Clinical and financial implications of robotically-assisted surgery

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ABSTRACT

Background

The use of minimally invasive surgery (MIS) in gynecologic oncology has been limited despite an exponential growth in some other specialties. Technological advances in the field of robotics may facilitate the application of MIS, thereby allowing more patients to benefit from the less invasive procedure. Despite the rising popularity of robotic surgery, questions remain as to its clinical and cost-effectiveness, contributing to resistance to changes in clinical practice and thus impeding its growth.

Objective

The objective of the current thesis was to evaluate the clinical and financial outcomes, from the perspective of patients and of the hospital, following the introduction of a robotic surgery program in gynecologic oncology.

Methods

Where applicable, data was retrieved from electronic health records, hospital information systems, and a series of retrospective and prospectively managed databases in the Division of Gynecologic Oncology at a tertiary center in Canada. Patient-level data included baseline characteristics, diagnostic information, operative outcomes, clinical outcomes, self-reported questionnaires, and resource use. All studies were approved by the institution's internal review board.

Results

The use of robotics in gynecologic oncology was found to result in a relatively rapid return to preoperative quality of life and patient-rated pain. Compared to open surgery, patients who underwent robotic surgery for the treatment of endometrial cancer used significantly less analgesics, including less opioids and a diminished use of patient-controlled analgesia, and this

was associated with a decrease in direct costs for the hospital. In ovarian cancer, where the use of robotics is rare, the approach was found to be feasible, improved perioperative results while maintaining oncologic outcomes, and was, on average, less expensive than open surgery. From the perspective of the hospital, the use of robotics largely replaced the use of open surgery, was found to decrease resource utilization and increase turnover on the inpatient ward, and was associated with a return on investment in the current setting.

Conclusion

The use of robotics in gynecologic oncology continues to expand. Insofar as its use in the setting examined, the current thesis demonstrates the clinical benefits of the procedure, the ability to achieve operational efficiencies and cost savings, and the potential to be a valuable investment in a high-volume center. The conceivable areas of innovation envisioned with such a technological platform are explored.

RÉSUMÉ

Contexte

L'utilisation de la chirurgie mini-invasive (CMI) en oncologie gynécologique a été limitée malgré une croissance exponentielle dans certaines autres spécialités. Les progrès technologiques dans le domaine de la robotique pourraient faciliter l'application des CMIs, permettant ainsi à plus de patients de bénéficier de cette procédure moins invasive. Malgré la popularité croissante de la chirurgie robotisée, des questions demeurent quant à son efficacité clinique et à son rapport coût-efficacité, contribuant ainsi à la résistance au changement dans la pratique clinique et entravant ainsi sa croissance.

Objectif

L'objectif de la thèse actuelle était d'évaluer les résultats cliniques et financiers, du point de vue des patients et de celui de l'hôpital, suite à l'introduction d'un programme de chirurgie robotique en oncologie gynécologique.

Méthodes

Le cas échéant, des données ont été extraites des dossiers électroniques de santé, des systèmes d'informations hospitaliers et d'une série de bases de données rétrospectives et prospectivement gérées de la Division de gynécologie-oncologique d'un centre de soins tertiaires au Canada. Les données relatives aux patientes incluaient les caractéristiques de base, les informations relatives au diagnostic, les résultats opératoires, les résultats cliniques, les questionnaires auto-déclarés et l'utilisation des ressources. Toutes les études ont été approuvées par le comité d'éthique de la recherche de l'établissement.

Résultats

L'utilisation de la robotique en oncologie gynécologique s'est avérée entraîner un retour relativement rapide à la qualité de vie et à la douleur préopératoires telles qu'évaluées par les patientes. Comparativement à la laparotomie (chirurgie ouverte), les patientes ayant subi une chirurgie robotique pour le traitement du cancer de l'endomètre utilisaient beaucoup moins d'analgésiques, incluant moins d'opioïdes ainsi qu'une diminution de l'usage d'analgésiques contrôlé par le patient, entraînant une diminution des coûts directs pour l'hôpital. Dans le cadre du cancer ovarien, où l'utilisation de la robotique est rare, l'approche a été jugée acceptable, a amélioré les résultats périopératoires tout en maintenant les résultats oncologiques, et était en moyenne moins chère que la chirurgie ouverte. Du point de vue de l'hôpital, l'utilisation de la robotique a largement remplacé l'utilisation de la chirurgie ouverte, a entrainé une réduction de l'utilisation des ressources, a augmenté le taux de roulement du service des patientes hospitalisées, et a démontré un retour sur investissement dans le contexte actuel.

Conclusion

L'utilisation de la robotique en oncologie gynécologique continue de s'étendre. Dans la mesure de son utilisation dans le cadre examiné, la thèse actuelle démontre les avantages cliniques de la procédure, la capacité de réaliser des efficacités opérationnelles et des économies de coûts, ainsi que le potentiel d'être un investissement rentable dans un centre à fort volume. Les domaines d'innovation envisagés avec une telle plate-forme technologiques sont discutés.

Note. French abstract translated using Google Translate (Alphabet, Inc., Mountain View, CA) and proofread for accuracy.

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I had finished my bachelor's degree and was looking to expand my training in an area that would combine three passions of mine: healthcare, technology, and economics. I came across the fascinating work on robotic surgery in the division of Gynecologic Oncology at the Jewish General Hospital and set up a meeting with Dr. Walter Gotlieb. I walked out of his office on July 10, 2012 around noon, and gave my parents a call: "I found exactly what I was looking for."

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CONTRIBUTIONS TO ORIGINAL KNOWLEDGE AND CONTRIBUTIONS OF CO-AUTHORS

The current thesis is organized in a manuscript (article)-based format. Chapter 1 describes the background on the subject matter, Chapters 2 to 7 present manuscripts either published, in submission, or ready for submission, and Chapter 8 discusses the thesis findings and future perspectives.

The first manuscript, shown in Chapter 2, presents new findings from a prospective study evaluating the short- and long-term impact of robotic surgery on the health-related quality of life of patients with gynecologic cancers. This was the first study to demonstrate the prospective evolution of health-related quality of life and self-reported body image using standardized and validated questionnaires before and after the use of robotics in gynecologic oncology.

Authors: Jeremie Abitbol, Susie Lau, Agnihotram V. Ramanakumar, Joshua Z. Press, Nancy Drummond, Zeev Rosberger, Sylvie Aubin, Raphael Gotlieb, Jeffrey H ow, Walter H. Gotlieb

Contribution of authors: JA, JH, and RG contributed to the acquisition of data. JA and AVR contributed to the analysis and interpretation of the results. JA, WHG, AVR, SL, and JZP contributed to drafting of the manuscript. ZR and SA provided critical revision. WHG, SL, JZP, and ND contributed to study conception and initial design.

In Chapter 3, the use of analgesics was quantified among patients who underwent robotic surgery and compared to a matched historical cohort of patients who were operated on by laparotomy. The direct hospital costs associated with analgesic use were measured and presented on a daily basis in order to control for the shortened length of stay of patients who underwent robotic surgery.

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Contribution of authors: JA contributed to study design, data analysis, and writing of the manuscript. WHG oversaw each step of the study's conception, design, and development. RC participated in the data management for the study. SH provided guidance on pain management protocols. EC and NL provided costs for medications and the preparations of medications. AR contributed to study initiation. SL and SS helped in the conception of the study. All authors reviewed, edited, and agreed with the final version of the manuscript.

There is a paucity of data demonstrating the use of robotics for the treatment of advanced stage ovarian cancer and most suffer from an inherent selection bias in favor of the robotic cohort. Chapter 4 presents the first study to demonstrate the feasibility of robotics in ovarian cancer while attempting to control for this selection bias.

Authors: Jeremie Abitbol, Walter H. Gotlieb, Xing Zeng, Agnihotram V. Ramanakumar, Roy Kessous, Liron Kogan, Valerie Pare-Miron, Marcelo Rombaldi, Shannon Salvador, Beste Kucukyazici, Sonya Brin, Jeffrey How, Susie Lau

Contribution of authors: JA contributed to the study design, data analysis, and writing of the manuscript. WHG and SL oversaw each step of the study's conception, design, and development. XZ contributed to study design, data collection, and writing of the manuscript. AR contributed to statistical analysis. RK and LK participated in the data collection and analysis. VPM, MR, SB, and JH contributed to data collection and data management. SS helped in the study design and its development. BK provided guidance on data analysis. All authors reviewed, edited, and agreed with the final version of the manuscript.

Chapter 5 is the first study to demonstrate the impact of robotic surgery on patient trajectories and hospital costs for the treatment of ovarian cancer.

Authors: Jeremie Abitbol, Beste Kucukyazici, Sonya Brin, Susie Lau, Shannon Salvador, Agnihotram V. Ramanakumar, Roy Kessous, Liron Kogan, John D. Fletcher, Valerie Pare-Miron, Gilbert Liu, Walter H. Gotlieb

Contribution of authors: JA contributed to study conception and design, data collection, analysis, and writing of the manuscript. WHG and SL oversaw each step of the process from initial conception to revision of the manuscript. BK contributed to study design and analysis and oversaw the operations management, health economics, and biostatistical aspect of the study. SB, RK, LK, VPM, and GL contributed to the data collection. SS provided guidance and critical revision. AVR provided expertise on the biostatistics aspect of the study revision of the manuscript. JDF contributed to the study methodology and provision of data.

Chapter 6 illustrates a novel approach to measuring the impact of robotics on the inpatient ward by using the total number of bed-days as the primary outcome of interest.

Authors: Annie Leung*, Jeremie Abitbol*, Agnihotram V. Ramana-Kumar, Bassam Fadlallah, Roy Kessous, Sabine Cohen, Susie Lau, Shannon Salvador, Walter H. Gotlieb

*Jeremie Abitbol and Annie Leung are co-first authors (equal contribution).

Contribution of authors: JA and AL contributed to study design, data analysis, and writing of the manuscript. WG oversaw each step of the study's conception, design, and development. SL and SS contributed to the study design and development. AR assisted in the data and statistical

analysis. BF and SC participated in the data management for the study. RK assisted with the data analysis. All authors reviewed, edited, and agreed with the final version of the manuscript.

Chapter 7 presents a unique capital budgeting approach to evaluate the net present value and return on investment of a robotics program.

Authors: Jeremie Abitbol, Aqsa Munir, Jeffrey How, Susie Lau, Shannon Salvador, Liron Kogan, Roy Kessous, Leslie Breitner, Russell Frank, Beste Kucukyazici, Walter H. Gotlieb

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This thesis contributes new findings to the current body of knowledge on the value of robotics in gynecologic oncology. The most significant contributions include the demonstration of both the clinical feasibility and cost impact of robotic surgery for the treatment of ovarian cancer while adjusting for selection biases. An innovative approach was also developed to demonstrate the rapid turnover of patients on the inpatient ward following the introduction of a robotic surgery program and its effects on inpatient demographics, resource utilization, and potential implications for hospital operations. Finally, investment appraisal methods were uniquely applied to demonstrate a new way to assess the value of a robotics program; this approach could be tailored to other settings and interventions.

CHAPTER 1 – INTRODUCTION

1.1 Surgical Treatment of Gynecologic Cancers

One in twenty Canadian women are expected to be diagnosed with endometrial, cervical, or ovarian cancer during their lifetime [1]. With some exceptions, the mainstay primary treatment for most of these involves surgery [2-5]. While some advances have been made with novel formulations of existing chemotherapeutic agents [6], the use of radiotherapy [7, 8], targeted therapy such as PARP inhibitors [9], and prophylactic vaccines [10], the surgical approach employed for most surgical candidates with a gynecologic cancer tends to involve a laparotomy (from the Greek *lapara* for 'flank' and *-tomia* for 'cutting' [11]), a midline abdominal incision to explore the abdominopelvic cavity [4, 12-14]. This surgical incision dates back to the 1800's [15, 16].

Advancements in endoscopic technology and techniques throughout the 19th century enabled its application to abdominal surgeries in the early 1900's [17]. Despite extensive resistance to changes in surgical practice, developments in laparoscopic techniques continued inexorably among early adopters [17-19]. In 1983, John Wickham "coined the term 'minimally invasive surgery' (MIS)" (Litynski, 1999, p. 747) [18, 19] and suggested in an article titled "The new surgery" that while "surgeons applaud large incisions . . . patients, in contrast, want the smallest wound possible" (Wickham, 1987, p. 1581) [20]. By the late 1980's and early 90's, a tipping point was reached as laparoscopy attracted the media, patients demanded the latest surgical approach, and instrument manufacturers supported the training of surgeons, paving the way for a paradigm shift towards less invasive operations [18, 19].

Historically, the use of laparoscopy in gynecology was initially intended for examination and diagnostic purposes as well as minor procedures [17-19]. In 1989, Reich et al. reported the

first laparoscopic-assisted vaginal hysterectomy (LAVH) [21]. Three years later, Nezhat et al. (1992) described the first laparoscopic radical hysterectomy with pelvic and periaortic lymphadenectomy for a cervical cancer [22]. Since then, numerous studies have evaluated the role of laparoscopy for the treatment of cervical [23-27], endometrial [28-36], and ovarian [37-43] cancer. Many of these studies have reported a range of benefits associated with the use MIS including diminished intraoperative blood loss [23, 24, 28, 29, 31, 41], fewer complications [23, 29, 32, 35, 36], a shorter length of stay [23, 24, 28-32, 35, 36, 40, 41], lower hospital costs [30, 36], and improvements in patient recovery [28-30, 33] and aspects of quality of life [28, 29, 33, 35]. However, despite these benefits, while the use of laparoscopy in other disciplines expanded significantly over the past few decades [44-46], its use in gynecologic oncology remained limited [13, 14, 47] due in part to technical difficulties of the procedure in complex cases [48-51]. One challenging feature of laparoscopy is due to the rigidity of the instruments and the fulcrum effect created by the entry point of the trocar at the abdominal wall, resulting in counterintuitive maneuvering [48, 49, 52], a "perception of stiffness" (Nisky et al., 2012) [53], and negative effects on skill acquisition [52].

1.2 The Introduction of Robotic Surgery

Karel Čapek coined the term *robot*—from "the Czech word *robotnik* . . . [for] peasant or serf" and "*robota* [for] . . . servitude" (Stone, 2005, section 1.1.4) [54]—to refer to the automatons that work to serve mankind in his 1920 play *R.U.R.* (*Rossum's Universal Robots*) [51, 54-56]. Soon thereafter, science fiction writer Isaac Asimov wrote extensively about *robotics* [54-56]. However, long before these terms were created, the concept of devices made to alleviate human labor has appeared throughout history [54]. Even those modelled on human form have historical roots with one famous example being Leonardo da Vinci's designs during the Renaissance period of a

mechanical android that could mimic human movement [51, 57]. While humanoid robots have been and continue to be developed [58], robotics have been successfully implemented in a variety of industries including manufacturing and assembly lines, space exploration, the military, and the medical field [54-56].

The first robots to enter the surgical arena include a Unimation PUMA robot for CT-guided sterotactic brain biopsies in 1985 [51, 55, 59, 60], the PROBOT (for "**p**rostatectomy **robot**" (Mei et al., 1996, p. 582) [61]) for computer-assisted prostate surgeries [55, 60, 61], and the ROBODOC for total hip arthroplasty [51, 55, 56, 60, 62]. In the late 1980s, a collaboration between researchers at the National Aeronautics and Space Administration (NASA)'s Ames Research Center and the Standard Research Institute (SRI, later known as SRI International) led to the notion of "telepresence surgery" (Satava, 2003, p. 1491), whereby astronauts in space could be operated on remotely from Earth [56, 63]. Their work eventually piqued the interest of the United States military given the prospects of remotely operating on soldiers on the battlefield, which led to funding from the Defense Advanced Research Projects Agency (DARPA) [51, 56, 63].

Around this time, with funding from DARPA, a new company called Computer Motion, Inc. (Goleta, CA) developed AESOP® (Automated Endoscopic System for Optimal Positioning), a voice-activated robotic arm that served to control the endoscopic camera used in laparoscopy, thus replacing the laparoscopic assistant [51, 55, 56, 60, 63]. AESOP was cleared by the Food and Drug Administration (FDA) in 1994 [55, 56, 60] and this technology would eventually be integrated into the ZEUS® Robotic Surgical System [51, 55, 56, 60, 63].

In parallel, in the mid-1990's, licensing to some of SRI's intellectual property was acquired to found Intuitive Surgical, Inc. (Sunnyvale, CA) [56, 63, 64] (initially called Intuitive Surgical Devices, Inc. [64]), which ultimately developed the da Vinci® Surgical System [51, 55, 56, 60,

63, 65]. In 2000, the FDA approved the da Vinci® system for use in general laparoscopic surgery [55, 66] (clearance for gynecological procedures would come in 2005 [55, 67]). Following a series of patent infringement lawsuits between Computer Motion and Intuitive Surgical [68, 69], the two companies merged [70] and only the da Vinci® system continued to be marketed while the ZEUS® was discontinued [56, 71, 72]. Following Intuitive's acquisition, the da Vinci® system was the only FDA-approved robotic surgery system on the market for use in gynecology [55, 60, 71] until more recently [73].

1.3 Technical Description of the Robotic Surgery Platform

The birth of the robotic surgery machines described above have their roots in telesurgical applications [55, 56, 63]. Indeed, some have previously demonstrated the feasibility of long-distance surgeries [74-77]. In 2001, a 68-year-old patient in France was remotely operated on by surgeons located in New York using the Zeus system [74]. Building on the success of this transcontinental cholecystectomy [74], the Zeus system was employed by surgeons in Hamilton, Ontario to operate on patients in a remote rural hospital in North Bay, Ontario [75]. To evaluate the feasibility of using the da Vinci system on wounded individuals in the battlefield as initially intended, researchers tested the "Trauma Pod" (SRI International) on phantom patients [76]. In this scenario, an administrator and a surgeon located in a "control cell" could operate on a wounded soldier located remotely in the "surgical cell" without any other human involvement, demonstrating the possibility of automating certain tasks in the operating room (e.g., dispensing as well as tracking surgical tools and supplies) from afar [76]. Moreover, an open-source research kit is available for researchers to experiment with teleoperation and other technological possibilities of robotic surgery [78]. Nevertheless, besides few examples, the majority of robotic

surgery systems today are used within the same operating room with the components of the system physically connected by cables [72, 77].

The da Vinci system is composed of three units: the patient-side cart, the surgeon console, and the vision system [48, 51, 55, 60, 72]. Robotic arms on the patient-side cart are inserted into the patient's abdomen through 8-12mm ports [67, 72, 79]; one of the arms holds a camera while two to three additional arms hold the so-called *EndoWrist*® surgical instruments for manipulating tissues inside the abdominopelvic cavity (e.g., cutting, clamping, cauterizing, etc.) [51, 55, 60, 65, 67, 72]. All robotic arms are controlled by the surgeon seated at a nearby console: the camera in the patient's abdomen feeds into a binocular display on the surgeon console via the *vision system* while the surgeon has full control of the instruments using controllers at the surgeon's fingers [51, 55, 60, 67, 72]. In addition to computational and image processing, the vision system also includes a video monitor for the operating staff to view the live feed from the endoscopic camera [60, 72].

Of note is that the robot is not autonomous and all of the robotic arms' movements are controlled by the surgeon at the console in a master/slave configuration [48, 65, 77]. As such, while the surgeon does not directly manipulate the instruments (e.g., scissors for cutting), all commands at the surgeon console (e.g., movement of the joysticks and activation of the cutting tool) are directly translated at the patient-side cart [48, 51, 60]. In addition, an assistant laparoscopic surgeon is sometimes helpful for gynecologic procedures [60, 67].

The literature describes several advantages to using a robotic platform as opposed to conventional straight-stick laparoscopy:

1. Ergonomics: Unlike laparotomy or conventional laparoscopy, robotic surgery permits the surgeon to sit comfortably at the console in a more user-friendly manner [48, 49, 51], which

has been linked to improvements in parameters of physical workload, mental stress, and task performance [80].

2. Magnified three-dimensional (3D) high definition (HD) immersion visualization [48, 51, 55, 72]: The dual-camera endoscope [48, 51, 55, 72] allows for the surgeon to feel practically immersed in the patient's abdomen [48, 63]. In comparison to a 2D optical display option on the da Vinci system, the 3D view mode has been shown to facilitate some tasks [81].
3. Dexterity: In contrast to laparoscopy, robotic surgery affords wristed instrumentation with the tips of the EndoWrist® instruments replicating the more natural movements at the master controls, resulting in greater degrees of freedom and enhanced dexterity for the user [48, 49, 51, 65, 72]. In addition, tremor filtration in the robotic system overcomes a natural human challenge that is said to be worsened in conventional laparoscopy [48, 49], and motion scaling (i.e., a large or natural movement at the master controls is scaled down at the instrument-level) makes it easier for the user to perform precise movements at a fine scale [49, 65, 72, 82].

On the other hand, some disadvantages of robotic surgery remain including the lack of haptic feedback that is also noted in laparoscopy [48, 51, 55, 71], the size of the machinery [48, 51, 55], the extra training required [51, 55], potentially longer operating room time [51, 55, 71], the possibility of equipment failure [83], and the relatively high upfront costs [48, 51, 55, 71]. Still, despite ongoing limitations, the learning curve for robotic surgery has been found to be easier compared to conventional laparoscopy [84, 85].

1.4 Robotic Surgery in Gynecologic Oncology

Gynecologic procedures account for the greatest surgical specialty by volume in the United States for the manufacturer of the robot [86]. The incorporation of robotics in gyn-oncology has been particularly important in expanding the use of minimally invasive surgery and overcoming the shortfalls and limited use of laparoscopy in the treatment of many patients with gynecologic cancers [47, 60, 87-94]. The literature has numerous reports on outcomes for robotic surgery, with comparisons to laparotomy, laparoscopy, and both.

Much like studies that compared laparoscopy to laparotomy, robotics has been associated with similar results in the treatment of endometrial and cervical cancer including generally longer operating room or procedure times [84, 89, 90, 95-99] though less intraoperative blood loss [84, 87, 89, 91, 95-106], fewer complications [87, 89-91, 95-97, 99, 101, 105], and a shorter hospital stay [84, 87, 89-91, 95-106]. Some have reported other clinical benefits to patients associated with the use of robotic surgery including lower rates of hernia development [107], less pain [100], reduced time to regular diet [99, 100], and a quicker return to work or daily activities [96, 101, 102]. Moreover, preliminary reports have suggested no adverse impact of robotics on oncologic outcomes such as disease- or progression-free survival and overall survival in endometrial [89, 100, 105] and cervical cancer [104]. Other outcomes like lymph node yield (i.e., number of pelvic and/or paraaortic lymph nodes removed) have been less consistent with some studies favoring robotics [91, 95, 102, 104], some disfavoring [84, 98, 101], and others finding no significant difference [87, 89, 96, 99, 100, 103, 105, 106]. In absence of prospective studies, however, changes in practice patterns are important confounding factors for these outcomes [84]. Researchers have also evaluated the use of the robotic system's integrated near-infrared fluorescence imaging mode to facilitate the detection of sentinel lymph nodes in real-time [108-110].

Other studies have focused on comparing robotic-assisted to conventional laparoscopy. It has been said that there is not a significant difference in clinical outcomes between robotically-assisted and conventional laparoscopy [111, 112]. Still, some have reported that robotic surgery results in more favorable pain assessments or analgesia use [87, 100, 113, 114], even less blood loss [84, 85, 87, 94, 95, 97, 100, 105, 114-117], and shorter hospital stays [84, 85, 94, 95, 97, 114, 116, 118]. Further, while a high body mass index (BMI) is a risk factor that may preclude the accomplishment of a laparoscopic surgery without conversion to open [32, 116], many have reported on the feasibility of robotics in patients with obesity and morbid obesity [116, 119-125].

Minimally invasive surgery has played a limited role in the management of ovarian cancer [4, 126-128]. A small number of groups have laid the groundwork for the evaluation of the feasibility of robotics in the treatment of early stage [129-135], advanced stage [129, 130, 133-137], and recurrent [134, 135, 138-140] ovarian cancer, though the use of MIS for this malignancy remains controversial [134].

An important barrier to the continued adoption of robotic surgery is the robotic platform's steep upfront acquisition costs as well as the periodic maintenance costs required and the added variable costs for disposable instruments [55, 60, 141, 142]. Cost analyses comparing robotics, laparoscopy, and laparotomy in gyn-oncology have revealed varying results. Some have found the average robotic surgery case to be less expensive [96] or not significantly different [88, 105, 143] from laparotomy when the initial capital outlay and routine service costs of the robot(s) are included. Ignoring capital costs, Leitao et al. (2014) and Bogani et al. (2016) also showed that robotic surgery was less expensive than laparotomy in endometrial cancer [88, 90], though the latter study reported no significant difference after adjustments for covariates [90]. In comparison to laparoscopy, robotic surgery has also been said to be more expensive [88, 115, 144-147], comparable [88, 96, 105], or less expensive [26], though variations exist with respect to the setting,

study design, and assumptions around the treatment of the machines' upfront capital costs and maintenance costs. The aforementioned cost studies generally evaluated costs from the institutional or hospital's perspective. After incorporating additional costs from the societal perspective (i.e., including both hospital costs as well as "lost wages and caregiver costs" (Barnett et al., 2010, p. 686) [148] to patients), the robotic approach was found to be less expensive than laparotomy but costlier than laparoscopy [148, 149], although the authors of the latter study do describe a selection bias favoring the laparoscopy group [149].

1.5 Objectives and Hypotheses

While some have noted significant increases in the use of robotics in gynecologic oncology over the years [128], other authors have reported a much slower diffusion of robotic hysterectomies [150], with impediments to adoption [141] and public perceptions [151] that are important to address. The objectives of this thesis are to: (1) contribute new evidence to the current body of knowledge regarding clinical outcomes and the patient experience following the use of robotic surgery, and (2) determine the operational and financial implications of robotic surgery from a hospital or healthcare system perspective. Correspondingly, the thesis is divided into two parts: *I. Patient Outcomes* and *II. Hospital Outcomes*.

The hypothesis is that clinical outcomes would reflect similar benefits as laparoscopy vis-à-vis open surgery, with robotics being a gentler approach to surgery, and economic outcomes would demonstrate potential cost-effectiveness if increased intraoperative costs could be outweighed by savings postoperatively.

PART I. PATIENT OUTCOMES

CHAPTER 2 – PROSPECTIVE QUALITY OF LIFE OUTCOMES FOLLOWING ROBOTIC SURGERY IN GYNECOLOGIC ONCOLOGY

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2.1 Preface

Ernest Codman was undoubtedly a revolutionary when it came to the record-keeping of medical and surgical outcomes [152]. In contrast to more traditional clinical endpoints such as complications and survival, there has been increasing use of patient-reported outcome measures (PROMs), including quality of life assessments, to put the patient at the center of care and to reflect the greater focus on improving not just quantity but patients' quality of life [153-155].

Quality of Life (QOL) is a very broad concept that has, in principle, appeared throughout history. In the 4th century BC, Aristotle touched on "'the good life' or 'doing well'" (cited in Fayers and Machin, 2002, p. 5) [153], and the good of happiness (see Russell, 1972, p. 172-184) [156]. Epicurus described the ingredients for tranquility and pleasure [157]. John Locke postulated that "happiness . . . is the utmost pleasure we are capable of" (cited in Russell, 1972, p. 613), the pursuit of which ought to drive us [158]. The founding fathers of the United States enshrined this "pursuit of happiness" in the Declaration of Independence (US 1776) and also discussed the idea of "general welfare" [154]. Jeremy Bentham even developed a way to calculate the amount of pleasure over pain [159].

While there are many definitions of QOL, some have defined it as "personal well-being" and "satisfaction with life" (Fayers and Machin, 2002, p. 7) [153]. Health-Related Quality of Life

(HRQOL or HRQL) refers to QOL as it relates to health, disease, and treatment [160], and has been described to encompass physical, functional, emotional, and social well-being [154]. Throughout the following chapters, the terms QOL and HRQOL may be used interchangeably.

HRQOL assessments are increasingly included in clinical trials in oncology [155]. While the validity [161], relevance [162], and patient-centeredness [162] of some HRQOL measures have been questioned, and discrepancies have been noted between outcomes derived from quantitative questionnaire-based scales and qualitative sources [163, 164], it is nonetheless important to survey patients' perspectives and "simply . . . ask the patient" (Fayers and Machin, 2002, p. 42) [153] to ensure that their needs are met. During the first two years of our division's robotics program, a questionnaire was sent to patients postoperatively as part of a pilot study to assess patients' satisfaction with the surgery, pain, recuperation, and effects on QOL [165]. Following that pilot study, a new survey was developed consisting of standardized and validated instruments; results from this second study are described in the following manuscript [166].

The following manuscript was published in *Gynecologic Oncology* 134 (2014) 144-149 and included in Appendix I.

2.2 Abstract

Purpose

To characterize the health-related quality of life (HRQL) of patients undergoing robotic surgery for the treatment of gynecologic cancers.

Methods

211 patients completed a quality of life questionnaire before surgery. Postoperative questionnaires, consisting of the same assessment with the addition of postoperative questions, were given at 1 week, 3 weeks, 3, 6, and 12 months after surgery. The Functional Assessment of Cancer Therapy – General (FACT-G) and its subscales were used to evaluate HRQL. Patient-rated body image was evaluated using the Body Image Scale. Statistical significance was measured by the Wilcoxon signed-rank test. Minimally important difference (MID) values were analyzed to evaluate clinical significance.

Results

Overall HRQL and body image decreased at 1 week after surgery and returned to baseline by 3 weeks. Physical and functional well-being decreased at 1 week after surgery and returned to baseline by 3 months after surgery. However, using MID criteria, physical well-being returned to baseline by 3 weeks. Social well-being did not change significantly. Emotional well-being increased immediately by 1 week after surgery.

Conclusion

Patient-reported HRQL outcomes following robotic surgery for the treatment of gynecologic cancers suggests a rapid return to pre-surgery values.

2.3 Introduction

There is a growing interest to integrate the assessment of health-related quality of life (HRQL) into clinical practice [167-169] as its measurement has become pivotal in patient care [155, 160, 170]. In oncology, the symptoms of cancer as well as side-effects from treatment have been associated with a decrease in HRQL [171-173], and HRQL has become an important indicator of the value of health care programs and new technologies.

Gynecologic cancers and their treatments affect not only the general well-being of patients, but can have specific impacts on femininity [174, 175], self-esteem [175], and body image [174-176]. In addition, sexual health following gynecologic cancer surgery can be impacted by modification of genitalia and/or loss of childbearing capacity [174-179], decreased libido [174, 178, 179], and surgical menopause [176, 177]. The introduction of minimally invasive surgery has corresponded with improved patient HRQL when compared with traditional laparotomy [29, 33, 35]. Though HRQL is a broad term which many have attempted to define, some have narrowed it down to four domains: physical, functional, mental/psychological, and social functioning [154]. Following a pilot study showing good recovery at one postoperative evaluation [180], we initiated this prospective study comparing HRQL prior to and after surgery in an unselected consecutive series of patients following robotic surgery for gynecologic cancers.

2.4 Methods

Recruitment of patients

Patients were recruited to this study from the gynecologic oncology clinic of a publicly funded tertiary care hospital. All patients scheduled to undergo robotic surgery for the treatment of a gynecologic cancer (uterine, ovarian, cervical) were invited to participate in this study, and signed

an informed consent which was approved by the institution's Research Ethics Committee. Three surgeons experienced with robotic surgery performed the surgeries. Between December 2009 and December 2012, there were 211 consecutive subjects included in the study. None of the patients were part of our previous pilot study [180]. A flow chart of the study process is shown in Supplementary Figure S1. After giving written informed consent, participants were provided with the baseline questionnaire prior to surgery. On the day of surgery, patients were given a follow-up questionnaire to be completed one week after surgery. Patients were then asked to complete the same follow-up questionnaire at their in-clinic visit three weeks after surgery. Subsequent questionnaires were mailed to patients at 3, 6, and 12 months after surgery. Completed questionnaires were transferred to an electronic database by a trained data manager, and none of the surgeons had access to the answers of the patients. Participants were eligible to participate in this study if they completed a baseline questionnaire and were excluded if their surgery was converted to laparotomy (n = 11). Questionnaires were completed either in English or French.

Outcome measures

FACT-G: HRQL was measured using the validated cancer-specific FACT-G questionnaire. The FACT-G is a 27-item questionnaire that assesses HRQL across four domains: physical well-being, social well-being, emotional well-being, and functional well-being [181]. Higher FACT-G scores correspond to better HRQL [181]. Following established guidelines, FACT-G subscale scores were considered valid if more than 50% of the questions were answered; total FACT-G scores were considered valid if more than 80% of all 27 questions were answered and all comprising subscale scores were valid [181]. Participants with too many missing FACT-G answers were therefore excluded from the FACT-G analysis. If too many missing values were found in the baseline questionnaire, all subsequent subscale scores and/or total FACT-G scores were removed

for that participant. This ensured that all follow-up questionnaires have a corresponding baseline questionnaire as a control.

Body Image Scale: Body image was measured using the Body Image Scale (BIS) designed for cancer patients by Hopwood et al. (2001) [182]. Scores on the 10-item questionnaire range from 0-30, with higher scores indicating a more negative self-image [182]. For consistency with the FACT-G, where higher scores reflect better HRQL, all BIS scores were subtracted from 30 so that higher scores correspond to better body image. Similarly to the FACT-G scoring methodology, BIS questionnaires with more than two missing answers were excluded from the body image analysis; if more than two missing answers were in the baseline questionnaire, all BIS data was excluded for that participant. Two missing items were considered acceptable to impute in accordance with what has been reported [182].

Statistical Analysis

Statistical analysis was performed using STATA 12 statistical software (StataCorp) and Microsoft Excel 2003. Some distributions of HRQL scores by visits were not normally distributed. We therefore performed non-parametric Wilcoxon signed-rank tests to test for significant differences in questionnaire scores between different time points. To assess clinical differences, changes in questionnaire scores were also evaluated using minimally important difference (MID) values established for the questionnaires where applicable [181]. A difference of 3–7 points is suggested as a minimally important difference (MID) for the total FACT-G Score; 2–3 points for the physical and functional well-being subscales; 2 points for the emotional well-being subscale [181]; and 2 points for the social well-being subscale [183]. Kruskal Wallis analysis of variance was used to test differences in questionnaire scores by age and marital status.

A return to pre-surgery HRQL was considered if the difference between scores at postoperative time points were not significantly different from baseline. A significance level of $p < 0.05$ was used throughout the study.

2.5 Results

Patient characteristics

Patient demographics and lifestyle habits are shown in Table 1. The mean age was 61 years old (20–92). Most patients were treated for endometrial cancer (70.6%) and more than a third had a BMI greater than 30 (37%).

Quality of life

FACT-G subscale scores and overall FACT-G scores are tabulated in Table 2. Overall FACT-G scores are graphically represented by box plots in Figure 1.

Table 3 shows changes in questionnaire scores, with Wilcoxon signed-rank test results and minimally important difference (MID) values established for the questionnaires where applicable [181].

Overall HRQL, as measured by the total FACT-G score, decreased at the 1-week follow-up ($p < 0.0001$, MID = -6.5) and returned to baseline by 3 weeks after surgery ($p = 0.1$, MID = -1.2). In the long-term 12 months after surgery, overall HRQL was significantly higher than HRQL measured before surgery ($p = 0.0005$, MID = 8.0).

The four domains of the FACT-G questionnaire were further evaluated separately. **Physical well-being** decreased at 1 week after surgery ($p < 0.0001$, MID = -5.0) and returned to

baseline at 3-months follow-up ($p = 0.3$, MID = -0.6). By the recommended MID criteria, however, physical well-being returned close to baseline by the third week after surgery (MID = -1.5). **Functional well-being** decreased after surgery and returned to baseline at 3-months follow-up ($p = 0.4$, MID = 0.1). Mean **social well-being** increased from baseline after surgery though it was not significant and returned closer to baseline by 3 months after surgery. Changes in social well-being did not meet the minimally important difference values. **Emotional well-being** was found to increase significantly by 1 week after surgery ($p < 0.0001$, MID = 3.0) and remained significantly higher than baseline.

Body Image

Means and 95% confidence intervals of Body Image Scale scores are tabulated in Table 2 and box plots are illustrated in Figure 2, underlining the median and outliers. Wilcoxon signed-rank test results are shown in Table 3. Patient-rated body image was found to decrease by the first week after surgery ($p = 0.002$) and return closer to baseline by the third week ($p = 0.9$).

One expected advantage of robotic surgery is the minimally invasive approach resulting in small scars. The specific question concerning scars from the Body Image Scale [182] revealed (Figure 3) that at 1 week after surgery, 62% were "not at all dissatisfied with the appearance of their scar," and this increased to 82% by 3 weeks.

Kruskal-Wallis analysis of variance was used to evaluate the impact of age and marital status on HRQL. Age was dichotomized into two groups: below 70 years old and greater than or equal to 70. Patients younger than 70 displayed significantly higher emotional well-being ($p = 0.02$) and functional well-being ($p = 0.01$), while patients 70 years or older had higher body image ($p = 0.0001$). We chose 70 years of age as a clinical definition of elderly, though to mitigate the

potential sample size bias, we repeated the analysis by dividing the sample into tertiles of age and found similar results with the highest age group reporting lower emotional and functional well-being, and the lowest age group reporting lower body image. We also repeated the analysis by splitting the sample at the median age, 62, and found significance only with body image (p = 0.0001), again with older patients reporting better body image.

We found a significant difference by marital status for social well-being (p = 0.0001), functional well-being (p = 0.048), and overall FACT-G score (p = 0.025), with single/divorced/widowed patients having the lowest scores. Body image scores were not influenced by marital status (p = 0.6). However, physical well-being (p = 0.0002) and body image (p = 0.0001) were significantly worse in patients who completed any form of adjuvant therapy, either chemotherapy (33% of patients) and/or radiation (28% of patients).

2.6 Discussion

The aim of this study was to prospectively characterize the HRQL outcomes following robotic surgery in patients with gynecologic cancers. Results showed a decrease in overall HRQL at 1 week after surgery, and a return to baseline by 3 weeks. The total FACT-G score was then broken down into its component subscales. The results for physical well-being depended on the test used, e.g., using the MID values, there was a return to baseline by 3 weeks after surgery, but using the Wilcoxon signed-rank test, it returned to baseline by 3 months after surgery. This discrepancy may be due to the different methodologies of each test. Whereas the Wilcoxon signed-rank test evaluates the sign of the ranked score differences between time points, the MID values were used as a reference point when comparing average scores between time points. The latter is therefore more sensitive to outlier scores. The time gap between the 3-week and 3-month evaluations makes

it difficult to ascertain at which point within that time interval patients can be expected to recuperate physically and functionally. Adding an intermediate follow-up would be more appropriate for future studies. There was a non-significant increase in mean social well-being in the short term after surgery. The minimal impact on social well-being could be related to the additional social support usually provided to cancer patients [183, 184] in the intermediate term after surgery. The social well-being subscale evaluates how close individuals feel with their friends, family, and partner, which may be expected to be higher during times of illness. Social support has also been associated with a decrease in depressive symptoms in cancer patients [185], which may account in part for the improvement in emotional well-being after surgery. This improvement may also be attributed to an emotional distress at baseline after being diagnosed with cancer, as well as a heightened sense of emotional relief following surgery, perhaps encompassing the minimal impact of the surgery or the rapid rate of recovery.

The progression of HRQL and FACT-G domains following surgery in our study reminds us of what has been reported previously [33, 35] in laparoscopy trials. In the multicenter Gynecology Oncology Group study LAP2 [33] comparing laparoscopy to laparotomy, the FACT-G was used to assess overall HRQL. Although the authors did not report data on the FACT-G subscales nor the significance of changes in postoperative HRQL relative to baseline, their laparoscopy data seems comparable to ours [33]. Using a different validated instrument, the generic Short-Form SF-36, they also reported a decrease in mean physical functioning scores one week after surgery, gradually returning to baseline by six months after surgery [33]. Mean body image scores increased by one week after surgery in both their laparoscopy and laparotomy groups [33] though the use of a different questionnaire to assess body image again makes it difficult to compare with our data.

Three diagnoses were included in this study: endometrial, ovarian, and cervical cancer. We performed Kruskal Wallis analysis of variance to test any differences between the three groups at baseline and found a significant difference only for functional well-being with median baseline scores of 21, 21.5, and 24 for endometrial, ovarian, and cervical cancer patients, respectively (p = 0.0261). Compared to studies that have assessed HRQL following laparoscopy [29, 33, 35], we did not exclude patients at high risk, such as those with advanced stage cancer, poor performance status, and/or other major medical conditions: 95% of all operable patients with endometrial cancer, uterine sarcoma, or cervical cancer underwent robotic surgery in our center. Over a third of the patients (38%) in our study were at higher risk for complications or poor quality of life, either because of age (22% were 70 years old or older) and/or obesity (37% obese: 16% with BMI between 30.0 and 34.9 kg/m^2; 11% with BMI between 35.0 and 39.9, and 10% with BMI $\geq$ 40). The feasibility of robotics in the elderly and obese populations reflects the findings of our previous studies [119, 180].

When we dichotomized our sample at 70 years of age, older patients were found to have lower emotional and functional well-being though higher body image. Dichotomized at the median age of 62, only body image was significantly different, with older patients reporting better body image. Others have also found older age to be associated with higher body image [182] and lower functional well-being [169] in cancer patients. In contrast, some have reported emotional well-being [169] and depressive symptoms [185] to be worse in younger patients. Gil et al. (2007) [184] looked for factors that influence baseline HRQL in patients planned to undergo gynecologic oncology surgery. The group found age to be positively correlated with the physical and emotional well-being domains of the FACT-G questionnaire. In contrast to our findings that marital status influences the FACT-G scores, they found no differences in preoperative FACT-G scores between women who were married and not married though their analysis was not intended to evaluate the

course of treatment [184]. We noted a significant difference in overall FACT-G scores as well as social and functional well-being by marital status, with single/divorced/widowed women having the lowest scores. These same domains have similarly been shown to be significantly lower in patients who have help no at home [169].

One limitation with our study is the missing response data and the decrease in questionnaire response over time, especially at 3 weeks after surgery, as shown in Table 2. Based on questionnaire guidelines, we excluded questionnaires with too many missing responses. In addition, subjects who had not completed a valid baseline questionnaire were excluded to ensure that every patient at follow-up was her own control. To evaluate this potential bias, we re-calculated all our data by including the invalid questionnaires. Mean and median scores were graphically compared and showed similar results in FACT-G subscales, overall FACT-G, and Body Image Scale scores over time.

While a decrease in questionnaire response is usually observed over time in this type of study, we evaluated the association between HRQL with completion of questionnaires at 12 months. Though body image was significantly worse ($p = 0.0047$) in patients who completed the 12-month questionnaire, physical well-being ($p = 0.040$), emotional well-being ($p = 0.011$), functional well-being ($p = 0.0079$), and total FACT-G score ($p = 0.016$) were significantly better. This may be explained by the fact that patients who completed the 12-month follow-up were also more likely to have completed the 3-month (Odds Ratio = 2.2, $p = 0.001$) and 6-month (Odds Ratio = 2.9, $p < 0.001$) follow-up questionnaires, which were associated with a higher HRQL. We therefore repeated the analysis by looking at the HRQL at 3 months and 6 months after surgery and comparing HRQL scores in participants who completed the 12-month questionnaire to those who did not. We found no significant difference at either follow-up. We then used Pearson's chi-squared test and simple logistic regression in order to characterize the cohort that is responding at

12 months compared to the one with missing responses. Ovarian cancer patients were less likely to complete the 12-month follow-up questionnaires in comparison to endometrial cancer patients (Odds Ratio = 0.7, $p = 0.048$). Whether or not participants completed the 12-month questionnaire was not significantly affected by age (less than versus greater than 70 years old), marital status, or whether patients had received chemotherapy and/or radiotherapy at any point during the course of the study.

Results from this study demonstrated a decrease in HRQL and body image 1 week after surgery. Between 1 week and 3 weeks, HRQL and body image returned close to baseline, providing evidence that robotic surgery for the treatment of gynecologic cancers results in a rapid return to pre-surgery quality of life.

2.7 Funding

This study was supported in part by grants from the Quebec Network for Research on Aging (RQRV), the Israel Cancer Research Fund, The Weekend to End Women's Cancers, Gloria's Girls, and the Levy family.

2.8 Conflicts of Interest

Walter Gotlieb and Susie Lau obtained partial travel support for proctoring robotic surgery

2.9 Acknowledgements

We would like to give special thanks to Ioana Eniu who was instrumental to this study and volunteered her time to collect questionnaire data and input it into our electronic database.

2.10 Tables

Table 1. Patient demographics and lifestyle habits

	N=211 (%)
Diagnosis	
Endometrial cancer	149 (70.6)
Ovarian cancer	43 (20.4)
Cervical cancer	19 (9.0)
BMI	
<30	132 (62.6)
30.0-39.9	57 (27.0)
≥40	20 (9.5)
No answer	2 (0.9)
Ethnicity	
White/Caucasian/Canadian	160 (75.8)
Other	27 (12.8)
No answer	24 (11.4)
Highest education level*	
Elementary	19 (9.0)
Secondary	63 (29.9)
College/University	120 (56.9)
No answer	9 (4.3)
Language†	
English	167 (79.1)
French	152 (72.0)
Other language(s)	82 (38.9)
No answer	12 (5.7)
Work status	
Working	92 (43.6)
Not working or retired	116 (55.0)
No answer	3 (1.4)
Current relationship status	
Married	123 (58.3)
Cohabitating	15 (7.1)
Dating	6 (2.8)
Single, widowed, divorced	61 (28.9)
No answer	6 (2.8)
Children	
Yes	167 (79.1)
No	15 (7.1)
No answer	29 (13.7)
Alcohol drinking habits	
None	72 (34.1)
Occasionally	47 (22.3)
1-3/week	41 (19.4)
≥4/week	40 (19.0)
No answer	11 (5.2)
Cigarette consumption	
None	184 (87.2)
Very few or rarely	1 (0.5)
3-5/day	2 (0.9)
6-10/day	6 (2.8)
>10/day	9 (4.3)
No answer	9 (4.3)
Exercising habits	
Never	76 (36.0)
≤5 times per month	5 (2.4)
1-4 times per week	76 (36.0)
≥5 times per week	39 (18.5)
No answer	15 (7.1)

*Subjects who only reported years of schooling were categorized accordingly.

†Knowledge of language includes any or all of the following: speaking, reading, and/or writing

Table 2. Mean and 95% confidence interval values for FACT-G, FACT-G subscales, and Body Image Scale

Questionnaire	N	Mean (95% confidence interval)
Physical Well-Being, FACT-G		
Baseline	193	23.9 (23.2–24.7)
1 week after surgery	121	18.9 (17.9–20.0)
3 weeks after surgery	92	22.4 (21.6–23.3)
3 months after surgery	114	23.3 (22.4–24.3)
6 months after surgery	81	23.8 (22.8–24.8)
12 months after surgery	67	25.3 (24.5–26.1)
Social Well-Being, FACT-G		
Baseline	184	22.9 (22.1–23.7)
1 week after surgery	116	23.7 (22.9–24.5)
3 weeks after surgery	85	23.8 (22.7–24.9)
3 months after surgery	111	22.3 (21.2–23.5)
6 months after surgery	81	22.2 (20.8–23.5)
12 months after surgery	68	23.1 (22.0–24.3)
Emotional Well-Being, FACT-G		
Baseline	185	15.2 (14.5–16.0)
1 week after surgery	114	18.2 (17.3–19.1)
3 weeks after surgery	85	18.4 (17.5–19.3)
3 months after surgery	108	19.6 (18.9–20.3)
6 months after surgery	77	18.1 (17.1–19.2)
12 months after surgery	63	19.2 (17.9–20.4)
Functional Well-Being, FACT-G		
Baseline	191	19.9 (19.0–20.8)
1 week after surgery	119	15.1 (14.0–16.3)
3 weeks after surgery	89	16.2 (14.9–17.6)
3 months after surgery	115	20.0 (18.9–21.1)
6 months after surgery	82	19.8 (18.3–21.2)
12 months after surgery	69	22.6 (21.4–23.8)
Overall HRQL, FACT-G		
Baseline	177	82.1 (79.8–84.4)
1 week after surgery	107	75.5 (72.4–78.6)
3 weeks after surgery	79	80.9 (77.6–84.2)
3 months after surgery	106	85.6 (82.8–88.5)
6 months after surgery	76	83.5 (79.9–87.1)
12 months after surgery	63	90.0 (86.6–93.5)
Body Image Scale		
Baseline	172	25.9 (25.0–26.8)
1 week after surgery	103	23.7 (22.4–25.1)
3 weeks after surgery	79	26.1 (25.0–27.3)
3 months after surgery	104	24.9 (23.8–26.0)
6 months after surgery	71	24.6 (23.1–26.0)
12 months after surgery	60	26.5 (25.3–27.7)

Note: Higher scores correspond to better HRQL and Body Image.

Table 3. Minimally important differences and Wilcoxon signed-rank test results between HRQL scores at different postoperative time points relative to baseline

Questionnaire	z-score	p-value	difference between mean score and baseline	MID
Physical Well-Being, FACT-G				
1 week after surgery*	7.841	<0.0001	-5	Y
3 weeks after surgery*	4.125	<0.0001	-1.5	N
3 months after surgery	1.079	0.2807	-0.6	N
6 months after surgery**	1.694	0.0902	-0.2	N
12 months after surgery	-1.083	0.2789	1.3	N
Social Well-Being, FACT-G				
1 week after surgery	-1.199	0.2303	0.8	N
3 weeks after surgery	-0.803	0.4221	0.9	N
3 months after surgery	1.185	0.2361	-0.5	N
6 months after surgery	0.542	0.5877	-0.7	N
12 months after surgery	0.848	0.3967	0.3	N
Emotional Well-Being, FACT-G				
1 week after surgery*	-6.591	<0.0001	3	Y
3 weeks after surgery*	-5.227	<0.0001	3.2	Y
3 months after surgery*	-7.637	<0.0001	4.4	Y
6 months after surgery*	-5.175	<0.0001	2.9	Y
12 months after surgery*	-5.076	<0.0001	3.9	Y
Functional Well-Being, FACT-G				
1 week after surgery*	6.974	<0.0001	-4.7	Y
3 weeks after surgery*	5.161	<0.0001	-3.7	Y
3 months after surgery	0.912	0.3616	0.1	N
6 months after surgery	0.998	0.3184	-0.1	N
12 months after surgery*	-2.83	0.0047	2.7	Y
Overall HRQL, FACT-G				
1 week after surgery*	4.791	<0.0001	-6.5	Y
3 weeks after surgery**	1.649	0.099	-1.2	N
3 months after surgery**	-1.754	0.0794	3.6	Y
6 months after surgery	-0.383	0.7016	1.4	N
12 months after surgery*	-3.495	0.0005	8	Y
BIS				
1 week after surgery*	3.094	0.0020		n/a
3 weeks after surgery	-0.109	0.9135		n/a
3 months after surgery	1.512	0.1304		n/a
6 months after surgery	0.62	0.5352		n/a
12 months after surgery	-1.502	0.1331		n/a

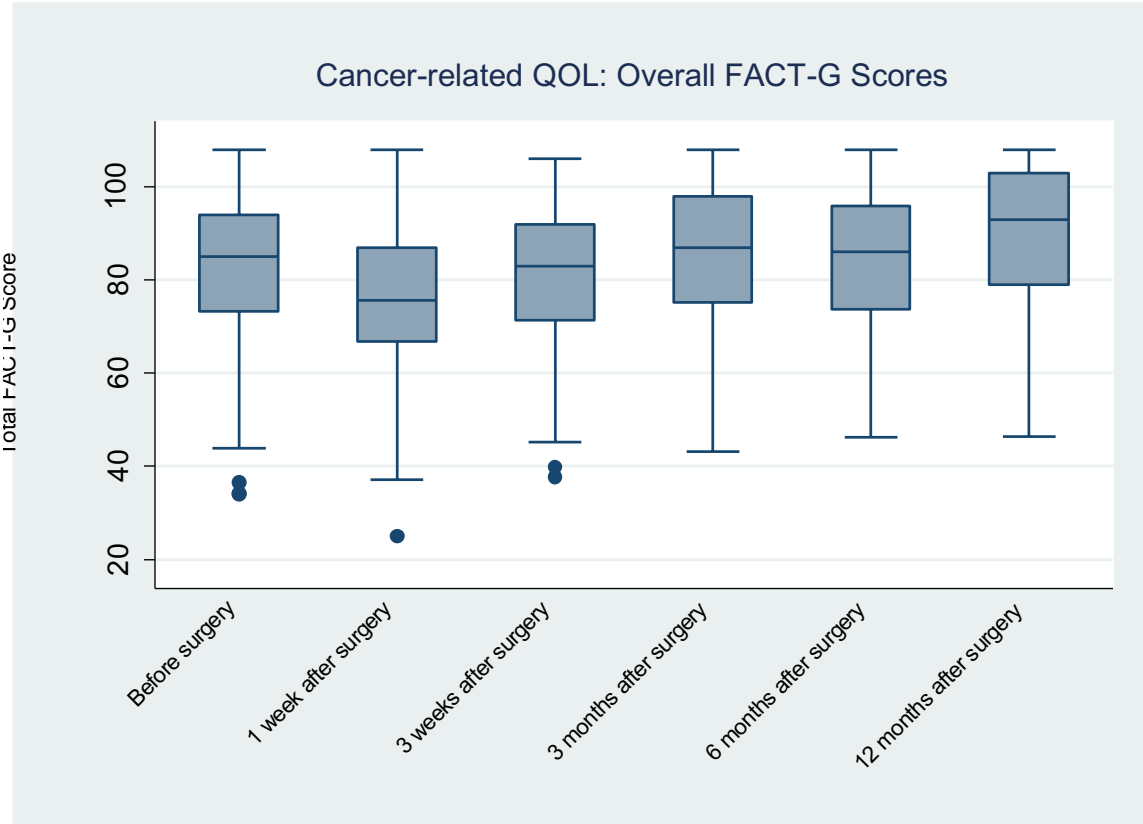
All postoperative questionnaire scores were compared to baseline scores using non-parametric Wilcoxon Signed-Rank Test. HRQL was considered to have returned to baseline if differences with baseline were non-significant.
Note: Similar significance results were obtained by the Mann-Whitney-Wilcoxon Rank Sum Test.

*Significance at $p < 0.05$

MID: Minimally important difference. A minimally important difference (Y) was reached if the difference in mean scores at baseline and at postoperative time points was greater than or equal to the referenced MID.

2.11 Figures

Figure 1. Cancer-related HRQL before and after robotic surgery

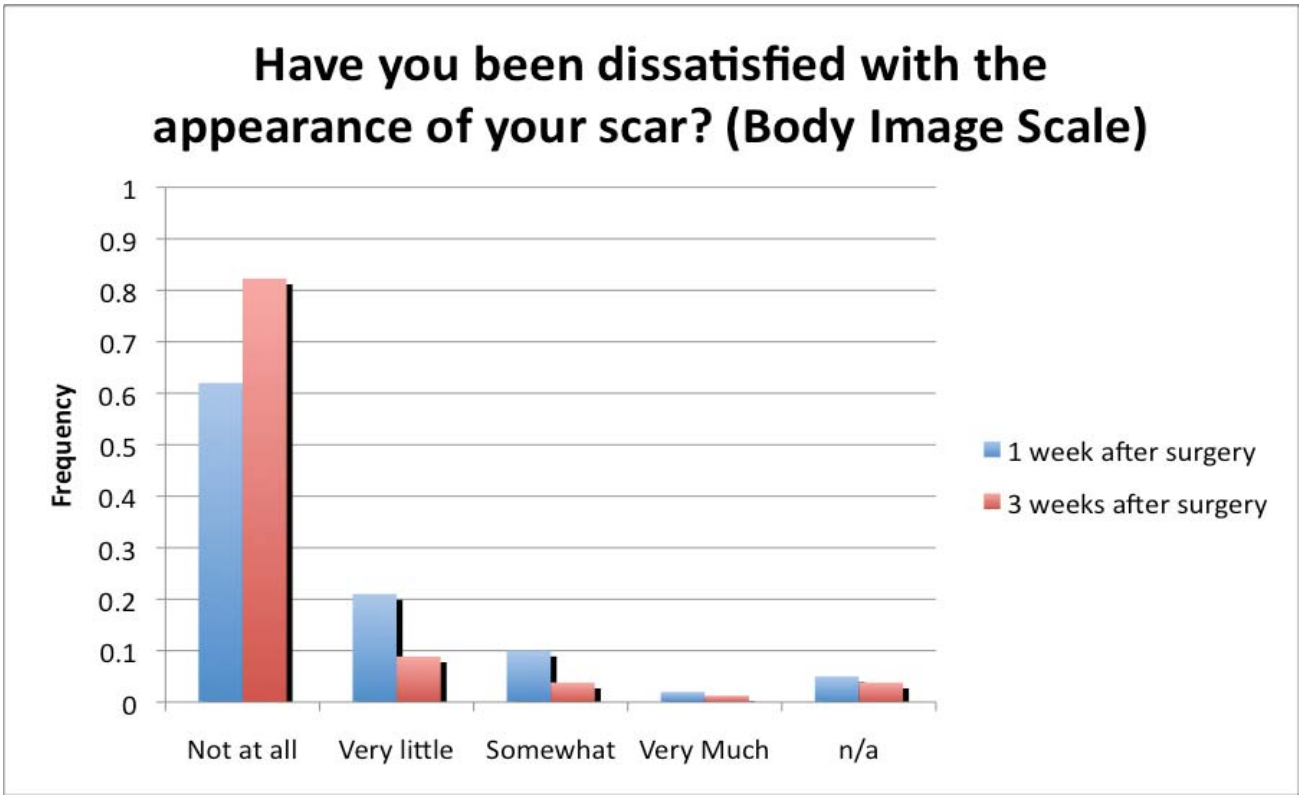


Box and whisker plots of FACT-G scores over time. The middle bar represents the median. Outer edges of the box represent the 25th and 75th percentiles. Whiskers represent the lower and upper adjacent values. Dots represent outliers.

Figure 2. Self-rated body image before and after robotic surgery

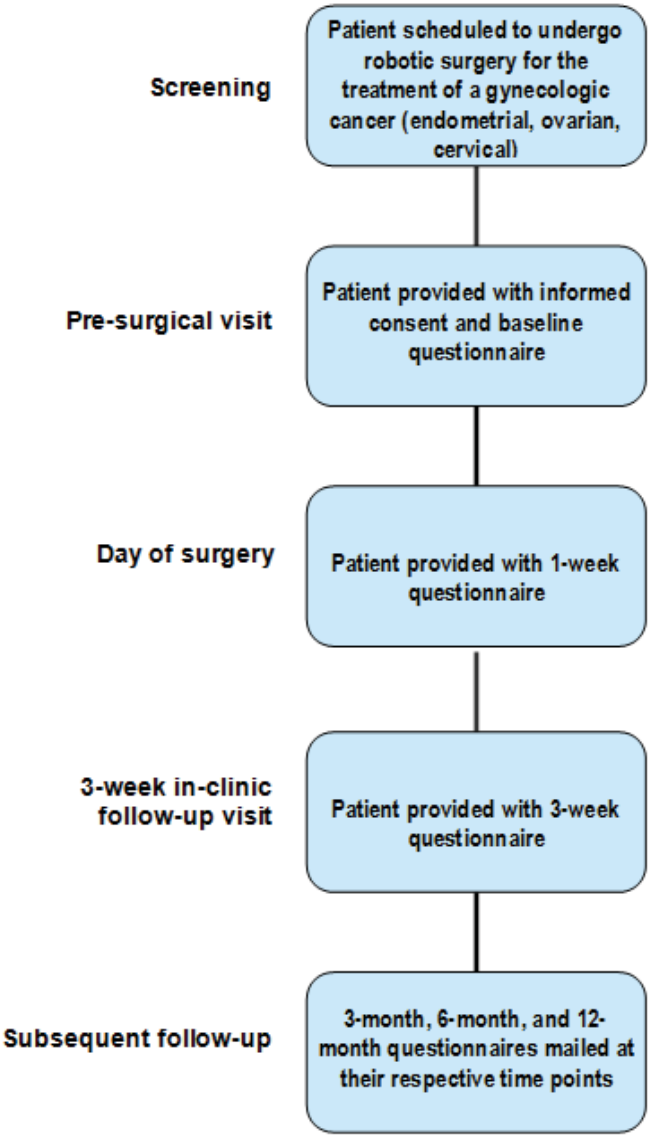
Box and whisker plots of body image scores over time. Body Image Scale (BIS) scores were subtracted from 30 so that higher scores correspond to better body image. The middle bar represents the median. Outer edges of the box represent the 25th and 75th percentiles. Whiskers represent the lower and upper adjacent values. Dots represent outliers.

Figure 3. Patient-rated satisfaction with scarring after robotic surgery.



2.12 Supplementary Material

S1. Flow chart of study procedure



CHAPTER 3 – MINIMIZING PAIN MEDICATION USE AND ITS ASSOCIATED COSTS FOLLOWING ROBOTIC SURGERY

J. Abitbol, R. Cohn, S. Hunter, M. Rombaldi, E. Cohen, R. Kessous, N. Large, A. Reiss, S. Lau, S. Salvador, W.H. Gotlieb

3.1 Preface

In conjunction with HRQOL, other important patient-reported outcomes that were evaluated as part of the previous study were patients' satisfaction with the surgery as well as patient-rated pain. Within the same HRQOL questionnaires described in the previous chapter, patients were asked to complete a validated pain assessment, the Brief Pain Inventory (BPI). Similarly to results from the HRQOL analysis in the previous chapter, results from this pain questionnaire demonstrated a return to pre-surgery levels of pain severity, pain interference with daily life, and the use of treatments for pain (e.g., pain medications), within three weeks of surgery [186]. Moreover, a satisfaction survey highlighted patients' contentment with the surgical approach [186] (published article enclosed in Appendix II).

The use of HRQOL and patient-reported outcomes is important to gain an understanding of patients' experiences as a result of treatment. Indeed, the increasing use of PROMs reflects a more holistic approach to treatment evaluation and a means to address the potential shortcomings of traditional measures [155]. However, it has been said that PROMs should be thought of as "added value" (Osoba, 2011, p. 64) rather than replace standard clinical outcomes [155, 187].

Together with patient-rated pain, a related pain assessment is the objective use of analgesics in the hospital. The following manuscript was published in *Gynecologic Oncology* 144 (2017) 187-192 and included in Appendix III.

3.2 Abstract

Introduction

Minimally invasive surgery (MIS) has been associated with diminished postoperative pain and analgesia requirements. The objective of the current study was to evaluate the use of analgesia in the postoperative period following robotic surgery for endometrial cancer.

Methods

All consecutive patients who underwent robotic surgery for the treatment of endometrial cancer were included in this study. The timing, dose, and type of analgesics administered postoperatively were recorded from patients' electronic medical records. Data was compared to a matched historical cohort of patients who underwent laparotomy before the introduction of the robotics program.

Results

Only eight patients (2.4%, 5 during the first 25 cases and 3 following mini-laparotomy) received patient-controlled analgesia (PCA) following robotic surgery. Most patients' pain was alleviated by over-the-counter analgesics (acetaminophen, non-steroidal anti-inflammatories). In comparison to laparotomy, patients who underwent robotic surgery required significantly less opioids (71 mg vs. 12 mg IV morphine, $p < 0.0001$) and non-opioids (4810 mg vs. 2151 mg acetaminophen, 1892 mg vs. 377 mg ibuprofen, and 1470 mg vs. 393 mg naproxen; all $p < 0.0001$).

Conclusion

Patients require less analgesics (opioids and non-opioids) following robotic surgery in comparison to conventional laparotomy, including the elderly and those with obesity. The diminished pain medication use is associated with some cost savings.

3.3 Background

In 1986 and again in 1996, the World Health Organization (WHO) developed guidelines to alleviate pain resulting from cancer and its treatments [188, 189], yet to this day pain in cancer patients continues to be undertreated [190, 191]. To further diminish post-surgical pain and limit the use of opioids, minimally invasive laparoscopic surgery (MIS) has been championed as a less traumatic approach to surgery. Since the introduction of robotically-assisted surgery, more patients have been able to benefit from the minimally invasive technique [47].

Recently, we reported that 40% of patients did not take any analgesics for pain at the time of their first post-op visit [165]. Using validated psychometric instruments, we demonstrated that pain severity, pain interference with daily life, and use of treatments for pain returned to pre-surgery levels within 3 weeks of surgery (*manuscript submitted for publication*). In the current study, we evaluate the use of pain medications during the postoperative hospital stay following surgery for endometrial cancer.

3.4 Methods

All consecutive patients who underwent robotic surgery for endometrial cancer were included in this study. A trained research assistant extracted medications, doses, routes of administration, and time of administration for every patient in the postoperative period, from every chart on the hospital's electronic medical record system. Time of administration was described as having been given after surgery on postoperative day 0 (POD0), POD1, and every day thereafter (POD2+). Patient characteristics and clinical data were obtained from a prospective computerized departmental database. Direct costs associated with the administration of pain medications were gathered from the hospital's pharmacy and purchasing departments. The following costs were

included: medications, needles, syringes, Patient Controlled Analgesia (PCA)-associated costs (PCA syringe, catheter, tubing, dressing, and labor costs for preparations by pharmacy personnel), epidural-associated costs (epidural kits, bags, tubing, labor costs for preparations, and anesthetist's fees for epidural injection and follow-up). All costs were expressed in 2015 Canadian dollars.

Since 2009, over 95% of patients with endometrial cancer undergo robotic surgery in our center, virtually eliminating laparotomy for this indication. We therefore evaluated pain medication usage in a cohort of consecutive patients treated by laparotomy for endometrial cancer, just prior to the introduction of the robotic platform. Electronic medical records were reviewed for both cohorts. Due to the greater number of patients in the robotic cohort, patients from the historical cohort were matched by stage (as a proxy for extent of disease) and age (as it can affect a drug's pharmacokinetics) in a 1:3 ratio to those treated by robotic surgery. Institutional IRB approval was obtained for this study. Outcomes were compared for statistical differences between the two cohorts using the Mann–Whitney U test, the chi-squared test, or Fisher's exact test, where applicable, using the STATA statistical software (StataCorp). A significance level of $p < 0.05$ was used throughout the study.

3.5 Results

A total of 356 patients were treated for endometrial cancer by robotically-assisted surgery since the introduction of the robotics program in December 2007 until April 2013, the time at which this study was designed. No differences in procedures occurred since that time. Sixteen patients were excluded because the final pathology demonstrated non-cancerous or benign disease (n = 4), the presence of multiple malignancies (n = 6), re-operation within the same admission (n = 3), incomplete pain medication chart (n = 1), or conversion to laparotomy for intolerance to

Trendelenburg (n = 2). Patients who underwent a mini-laparotomy for the removal of large uteri (n = 6) remained included in the robotic cohort, leaving 340 robotic cases for analysis.

The mean age was 65 years, and 34% were ≥70 years old (Table 1). The mean body mass index (BMI) was 32 kg/m^2; 51% were obese and 19% morbidly obese (BMI>40). Most patients had stage IA disease (62%) and most tumors were of endometrioid histology (74%).

The average surgical time (skin incision to closure) was 240 minutes (95% CI 234 to 245 minutes) with a mean estimated blood loss (EBL) of 70 mL (95% CI 60 to 80 mL). Patients stayed in the hospital, on average, 1.6 days (95% CI 1.4 to 1.7 days, median 1 day).

Pain medication use is tabulated in Table 2. Most patients' pain was alleviated by acetaminophen (mean 2294 mg) and NSAIDs (mean 461 mg ibuprofen, 375 mg naproxen). As part of the anesthesia protocol for minimally invasive procedures, patients were administered intravenous fentanyl (mean 53 mcg) in the Post-Anesthesia Care Unit. The average dose of morphine administered was 1.3 mg intravenously, 3.1 mg subcutaneously, and 1.2 mg orally. Only eight (2.4%) patients were on Patient-Controlled Analgesia (PCA), six on IV morphine and two on IV fentanyl. No patients required continuous epidural analgesia. Five of those on PCA were during the learning curve in the first 25 cases and three had a mini-laparotomy for retrieval of a large uterus. All opioids were converted into a Morphine IV scale to estimate the total narcotic use. Including patients on PCA, on average 12.8 mg of morphine were administered.

Comparing to matched laparotomy group

59 non-selected patients in the historical laparotomy group had available electronic records containing data on pain medications administered after surgery. Patients in the laparotomy group

were then matched in a 1:3 ratio (for n = 177 robotic cases) by stage and age to those in the robotics group.

Patient and oncologic characteristics for the matched cohorts are shown in Table 3. There was no significant difference in the mean age (67 years old in both groups, $p = 1.0$), BMI (29 vs. 30 in the laparotomy and robotic groups, respectively; $p = 0.3$), and ASA scores (58% vs. 62% had an ASA level of 2, $p = 0.6$). Most tumors were of endometrioid histology (75% vs. 66%, $p = 0.3$), most patients had stage I disease (68% in both cohorts), and one fifth of patients in both cohorts had stage III disease.

The robotic cohort tended to have longer mean surgical times (247 vs. 202 min, $p < 0.0001$) though significantly lower estimated blood loss (76 vs. 314 mL, $p < 0.0001$) and length of stay (1.5 vs. 6.1 days, $p < 0.0001$).

Table 4 shows pain medication use comparing the laparotomy and robotic cohorts. There are standard order sheets but no protocol per se for patients undergoing laparotomy. Overall, patients who had a laparotomy tended to require significantly more narcotic and non-narcotic analgesics. The laparotomy cohort required more acetaminophen (4810 mg vs. 2151 mg, $p < 0.0001$), ibuprofen (1892 mg vs. 377 mg, $p < 0.0001$), and naproxen (1470 mg vs. 393 mg, $p < 0.0001$). In addition, all but one patient in the laparotomy cohort were either on PCA (90%) or continuous epidural analgesia (9%). In contrast, only three (2%) patients in the matched robotics cohort were on PCA ($p < 0.0001$): two with morphine and one with fentanyl and no patients were on continuous epidural analgesia ($p < 0.0001$). Among those who were on PCA, there was no difference in the doses administered via PCA (57.9 mg morphine and 611 mcg fentanyl in the laparotomy group; 53.4 mg morphine and 720 mcg fentanyl in the robotic group).

Taking into account all opioids on a morphine IV equivalent scale, patients who had a robotic surgery were administered significantly less opioids than those who were operated by laparotomy (12 vs. 71 mg, $p < 0.0001$).

Neither BMI nor age were associated with a difference in the use of the NSAIDs (acetaminophen, ibuprofen, naproxen) or opioids (morphine IV equivalent), but both obese and elderly patients used significantly less of these analgesics following robotic surgery compared to laparotomy ($p < 0.01$).

Due to the difference in length of stay between the two cohorts, the use of analgesics is represented on the basis of daily use (Figures 1 and 2).

While patients were matched between the laparotomy and robotic cohorts, to control for a selection bias, the statistical analysis was run again between the laparotomy cohort and the entire robotic sample (n = 340), and yielded similar results.

Cost analysis

The average direct costs associated with postoperative analgesia in the laparotomy cohort were higher than that of the robotic cohort ($47.57 vs. $6.39, $p < 0.0001$). The most expensive costs were attributed to the epidural analgesia, though even when these were excluded, costs were still higher in the laparotomy cohort ($29.31 vs. $6.39, $p < 0.0001$). To control for the longer hospitalization among laparotomy patients, total analgesia costs per day were calculated and were still significantly higher in the laparotomy cohort ($7.89 vs. $2.52, $p < 0.0001$).

3.6 Discussion

The current study demonstrates reduced pain medication utilization in the immediate postoperative period following robotic surgery in comparison to laparotomy. Overall, patients who underwent robotic surgery used, on average, significantly less non-opioids (acetaminophen, ibuprofen, and naproxen; all $p < 0.0001$), opioids ($p < 0.0001$), and PCA or continuous epidural analgesia ($p < 0.0001$).

Incision size has been found to be an important predictor for severe postoperative pain in the first hour after surgery [192]. Some mathematical models also suggest that wound tension is not linearly but exponentially related to the length of an incision, suggesting that multiple small incisions result in less morbidity than a single large open incision [193]. Indeed, compared to laparotomy, minimally invasive laparoscopic surgery is associated with reduced patient-rated pain [33] and analgesic requirement [194, 195]. In comparison to laparoscopy, robotic surgery has been shown to be associated with significantly less use of opioids following surgery for cervical [196] and endometrial cancer [114]. The latter study reported high rates of intravenous PCA use (86% in the robotic cohort and 88% in the laparoscopy cohort), though the authors describe having ceased the routine administration of PCA in their robotic surgery patients [114]. With only eight (2%) patients on IV PCA in our robotic cohort (three of whom required a mini-laparotomy), the current study is evidence that the routine use of PCA is not required in patients undergoing robotic surgery. While patients with a mini-laparotomy might be expected to experience greater pain, these were included in the robotic cohort as these were not considered full conversions. These patients were excluded in a sensitivity analysis yielding similar results. All eligible consecutive patients surgically treated for endometrial cancer by laparotomy and robotic surgery were included in the analysis. Three patients in the matched robotic cohort had a previous hysterectomy (one subtotal) and salpingo-oophorectomy and were re-operated robotically for completion staging. One patient

with stage IV disease had biopsies and a pelvic lymphadenectomy but complete debulking was abandoned due to diffuse metastases. All other patients had full staging with hysterectomy, salpingo-oophorectomy, and pelvic lymphadenectomy. Some also had periaortic lymph nodes removed (78 in the matched robotic cohort, 37 in the laparotomy cohort), omentectomy or omental biopsy (41 robotic, 37 laparotomy), appendectomy (1 in each matched cohort), and hernioplasty (1 in each matched cohort).

To account for the quicker discharge of patients after robotic surgery, the daily use of analgesics was evaluated, further reflecting the significantly reduced need for opioids in the robotic cohort ($p < 0.0001$ on POD0, POD1, and POD2 onwards).

The benefits of robotic surgery remained regardless of body habitus or age. The total use of opioids among the elderly was significantly reduced in the robotic cohort compared to the laparotomy cohort (67 mg vs. 10 mg, $p < 0.0001$). This is particularly relevant considering the increased risk of adverse events associated with the use of opiates in the geriatric population [197].

The decrease in the use of postoperative pain medications following the introduction of robotic surgery was associated with a 70% decrease in pain medication costs per day. While these costs take into account the costs of medications and supplies for the injection of parenteral medications, they underestimate cost savings attributed to the reduced nursing hours required to tend to patients for the alleviation of pain. Robotic surgery has similarly been found to decrease pain medication costs compared to laparoscopy [113].

In addition to decreased analgesic use, robotically-assisted surgeries were associated with longer surgical times but less blood loss and shorter hospital stay. A recent study by Bogani et al. (2016) similarly noted significantly longer surgical times but shorter hospitalizations in endometrial cancer patients undergoing robotic surgery compared to open surgery [90]. Similar

trends were previously described following the introduction of laparoscopy for apparent early stage gynecologic cancers, noting a significant growth in the use of laparoscopy relative to open surgery, and associated with decreased blood loss and shortening of hospital stay [198].

There are some limitations in the current study. First, data was gathered retrospectively. For the most part, the availability of medications was similar between the two eras, with only few exceptions (e.g., Rofecoxib was withdrawn from the market in 2004 but was only used once by a single laparotomy patient). Prior to the introduction of robotics in our department, only up to 17% of patients were operated by MIS [89]. In the first year of our robotics program, 66% of endometrial cancer patients underwent robotic surgery though this was only due to limited access to the robotic system [199]. From 2009 and onwards, over 95% of operable endometrial cancer patients underwent robotic surgery [89, 199].

The analysis was also limited to postoperative use of pain medications only. Intraoperatively, all robotic trocar sites are routinely infiltrated with Bupivacaine 0.5% without Epinephrine before skin incision and at the conclusion of surgery to diminish pain. This procedure is not done for patients undergoing laparotomy. Preoperative use of chronic pain medications was also not taken into account when calculating equianalgesic values. However, the differences in opioid usage in the robotic and laparotomy cohorts were so apparent that it is unlikely to have made a difference. Opioids were prescribed “as needed” in the routine post-op orders and were therefore available to all patients. Due to the rapid onset and excretion of fentanyl, intravenous fentanyl is administered to patients in the PACU following minimally invasive procedures as part of a standard recovery room protocol.

Our previous studies on outcomes following robotic surgery have demonstrated a rapid return to preoperative patient-reported pain scores (*manuscript submitted*). The current study

supports these findings by demonstrating the low use of both opioid and non-opioid pain medications, and although the absolute cost reduction is not abundant, there were some cost savings attributed to the reduction in the use of analgesia.

3.7 Funding

This study was supported by grants from the Israel Cancer Research Foundation, the Gloria's Girls Fund, the Levi Family Fund, and the Weekend to End Women's Cancers.

3.8 Conflicts of Interest

Walter Gotlieb and Susie Lau obtained partial travel support for proctoring robotic surgery

3.9 Acknowledgements

We would like to extend a sincere thanks to our pivot nurse, Nancy Drummond, without whom this study would not have been possible.

3.10 Tables

Table 1. Baseline characteristics of all patients with robotic surgery

	Robotic (n=340)
Age, mean (SD)	64.8 (11.5)
BMI, mean (SD)	31.9 (8.7)
ASA	
1	10.3%
2	62.1%
3	27.1%
4	0.6%
Final histology	
Endometrioid	73.8%
Serous	10.9%
Clear cell	5.0%
Carcinosarcoma	4.1%
Adenosquamous	3.5%
Mucinous	1.2%
Sarcoma	1.2%
Unclassified	0.3%
Grade	
1	42.1%
2	23.8%
3	34.1%
Surgical stage	
IA	61.5%
IB	16.2%
II	5.0%
IIIA	3.5%
IIIB	0.6%
IIIC	10.9%
IVA	0.6%
IVB	1.8%

Table 2. Pain medication use following robotic surgery

Medication	Full robotic sample (n=340)			
	n	Mean	SD	Median
Acetaminopen				
Acetaminopen	300	2294.0	2293.4	1650
NSAIDS				
Ibuprofen	145	461.2	702.0	0
Toradol	34	1.0	3.0	0
Naproxen	122	375.4	655.7	0
Diclofenac (PO/PR)	20	7.1	32.0	0
Meloxicam	2	0.1	1.1	0
Ketoprofen	0	0.0	0.0	0
Rofecoxib	0	0.0	0.0	0
Indomethacin	0	0.0	0.0	0
Celecoxib	1	0.6	10.8	0
Oral opioids				
Codeine	20	3.2	15.1	0
Oxycodone	4	0.1	1.1	0
Hydromorphone (PO)	24	0.3	1.9	0
Morphine				
Morphine (IV)	48	1.3	4.2	0
Morphine (SC)	69	3.1	10.0	0
Morphine (PO)	43	1.2	3.8	0
Other				
Fentanyl (IV)	177	0.1	0.1	0.03
Neurontin (PO)	2	3.5	45.9	0
Demerol (IV/IM)	4	0.3	2.7	0
Hydromorphone (IV/SC)	17	0.1	0.4	0
Empracet (PO)	10	1.3	8.4	0
Patient-controlled analgesia				
# on PCA	8			
Morphine (IV PCA)	6	0.8	7.2	0
Fentanyl (IV PCA)	2	0.002	0.04	0
Continuous epidural anlagesia				
# on CEA	0			
Morphine IV equivalence				
Including PCA/CEA	280	12.8	17.1	7.8

Note: All doses presented are in milligrams (mg).

Table 3. Baseline characteristics in matched laparotomy and robotic sample

	Laparotomy (n=59)	Robotic (n=177)	P-value
Age, mean (SD)	67.4 (10.2)	67.3 (10.3)	0.95
BMI, mean (SD)	29.3 (6.5)	30.2 (6.6)	0.29
ASA			
1	16.9%	11.9%	0.32
2	57.6%	61.6%	0.59
3	23.7%	26.0%	0.73
4	1.7%	0.6%	0.44†
Final histology†			
Endometrioid	74.6%	66.1%	0.26
Serous	8.5%	15.3%	0.27
Clear cell	6.8%	6.2%	1.0
Carcinosarcoma	6.8%	5.6%	0.75
Adenosquamous	3.4%	4.5%	1.0
Mucinous	0.0%	1.1%	1.0
Sarcoma	0.0%	0.6%	1.0
Unclassified	0.0%	0.6%	1.0
Grade			
1	25.4%	33.9%	0.23
2	40.7%	21.5%	0.004
3	33.9%	44.6%	0.15
Surgical stage†			
IA	54.2%	54.2%	1.0
IB	13.6%	13.6%	1.0
II	6.8%	6.8%	1.0
IIIA	1.7%	1.7%	1.0
IIIB	0.0%	0.0%	
IIIC	20.3%	20.3%	1.0
IVA	0.0%	0.0%	
IVB	3.4%	3.4%	1.0

†Significance tested using Fisher's exact test

Table 4. Comparing pain medication use following laparotomy and robotic surgery

Medications	Laparotomy (n=59)				Robotic (n=177)				P-value
	n	Mean	SD	Median	n	Mean	SD	Median	
Acetaminopen									
Acetaminopen	57	4810.2	2194.6	4875	153	2151.1	2216.5	1650	<0.0001
NSAIDS									
Ibuprofen	48	1891.5	1498.2	1600	68	377.4	593.5	0	<0.0001
Toradol	2	1.4	7.5	0	21	1.2	3.2	0	0.071
Naproxen	34	1470.3	2716.5	1000	67	393.4	704.6	0	<0.0001
Diclofenac (PO/PR)	6	11.9	37.5	0	13	9	37.4	0	0.49
Meloxicam	0	0.0	0.0	0	1	0.1	1.1	0	0.56
Ketoprofen	1	13.6	104.2	0	0	0	0.0	0	0.083
Rofecoxib	1	1.7	13.0	0	0	0	0.0	0	0.083
Indomethacin	2	4.7	25.2	0	0	0	0.0	0	0.014
Celecoxib	0	0.0	0.0	0	1	1.1	15.0	0	0.56
Oral opioids									
Codeine	0	0.0	0.0	0	13	4.1	17.3	0	0.033
Oxycodone	1	0.1	1.0	0	1	0.1	1.1	0	0.42
Hydromorphone (PO)	0	0.0	0.0	0	14	0.4	2.6	0	0.026
Morphine									
Morphine (IV)	2	0.3	1.4	0	23	1.2	4.0	0	0.039
Morphine (SC)	38	14.8	22.4	5	37	3	8.8	0	<0.0001
Morphine (PO)	0	0.0	0.0	0	18	1	3.7	0	0.011
Other									
Fentanyl (IV)	1	1.0	7.8	0	85	46.5	64.6	0	<0.0001
Neurontin (PO)	1	81.4	624.9	0	1	3.4	45.1	0	0.41
Demerol (IV/IM)	1	1.7	13.0	0	2	0.3	2.6	0	0.73
Hydromorphone (IV/SC)	1	0.1	0.9	0	11	0.1	0.5	0	0.18
Empracet (PO)	6	15.8	60.9	0	6	1.5	9.2	0	0.034
Patient-controlled analgesia									
# on PCA	53				3				<0.001†
Morphine (IV PCA)	51	50.0	39.2	43	2	0.6	6.4	0	<0.0001
Fentanyl (IV PCA)	4	0.04	0.2	0	1	0.004	0.1	0	0.0043
Continuous epidural analgesia									
# on CEA	5				0				0.001†
Bupivacaine (IV CEA)	5	23.5	79	0	0				0.0001
Morphine (IV CEA)	3	1.0	4.5	0	0				0.0026
Sufentanil (IV CEA)	3	0.003	0.01	0	0				0.0026
Morphine IV equivalence:									
Including PCA/CEA	59	71.0	47.2	59	144	12.2	17.1	8	<0.0001

Note: All doses presented are in milligrams (mg).

†Significance tested using Fisher's exact test.

3.11 Figures

Figure 1. Daily use of non-opioids following laparotomy and robotic surgery for endometrial cancer

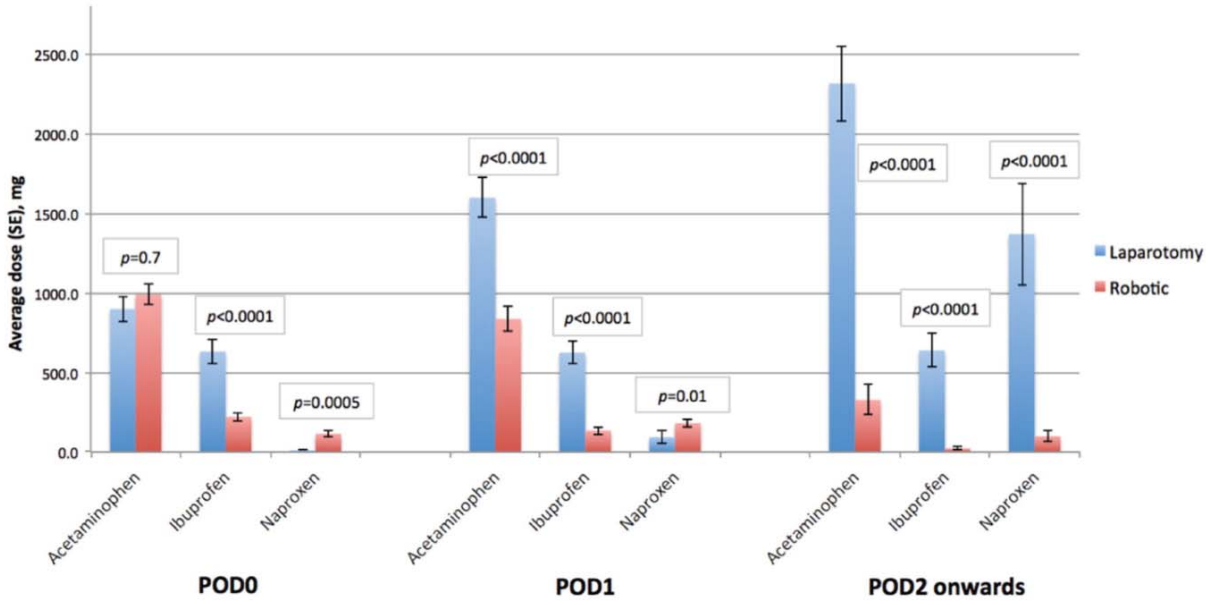
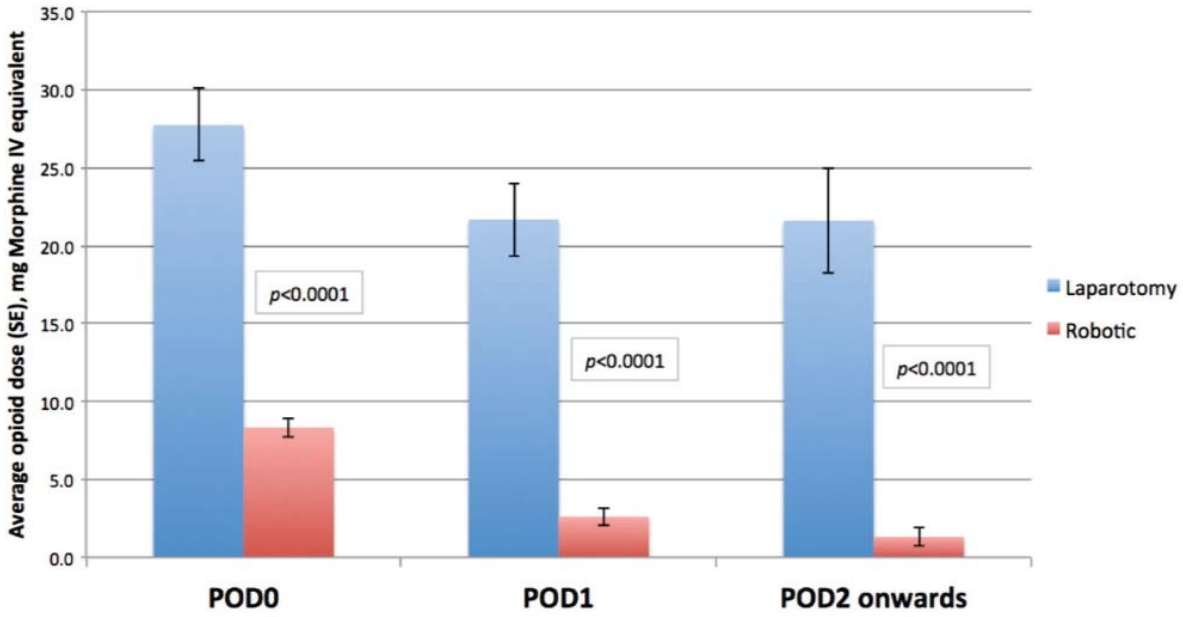


Figure 2. Daily use of opioids following laparotomy and robotic surgery for endometrial cancer



CHAPTER 4 – INCORPORATING ROBOTIC SURGERY INTO THE MANAGEMENT OF ADVANCED STAGE OVARIAN CANCER

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4.1 Preface

In addition to PROMs (HRQOL, patient-rated pain, satisfaction survey) and the perioperative outcomes (e.g., analgesic use, estimated intraoperative blood loss, length of hospital stay) described in the preceding chapters, other clinical outcomes that were evaluated following robotic surgery include lymph node yield, conversions to open surgery, complications and adverse events, transfusion rates, emergency room visits, and readmissions to the hospital. Our team has published on many of these variables [199-202], with key results summarized in another published mini-review [203] (Appendix IV), and our division has also contributed this data to a prospective pan-Canadian multicenter study comparing laparotomy, laparoscopy, and robotic surgery for apparent early stage endometrial cancer (GOC2 study, registered on ClinicalTrials.gov with identifier NCT01480999). Preliminary results from this trial have been presented [204, 205].

An additional measure that is crucial to evaluate when assessing a new technology in oncology is survival and recurrence. Our team has analyzed overall survival as well as the recurrence patterns, including time and location(s) of recurrence, following robotic surgery versus laparotomy for the staging and treatment of endometrial cancer (*manuscript in preparation*) [206] as well as for the treatment of early stage cervical cancer [207].

In contrast to endometrial cancer, most patients presenting with ovarian cancer tend to be diagnosed at an advanced stage (over 75%), resulting in a poor prognosis for many patients [208]. Our team has described the often long treatment pathways in ovarian cancer, with up to ten lines of chemotherapy administered (*manuscript in submission*) [209], as well as the comparison of different treatment protocols (specifically, the use of neoadjuvant chemotherapy versus upfront primary debulking surgery) [210]. However, because of the nature of the disease, very little has been published with regard to the use of robotics in the management of ovarian cancer.

4.2 Abstract

Introduction

Despite the rapid uptake of robotics in surgical oncology, its use in the treatment of ovarian cancers remains controversial. Extensive cytoreductive surgery via midline laparotomy remains the mainstay treatment, though in some cases the extent of disease would enable minimally invasive surgery. The objective of the current study was to evaluate the impact of introducing robotic surgery for selected patients with stage III–IV ovarian cancer.

Methods

Since the introduction of robotics for ovarian cancer in 2008, patients were selected to undergo robotic surgery (n = 75) or laparotomy (n = 61) either for primary debulking surgery (PDS) or following neoadjuvant chemotherapy (NACT). Prior to the use of robotic debulking surgeries, all patients (n = 62) were offered a laparotomy. Overall survival (OS), progression-free survival (PFS), and perioperative outcomes were compared for the entire patient cohort with advanced ovarian cancer before and after the introduction of robotic surgery.

Results

The median OS was 47.2 ± 5.4 months in the period where both robotic surgery and laparotomy were offered, compared to 40.0 ± 5.3 months in the immediately preceding period where only laparotomy was performed ($p = 0.64$). There were no significant differences in OS or PFS after controlling for the use of NACT. Among patients selected to undergo robotic surgical debulking, adequate cytoreduction was achievable (72% complete cytoreduction), blood loss was minimal (mean of 145 mL), and hospital stay was short (median of one day).

Conclusion

The integration of robotics into the surgical management of patients with ovarian cancer seems feasible in patients who are triaged, resulting in comparable survival rates and improved perioperative outcomes. Complete cytoreduction remains the surgical objective and future studies should aim to define which patients are best suited to be selected for minimally invasive debulking surgery.

4.3 Introduction

Cytoreductive surgery as described by Griffiths (1975) has been the prevailing paradigm in treating ovarian cancer [211], including in the era of platinum, taxanes, and precision medicine [212]. Despite this radical approach, ovarian cancer has poor survival [213], and its treatments have been associated with significant morbidity, including physical as well as psycho-emotional impairment [171, 177, 214, 215].

The use of neoadjuvant chemotherapy followed by interval surgical cytoreduction and adjuvant chemotherapy has become an option for some women with advanced ovarian cancer, offering comparable survival [216] and decreased morbidity [217, 218] compared to extensive cytoreductive surgery upfront followed by adjuvant chemotherapy. Since the approval of the da Vinci® Surgical System for gynecologic procedures in 2005 [67], it has rapidly integrated into the treatment of endometrial and cervical cancer, and, like laparoscopy, it has resulted in reduced operative blood loss, lower incidence of postoperative complications, and faster recovery [89, 95, 99, 219].

In view of the decreased tumor burden observed following neoadjuvant chemotherapy, with sometimes minimal or no visible residual disease at the time of interval cytoreduction by laparotomy, the objective of the current study was to evaluate whether the introduction of a robotics program can improve perioperative results while maintaining oncologic outcomes for women with ovarian cancers. In this manuscript we evaluated how the addition of robotics as a surgical option for a carefully selected group of patients affected the outcomes of our entire patient population with advanced stage ovarian cancer by comparing it to an immediately preceding historical cohort to whom laparotomy was the surgical approach offered.

4.4 Materials and Methods

Prior to November 2008, all patients who were offered debulking surgery for ovarian cancer underwent abdominal surgery via laparotomy. Starting in November 2008, the use of robotically-assisted surgery was offered to a carefully selected group of patients who were prospectively evaluated; if deemed not feasible, patients continued to undergo open cytoreductive surgery. To evaluate the impact of incorporating robotics into the surgical management of patients with ovarian cancer, all patients who were operated in the robotic period (i.e., via both laparotomy and robotic surgery) from November 2008 to 2014 were compared to all patients who were operated between January 2006 and November 2008, immediately prior to the use of robotic surgery for ovarian cancers. A diagram illustrating the surgical approaches in the pre-post analysis is included in Supplementary Material S1. The current analysis focuses on patients with advanced stage (III–IV) disease only.

Patients were informed about the evaluation of the robotic approach for the surgical treatment of their disease. An information booklet was provided to each patient and all patients who were offered robotic surgery signed an informed consent for the evaluation of outcomes in addition to the regular surgical consent form. This study was approved by the hospital's Institutional Review Board.

In this evaluation period, the decision to proceed with robotically-assisted surgery rather than laparotomy was made by the gynecologic oncology tumor board following an initial assessment of whether complete cytoreduction could be expected to be achieved robotically, including a clinical evaluation and the review of CT images with an expert radiologist in abdominal imaging. In patients who received neoadjuvant chemotherapy (NACT), the decrease in CA125 values, the resolution of ascites, and a comparison of CT scan images prior to and after neoadjuvant chemotherapy was included. During this pilot period, no absolute criteria were defined, and a

conservative approach was taken favoring laparotomy in suspected complex surgical cases, especially requiring bowel resection, leading to a selection of patients with the highest likelihood of successful debulking in the robotics cohort. Complete cytoreduction was defined as no visible residual disease. The chemotherapy administered was a combination of platinum-taxane chemotherapy.

All procedures were performed by one of four gynecologic oncologists with experience in robotic surgery. Robotic-assisted surgery was performed using the da Vinci® Surgical System, introduced in December 2007 in the Division of Gynecologic Oncology.

Robotic surgery followed established oncological standards and included careful evaluation of the abdomino-pelvic cavity, peritoneal washings, hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic/paraaortic lymphadenectomy for staging or presence of enlarged lymph nodes, omentectomy, and removal of all visible peritoneal disease including upper abdominal implants in order to attempt to achieve complete cytoreduction.

The patient was placed on an egg crate mattress with the lower extremities in padded lithotomy stirrups. The entire upper extremities were wrapped in foam padding. Shoulder braces covered with gel foam pads were used as additional safety devices. This prevented the patient from sliding and avoided injury to the brachial and ulnar nerves. All patients were monitored with an arterial line and were maintained in steep (almost 30 degrees) Trendelenburg position throughout the procedure, with insufflation pressures between 8 to 15 mmHg. Patients received standard antibiotherapy with piperacillin and tazobactam, subcutaneous heparin, and pneumatic compression stockings to the lower extremities. Since May 2009, we have adopted positioning of the robot at a 30-degree angle at the side of the patient's bed to allow easy repositioning of the robot (double docking) and better access to the perineum to extract specimens. Repositioning of

the robot was performed for upper abdominal and diaphragmatic surgery. Specimens were extracted in endobags through the vaginal opening unless a hysterectomy had been performed in the past, in which case a port site was slightly enlarged to allow for the removal of specimens within endobags.

Patients were seen in the clinic after one week for routine postoperative care and to plan for adjuvant chemotherapy. Following the end of adjuvant treatment, patients in remission were followed every four months for two years, followed by every six months up to five years, and yearly thereafter. Physical examination and standard blood tests including tumor markers were ordered routinely, and imaging studies were performed only if indicated.

The inclusion criteria for the study included a debulking surgery by laparotomy or robotic-assistance for a confirmed stage III–IV ovarian, fallopian tube, or primary peritoneal cancer. Borderline or benign tumors as well as germ cell tumors were excluded from this study. Other exclusion criteria included patients being treated concurrently for a non-gynecologic cancer as well as secondary debulking surgeries and diagnostic surgeries without an attempt at debulking.

Statistical analysis

Statistical tests were performed using Fisher's exact test for categorical variables, the Wilcoxon rank-sum test for continuous variables, and exact logistic regression for odds ratios (presented as OR ± standard error). Oncologic outcomes such as survival and progression-free survival were analyzed using Kaplan-Meier curves and the log rank test for statistical significance. Cox proportional hazard models were used to control for the use NACT, stage (III, IV), and age, with hazard ratios presented as HR ± standard error. Overall survival (OS) was measured from the date of first treatment (date of surgery for the primary debulking group; date of first chemotherapy

treatment for the neoadjuvant chemotherapy group) to the date of last follow-up or death. Progression-free survival (PFS) was measured from the date of first treatment to the date of recurrence, death, or last follow-up. Patients who progressed without a disease-free interval were estimated to recur on the day of their last treatment. Recurrences were diagnosed on imaging or physical exam. Survival time is presented as median survival ± standard error. Statistical analyses were performed using Stata 13.0 (StataCorp). A two-sided significance level of $p < 0.05$ was used throughout the study.

4.5 Results

Description of patient population

During the period of November 2008 (one year after starting the robotics program) to November 2014, 108 patients with ovarian cancer underwent robotically-assisted surgery as part of their first line treatment, of whom 75 (69%) had stage III or IV disease and represent the cohort studied in this manuscript (Supplementary Material S1). Among those 75 patients with advanced stage disease, 18 underwent upfront primary debulking surgery (PDS) and 57 underwent interval debulking surgery after neoadjuvant chemotherapy (NACT). During the same period that robotic debulking surgeries were performed, 61 patients underwent a traditional midline laparotomy for advanced stage disease, of whom 27 had PDS and 34 had received NACT.

Comparison between the eras prior to robotics and after the introduction of robotics

To evaluate how the introduction of robotics for selected patients affected the outcome of our entire patient population with advanced ovarian cancer, surgical outcomes as well as the pattern of recurrence were examined for all patients who underwent upfront PDS (combining n = 27 via

laparotomy and n = 18 via robotics) or interval debulking (n = 34 via laparotomy and n = 57 via robotics) for ovarian cancer since the first robotic surgery for ovarian cancer in November 2008. These were compared to a historical cohort of patients in the immediately preceding period who underwent upfront primary (n = 40) or interval (n = 22) debulking surgery by laparotomy, prior to the use of robotics for ovarian cancer, from January 2006 to November 2008.

Patient and tumor characteristics for patients prior to and after the addition of the robot as a potential tool for the surgery of patients with ovarian cancer are shown in Table 1. In both the NACT and the PDS groups, there were no statistically significant differences in age, American Society of Anesthesiologists' physical status classification score (ASA), stage, or histology. In the NACT group, patients in the robotic era tended to have more grade 3 disease ($p = 0.005$). In the PDS group, there was no statistically significant difference in grade ($p = 0.9$) but patients in the robotic era had a higher body mass index (BMI, $p = 0.007$).

Table 2 describes perioperative outcomes in the pre-robotic era as well as in the period combining laparotomy and robotics. In both the NACT and PDS groups, the latter period tended to have better cytoreduction rates ($p = 0.005$ in both the NACT and PDS groups) and significantly shortened hospital stay ($p = 0.0001$ and $p = 0.03$ in the NACT and PDS groups, respectively). In the NACT group, intraoperative blood loss was also significantly reduced in the robotic era ($p = 0.001$). In both the NACT and PDS groups, there were relatively fewer patients transfused intraoperatively as well as postoperatively in the robotic era, though the results were not statistically significant. Within the robotic era, patients who were transfused were significantly more likely to have undergone a laparotomy than a robotic surgery, and this applied to both intraoperative (NACT: OR = 12.2 ± 8.3, $p < 0.001$; PDS: OR = 18.3 (standard error not available), $p = 0.001$) and postoperative (NACT: OR = 4.9 ± 2.3, $p = 0.0007$; PDS: OR = 31.2 ± 34.2, $p < 0.001$) transfusions.

Complications were evaluated intraoperatively (for excess bleeding as well as injuries to the bladder, ureters, bowels, nerves, and blood vessels) and postoperatively (for fever, infection, abscess formation, cardiac complications, poor glucose control, cerebrovascular morbidity, ileus, lymphocyst formation, pulmonary complications, renal morbidity, septicemia, thromboembolic complications, urinary retention, urinary tract infection, vault complications, wound complications, and postoperative death). In both the NACT and PDS groups, there were no significant differences in the above complications between the two time periods (all $p > 0.05$).

Figures 1A and 1B illustrate the overall survival (OS) and progression-free survival (PFS), respectively, before and after the first use of robotics for ovarian cancer. Women in the era combining laparotomy and robotics merely trended towards a longer OS (Figure 1A1: median survival of 40.0 vs. 47.2 months before and after the initial use of robotics, respectively, $p = 0.6$) and PFS (Figure 1B1: 12.7 vs. 16.1 months, $p = 0.4$) when compared to the laparotomy only era, though there were no significant differences between the two groups.

The addition of robotics did not adversely affect the OS or PFS following either NACT (OS: median survival of 37.9 vs. 42.8 months, $p = 0.6$, Figure 1A2; PFS: 11.9 vs. 16.5 months, $p = 0.4$, Figure 1B2) or upfront PDS (OS: median survival of 40.1 vs. 62.4 months, $p = 0.8$, Figure 1A3; PFS: 12.8 vs. 13.5 months, $p = 0.7$, Figure 1B3).

After controlling for the use of NACT, stage, and age, the robotic era was not a significant predictor of OS (HR = 0.9 ± 0.2, $p = 0.6$) or PFS (HR = 0.9 ± 0.2, $p = 0.4$); none of the covariates were significant.

Perioperative and oncologic outcomes following robotic surgical debulking

Patients who underwent robotically-assisted debulking surgery were analyzed independently. Patient and tumor characteristics are presented in Table 3. The majority of patients had high grade (96%), serous (88%), and stage III (76%) disease. Surgical outcomes following robotic debulking surgery are summarized in Table 4. Complete cytoreduction was achieved in 72% of cases and an additional 24% of patients attained less than 1 cm residual disease. Only three patients in the robotic cohort had major residual disease and all three were in the PDS group. One patient had intraparenchymal hepatic metastases, the second presented with infiltration of the base of the mesentery, and the third had extensive carcinomatosis involving all peritoneal surfaces.

There were five conversions to laparotomy (7%) in the robotic cohort in order to achieve optimal debulking. In the PDS group, two conversions were performed: one for disease invading the sigmoid colon and mesentery, and one surgery for the removal of a large immobile ovarian mass involving the parametrium and the ureter. In the interval debulking group, three conversions were performed for debulking that necessitated a rectosigmoid resection, a hemicolectomy, and dissection of a densely adherent omentum. In addition, three left upper quadrant mini-laparotomies were performed to remove omental disease densely adherent to the splenic flexure and the spleen.

The mean blood loss for the robotic cohort was 145 mL and patients were relatively unlikely to require blood transfusions intraoperatively (4%). Postoperatively, 15 patients (20%) were transfused, all but one of whom had received neoadjuvant chemotherapy. Because some patients may be transfused for a low preoperative hemoglobin due to neoadjuvant chemotherapy, the number of patients transfused was analyzed among those with a preoperative hemoglobin level of at least 100 g/L, yielding transfusion rates of 3% intraoperatively and 11% postoperatively. Patients in the robotic cohort also had a median hospital stay of one day, with 81% of patients

discharged within the first two days postoperatively. Adjuvant chemotherapy was given after reception of final pathology after a median of 14 days from surgery [6–75 days].

After a median duration of follow-up of 43 months among patients who underwent robotic surgery, we note, as preliminary results, a median OS of 55.1 ± 9.1 months, including two patients in the robotic cohort who passed away due to reasons unrelated to their ovarian cancer. We also note a median PFS of 20.4 ± 2.9 months. There were no isolated incidences of port-site metastasis though three patients had port-site implants in the context of abdominal carcinomatosis at the time of recurrence with diffuse peritoneal disease.

Comparison between robotic and laparotomy cases

To control for the time bias and to ensure that the non-inferiority of patients in the robotic era is not due to an outperforming laparotomy group in that time period, the survival analysis was repeated and compared between patients who were debulked robotically and those who were operated on by laparotomy in the pre-robotic era and in the robotic era. In all cases, the robotic group tended to have comparable or superior overall survival (Figure 2A) and progression-free survival (Figure 2B) given that patients were selected prior to being offered robotically-assisted surgical debulking. Cox proportional hazard models were employed to control for the aforementioned covariates and patients who underwent robotic debulking surgery were associated with better OS (HR = 0.6 ± 0.1, $p = 0.03$) and PFS (0.6 ± 0.1, $p = 0.01$).

Sensitivity analysis

The PFS analyses were repeated using a clinical date of recurrence when patients began a second line of treatment (chemotherapy, radiotherapy, or surgery). If patients refused or were incapable

of receiving a second line intervention, the date the treatment was offered was used instead. Similar results were obtained as the primary analysis and there were no significant differences between the pre-robotic and the robotic eras as above.

4.6 Discussion

In the 1990's, it was suggested that for the treatment of ovarian cancer "the incision must be as ruthless as the cancer itself" (Barber, 1993, p. 695) [220].

In contrast to the wide incorporation of minimally invasive surgery in the treatment of cervical and uterine cancers, the standard approach for ovarian cancer remained debulking surgery via laparotomy. Fear of intraoperative spillage and port-site metastases, incomplete debulking, and adequacy of lymphadenectomy were some of the obstacles to the adoption of any minimally invasive surgical technique to this setting [4, 43, 126]. Nevertheless, obstacles are being sequentially overcome as expertise and technology advance.

In 1990, Reich et al. published a single case report on the management of a stage I ovarian cancer by laparoscopy [221]. In 1994, Querleu and Leblanc reported a case series on the first full pelvic and infra-renal paraaortic lymphadenectomy via laparoscopy for restaging and second look procedures [222]. In the following years, reports emerged demonstrating the feasibility of the laparoscopic management of ovarian cancer, but its use has been largely limited to exploratory surgeries for diagnosis as well as the assessment of resectability and second look procedures [37, 126, 223], and in the treatment of select cases of early stage disease [37, 41]. Rare studies have reported on laparoscopic staging in highly selected patients with advanced ovarian cancer [39].

Because neoadjuvant chemotherapy can considerably decrease the tumor burden, we observed that in some patients there remained only low volume and sometimes no disease at the

time of interval cytoreduction by laparotomy. This had led our group to evaluate the possibility of using robotic surgery in these selected cases after neoadjuvant chemotherapy to decrease surgical morbidity.

To date, only a few studies have published on the feasibility of robotic debulking surgery in ovarian cancer [129, 130, 133] as well as secondary debulking surgery for recurrent disease [138, 139]. In 2011, Magrina et al. published a case control study with 25 patients who underwent robotic surgery, 15 of whom had advanced stage ovarian cancer and 6 of whom received neoadjuvant chemotherapy [129]. While they report greater progression-free survival in their robotic and laparoscopy groups compared to laparotomy, this is likely due to a selection process, similarly to our data, wherein patients who underwent a laparotomy were more likely to have advanced stage disease, undergo more extensive debulking procedures, and less likely to be completely debulked [129]. Feuer et al. (2013) compared 63 selected patients (37 with advanced stage, 33 received NACT) who were robotically debulked to 26 patients (19 with advanced stage, 4 received NACT) debulked by laparotomy for ovarian cancer [130]. This study also reported on the decreased blood loss and the shorter hospital stay, with adequate survival at one year [130]. The MISSION trial evaluated the feasibility of minimally invasive interval debulking surgery (n = 26 laparoscopically, n = 4 robotically) in a highly selected cohort of patients who had a clinical complete response (cCR) to NACT for advanced ovarian cancer [136]. While median follow-up was limited (10.5 months), perioperative and psycho-oncological outcomes were promising [136].

Our study evaluated the effect of introducing a cutting-edge surgical tool to improve the feasibility of minimally invasive surgery in selected patients with advanced epithelial ovarian cancers. In order to mitigate the selection bias, we sought to evaluate whether there were any changes in the outcomes of our entire patient population as a result of the availability and selected utilization of robotics. Overall, out of the one hundred and eight patients with ovarian cancer who

were treated robotically, seventy-five had stage III or IV disease with a median follow-up of 43 months. We demonstrate that the robotic approach, whether in the primary cytoreductive or interval debulking setting, allowed for satisfactory rates of complete cytoreduction (72%), albeit in selected patients, with adequate surgical and oncologic outcomes. Indeed, the careful selection of some patients for robotic debulking surgery at our center combined with the use of neoadjuvant chemotherapy, where appropriate, has not compromised the overall or the progression-free survival of our patient population, and has improved some perioperative outcomes.

The rate of conversion to laparotomy was higher in the primary debulking group (two patients or 11.1%) than the interval debulking group (three patients or 5.3%). This trend towards less need for open surgery is likely a reflection of the efficacy of neoadjuvant chemotherapy. Our management of conversion for advanced disease necessitating complex bowel or additional procedures coincides with the suggestion by Magrina et al. (2011) that such patients might be better served by an open approach [129]. Of note is that all conversions were done to safely remove extensive disease and there were no conversions for intraoperative complications. While the primary focus of the current study was on survival and oncologic outcomes, the use of robotics in combination with laparotomy did not have a statistically significant impact on complication rates. A secondary analysis is currently being undertaken to report further on complication rates and costs of robotic surgery in ovarian cancer.

There are several limitations to our study. First, this was a retrospective study which carries some inherent biases, though all data was collected from prospectively maintained electronic medical records and all consecutive patients were included. Second, patients who underwent robotic debulking surgery were a highly selected group of patients undergoing operations by a group of surgeons experienced in robotics (over 1,400 robotic cases performed to date) in a single institution, which may restrict the generalizability of the findings. Patients with extensive disease

who were deemed unlikely to be optimally debulked by robotic surgery underwent a laparotomy, thus there is a clear selection bias that would favor the robotic surgery group. This selection bias was addressed by including all the patients in a pre-post analysis, including those who underwent a laparotomy in the robotic period. As in all such analyses, there is the possibility of confounders such as other changes in the management of pelvic epithelial cancers including changes in chemotherapy regimens, variations in the performance of imaging studies, and developments in perioperative care. For this reason we compared the outcomes of patients who underwent a laparotomy during both periods, and these were similar, consistent with the survival rates for ovarian cancer that have only marginally improved over this period [213]. While the degree of aggressiveness of debulking surgeries continues to be debated in the literature [224], the comparable oncologic outcomes between the pre-robotic and the robotic era might be attributed to a controlled utilization of radical procedures in our laparotomy series as well as the use of neoadjuvant chemotherapy, which permitted us to achieve optimal cytoreductive surgeries. Nonetheless, it appears that, at least when combining the use of robotics in a well-selected group of patients while maintaining the use of laparotomy for patients with larger and less easily resectable tumor burdens, overall survival and progression-free survival are not negatively impacted compared to a historical cohort just prior to the introduction of robotics and treated only by laparotomy.

4.7 Conclusion

Robotic surgery for the management of selected patients with ovarian, tubal, and peritoneal cancers, whether in the primary cytoreductive or interval debulking setting, seems feasible with good surgical outcomes and warrants further investigation as a surgical option. Patients with extensive disease who are unlikely to be optimally debulked by robotic surgery should continue to

be offered cytoreductive surgery by laparotomy. Further follow up is necessary to validate survival outcomes following robotic surgery compared to standard surgical treatment via laparotomy. Future studies should also elucidate the specific population that may benefit most from the incorporation of robotic surgery into their surgical management.

4.8 Funding

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4.9 Conflicts of Interest

Walter Gotlieb and Susie Lau obtained partial travel support for proctoring robotic surgery.

4.10 Acknowledgements

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4.11 Tables

Table 1. Description of population before and after the use of robotic surgery for ovarian cancer

	NACT			PDS		
	Pre-robotic era: laparotomy only (n=22)	*Robotic era:* laparotomy + robotics (n=91)	P value	*Pre-robotic era:* laparotomy only (n=40)	*Robotic era:* laparotomy + robotics (n=45)	P value
Age, mean (SD)	65.4 (9.2)	64.1 (13.5)	0.98	59.5 (11.2)	58.6 (11.6)	0.80
BMI, mean (SD)	27.3 (5.8)	26.7 (6.3)	0.52	24.3 (4.9)	27.8 (6.0)	0.007
ASA			0.41*			0.61*
1	2 (9.1%)	3 (3.3%)		3 (7.5%)	9 (20.0%)	
2	11 (50.0%)	54 (59.3%)		17 (42.5%)	25 (55.6%)	
3	7 (31.8%)	33 (36.3%)		8 (20.0%)	9 (20.0%)	
4	0 (0%)	0 (0%)		0 (0%)	1 (2.2%)	
Unknown	2 (9.1%)	1 (1.1%)		12 (30.0%)	1 (2.2%)	
Stage			1.00			0.78
III	17 (77.3%)	71 (78.0%)		32 (80.0%)	38 (84.4%)	
IV	5 (22.7%)	20 (22.0%)		8 (20.0%)	7 (15.6%)	
Grade			0.005			0.91
1	0 (0%)	1 (1.1%)		2 (5.0%)	3 (6.7%)	
2	4 (18.2%)	1 (1.1%)		5 (12.5%)	4 (8.9%)	
3	18 (81.8%)	89 (97.8%)		33 (82.5%)	38 (84.4%)	
Histology			0.37			0.21
Serous	19 (86.4%)	79 (86.8%)		32 (80.0%)	31 (68.9%)	
Endometrioid	1 (4.6%)	3 (3.3%)		6 (15.0%)	6 (13.3%)	
Clear cell	0 (0%)	5 (5.5%)		0 (0%)	1 (2.2%)	
Carcinosarcoma	0 (0%)	1 (1.1%)		0 (0%)	5 (11.1%)	
Adenosquamous	1 (4.6%)	0 (0%)		1 (2.5%)	1 (2.2%)	
Mucinous	0 (0%)	0 (0%)		1 (2.5%)	1 (2.2%)	
Not defined	1 (4.6%)	3 (3.3%)		0 (0%)	0 (0%)	
Follow-up time (months)			0.56			0.46
Mean (SD)	46.0 (29.5)	38.2 (19.1)		51.1 (37.9)	41.4 (25.2)	
Median (range)	36.2 (9.0–104.3)	37.0 (5.6–91.4)		39.9 (0.7–122.7)	40.7 (0.2–90.4)	

Data is presented as n (%) unless stated otherwise

NACT: Neoadjuvant chemotherapy group

PDS: Primary debulking surgery group

BMI: Body Mass Index (m/kg^2)

ASA: American Society of Anesthesiologists physical status classification system

*Statistical significance excludes unreported/missing data

Table 2. Surgical outcomes before and after the use of robotic surgery for ovarian cancer

	NACT			PDS		
	Pre-robotic era: laparotomy only (n=22)	*Robotic era:* laparotomy + robotics (n=91)	P value	*Pre-robotic era:* laparotomy only (n=40)	*Robotic era:* laparotomy + robotics (n=45)	P value
Cytoreduction			0.005			0.005
Complete cytoreduction, n (%)	9 (40.9%)	69 (75.8%)		7 (17.5%)	23 (51.1%)	
≤1cm residual disease, n (%)	11 (50.0%)	18 (19.8%)		20 (50.0%)	13 (28.9%)	
>1cm residual disease, n (%)	2 (9.1%)	4 (4.4%)		13 (32.5%)	9 (20.0%)	
Estimated blood loss (mL), mean (SD)	505 (599)	271 (307)	0.001	508 (390)	530 (596)	0.34
Hgb differential*, mean (SD)	-15.1 (13.0)	-11.9 (15.5)	0.49	-24.9 (17.8)	-17.0 (19.4)	0.12
Blood transfusion†, n (%)						
Intraoperative blood transfusion	5 (25.0%)	17 (18.7%)	0.54	10 (34.5%)	12 (26.7%)	0.60
Intra-op transfusion with pre-op Hgb≥100‡	4 (20.0%)	5 (5.5%)	0.054	10 (34.5%)	9 (20.0%)	0.18
Postoperative blood transfusion	12 (60.0%)	35 (38.5%)	0.087	15 (51.7%)	19 (42.2%)	0.48
Post-op transfusion with pre-op Hgb≥100‡	8 (40.0%)	21 (23.1%)	0.16	14 (48.3%)	17 (37.8%)	0.47
Length of stay (days)			0.0001			0.034
Mean (SD)	8.6 (6.3)	4.6 (5.7)		12.3 (13.8)	7.4 (6.5)	
Median (range)	6 (4–27)	2 (1–35)		7 (3–69)	7 (1–35)	

NACT: Neoadjuvant chemotherapy group

PDS: Primary debulking surgery group

*Postoperative minus preoperative hemoglobin (Hgb)

†Transfusion of blood products documented in 49 out of 62 subjects in the pre-robotic era (20 NACT, 29 PDS). Data represents number of patients transfused with blood products including packed red blood cells, fresh frozen plasma, platelets, and/or albumin.

‡Transfusion of blood products among patients with a preoperative hemoglobin (Hgb) of 100g/L or more in order to control for low Hgb due to reasons other than surgery (e.g., NACT).

Table 3. Description of robotic surgery population

	Robotic surgery cohort (n=75)
Age, mean (SD)	62.6 (13.8)
BMI, mean (SD)	27.1 (6.0)
ASA	
1	5 (6.7%)
2	50 (66.7%)
3	19 (25.3%)
4	0 (0%)
Unknown	1 (1.3%)
Stage	
III	57 (76.0%)
IV	18 (24.0%)
Grade	
1	2 (2.7%)
2	1 (1.3%)
3	72 (96.0%)
Histology	
Serous	66 (88.0%)
Endometrioid	3 (4.0%)
Clear cell	3 (4.0%)
Carcinosarcoma	0 (0%)
Adenosquamous	1 (1.3%)
Mucinous	0 (0%)
Not defined	2 (2.7%)
Follow-up time (months)	
Mean (SD)	42.8 (20.5)
Median (range)	42.5 (0.2–85.5)

Data is presented as n (%) unless stated otherwise

BMI: Body Mass Index (m/kg^2)

ASA: American Society of Anesthesiologists physical status classification system

Table 4. Surgical outcomes following robotic surgery

	Robotic surgery cohort (n=75)
Cytoreduction	
Complete cytoreduction, n	54 (72.0%)
≤1cm residual disease, n	18 (24.0%)
>1cm residual disease, n	3 (4.0%)
Estimated blood loss (mL), mean(SD)	145 (194)
Hgb differential*, mean (SD)	-13.9 (13.0)
Blood transfusion†, n (%)	
Intraoperative blood transfusion	3 (4.0%)
Intra-op transfusion with pre-op Hgb≥100‡	2 (2.7%)
Postoperative blood transfusion	15 (20.0%)
Post-op transfusion with pre-op Hgb≥100‡	8 (10.7%)
Length of stay (days)	
Mean (SD)	2.3 (2.6)
Median (range)	1 (1–17)

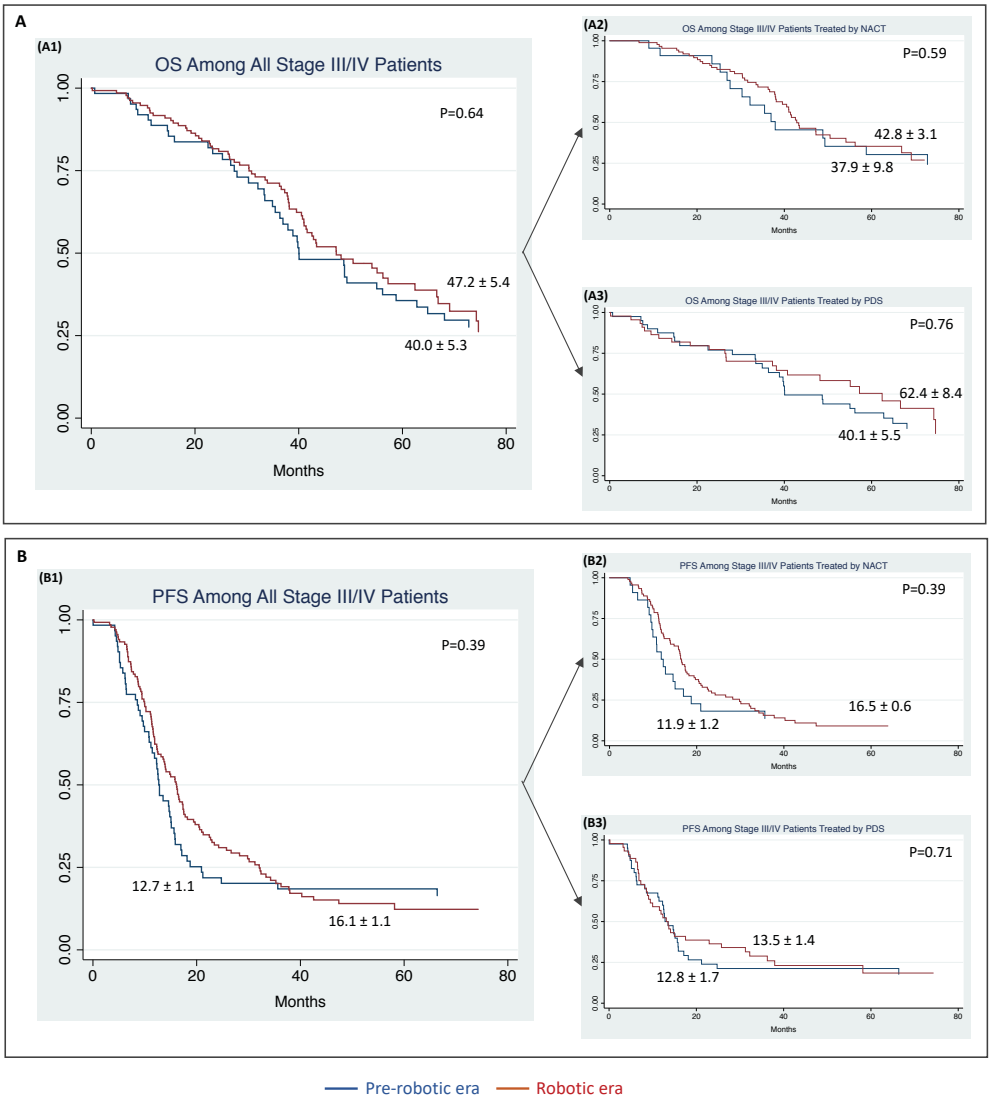
*Postoperative minus preoperative hemoglobin (Hgb)

†Data represents number of patients transfused with blood products including packed red blood cells, fresh frozen plasma, platelets, and/or albumin.

‡Transfusion of blood products among patients with a preoperative hemoglobin (Hgb) of 100g/L or more in order to control for low Hgb due to reasons other than surgery (e.g., NACT).

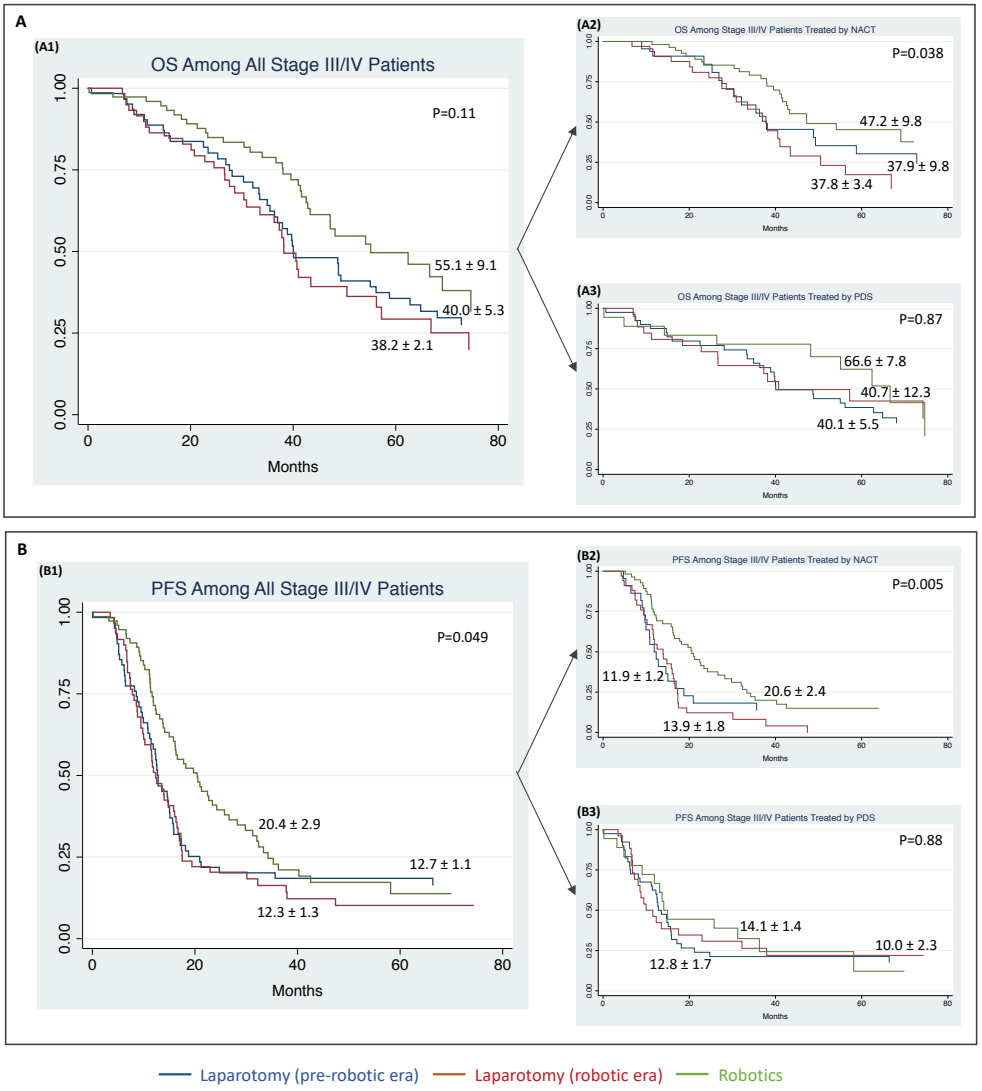
4.12 Figures

Figure 1. Overall survival and progression-free survival before and after the use of robotic surgery for ovarian cancer



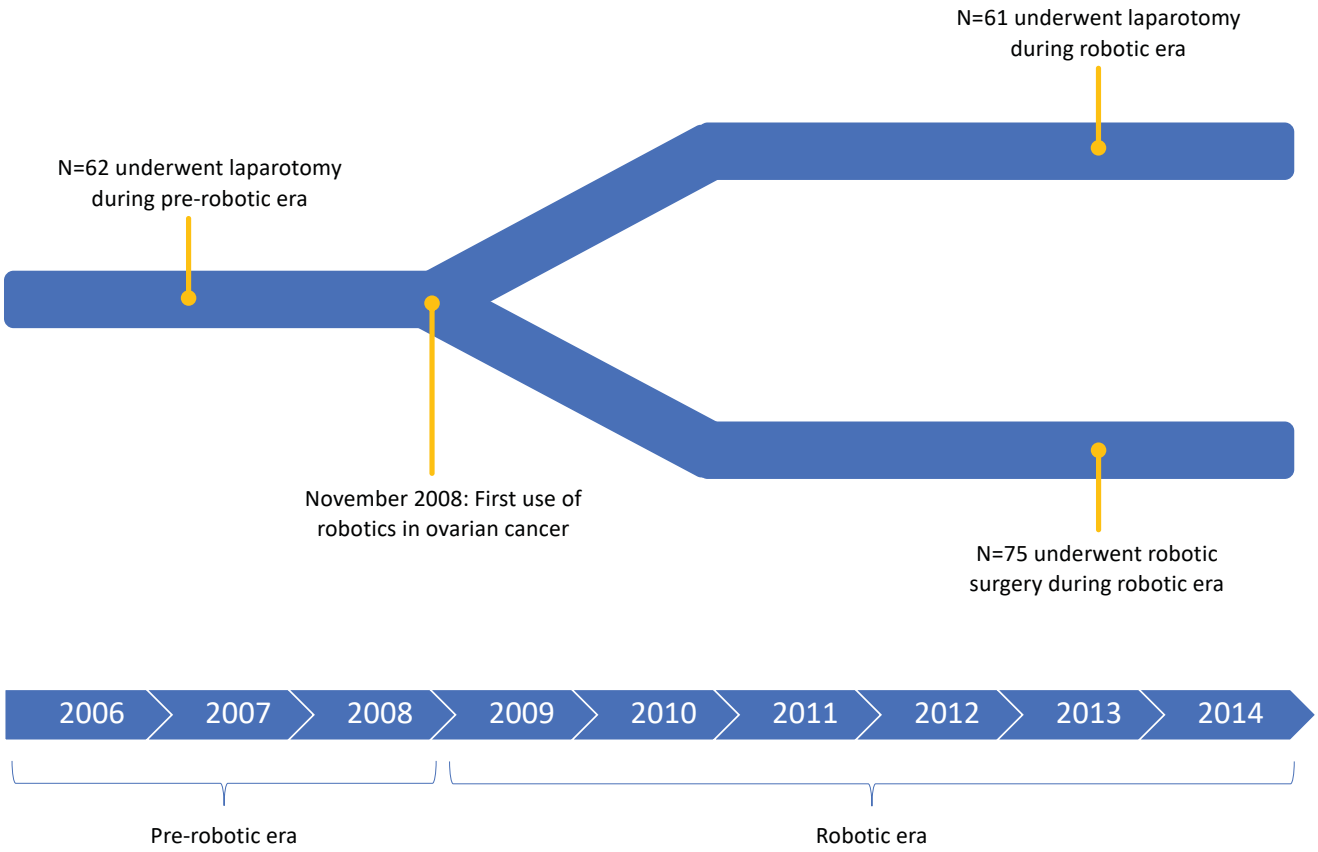
Overall survival (OS, Figure 1A) and progression-free survival (PFS, Figure 1B) were compared between patients in the pre-robotic era (laparotomy only) and the robotic era (combination of laparotomy and robotics in selected cases). Survival outcomes were analyzed among all patients (A1: OS, B1: PFS), patients treated by NACT (A2: OS, B2: PFS), patients treated by PDS (A3: OS, B3: PFS).

Figure 2. Overall survival and progression-free survival before and after the use of robotic surgery for ovarian cancer, by surgical approach



Overall survival (OS, Figure 2A) and progression-free survival (PFS, Figure 2B) were compared between patients who underwent laparotomy during the pre-robotic era, laparotomy during the robotic era, and robotic surgery during the robotic era. Survival outcomes were analyzed among all patients (A1: OS, B1: PFS), patients treated by NACT (A2: OS, B2: PFS), patients treated by PDS (A3: OS, B3: PFS).

S1. Timeline chart illustrating surgical approach for stage III–IV ovarian cancer over time



PART II. HOSPITAL OUTCOMES

CHAPTER 5 – IMPACT OF ROBOTIC SURGERY ON PATIENT FLOW AND RESOURCE USE INTENSITY IN OVARIAN CANCER

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5.1 Preface

The previous chapter evaluated the perioperative as well as oncologic and survival outcomes following robotic surgery in ovarian cancer. The following chapter uses the same cohort to evaluate the cost impact of robotics in ovarian cancer from the hospital's perspective. To date, this is the first study to examine this.

5.2 Abstract

Objective

To evaluate the impact of integrating minimally invasive robotic surgery on patient flow, resource utilization, and hospital costs associated with the treatment of ovarian cancer during the in-hospital and post-discharge processes.

Methods

261 patients operated for the primary treatment of ovarian cancer between January 2006 and November 2014 at a Canadian university-affiliated tertiary hospital were included in this study. Outcomes were compared by surgical approach (robotic versus open surgery) as well as pre- and post-implementation of the robotics platform for use in ovarian cancer. The in-hospital patient flow and number of emergency room visits within 3 months of surgery were evaluated using multi-state Markov models and generalized linear regression models, respectively.

Results

Robotic surgery cases were associated with lower rates of postoperative complications, resulted in a more expedited postoperative patient flow (e.g., shorter time in the recovery room, ICU, and inpatient ward), and were between $7,421 and $10,376 less expensive than the average laparotomy depending on the depreciation and amortization assumptions of the robotic platform. Post-discharge, patients who underwent robotic surgery were less likely to return to the ER (IRR: 0.42, $p = 0.02$, and IRR: 0.47, $p = 0.055$, in the univariate and multivariable models, respectively).

Conclusions

With appropriate use of the technology, the addition of robotics to the medical armamentarium for the management of ovarian cancer may lead to reduced hospital costs and may be a powerful cost-saving option.

5.3 Introduction

Ovarian cancer is the eighth most common malignancy among women with over 25,000 cases estimated to have been diagnosed in 2017 in the United States and Canada [1, 225]. Over 75% of patients present with the disease at an advanced stage [208, 225], rendering it the gynecologic cancer with the highest mortality rate [1, 225]. Little has changed in the modus operandi for ovarian cancers, where aggressive debulking surgery via a large abdominal incision (laparotomy) remains the primary treatment in most instances [4]. This has significant implications for patients, as debulking surgeries take a heavy toll on patients' quality of life [215], as well as hospitals and providers as this treatment phase is resource intensive [226-230].

Using data from the SEER-Medicare database, both initial treatment costs [230] as well as "patient time costs" (Yabroff, 2007) [231] have been found to be substantial in ovarian cancer. In a study using a database on patients covered by employer-sponsored commercial insurance, median total expenditures for ovarian cancer treatment including out-of-pocket costs were over $30 thousand (2013 USD) per patient within the first thirty days of surgery alone [229].

In other indications, the use of robotic surgery has been a promising means of diminishing the invasiveness of laparotomy, improving clinical outcomes [90, 91, 96, 232, 233], and shortening individuals' return to daily activities [96, 233]. The impact of robotics on hospital costs is still rather conflicting [90, 96, 105, 143, 148, 233].

The uptake of robotics has been slower in ovarian cancer though studies are demonstrating its clinical effectiveness [234]. Our previous study demonstrated that robotically-assisted debulking surgery is feasible in selected patients who are likely to have little to no residual disease at the end of surgery (*manuscript in submission, 2018*). The current study evaluates whether a robotics program for patients with ovarian cancer is associated with distinct patient trajectories,

both within the in-hospital process and after discharge, and whether a robotics program reduces hospital resource use, as gauged by average costs.

5.4 Methods

Between January 2006 and November 2008, 74 consecutive patients were treated for epithelial ovarian cancer (including cancer of the ovary, fallopian tube, and peritoneum) by the traditional midline laparotomy incision. Within this historical cohort, seventeen patients had incomplete electronic medical charts (i.e., missing postoperative nursing notes) and were therefore excluded from the current analysis, resulting in 57 patients in the historical cohort with data on complications and resource use available.

Since November 2008, one year after the start of the robotics program in our department, patients with ovarian cancer were offered a robotic approach to debulking surgery if the surgeons judged that the patient could be debulked satisfactorily based on imaging, clinical exam, and ca-125 markers. The robotic procedure was performed by means of the *da Vinci® Surgical System* using the previously described surgical set up (*manuscript in submission, 2018*). Between November 2008 and November 2014, 108 patients underwent robotic surgery and 79 underwent a midline laparotomy for an ovarian cancer.

Patient characteristics, clinical outcomes, and both intraoperative and postoperative complications up to six weeks postoperatively were gathered from the patient's electronic medical record. Postoperative resource use was captured in the perioperative period until discharge as well as until 3 months after surgery.

For all patients in the study, their trajectory in the hospital was recorded until 3 months after surgery and included operating room time (estimated from the time the patient started

anesthesia to when they left the operating room), procedure time (skin incision to skin closure), time in the post-anesthesia care unit (PACU), time on the inpatient ward, time in the intensive care unit (ICU), and time in any subsequent operations, emergency room (ER) visits, and readmissions to the hospital. Outpatient hospital visits, aside the ER, as well as outpatient same-day treatments (e.g., for intravenous chemotherapy treatment, clinic visits, etc.) were ignored. ER visits and rehospitalizations due to reasons unrelated to the surgery were excluded. The following resources used postoperatively until discharge were recorded: imaging (e.g., X-rays, CT scans, interventional radiology, etc.), major interventions on the ward (e.g., total parenteral nutrition, fluid drainage, blood transfusions, etc.), and consultations to other medical services. Imaging was also recorded between discharge and four weeks postoperatively in order to capture scans that were most relevant to the surgery.

This study was approved by the hospital's Institutional Review Board.

Statistical analyses

Two sets of comparisons were done throughout the analysis:

(1) to evaluate differences between robotic cases and laparotomies, the robotic cohort was compared to all patients who had a laparotomy;

(2) to control for the biased selection of patients in the robotic group, a pre-post analysis was conducted to compare all patients operated in the *robotic era* (i.e., the combination of selective laparotomy and robotic surgery since the first use of robotics for ovarian cancer in November 2008) to the historical cohort of patients who were only offered debulking via laparotomy prior to November 2008 (described as the *pre-robotic era*).

General statistical tests were performed using the Fisher's exact test and the Mann-Whitney-Wilcoxon rank sum test for categorical and continuous variables, respectively. Descriptive statistics were run using Stata (version 13.0). A statistical significance of $p < 0.05$ was used throughout the analysis.

Multi-state Markov models [235-237] were used to study our proposed patient flow during the in-hospital stay following the surgery. A typical multi-state process consists of a finite number of states, either transient states or absorbing states, in which transitions are allowed from transient states but not from absorbing states. Our proposed multi-state model is described in Supplementary Figure S1. Every subject in the current analysis was recorded from the starting point of the surgery to the recovery room (post-anesthesia care unit, PACU), the general ward, the intensive care unit (ICU), any secondary surgery or reoperation in the perioperative period, and discharge home (only absorbing state). In summary, this model had five transient states, one absorbing state, and ten possible transitions (see S1). Predicted transition intensities (probabilities) of the absorbing state were computed at 1, 2, 3, 7, 14, 21, 28, and 35 days from surgery. Hazard ratios with their 95% confidence limits for transitions were estimated for several selected covariates. Analysis of multi-state models was performed in R (version 3.2.1) using package *msm*.

Following discharge, the number of ER visits within a 3-month period was defined as the primary outcome variable. The effects of different independent variables (age, body mass index (BMI), use of neoadjuvant chemotherapy (NACT) before surgery, and disease stage) were tested using a generalized linear model (GLM) with a negative binomial distribution to take into account the skewed nature of the data [238]. An offset variable was included in the model to only account for the time at risk (i.e., when the patient was not hospitalized). A multivariable model was also developed to control for the covariates above. Incidence Rate Ratios (IRR) and 95% confidence

intervals were computed for all independent variables. These analyses were conducted with SAS (version 9.4).

Cost analysis

The cost analysis was designed from the institutional perspective. Unit costs were attributed to the above-mentioned resources. Average direct and indirect (overhead) costs of scans, interventional radiology, and room and board costs for the different nursing units were obtained from MedGPS (Logibec Inc, Montreal, Canada), a hospital-based data warehouse that calculates the costs of resources used in the hospital at the patient level. The software was also used to estimate the average daily costs of pharmacy (e.g., medication use), laboratory (e.g., blood work and microbiology), allied health services (e.g., social work, nutrition, and physiotherapy), and other costs among surgical admissions under the gynecologic oncology service. Blood transfusion costs were obtained from the hospital's transfusion service. Total hourly operating room salary costs were estimated using data from the hospital's financial report. An average cost for materials used in the operating room was calculated for laparotomies and robotic surgeries based on an electronic intraoperative data collection system implemented in January 2013 to record, among other things, the use of resources (e.g., sutures, clips, thrombotic materials, disposable bags, and other disposable instruments). The costs of these surgical supplies were retrieved from the hospital's operating room management solution software. While physician billing fees are not paid out of hospital budgets in the current setting, they were included in the analysis in order to incorporate physician time as a hospital resource and their remuneration fees were obtained from the regional health insurance board (*Régie de l'assurance maladie du Québec*). An hourly emergency department rate was applied using the average ER cost in the hospital using data from the MedGPS software. Capital costs of imaging scanners and of the robot were depreciated using straight line

depreciation over their useful life and over the average number of procedures performed per year across the hospital. Robotic instruments were assumed to have ten lives as advertised [239] and annual service costs were amortized across the yearly average number of robotic surgeries.

All costs are expressed in real terms and were adjusted for inflation to 2017 Canadian dollars using the Bank of Canada Inflation Calculator [240]. Discounting was ignored as subjects were only followed for three months.

Three scenarios were utilized for the robotic system costs:

(1) a *donated scenario*, where the capital and service costs of the robot are assumed to be off-budget and covered by charitable funds, as is the case at our center,

(2) an *actual usage scenario*, where fixed robot costs including upfront capital costs and annual maintenance costs were depreciated and amortized, respectively, over the actual number of robotic surgeries performed and forecasted to be performed across the hospital for the remaining useful lives of the robots, and

(3) an *optimal usage scenario*, where a plausible two surgeries per robot per day per five-day workweek, for two robots used across the hospital, is employed.

5.5 Results

Patient population and complications

Characteristics of the patient population are described in Table 1. There were fifty-seven patients in the pre-robotic era (before the start of robotics for ovarian cancer), all of whom had a laparotomy. Of these, over a third (35.1%) received neoadjuvant chemotherapy (NACT) prior to their surgery. In the robotic era, seventy-nine patients were operated by laparotomy, 43% of whom

had received NACT, and one hundred and eight patients were selected to undergo robotic surgery (57% NACT). Statistical significance was tested between those who underwent a laparotomy and robotic surgery as well as between the pre-robotic and robotic time periods. In either case, there were no significant differences in age, body mass index (BMI), American Society of Anesthesiologists' physical status classification score (ASA), stage, or grade. Compared to the robotic group, patients in the laparotomy group had higher rates of omentectomy (94% vs. 99% in the robotics and laparotomy groups, respectively, $p = 0.02$), appendectomy (5% vs. 21%, $p < 0.001$), and digestive surgeries including bowel resection, low anterior resection, hepatectomy, pancreatectomy and/or splenectomy (3% vs. 18%, $p < 0.001$).

Complication rates are described in Supplementary Material S2. Intraoperatively, patients selected to undergo robotic surgery were associated with lower rates of blood transfusions (4% vs. 34%, $p < 0.001$) and higher rates of minor mucosal vaginal tears (5% vs. 0%, $p < 0.001$) mainly at the level of the introitus due to tearing of the vagina during removal of the endobags containing the surgical specimens. Postoperatively until six weeks post-surgery, patients in the robotic group were less likely to develop ileus (1% vs. 11%, $p = 0.001$), require blood transfusions (15% vs. 50%, $p < 0.001$), and develop urinary tract infections (6% vs. 14%, $p = 0.035$). There were two postoperative deaths in this series: one 88-year-old patient in the robotic group died on postoperative day five from septic peritonitis due to an occult intraoperative bowel perforation and one patient in the laparotomy group experienced failure to thrive with severe respiratory distress, massive anasarca, and shock. There were four re-operations in the robotic group: two were laparotomies done within the same admission to control postoperative bleeding and to repair a bowel injury, one was performed robotically to repair a vesicovaginal fistula, and one had an infected peritoneal port-a-cath removed. In the laparotomy group, one patient was re-operated for small bowel obstruction.

As previously described (*manuscript in submission, 2018*), seven patients in the robotic cohort were converted to laparotomy in order to ensure the safe removal of extensive disease; none were converted for intraoperative complications and all bowel serosal, bladder, and vascular injuries were repaired robotically.

Patient trajectories

On average, patients who underwent robotic surgery spent more time in the operating room (mean of 369 vs. 304 minutes, $p < 0.0001$) but were transferred through the PACU more rapidly (268 vs. 458 minutes, $p < 0.0001$), were less likely to visit the ICU (0.9% vs. 7%, $p = 0.03$), and spent less time on the inpatient ward (45 hours vs. 206 hours, $p < 0.0001$). There was no significant difference in the proportion of patients who were re-operated within the same admission (1.9% vs. 0.7%, $p = 0.6$). Statistical significance persisted in the pre-post analysis except for ICU admissions.

Figure 1 shows the probabilities of being discharged from the hospital using the multi-state model. Patients who underwent robotic surgery were significantly more likely to be discharged home in a shorter time frame than those who had a laparotomy (Figure 1A). Following a laparotomy, patients with advanced stage disease were significantly more likely to remain longer in the hospital than those with early stage disease (in terms of crude proportions, 23% of patients with stage I–II disease were still in the hospital one week postoperatively versus 43% with stage III–IV disease); following robotic surgery, cancer stage was not as important a predictor of length of stay (within two days postoperatively, 88% and 81% of patients with stage I–II and stage III–IV cancer, respectively, had been discharged) and around 95% had returned home within the first week, irrespective of disease severity (see Figure 1B for results from the multi-state model). These

findings were also reflected in the analysis comparing the pre-robotic and robotic eras (Figures 1C and 1D).

Post-discharge, the association between the use of robotics and the number of ER visits was evaluated and shown in Table 2. In the univariate model, patients who underwent robotic surgery were significantly less likely to return to the ER (IRR: 0.42, $p = 0.02$). After controlling for age, BMI, stage, and the use of NACT, the impact of robotics on ER visits was still apparent (IRR: 0.47, $p = 0.055$). Stage was not a significant predictor of ER visits in either the univariate or multivariable analyses. The regressions were repeated for the pre-post analysis and the use of NACT was found to be the only factor significantly associated with ER visits (IRR: 0.44, $p = 0.039$ in the multivariable model), as shown in Supplementary Material S3.

Resource use intensity and cost outcomes

Hospitalization costs from surgery until three months postoperatively are described in Table 3. While intraoperative costs were higher among robotic surgeries ($p < 0.0001$), they were offset by significantly lower postoperative costs, primarily on the inpatient ward ($p < 0.0001$). The primary driver of the lower ward costs among robotic cases was the reduced length of stay (median of 1 day [range: 1 to 17] vs. 7 days [3 to 63] among all robotic and open surgeries, respectively, $p < 0.0001$). In addition, though less substantial individually, costs pertaining to imaging (mean \$59 vs. \$180, $p = 0.0001$), blood transfusions (\$201 vs. \$806, $p < 0.0001$), and consultations to other services (\$26 vs. \$84, $p < 0.001$) were lower among robotic cases.

Figure 2 illustrates the total hospitalization costs from surgery until discharge for the three scenarios described in the Methods section. The average robotic surgery cost was significantly lower than the average laparotomy by \$10,376 if the capital costs of the robots and their annual

maintenance are excluded and by $7,421 if they are included. Across all three scenarios, the combination of selective robotics and standard laparotomy in ovarian cancer resulted in cost savings compared to the pre-robotic era: $4,319 and $3,743 when the robots' capital expenditures are excluded and included, respectively. The optimal usage scenarios suggest that even greater savings can be realized with increasing use of the robotic systems across the hospital.

5.6 Discussion

The first laparoscopic cholecystectomy was performed September 12, 1985 by Dr. Erich Mühe, the first major revolution of the procedure in 103 years [241, 242], yet this pioneering work was met with immense resistance and "derogatory remarks such as 'Mickey Mouse surgery' and 'small brain—small incision'" (Litynski, 1998, p. 343) [242]. Since then, minimally invasive cholecystectomy has become the gold standard [44].

The use of conventional laparoscopy for the surgical treatment of ovarian cancer has been largely limited as the ability to properly explore the abdominopelvic cavity remains in question [4] and only a handful of studies have reported on the feasibility of laparoscopic debulking surgery [39, 243]. In a 2003 survey of members of the Society of Gynecologic Oncologists (SGO) and fellows-in-training, only a single respondent thought that conventional laparoscopy would be appropriate for the debulking of a known ovarian cancer; rather, most respondents reported using laparoscopy for its initial management and/or for second-look procedures [244]. Following the diffusion of the robotic platform to facilitate the performance of MIS, an updated survey of the SGO in 2012 indicates an interest in robotically-assisted debulking surgery among some early adopters [128].

Using the same patient population as the current study, we have previously shown that the

selective use of robotic surgery in combination with standard laparotomy for patients with more extensive disease (the robotic era) did not adversely affect overall or progression-free survival and resulted in improved perioperative outcomes (*manuscript in submission, 2018*). While a small number of other groups have also reported on the feasibility of robotics for selected ovarian cancer cases [134], to our knowledge, this is the first study to evaluate the impact of robotic surgery on resource use and hospital costs in ovarian cancer. To date, most cost-effectiveness studies evaluating treatment costs in ovarian cancer have focused on clinical trials comparing different chemotherapy regimens [245, 246] or on the use of NACT [247].

The current analysis suggests that the selective use of robotic surgery for the treatment of ovarian cancer can be a cost-saving intervention. The major source of savings emanating from the robotics program was undoubtedly the reduced length of stay, which can be prolonged following aggressive debulking surgeries by laparotomy. This finding has similarly been reported by others in the context of endometrial cancer [90, 96]. The impact of robotics in shortening length of stay has been shown to support the high demand of hospital beds by freeing them up sooner [90, 248]. This has become especially important given reports of hospital bed shortages [249, 250]. Indeed, most OECD countries have seen a reduction in the number of hospital beds per capita over the last decade [251]. This has been attributed to both technological advancements, which have permitted, for example, many surgeries to be done in an outpatient setting, as well as to budgetary constraints and economic pressures to contain healthcare costs [251]. Prolonged hospital bed occupancy can be an important bottleneck that impairs patient flow [249, 252, 253], the costs of which can be exacerbated by growing healthcare workforce spending [254], highlighting the need for solutions that could safely improve hospital throughput from a logistics standpoint.

While length of stay is an indicator of operational efficiency, hospital readmission rates are sometimes regarded as a marker for quality of care [255-257]. Several studies have investigated

whether early or premature discharges might be associated with increased readmission risk [255-257]. Despite shortening the required hospital stay in the perioperative period, the implementation of the robotics program did not adversely affect the number of ER visits or readmissions to the hospital. Although this could have been affected by the sample size in the current study, Clark et al. (2013) also found that decreasing surgical radicality in ovarian cancer did not affect thirty-day readmission rates despite being associated with a shorter length of stay [258].

While patients in the robotic cohort spent more time in the operating room, they spent significantly less time in the recovery room and on the ward. Further, while patient flows were lengthened in patients with advanced stages compared to early stages among those operated via the open technique, the use of robotics *neutralized* this effect in large part. With markedly different patient trajectories following robotic surgery, this has implications from a hospital operations management standpoint. While additional allocation of resources may be required in the operating room, the postoperative in-hospital process can allow for considerable performance improvements without increasing returns to the ER or readmissions to the hospital.

There are several limitations to the current analysis. First and foremost, many of the costs in this retrospective study are estimates based on average costs calculated for hospital-based activities for patients treated by our division or across the hospital. Given that the machines were donated to our hospital, the costs of the robots did not include the opportunity costs of owning them. Additionally, the training of personnel for the use of the robot was ignored. On the other hand, indirect economic benefits such as decreased productivity losses, the impact on families and caregivers, improved leisure time, and other societal costs were not considered. However, because most of the patients in the current analysis were given adjuvant chemotherapy, that would likely be the driving factor of many of such losses. Finally, the findings of the current study pertain to a single tertiary center in a Canadian setting with multi-departmental use of robotics. As more

specialties share the robotic system and the surgical caseload is increased, the unit cost of the capital outlay diminishes. The economies of scale are apparent given the higher cost savings projected in the optimal usage scenario.

5.7 Conclusion

A surgical oncology program that combines laparotomy and robotic surgery for the treatment of ovarian cancer can potentially attain substantial cost-effective dominance. The impact on patient trajectories has important implications form a hospital operations management standpoint.

5.8 Funding

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5.9 Conflicts of Interest

Walter Gotlieb and Susie Lau obtained partial travel support for proctoring robotic surgery.

5.10 Acknowledgments

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5.11 Tables

Table 1. Description of population before and after the use of robotic surgery for ovarian cancer

	Laparotomy during pre-robotic era (n=57)	Laparotomy during robotic era (n=79)	Robotic surgery during robotic era (n=108)	P value*	
Age, mean (SD)	61.0 (10.2)	61.8 (12.2)	61.3 (13.7)	0.81	0.42
BMI, mean (SD)	26.2 (5.8)	26.7 (6.7)	27.4 (6.7)	0.32	0.42
ASA				0.50	0.63
1	10 (17.5%)	10 (12.7%)	11 (10.2%)		
2	28 (49.1%)	41 (51.9%)	66 (61.1%)		
3	17 (29.8%)	25 (31.7%)	28 (25.9%)		
4	0 (0%)	1 (1.3%)	0 (0%)		
Unknown	2 (3.5%)	2 (2.5%)	3 (2.8%)		
Stage				0.13	0.24
I	6 (10.5%)	12 (15.2%)	21 (19.4%)		
II	2 (3.5%)	6 (7.6%)	12 (11.1%)		
III	39 (68.4%)	52 (65.8%)	57 (52.8%)		
IV	10 (17.5%)	9 (11.4%)	18 (16.7%)		
Grade				0.52	0.24
1	6 (10.5%)	6 (7.6%)	8 (7.4%)		
2	6 (10.5%)	5 (6.3%)	5 (4.6%)		
3	45 (79.0%)	68 (86.1%)	95 (88.0%)		
Histology				0.046	0.066
Endometrioid	7 (12.3%)	13 (16.5%)	11 (10.2%)		
Serous	41 (71.9%)	51 (64.6%)	85 (78.7%)		
Clear cell	2 (3.5%)	6 (7.6%)	8 (7.4%)		
Carcinosarcoma	0 (0%)	6 (7.6%)	0 (0%)		
Adenosquamous	3 (5.3%)	0 (0%)	1 (0.93%)		
Mucinous	3 (5.3%)	2 (2.5%)	0 (0%)		
Not defined	1 (1.8%)	1 (1.3%)	3 (2.8%)		
Surgical procedures done					
Hysterectomy	53 (93.0%)	65 (82.3%)	101 (93.5%)	0.093	0.46
Salpingo-oophorectomy†	57 (100%)	78 (98.7%)	107 (99.1%)	1.00	1.00
Lymphadenectomy‡	48 (84.2%)	56 (70.9%)	99 (91.7%)	0.002	1.00
Omentectomy	57 (100%)	78 (98.7%)	101 (93.5%)	0.023	0.20
Lysis of adhesions	27 (47.4%)	25 (31.7%)	50 (46.3%)	0.24	0.36
Appendectomy	15 (26.3%)	14 (17.7%)	5 (4.6%)	<0.001	0.004
Cholecystectomy	2 (3.5%)	1 (1.3%)	0 (0%)	0.26	0.14
Hernioplasty	0 (0%)	3 (3.8%)	3 (2.8%)	1.00	0.34
Digestive surgery§	10 (17.5%)	15 (19.0%)	3 (2.8%)	<0.001	0.15
Neoadjuvant chemotherapy	20 (35.1%)	34 (43.0%)	61 (56.5%)	0.010	0.048

Data is presented as n (%) unless stated otherwise

BMI: Body Mass Index (in m/kg^2)

ASA: American Society of Anesthesiologists physical status classification system

*First P value between robotic cases (n=108) and all laparotomy cases (n=136); second P value between pre-robotic era (n=57) and entire robotic era (n=187)

†Removal of one or both ovaries and/or fallopian tube(s)

‡Pelvic and/or para-aortic lymphadenectomy

§Includes any bowel or rectal resection, gastrointestinal surgery, or related surgery (e.g., splenectomy, pancreatectomy, hepatectomy)

Table 2. Negative binomial regression models for number of ER visits within 3 months of surgery

			Univariate models (5 models)		Multivariable model (1 model)	
	n	mean (SD)	IRR	P-value	IRR	P-value
	243					
Age						
<65	146	0.20 (0.6)	1.00		1.00	
65+	97	0.11 (0.3)	0.58	0.175	0.59	0.189
BMI						
<30	164	0.13 (0.4)	1.00		1.00	
30+	60	0.18 (0.5)	1.34	0.504	1.40	0.452
missing	19	0.37 (1.0)	2.64	0.138	2.53	0.117
NACT						
No	128	0.21 (0.6)	1.00		1.00	
Yes	115	0.11 (0.3)	0.53	0.095	0.58	0.186
Type of surgery						
Laparotomy	136	0.22 (0.6)	1.00		1.00	
Robotic	107	0.09 (0.3)	0.42	0.024	0.47	0.055
Stage						
I—II	59	0.15 (0.6)	1.00		1.00	
III—IV	184	0.17 (0.5)	1.14	0.811	1.45	0.406
Interaction test						
Robotic & Stage				0.425		
Robotic & Age				0.351		
Robotic & NACT				0.683		

Univariate and multivariable regression models for the number of emergency room visits within 3 months of the initial surgery date as the count outcome.

Potential interaction between the use of robotics and the cancer stage was tested at alpha 0.1 by adding the interaction term in the multivariable model.

IRR: Incidence Rate Ratio; adjusted for the time at risk (i.e., if the patient was admitted, they are not at risk of returning to the emergency department)

BMI: Body Mass Index (in kg/m^2)

NACT: Neoadjuvant chemotherapy

Table 3. Hospitalization costs before and after the use of robotic surgery for ovarian cancer

	Laparotomy during pre-robotic era (n=57)	Laparotomy during robotic era (n=79)	Robotic surgery during robotic era (n=108)	P value*	
Total intraoperative costs[†]	5,987 (2,319)	6,439 (2,526)	9,454 (1,681)	<0.0001	<0.0001
Total PACU costs	750 (913)	744 (974)	437 (451)	<0.0001	0.0038
Total ICU costs	263 (1212)	500 (1875)	13 (131)	0.016	0.32
Total inpatient ward costs	16,701 (16,198)	15,492 (11,153)	3,768 (4,564)	<0.0001	<0.0001
Total reoperation costs	44 (330)	0 (0)	41 (304)	0.43	0.68
Total costs until discharge	**23,745 (18,140)**	**23,175 (13,697)**	**13,712 (5,993)**	<0.0001	0.0001
Total ER costs	114 (410)	312 (898)	128 (485)	0.20	0.36
Total readmission costs	68 (516)	2,596 (9,920)	940 (5,506)	0.72	0.11
Total secondary surgery costs	0 (0)	39 (346)	23 (263)	0.22	0.27
Total imaging costs (<4 weeks)[‡]	44 (150)	57 (173)	52 (160)	0.60	0.64
Total costs from initial discharge to 3 months postop	**226 (907)**	**3,004 (10,586)**	**1,166 (5,848)**	0.84	0.22
Total costs from primary surgery to 3 months postop	**23,971 (18,168)**	**26,180 (19,172)**	**14,878 (8,265)**	<0.0001	0.0012

Data is presented as mean (SD), in Canadian dollars

PACU: Post Anesthesia Care Unit

ICU: Intensive Care Unit

ER: Emergency Room

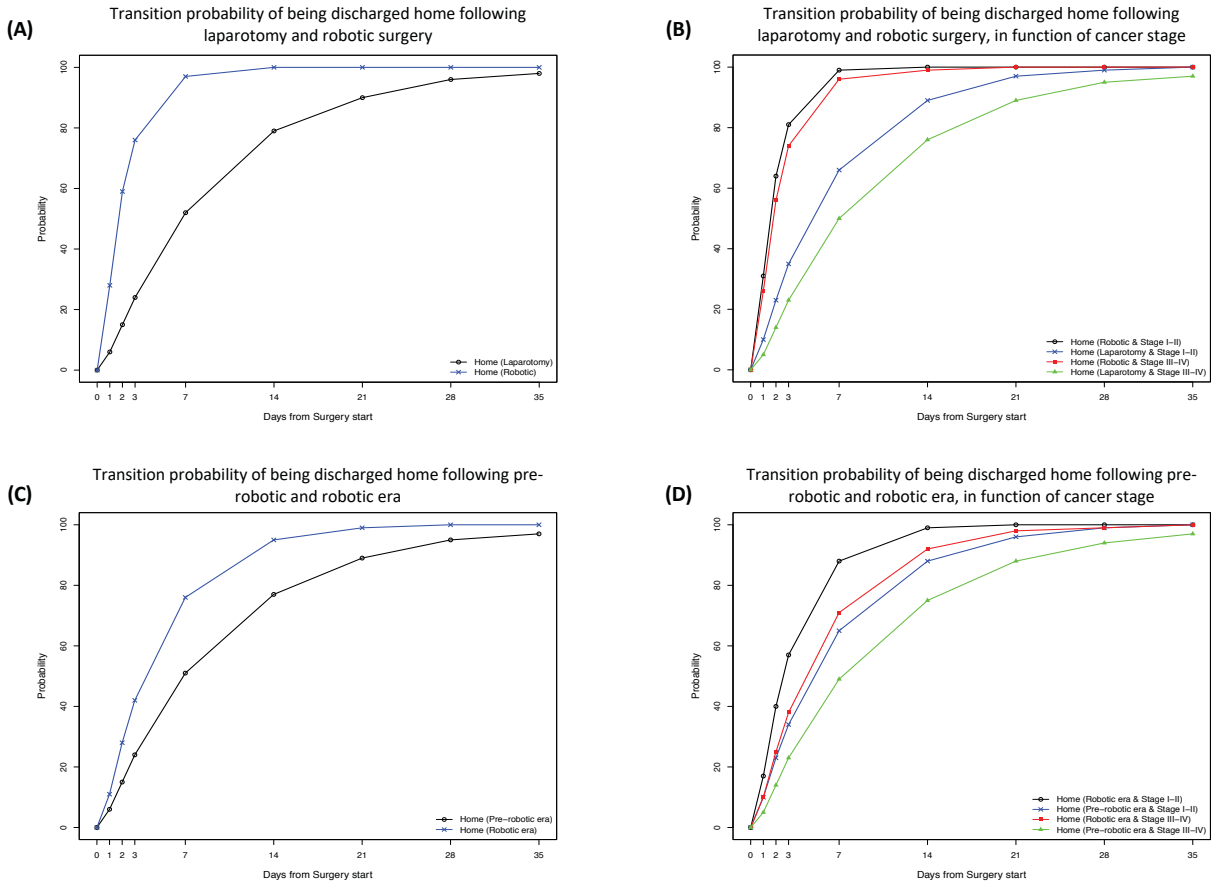
[*] First P value between robotic cases (n=108) and all laparotomy cases (n=136); second P value between pre-robotic era (n=57) and entire robotic era (n=187)

[†] Intraoperative robotic costs exclude acquisition costs of the robot and annual maintenance costs

[‡] Total imaging costs between initial discharge and 4 weeks postoperatively

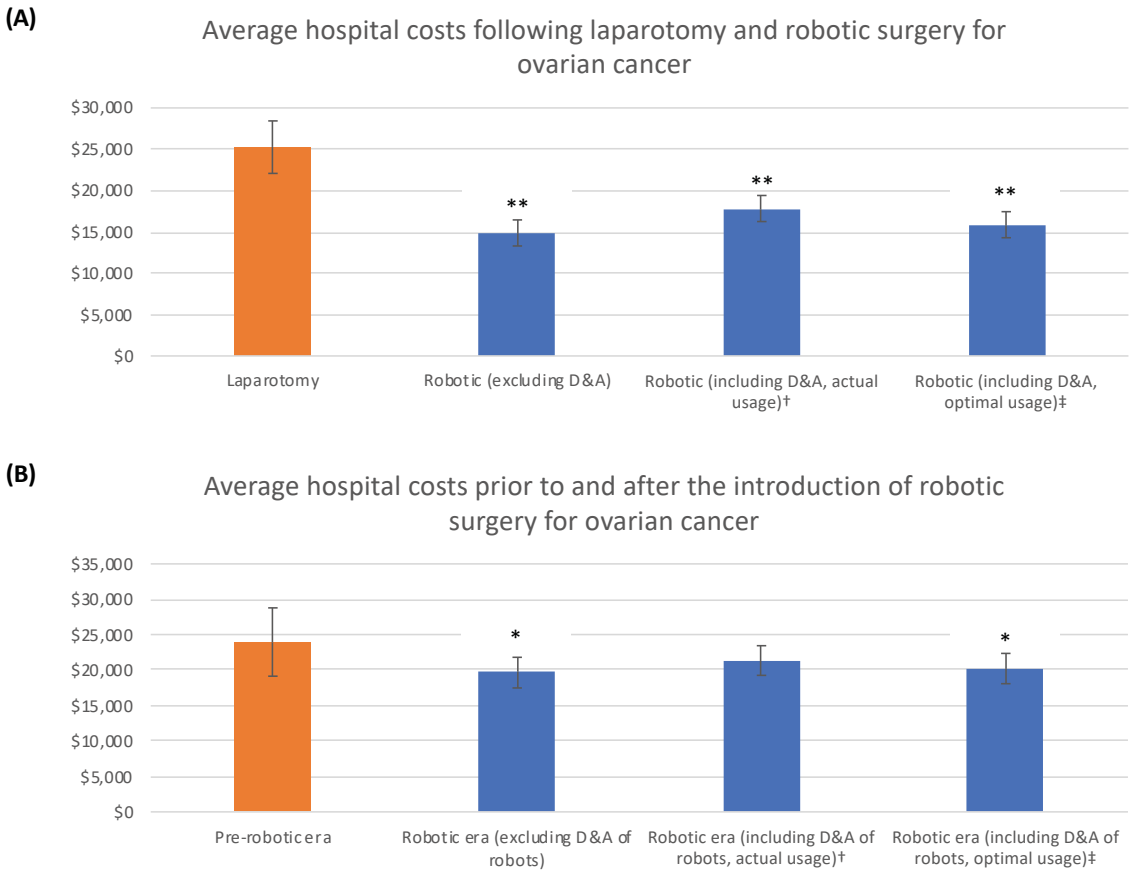
5.12 Figures

Figure 1. Transition probabilities of absorbing states



Results from the multistate model characterizing the patient flow during the in-hospital process after surgery. Predicted transition intensities (probabilities) of the absorbing state were computed at 1, 2, 3, 7, 14, 21, 28, and 35 days from surgery. Figures A and B compare laparotomy and robotic cases; figures C and D compare the pre-robotic and robotic eras.

Figure 2. Average hospital costs for the surgical treatment of ovarian cancer



Significance tests are compared to entire laparotomy cohort (Figure A) or to pre-robotic era (Figure B). *P<0.01, **P<0.0001.

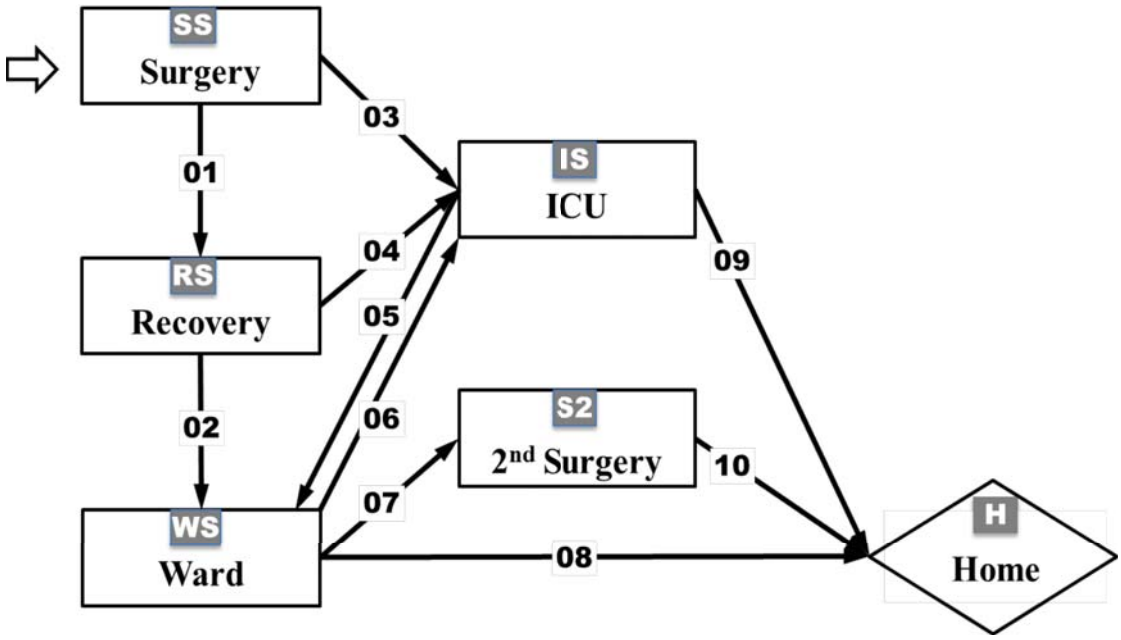
D&A: Depreciation and amortization of capital and maintenance costs of the robots.

†Including D&A of robots using actual hospital usage of the robotic systems (actual usage scenario).

‡Including D&A of robots using theoretical model based on 2 cases per robot per workweek (optimal usage scenario).

5.13 Supplementary Material

S1. Multi-state model from surgery until discharge



SS: starting point of the surgery; ***RS***: the recovery room (post-anesthesia care unit, PACU); ***WS***: the general ward; ***IS***: intensive care unit (ICU); ***S2***: any secondary surgery or reoperation in the perioperative period; ***H***: discharged home or death (absorbing state)

S2. Complication rates before and after the use of robotic surgery for ovarian cancer

	Laparotomy during pre-robotic era (n=57)	Laparotomy during robotic era (n=79)	Robotic surgery during robotic era (n=108)	P value*	
Any complication	40 (70%)	63 (80%)	44 (41%)	<0.001	0.090
Any complication (excluding transfusions)†	23 (40%)	42 (53%)	35 (32%)	0.018	1.00
Any complication (including transfusions where pre-op Hgb ≥100)‡	38 (67%)	58 (73%)	39 (36%)	<0.001	0.067
Intra-operative complication(s)	16 (28%)	34 (43%)	17 (16%	<0.001	1.00
Intra-operative complication(s) (excluding transfusions)†	4 (7%)	14 (18%)	15 (14%)	1.00	0.12
Intra-operative complication(s) (including transfusions where pre-op Hgb ≥100)‡	15 (26%)	24 (30%)	16 (15%)	0.013	0.47
Bleeding§	3 (5%)	6 (8%)	3 (3%)	0.24	1.00
Intra-operative blood transfusion	16 (28%)	30 (38%)	4 (4%)	<0.001	0.13
Intra-operative blood transfusion (where pre-op Hgb <100)††	1 (2%)	14 (18%)	1 (1%)	0.001	0.13
Intra-operative blood transfusion (where pre-op Hgb ≥100)‡‡	15 (26%)	16 (20%)	3 (3%)	<0.001	0.004
Injury to bladder	0 (0%)	4 (5%)	3 (3%)	1.00	0.21
Bowel injury	0 (0%)	5 (6%)	7 (6%)	0.38	0.074
Vascular injury	2 (4%)	5 (6%)	4 (4%)	0.76	1.00
Vaginal laceration	0 (0%)	0 (0%)	5 (5%)	<0.001	0.079
Other intra-operative complication(s)	0 (0%)	1 (1%)	0 (0%)	1.00	1.00
Post-operative complication(s)	35 (61%)	57 (72%)	37 (34%)	<0.001	0.17
Post-operative complication(s) (excluding transfusions)†	21 (37%)	32 (41%	27 (25%)	0.028	0.52
Post-operative complication(s) (including transfusions where pre-op Hgb ≥100)‡	33 (58%)	52 (66%)	32 (30%)	<0.001	0.097
Fever	5 (9%)	5 (6%)	3 (3%)	0.15	0.19
Infection	5 (9%)	8 (10%)	7 (6%)	0.48	0.79
Abscess formation	1 (2%)	0 (0%)	0 (0%)	1.00	0.23
Cardiac complication	3 (5%)	0 (0%)	0 (0%)	0.26	0.012
Poor blood pressure	1 (2%)	1 (1%)	0 (0%)	0.51	0.41
Ileus	3 (5%)	12 (15%)	1 (1%)	0.001	0.77
Lymphocyst formation	1 (2%)	0 (0%)	4 (4%)	0.17	1.00
Post-operative blood transfusion	28 (49%)	40 (51%)	16 (15%)	<0.001	0.011
Post-operative blood transfusion (where pre-op Hgb <100)††	5 (9%)	9 (11%)	7 (6%)	0.36	1.00
Post-operative blood transfusion (where pre-op Hgb ≥100)‡‡	23 (40%)	31 (39%)	9 (8%)	<0.001	0.006
Pulmonary complication	5 (9%)	4 (5%)	2 (2%)	0.12	0.14
Renal morbidity	0 (0%)	2 (3%)	0 (0%)	0.51	1.00
Septicemia	0 (0%)	3 (4%)	1 (1%)	0.63	0.58
Thromboembolic complication	2 (4%)	5 (6%)	1 (1%)	0.08	1.00
Urinary retention	0 (0%)	2 (3%)	0 (0%)	0.51	1.00
Urinary tract infection	8 (14%)	11 (14%)	6 (6%)	0.035	0.32
Vault complication	0 (0%)	1 (1%)	2 (2%)	0.59	1.00
Wound complication	3 (5%)	6 (8%)	4 (4%)	0.40	1.00
Other post-operative complication(s)	4 (7%)	10 (13%)	7 (6%)	0.36	0.79
Post-operative death	1 (2%)	0 (0%)	1 (1%)	1.00	0.41
Re-operation	1 (2%)	0 (0%)	4 (4%)	0.17	1.00

Data is presented as n (%) unless stated otherwise

Hgb: Hemoglobin (expressed in g/L)

*First P value between robotic cases (n=108) and all laparotomy cases (n=136); second P value between pre-robotic era (n=57) and entire robotic era (n=187)

†Complication rate excludes blood transfusions

‡Complication rate only includes blood transfusions if the pre-operative Hgb was greater than or equal to 100g/L

§Intra-operative bleeding was defined as bleeding from a vessel injury, bleeding that required an intensive care unit (ICU) admission, or at least 2L of blood loss for laparotomies or 1L for robotic surgeries.

††Blood transfusion counted only if patient's pre-operative Hgb was less than 100g/L

‡‡Blood transfusion rate counted only if patient's pre-operative Hgb was greater than or equal to 100g/L

S3. Negative binomial regression models for number of ER visits within 3 months of surgery, by robotic era

			Univariate models (5 models)		Multivariable model (1 model)	
	n	mean (SD)	IRR	P-value	IRR	P-value
	243					
Age						
<65	146	0.20 (0.6)	1.00		1.00	
65+	97	0.11 (0.3)	0.58	0.175	0.63	0.237
BMI						
<30	164	0.13 (0.4)	1.00		1.00	
30+	60	0.18 (0.5)	1.34	0.504	1.21	0.654
missing	19	0.37 (1.0)	2.64	0.138	2.30	0.134
NACT						
No	128	0.21 (0.6)	1.00		1.00	
Yes	115	0.11 (0.3)	0.53	0.095	0.44	0.039
Time period						
Pre-robotic era	57	0.16 (0.6)	1.00		1.00	
Robotic era	186	0.17 (0.5)	1.10	0.866	0.47	0.055
Stage						
I—II	59	0.15 (0.6)	1.00		1.00	
III—IV	184	0.17 (0.5)	1.14	0.811	1.45	0.406
Interaction test						
Robotic era & Stage				0.056		
Robotic era & Age				0.464		
Robotic era & NACT				0.974		

Univariate and multivariable regression models for the number of emergency room visits within 3 months of the initial surgery date as the count outcome.

Potential interaction between the use of robotics and the cancer stage was tested at alpha 0.1 by adding the interaction term in the multivariable model.

IRR: Incidence Rate Ratio; adjusted for the time at risk (i.e., if the patient was admitted, they are not at risk of returning to the emergency department)

BMI: Body Mass Index (in kg/m^2)

NACT: Neoadjuvant chemotherapy

CHAPTER 6 – OUTSIDE THE OPERATING ROOM: HOW A ROBOTICS PROGRAM CHANGED RESOURCE UTILIZATION ON THE INPATIENT WARD

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6.1 Preface

The previous chapter demonstrated that the greatest source of cost savings in ovarian cancer using an already existing robotic platform is the length of hospital stay—in other words, the inpatient unit. Using a similar methodology of comparing the pre-robotic to the robotic era, the following chapter zooms in to the inpatient unit and extends the analysis to the entire gynecologic oncology division.

The following manuscript was published in *Gynecologic Oncology* 145 (2017) 102-107 and included in Appendix V.

6.2 Abstract

Objective

To analyze the changes in the composition of the gynecologic oncology inpatient ward following the implementation of a robotic surgery program and its impact on inpatient resource utilization and costs.

Methods

Retrospective review of the medical charts of patients admitted onto the gynecologic oncology ward the year prior to and five years after the implementation of robotics. The following variables were collected: patient characteristics, hospitalization details (reason for admission and length of hospital stay), and resource utilization (number of hospitalization days, consultations, and imaging).

Results

Following the introduction of robotic surgery, there were more admissions for elective surgery yet these accounted for only 21% of the inpatient ward in terms of number of hospital days, compared to 36% prior to the robotic program. This coincided with a sharp increase in the overall number of patients operated on by a minimally invasive approach (15% to 76%, $p < 0.0001$). The cost per surgical admission on the inpatient ward decreased by 59% ($9,892 vs. $4,058) in the robotics era. The robotics program contributed to a ward with higher proportion of patients with complex comorbidities (Charlson ≥5: RR 1.06), Stage IV disease (RR 1.30), and recurrent disease (RR 1.99).

Conclusion

Introduction of robotic surgery allowed for more patients to be treated surgically while simultaneously decreasing inpatient resource use. With more patients with non-surgical

oncological issues and greater medical complexity, the gynecologic oncology ward functions more like a medical rather than surgical ward after the introduction of robotics, which has implications for hospital-wide resource planning.

6.3 Introduction

The assessment of new technology in healthcare generally involves evaluating its safety, clinical effectiveness, economic impact, as well as effects on a local organizational level [259]. In order to fully capitalize on the introduction of a new technology in a hospital setting, changes in organizational processes and workflow need to also be measured and adapted accordingly [260].

The introduction of robotic surgery in gynecologic oncology is a prime example of a practice-changing technological conversion, allowing for an accelerated transition from laparotomy to minimally invasive surgery (MIS), especially for patients with endometrial and cervical cancers [261]. Since the introduction of the da Vinci Surgical System at our institution in December 2007, all the patients with cancer of the cervix undergoing surgery went from being operated on by laparotomy to robotics [99] and the rate of MIS for the treatment of endometrial cancer rose from 17% by laparoscopy to over 95% using robotics by 2012 [89]. The use of robotic surgery for ovarian cancer at our institution is also steadily increasing (66% in 2013).

Systematic reviews have demonstrated the safety and effectiveness of robotic surgery for endometrial and cervical cancer [262] with similar oncological outcomes [263, 264] when compared to laparoscopy and laparotomy. The high initial equipment and ongoing maintenance costs of robotic surgery are offset by the decreased length of hospitalization and decreased morbidity [89, 95, 96, 99, 148], and its potential to convert cases to outpatient same-day surgeries [265, 266]. From a hospital administration and resource allocation perspective, however, there is a paucity of data evaluating the organizational impact of introducing a robotic surgery program in gynecologic oncology. The objective of this study was to analyze the changes in the demographics of hospitalized gynecologic oncology patients (i.e., the composition on the inpatient ward) with the introduction of robotic surgery and its impact on resource utilization and implications for the management of the inpatient ward.

6.4 Methods

A retrospective chart review was conducted on patients admitted onto the gynecologic oncology ward at a university-affiliated tertiary care hospital, the year prior to (2007) and 5 years after the implementation of the robotic surgery program (2013), at the time when a learning curve plateau and a steady state had been reached with the robotics program. Admissions data from January to December of 2007 and 2013 were collected from the hospital's database following approval from the hospital institutional review board.

The design of the study was a non-experimental pre-test/post-test study. With robotic surgery as the intervention, the variables were analyzed before (pre-test) and after (post-test) the introduction of robotic surgery. The selected unit of analysis was the absolute number of hospitalization days rather than the number of admissions because patients could be admitted once for a prolonged period on the ward or have multiple admissions in that year for short periods of time. In order to capture a snapshot of the inpatient ward in the pre-robotic and robotic era, the relative risk (RR) of being on the ward with a particular clinical characteristic was calculated by comparing the proportion of total days spent on the ward by patients with those characteristics in both eras. For example, if 20% of the hospitalization days were spent by patients admitted for bowel obstruction in 2007 and 40% in 2013, one would be twice as likely to see a patient on the ward for bowel obstruction in 2013. Since the length of stay is often shorter for robotic surgeries, we hypothesized that the introduction of a robotic surgery program would affect the length of stay for patients hospitalized for elective surgeries to a relatively greater extent compared to those hospitalized for non-surgical reasons. Thus, the analysis was divided to those who were admitted for elective surgery, "surgical," and those admitted for any other reason, "non-surgical." Patients who were discharged postoperatively and at any point re-admitted for surgical complications (e.g.,

wound infection) were included in the latter non-surgical group to create the distinction with patients admitted for the elective surgery itself.

Patient charts (both electronic and paper) from all admissions were reviewed for patient characteristics (e.g., age, cancer type and stage, comorbidities), hospitalization details (e.g., reason for admission, length of hospitalization, complications), and resources used. Cancer type and stage were retrieved post-hoc, after a final diagnosis could be made, rather than at time of admission where these are often not yet available. The Charlson comorbidity score [267-269] was used as a measure of comorbidities in our population; a score equal to or greater than 5 was chosen as the dividing point for analysis because of the associated exponential increase in the risk of mortality. Moreover, while medical issues may arise during hospitalizations and diagnoses may change, the initial admitting diagnosis was used as the reason for admission.

Variables pertaining to inpatient resource utilization included number of hospitalization days (e.g., cost for room, nursing, pharmacy, laboratory, and overhead costs), specialty consultations (e.g. Internal Medicine, Surgical subspecialties, Palliative Care, Geriatrics, etc.), inpatient imaging studies (e.g., X-Ray, MRI, CT, Ultrasound, PET), and inpatient procedures (e.g., drain insertion by interventional radiology or rectal stent insertion by gastroenterology). Resources used intraoperatively (e.g., the robot, surgical instrumentation, anesthesia, etc.) were excluded to focus on the inpatient ward. Average direct and indirect costs of each of the above-mentioned tests were obtained from hospital and departmental administrative databases, including MedGPS (Logibec Inc., Montreal, Canada), a data warehouse that archives patient-level administrative and clinical data on health care utilization and calculates the costs of resources used in the hospital. Capital costs of imaging machines were depreciated over the expected life of the machines and the average number of hospital-wide exams per year, and included in imaging costs. Physician remuneration fees were obtained from the provincial health insurance board (*Régie de l'assurance*

maladie du Québec). All cost estimates in this study were adjusted for inflation to 2016 Canadian dollars.

Statistically significant differences were also calculated for categorical and continuous variables using the Chi-squared test and the Wilcoxon rank-sum test, respectively. Statistical analysis was performed using commercially available statistical software, STATA 14 (StataCorp, Texas). A two tailed *p*-value less than 0.05 was considered statistically significant throughout the study.

6.5 Results

Description of admissions: Surgical vs. non-surgical

There were more individuals admitted in 2013 than 2007 (291 vs. 246 patients admitted at least once) and among these patients, some were admitted multiple times during the year and there were overall more admissions to the gynecologic oncology service in 2013 than 2007 (395 vs. 356). Despite more admissions, the overall total number of hospitalization days decreased by 12% (2964 vs. 3358 in 2013 and 2007, respectively).

There were 207 admissions for elective surgery (52% of total admissions) in 2013 compared to 163 (46%) in 2007. Of these, the number of elective surgeries performed with a minimally invasive approach increased to 76% (94.3% of which were performed robotically) in 2013 from 15% (all by laparoscopy) in 2007 ($p < 0.0001$).

Figure 1 illustrates the total number of bed days on the gynecologic oncology ward by reason for admission in 2007 and 2013. Despite performing more surgeries in 2013, only 21% of the inpatient bed days were dedicated to patients admitted for surgery, compared to 36% in 2007, saving 585 bed-days for surgery. This is likely due to the increase in number of patients who

underwent robotic surgery resulting in a decrease in the median length of stay for surgical patients to 1 day in 2013 from 6 days in 2007 ($p < 0.0001$). Thus, patients were less likely to be on the ward for elective surgery in 2013 (RR 0.58; 95% CI 0.54 to 0.64). Moreover, of the patients admitted for surgical reasons in 2013, 50% of the days on the ward were dedicated to post-laparotomy patients even though only 17% of surgeries were done by laparotomy.

For non-surgical admissions, the number of hospitalization days increased (79% vs. 64% of the inpatient bed days in 2013 and 2007, $p < 0.0001$) for an additional 191 days, without a significant change in median length of stay (5 vs. 6 days, $p = 0.1$). Among these patients, there was an increase in admissions for bowel obstruction, symptomatic ascites or pleural effusion, and pneumonia, and a decrease in admissions for urosepsis, wound infection, pelvic mass, and febrile neutropenia (all statistically significant, $p < 0.05$) (Figure 1).

Changes in cancer diagnoses

The total number of hospitalization days was analyzed based on admitting diagnosis (Table 1). In 2013, there were fewer hospital bed days on the inpatient ward for patients with endometrial (RR 0.74; 95% CI 0.68 to 0.81) and cervical cancer (RR 0.51; 95% CI 0.42 to 0.62), and a greater number of hospital days for patients with ovarian/fallopian/peritoneal (RR 1.36; 95% CI 1.29 to 1.44) and vulvar cancer (RR 2.28; 95% CI 1.87 to 2.78). This is consistent with the decreased length of stay following robotic surgery and that majority of robotic cases were performed for endometrial and cervical cancers. This trend was also seen when the analysis was subdivided into surgical and non-surgical groups.

Changes in medical complexity of patients

The average age of patients did not differ between the two cohorts (59.8 ± 14.3 vs. 59.7 ± 15.1, $p = 0.9$). In the robotics era, inpatients were more likely to have stage IV disease (RR 1.30; 95% CI 1.21 to 1.39), twice as likely to have recurrence of disease at the time of admission (RR 1.99; 95% CI 1.86 to 2.13), and more likely to have a Charlson score ≥5 (RR 1.06; 95% CI 1.04 to 1.08), indicating an overall increase in the medical complexity and disease severity of patients found on the ward in the robotic era.

Resource Utilization: Imaging Tests and Consults

As shown in Table 2, in 2013 there were less X-rays (-14.7%), ultrasounds (-34.2%), and nuclear imaging (-45.5%) studies requested, but an increase in the number of computed tomography (CT) (+18.1%) and magnetic resonance imaging (MRI) studies (+41.7%). The number of interventional radiology (IR) procedures doubled and the number of gastroenterology (GI) procedures remained unchanged. The number of consults decreased to 665 from 703 in 2007 (-5.4%) and there were less consults for postoperative issues such as pain management (5 vs. 27), general surgery (13 vs. 29), urology (14 vs. 22), and wound care (9 vs. 16). Among admissions for elective surgery only, there were fewer consults to other specialties and fewer imaging tests across the board with less X-rays, ultrasounds, CT, MRI, PET, although more IR and GI procedures.

Inpatient Costs

Despite a greater number of admissions for surgery (207 in 2013 vs. 163 in 2007), the amount of time spent on the ward by postoperative patients decreased substantially from 1215 days to 630 days, with less use of resources for radiology, nuclear medicine, and consultations to other

services, representing an estimated cost savings of $5,834 on the inpatient ward per surgical admission at our institution, a 59% decrease in surgical admission costs ($4,058 vs. $9,892) in the robotics era (Table 2).

If the unit cost per admission of surgical patients from 2007 is extrapolated to the increased volume seen in 2013 (44 additional surgical admissions), the additional cost incurred if the robotics program were not implemented would have been $435,250, assuming all these patients would have been suitable candidates for robotic surgery and rates of MIS remained the same.

The unit cost per non-surgical admission increased by 13% ($17,386 vs. $15,413). This is likely in part due to the increased medical complexity of the non-surgical patients as described, with the associated greater demand for imaging investigations and consults. Despite the increased cost of non-surgical patients, the overall estimated cost savings obtained following the introduction of the robotics program from the inpatient ward perspective was $478,434 (Table 2).

6.6 Discussion

The current study demonstrates the changes in the makeup of the inpatient ward before and after the introduction of robotic surgery, with the later era representing a ward that is more medically complex, more likely to have patients with greater comorbidities, advance stage, recurrent disease, and with ovarian and vulvar cancer, as opposed to endometrial and cervical cancer who tend to undergo robotic surgery. The inpatient ward also consisted of patients less likely to be present for elective surgery following the introduction of robotics due to the shortened postoperative in-hospital convalescence following robotic surgery. The changes in the makeup of the inpatient ward following the expansion of our MIS program were associated with changes in the resource use and the day-to-day operation of the inpatient ward.

The faster turnover of patients admitted for surgery and the associated decreased cost is consistent with previous studies comparing laparotomy to laparoscopy [30, 270, 271] and robotic surgery [88, 89, 96, 99, 143]. Since the volume of surgeries performed at a center is not only limited by availability of operating room time but also availability of beds on the ward, the robotics program allows for an increase in the number of elective surgeries as hospital bed availability is less of a limiting factor. At our center, the introduction of robotic surgery allowed for an increase of 27% in the number of elective surgeries performed (from 163 to 207) while simultaneously decreasing resource use and reducing the total number of bed-days required by 585 days. It should be noted that we have in the last two years begun discharging some patients following robotic surgery on the same day, where appropriate, potentially making this effect even more pronounced.

On the other hand, the proportion of non-surgical patients in the ward has simultaneously increased (79% in 2013 compared to 64% in 2007, increase of 191 bed-days). This may also reflect the evolution of any oncology department where more patients accumulate over time with prolonged survival due to treatment advances over the five-year period of the study. These non-surgical patients are more medically complex, demanding greater resource use with an increased cost per admission ($17,386 in 2013 compared to $15,413 in 2007, increase of 13%). What the robotics program has enabled the inpatient ward to do is to liberate beds for non-surgical patients, thus accommodating their increased demand. This was possible while decreasing the overall cost of the inpatient ward by $478,434 in our cohort.

Hence, following the introduction of a robotics program, surgeons, nurses, and administrators could expect a greater turnover of surgical patients on the inpatient ward with some of them becoming outpatient procedures and hospital beds becoming available more frequently. With the focus shifting from fewer postoperative to greater medical issues, there are several implications in terms of resource planning. Firstly, nursing and allied healthcare expertise need to

be adapted. Nursing expertise should include comfort with managing issues such as chemotherapy side effects, pain management, and end-of-life care. Allied healthcare expertise should be expanded with more resources for services such as physiotherapy, nutrition, social work, and palliative care. Secondly, our data suggests that this growing population of non-surgical patients require more resources such as imaging and consultations, which should be accounted for in ward resource planning. Thus, the contrast in care pathways between surgical and non-surgical patients appears more pronounced with the introduction of robotic surgery. This suggests that perhaps a ward structure of post-robotic surgery "fast track" care separate from a "gynecology oncology" ward might be more efficient from a resource-planning perspective, similar to how "centers of excellence" developed standardized care maps and clinical pathways [272, 273].

Understanding the implications of implementing a robotic surgery program on the inpatient ward is important in preparing the organization's "readiness for change" (Weiner, 2009) [274] in anticipating how it could change nursing tasks, workflows, and resource requirements. It should be noted that the data in the robotics era is derived from a time period when the robotics program was already well established at our institution in order to allow for the analysis of the inpatient ward at a plateau steady state. One might expect a transitional period with a steeper learning curve for personnel on the ward and associated costs in the short term after implementing such a program. In this study, we did not evaluate the pattern of transition in the early phase of introducing a robotics program, prior to reaching stability. Implications for changes outside of the inpatient ward, such as intraoperative costs, outfitting of operating room suites, changes in pre-surgical admission testing units, and impact on the emergency room, were not considered in the current study, and were addressed in a previous study [89]. Moreover, within the inpatient ward, the amount of time on the ward may not correlate fully with time spent on nursing tasks at the patient level. For instance, while patients may be spending less time on the ward, they may require certain

nursing tasks such as patient education and discharge planning to occur in a more compressed manner, especially in "extended recovery beds." The impact on community resources used outside of the hospital were also not examined and might be a point of interest for future studies. Nonetheless, the unique methodology of taking a snapshot of a year in the inpatient ward offers a new dimension for assessing the impact of robotic surgery.

There are several limitations to our study. This was a non-experimental study design and lacks a control group of two groups during the same time period, thus it is difficult to determine what would have happened in the absence of the robotics program. A comparable laparotomy group was not possible as the robotics program was offered to every operable patient with endometrial, cervical, or uterine cancer. The observed changes in resource use could have also been confounded by new developments in treatments and other administrative changes within our institution. For instance, the use of neoadjuvant chemotherapy at our center, while mostly relevant to ovarian cancers, coincided with the introduction of robotics, also contributing to a trend from aggressive primary debulking surgeries to more conservative surgical management and allowing for robotically-assisted interval debulking surgeries. In addition, administrative pushes for cost containment strategies across the board may have also resulted in some diminished resource use in the robotic era. However, while not technically a control group, given that the cost of non-surgical admissions did not experience a parallel dramatic decrease, this acts as an indicator to suggest that the robotics program was likely a dominant driver of decreasing surgical admission costs. The cost variables chosen might not account for all costs incurred by the hospitalization. The unit cost of a hospitalization day ($1,288) was meant to capture some of the overhead, nursing staff, and ancillary costs associated with an average admission to the gynecologic oncology ward. Costs incurred intraoperatively, in the outpatient setting, and in emergency room visits that did not lead to admission to the hospital were omitted to focus on the impact on the inpatient ward. Lastly,

the cost estimates are for a single institution in one Canadian province and therefore may limit the study's generalizability.

A decade after its introduction, the debate on robotic technology is ongoing in the literature. Organizations are beginning to recognize that the economic implications of introducing a robotics program extend beyond the operating room. Regardless of whether a robotics program is sensible in a given local context, it is timely to evaluate the broader ripple effect robotics has on hospital departments outside of the operating room (i.e., inpatient ward, radiology, etc.). The methodology presented here provides a unique, intuitive, and pragmatic approach, which may be used to evaluate changes in the hospital setting. The results of this study could help inform administrators in hospitals with an established robotics program as well as those evaluating the cost-benefit of incorporating robotics into their surgical program.

6.7 Funding

This study was supported in part by grants from the Israel Cancer Research Fund, the Francine Grzywacz Memorial Fund, the Weekend to End Women's Cancers, and the Gloria's Girls Fund. Dr. Kessous has obtained a grant from Intuitive Surgical.

6.8 Conflicts of Interest

Roy Kessous obtained a fellowship training grant from Intuitive Surgical.

6.9 Tables

Table 1. Total hospitalization days based on cancer type, cancer stage, recurrence, and Charlson score

	SURGICAL			NON-SURGICAL			OVERALL		
	2007	2013	RELATIVE RISK	2007	2013	RELATIVE RISK	2007	2013	RELATIVE RISK
CANCER TYPE									
Endometrial	348	134	0.71 (0.62–0.88)**	638	511	0.75 (0.67–0.81)**	986	645	0.74 (0.68–0.81) **
Ovarian	430	200	0.90 (0.78–1.03)	867	1359	1.44 (1.35–1.53)**	1297	1559	1.36 (1.29–1.44) **
Cervical	92	23	0.48 (0.31–0.75)*	221	118	0.49 (0.40–0.61)**	313	141	0.51 (0.42–0.62) **
Uterine sarcoma	29	63	4.19 (2.73–6.44)**	160	80	0.46 (0.53–0.60)**	189	143	0.86 (0.69–1.06)
Vulvar	111	160	2.78 (2.23–3.47)**	28	120	3.94 (2.62–5.91)**	139	280	2.28 (1.87–2.78)**
GTN	3	2	1.29 (0.22–7.67)	15	4	0.24 (0.08–0.74)*	18	6	0.38 (0.15–0.95)*
Vaginal	26	22	1.63 (0.93–2.86)	90	12	0.12 (0.07–0.22)**	116	34	0.33 (0.23–0.48)**
Benign	55	3	0.11 (0.03–0.33)*	15	0	0.03 (0.00–0.49)*	70	3	0.05 (0.02–0.15)**
Other	121	23	0.37 (0.24–0.57)**	109	130	1.10 (0.85–1.40)	230	153	0.75 (0.62–0.92)*
STAGE									
Benign	161	35	0.42 (0.29–0.60)**	63	50	0.73 (0.51–1.05)	224	85	0.43 (0.34–0.55)**
Pre-malignant	25	10	0.77 (0.37–1.60)	7	0	0.06 (0.00–1.07)	32	10	0.35 (0.17–0.72)*
I	343	229	1.29 (1.12–1.48)*	125	116	0.85 (0.67–1.09)	468	345	0.84 (0.73–0.95)*
II	101	33	0.63 (0.43–0.92)*	84	130	1.42 (1.09–1.86)*	185	163	1.00 (0.81–1.22)
III	430	230	1.03 (0.91–1.17)	714	824	1.06 (0.98–1.15)	1144	1054	1.04 (0.98–1.12)
IV	69	30	0.84 (0.55–1.27)	986	1178	1.10 (1.03–1.17)*	1055	1208	1.30 (1.21–1.39)**
Unclassified	86	63	1.41 (1.04–1.93)*	164	36	0.20 (0.14–0.29)**	250	99	0.45 (0.36–0.56)**
RECURRENCE									
No Recurrence	1197	483	15.75 (9.75 - 25.45)**	1291	954	1.49 (1.40–1.58)**	2488	1437	1.99 (1.86–2.13) **
Recurrence	18	147		852	1380		870	1527	
CHARLSON SCORE									
Charlson 0-4	294	113	1.08 (1.03–1.14)*	115	90	1.02 (1.00–1.03)*	409	203	1.06 (1.04–1.08) **
Charlson >=5	921	517		2028	2244		2949	2761	
TOTAL	1215	630		2143	2334		3358	2964	

Statistically significance: * p<0.05, ** p<0.0001.

GTN = Gestational Trophoblastic Neoplasia. Ovarian includes primary peritoneal and fallopian carcinoma. "Other" cancer types include non-mullerian carcinomas (e.g. gastrointestinal primary) and synchronous carcinomas (e.g., ovarian and endometrial together)

Table 2. Costs of hospitalizations for surgical, non-surgical, and all admissions

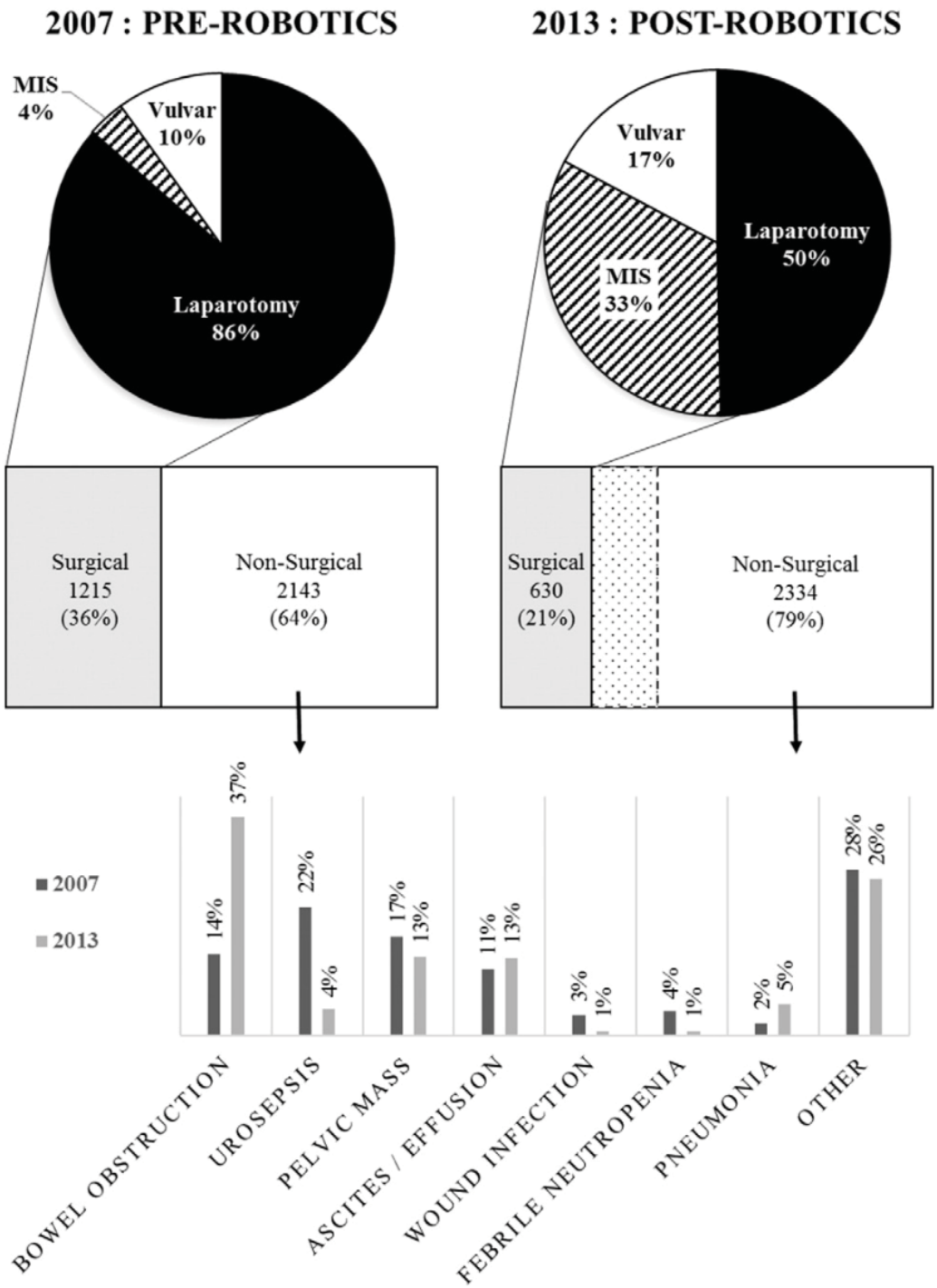
Number of Admissions:	Surgical				Non-Surgical				Overall			
	2007		2013		2007		2013		2007		2013	
	163		207		193		188		356		395	
	Units	Cost ($)	Units	Cost ($)	Units	Cost ($)	Units	Cost ($)	Units	Cost ($)	Units	Cost ($)
Hospitalization ($1,288)	1,215	$ 1,564,920	630	$ 811,440	2,143	$ 2,760,184	2,334	$ 3,006,192	3,358	$ 4,325,104	2,964	$ 3,817,632
X-Ray ($76)	113	$ 8,588	51	$ 3,876	357	$ 27,132	350	$ 26,600	470	$ 35,720	401	$ 30,476
US ($98)	13	$ 1,274	8	$ 784	69	$ 6,762	46	$ 4,508	82	$ 8,036	54	$ 5,292
CT ($187)	37	$ 6,919	19	$ 3,553	151	$ 28,237	203	$ 37,961	188	$ 35,156	222	$ 41,514
MRI ($400)	4	$ 1,600	0	$ -	8	$ 3,200	17	$ 6,800	12	$ 4,800	17	$ 6,800
PET ($747)	5	$ 3,735	1	$ 747	17	$ 12,699	11	$ 8,217	22	$ 16,434	12	$ 8,964
IR ($746)	0	$ -	3[†]	$ 2,238	52	$ 38,792	106	$ 79,076	52	$ 38,792	109	$ 81,314
GI ($409)	0	$ -	2[‡]	$ 818	12	$ 4,908	10	$ 4,090	12	$ 4,908	12	$ 4,908
Consults ($168)	151	$ 25,368	99	$ 16,632	552	$ 92,736	566	$ 95,088	703	$ 118,104	665	$ 111,720
TOTAL COST ($)		**$ 1,612,404**		**$ 840,088**		**$ 2,974,650**		**$ 3,268,532**		**$ 4,587,054**		**$ 4,108,620**
COST/ADMISSION ($)		**$ 9,892**		**$ 4,058**		**$ 15,413**		**$ 17,386**		**$ 12,885**		**$ 10,402**

[†] One patient required one PICC line insertion under ultrasound guidance for total parenteral nutrition as well as transgluteal pigtail draining for a postoperative pelvic abscess. A second patient required pleural tapping by interventional radiology for pleural effusion.

[‡] One patient underwent surgery for a suspected ovarian carcinoma and postoperatively had two GI procedures (colonoscopy and gastroscopy) to confirm suspicion that the cancer was of gastrointestinal tract origin.

6.10 Figures

Figure 1. Proportion of total hospital days spent on the inpatient ward in 2007 and 2013 based on reason for admission



CHAPTER 7 – THE SHIFTING TRENDS TOWARDS A ROBOTICALLY-ASSISTED SURGICAL INTERFACE: CLINICAL AND FINANCIAL IMPLICATIONS

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7.1 Preface

The introduction of robotics in gynecologic oncology, among other developments, was said to have had a substantial impact on the inpatient unit and the use of resources on the ward. Many of the changes noticed in the inpatient unit were attributed, at least in large part, to an important trend that the study highlighted: the shift towards a greater use of minimally invasive surgery in gynecologic oncology [248]. This was done by comparing a snapshot of the inpatient ward in 2007, immediately prior to the introduction of robotics in the division, to that of 2013, five years into the robotics program where a steady state was assumed to have been reached [248].

The following chapter elaborates on this trend by plotting a course from the start of the gynecologic oncology division in 2003 to 2017, and tracking the evolving use of minimally invasive surgery over time, the associated changes in certain clinical outcomes, and estimating the financial impact attributed to the use of robotics for gynecologic cancers.

7.2 Abstract

Introduction

Some hospitals have invested in robotic surgery platforms to stimulate the uptake of minimally invasive surgery (MIS) and offer its benefits to more patients. The primary objective of this study was to evaluate the impact of a robotics program on the use of MIS in an academic gynecologic oncology division over time. The secondary objectives were to determine the clinical and financial effects of this trend and the policy implications.

Methods

Patients treated for endometrial, cervical, and ovarian cancer within a gyn-oncology division between 2003 and 2016 were included in the current study. Clinical outcomes were described in function of surgical approach (laparotomy, laparoscopy, and robotic surgery) and tumor site. The net present value and the return on investment of the robotics program were approximated using previously reported treatment costs.

Results

The use of MIS soared from a high of 15% to 91% before and after the introduction of robotics, respectively. Across all tumor sites, MIS procedures were associated with diminished blood loss and a shorter hospital stay ($p < 0.0001$). The use of robotics in gyn-oncology resulted in cost savings.

Conclusion

Robotic surgery was instrumental in catalyzing the shift from open surgery to MIS and amplifying the number of patients who benefited from less invasive surgery. Continued investments in robotics and the digitization of surgery could help further drive innovation and expand its applications.

7.3 Introduction

Minimally invasive surgery (MIS) has revolutionized the concept of surgery, from the old paradigm "Big Surgeon—Big Incision" (Litynski, 1998, p. 344) [242], where the accomplishment of a surgery was defined by how invasive and radical it was, to the modern-day push for minimizing invasiveness as much as possible, where the smaller the incision, the higher the value for the patient.

Despite evidence of the clinical benefits of laparoscopy [32], most surgeons did not perform laparoscopic surgeries in gynecologic oncology [13, 14, 47] due to its steep learning curve and the technical difficulties of the surgery in complex cases [49, 84]. The enhanced user-friendly interface of robotically-assisted MIS [49] has made the minimally invasive technique easier to adopt among surgeons, allowing them to offer more patients the benefits of MIS [60, 89, 91, 92].

The dominant robotic surgery platform on the market has been Intuitive Surgical's *da Vinci*® Surgical System, with 877,000 surgical procedures reported worldwide in 2017 [86]. In the United States, gynecologic procedures continue to be the most frequent interventions performed with the robotic platform with 252,000 procedures in 2017 [86]. The growth in the rate of robotic surgeries in gynecology has been attributed in part to gynecologic oncology [86].

The current study analyzed an academic center's experience with MIS and how the introduction of robotics has catalyzed the shift from 'big incision' to 'small incisions', and the resulting changes in patient outcomes and hospital costs. To determine whether the robotics program was a worthwhile investment from the point of view of one division, a cash flow-based methodology was uniquely adapted from capital budgeting techniques, offering a novel way to assess the value of surgical robotics.

7.4 Methods

Patient population and data collection

All patients who underwent a primary surgery including hysterectomy for endometrial, cervical, and/or tubo-ovarian cancer at a tertiary center between March 2003 and August 2016, were included in the current study. The following clinical data was gathered from patients' electronic health records: patient characteristics (age, body mass index, American Society of Anesthesiologists' physical status score), diagnostic information (cancer origin, stage, grade, and histology), and perioperative data (surgical approach (laparotomy, laparoscopy, robotic), procedures done, surgical time from skin incision to skin closure, and length of hospital stay).

The average costs of an open and robotic surgery in real terms were estimated using previously reported data from our center in endometrial [89], cervical [99], and ovarian (*manuscript in submission*) [275] cancer. The figures in the first two articles [89, 99] were adjusted for inflation to 2017 Canadian dollars and the costs of the robots and associated service costs were obtained from data gathered for the latter study [275] to reflect the upgrade of one robot and the acquisition of a second robot.

The net present value (NPV) of the robotics program was estimated by multiplying the average laparotomy and robotic surgery costs to the corresponding number of surgeries over the course of the robotics program and discounting the total costs to the start of the program at 1.5% [276], with sensitivity analyses using discount rates of 0% and 3% [277]. The NPV was compared to what it would have cost had all surgeries been performed without the use of the robot, i.e., using the same case-mix of laparotomy/MIS that was used before the use of the robotic platform. Because it was estimated that the latest robot purchased would be viable until the year 2022 (six years past the cutoff of the current analysis), the number of surgeries were projected forward using

the average of the last two years of available data (2016–2017), for a total of a fifteen-year robotics program. Due to there being a relatively low number of laparoscopic procedures following the introduction of the robot, the cost of a robotic surgery was used as a proxy for any MIS procedure performed in the robotic years. Three primary analyses were conducted:

a) In the base case analysis, the capital investment costs as well as the maintenance costs of the robots were excluded as these costs are covered by the hospital's philanthropic foundation, thus representing the actual scenario at our center.
b) A secondary analysis was conducted wherein the annual maintenance costs were included (and forecasted to the year 2022 to reflect the estimated useful life of the robots) and the capital costs of the robot were excluded.
c) A third analysis included the acquisition costs of the robots as well as their annual maintenance costs.

Where applicable, the robots' capital and annual maintenance costs were deducted as capital expenditures in the years they were incurred and discounted as described above using end-of-year discounting for simplicity, except for the acquisition of the first robot at time zero. Due to the fact that the robotic platforms are shared among several services in the hospital, their capital costs were scaled down to reflect the use of the machine for gynecologic cancers as a proportion of all robotic procedures performed in the hospital in the same time period.

A return on investment (ROI) was calculated for the third analysis: the costs of the investments (the upfront capital costs and the annual maintenance costs to date) were subtracted from the gains of the investment (the estimated savings from the robotics program), divided by the aforementioned investment costs.

This study was approved by the hospital's Institutional Review Board (IRB number: CODIM-MBM-CR18-07).

Statistical analysis

Patient characteristics as well as surgical and clinical outcomes were compared between patients who underwent laparotomy and MIS and stratified by tumor origin (uterus, cervix, and ovary), with endometrial cancer and uterine sarcoma classified under "uterus," and ovarian, fallopian tube, and primary peritoneal cancer classified under "ovary." Laparoscopic and robotic procedures were combined for the statistical analysis. Continuous variables were compared using the Student's *t*-test and categorical variables were compared using Fisher's exact test. A *p*-value threshold of <0.05 was used throughout the study. Data was collected on Microsoft Excel and statistical analyses were performed on Stata 13 (StataCorp).

7.5 Results

Utilization of minimally invasive surgery over time

From the launch of the robotics program in December 2007 until August 2016, 1,125 surgeries were performed robotically in the department of gynecologic oncology. Of these, 232 were excluded due to non-gynecologic malignancy or due to benign, borderline, and pre-malignant lesions. Of the remaining 893 surgeries, 19 were performed for recurrent disease, 24 for surgical treatment of cervical cancer without full hysterectomy, 16 were completion staging surgeries, 3 were diagnostic surgeries, and 1 was performed to repair a vesicovaginal fistula. The remaining 830 robotic surgeries were performed as primary treatment for cancer, among which seven had a

prior hysterectomy, leaving 823 robotic surgeries in the current analysis: 625 for uterine cancer (including nine with uterine sarcoma), 85 for cervical cancer, and 113 for ovarian cancer.

Since the start of the department in March 2003 until August 2016, 429 hysterectomies for a gynecologic cancer were performed via laparotomy and 69 via laparoscopy. An additional two vaginal hysterectomies were performed for stage I endometrial cancer and were excluded from the current analysis.

Figure 1 illustrates the expansion in the use of MIS for all gynecologic cancers since the start of the department. Before the introduction of robotics, a cumulative 10% of patients were offered MIS via laparoscopy, with an annual peak of 15% in 2006 (Figure 1A). One year after the start of the robotics program, MIS was offered to over 80% of patients yearly, except for 2015 (77%) due to a temporary pullback in administrative funding for robotic surgery that year.

Figure 1B breaks down the relative frequency of MIS use over time by disease site. Patients with cervical cancer saw the most drastic shift in MIS use from 0% to 99% cumulatively before and after the introduction of robotics, respectively. Since 2009, 100% of all cervical cancers were operated by MIS and all were performed robotically except for one that was completed laparoscopically. In parallel, the shift for endometrial cancer was slightly more gradual with 15% to 94% cumulatively operated by MIS before and after the introduction of robotics. As was the case with cervical cancer, all patients with ovarian cancer were operated by midline laparotomy prior to 2008. Thenceforth, 47% of patients were offered MIS for an ovarian cancer (3 laparoscopically, 113 robotically). The use of robotics in ovarian cancer began once enough experience was acquired one year after the start of the robotics program, and the procedure was selectively offered to patients with a greater likelihood of resectable disease upfront or following neoadjuvant chemotherapy.

Clinical and financial implications of an expanding MIS program

Table 1 describes patient and tumor characteristics as well as perioperative outcomes by mode of operation. Between laparotomy and MIS procedures, differences in patients' age at surgery as well as mean American Society of Anesthesiologists' physical status classification score (ASA) were not statistically significant. Mean body mass index (BMI) was higher in patients treated by MIS for uterine cancer ($p = 0.006$) but not cervical or ovarian cancer. Patients treated by MIS for uterine and cervical cancer were more likely to be associated with well-differentiated disease ($p < 0.001$ and $p = 0.008$, respectively). Patients treated by MIS were also more likely to have stage I uterine cancer ($p = 0.008$) and less likely to have stage III ovarian cancer ($p = 0.048$).

Among the thirty patients who were operated by laparoscopy prior to the start of robotics in December 2007, all had endometrial cancer, 26 (87%) had stage I disease, the average age was 58.5 (±8.9) years old, and the average BMI was 25.5 (±5.3) kg/m^2. In contrast, robotic surgery was offered to patients regardless of age (31% were 70 years old or older), BMI (46% with BMI ≥30 including 15% with BMI ≥40; range: 16.1 to 85.6 kg/m^2), and was feasible in patients with distant metastases (24% had stage III or IV disease).

Procedure times (skin incision to skin closure) were higher in the MIS cohorts for uterine and ovarian cancer ($p = 0.004$ and $p < 0.0001$, respectively) though not for cervical cancer ($p = 0.96$). Across all disease sites, MIS was associated with significantly less blood loss and a shortened length of hospital stay ($p < 0.0001$ for all).

The financial impact of using a robotics platform to accelerate the use of MIS was evaluated using the average costs of surgeries described elsewhere [89, 99, 275]. Figure 2 shows the estimated cost savings associated with the use of the robotics program over a fifteen-year

period in the base case analysis. While the use of robotics resulted in cost savings across all disease sites, the greatest savings came from its use in uterine cancer ($3.5 million over the course of fifteen years), where there was greatest utilization of the robot, followed by ovarian cancer ($1.5 million), and cervical cancer ($582 thousand). Therefore, after a potential fifteen years of applying robotics in gynecologic oncology, from the perspective of the gyn-oncology division alone, the current analysis estimated savings of $5.6 million to the hospital's operating budget (Figure 3), given that the robots and associated maintenance costs were philanthropically funded. Had the robots been purchased by the hospital, the savings from the standpoint of surgeries for gynecologic cancer would have been approximately $717 thousand, with an ROI of 15%.

Sensitivity analyses

The NPV analysis was repeated using a more efficient surgical caseload, which is currently achieved in the division, of six hysterectomies per week, times 50 workweeks, over the fifteen-year period. Using a 1.5% discount rate and the same yearly proportions as the current analysis in terms of diagnosis and surgical approach, the estimated cost savings over the fifteen-year period came to $12.6 million excluding the capital expenditures, $10.6 million including annual maintenance costs, and $7.7 million including both capital and maintenance costs (Supplementary Material S1).

Another sensitivity analysis was performed to assess a worst-case scenario whereby the full costs of the robots and maintenance costs are included as though the platform were not shared with other services but purchased solely for the gynecologic cancer surgeries in the current study. At a 1.5% discount rate, the results demonstrate that the NPV of the surgical program with robotics would have been $32 million, compared to $25 million in costs without robotics.

In a third sensitivity analysis, if the analysis were strictly retrospective in nature and the remaining useful years of the robots' lives were ignored by not forecasting the number of surgeries to 2022 and by cutting off maintenance costs at the end of year nine, the NPV of the surgical program with robotics would have been $11.6 million and $15.4 million excluding and including capital plus maintenance costs, respectively, compared to $14.7 million without the robotics program.

7.6 Discussion

Until the 1970s, one would practically have to be a programmer to use a computer with command-line operating systems. The arrival of the graphical user interface transformed the computer market by rendering the PC more interactive and user-friendly for anyone to use, thereby increasing its diffusion [278, 279]. The objective of the current study was to evaluate how the introduction of a robotically-assisted surgical interface impacted the use of MIS over time in one gynecologic oncology division.

Data from the Nationwide Inpatient Sample suggests a declining rate of inpatient hysterectomies in the United States except for hysterectomies for gynecologic cancers [14]. Between 1998 and 2010, 79% of inpatient hysterectomies for a gynecologic cancer were performed via an abdominal approach, while only 9% were performed by MIS (roughly two thirds laparoscopically and one third robotically) [14]. Another study using the Nationwide Inpatient Sample database demonstrated a shift away from abdominal surgery and towards MIS for the treatment of early stage endometrial cancers, from 22% in 2007 to 51% in 2011 ($p < 0.001$), which the authors attributed primarily to the increasing use of robotic surgery [47].

In the current study, over 1,100 robotic surgeries were performed, of which 823 included a hysterectomy for a gynecologic cancer. Before the use of robotics in December 2007, only 30 patients (10% of the patient population) were offered MIS by laparoscopy and it was limited to few low-risk patients. The introduction of robotics in the department was instrumental in transforming the availability of MIS from one in ten to over eight in ten patients, including those with cervical and ovarian cancer as well as those with advanced stage disease, high BMI (up to 85.6 kg/m^2), and elderly patients (up to 93 years old). While increasing age, BMI, and presence of metastatic disease were associated with a higher risk of conversion in the LAP-2 trial comparing laparotomy to laparoscopy (25.8% of patients assigned to laparoscopy were converted to laparotomy) [32], the overall conversion rate for those undergoing robotic surgery in the current study was low: 2% were converted to midline laparotomy and an additional 2% had a mini-laparotomy to remove a large uterus. Paley et al. (2011) found similar conversion rates (2.9%) after 1,000 robotic surgeries [91]. The feasibility of MIS in the elderly and the obese is especially important given current demographic trends. Across OECD countries, it is estimated that more than half of adults are currently overweight, including 19% with obesity, and 17% are aged 65 years old or older and that figure is expected to reach 28% by 2050 [251].

Uterine cancer is the most commonly diagnosed gynecologic cancer [1, 225]. In absolute terms, the use of robotics in uterine cancer impacted the greatest number of patients (n = 624). On an annual basis, between 91% and 99% of patients with uterine cancer were operated by MIS since the implementation of the robotics program. Others have reported substantial increases in the use of MIS for endometrial cancer following the start of a robotics program [60, 91, 92], from 43 percentage points within twelve months [92] to 74 percentage points within three years [91] of starting their robotics programs compared to the twelve months prior. A trend analysis using the Premier Hospital Perspective Database also demonstrated a shift from open to MIS following the

use of robotic surgery for endometrial cancer, from 28% MIS (9% robotics) in 2008 to 71% (57% robotics) in 2015 [93]. In order to be cognizant of the marginal cost of each surgery, the use of laparoscopy was reintroduced by our team starting in 2014 and offered to patients in whom laparoscopy is feasible and at a low risk of conversion.

The introduction of robotics in our study allowed for the introduction of MIS in the surgical management of patients with cervical and ovarian cancer. Prior to robotics, all patients who were surgically treated for cervical or ovarian cancer underwent a laparotomy. Except for one patient who presented with an unusual 6.6cm stage 3B carcinosarcoma post neoadjuvant chemotherapy, all patients who had surgery for cervical cancer were offered MIS following the introduction of the robotics program. In a survey of members of the Society of Gynecologic Oncology (SGO) in 2012, 97% of respondents reported performing robotic surgery, 75% of whom indicated that they would perform radical hysterectomies with pelvic lymphadenectomy for cervical cancer robotically but not laparoscopically [128]. In ovarian cancer, aggressive cytoreductive surgeries are associated with significant morbidity in patients [214]. Early publications are describing the feasibility of robotics in ovarian cancer [129, 130, 133, 280].

Total health expenditures currently account for approximately 11.5% [254] and 18.0% [281] of Canada's and the United States' Gross Domestic Product (GDP), respectively, with the majority of funds being used on hospital care [254, 281]. In Canada, healthcare is the highest budgetary line item for provincial governments [282] and spending has been curtailed in the last few years in order to tackle fiscal deficits [254]. Accordingly, capital expenditures, such as investments in new medical equipment, often face resistance depending on economic conditions [251]. Indeed, the high fixed costs of robotic surgery platforms as well as the costs of disposable instruments is an oft-cited argument against its acquisition [142]. Across the three diagnoses evaluated here, the average annual net cost savings calculated in the current analysis amounted to

$371 thousand per year in the base case scenario and $48 thousand per year if both the initial capital outlay and the annual maintenance costs are included. These savings were considerably higher when the surgical caseload was increased to a reasonable total of six surgeries per week. Of note is that at our center the upfront capital costs as well as maintenance and service costs are funded by our hospital's foundation. Thus, the base case "donated" scenario illustrates the actual impact on the hospital's operating budget. In lieu of the donated scenario, a center with a pre-existing robotic system, wherein the acquisition of the robot is a sunk cost, could perhaps instead compare potential savings to an opportunity cost or the resale value of the robot.

There are several limitations to the current study. For one, the analysis was retrospective in nature and the comparisons to laparotomies performed during the initial years of the department contain inherent biases. It is plausible that changes in organizational processes, rising administrative pressures to contain costs, surgical performance, as well as possible changes in the patient population, could have all influenced the results of the study. For instance, a division with a reputation for experience with robotics could, theoretically, alter how patients are referred to the department by attracting more patients who are well suited for MIS. In addition, while robotics helped jumpstart the use of MIS, it is possible that the use of laparoscopy would have increased to some extent in the absence of robotics. Furthermore, the increasing number of surgical cases over time could have also magnified cost savings. This may be partially attributed to natural departmental growth and additional healthcare staff over time. At the same time, the rapid turnover of surgical patients associated with robotics may have also, in turn, allowed for more patients to be operated in a given year [248]. Moreover, the use of robotics, while currently employed for a majority of surgical cases overall and 95% of patients with uterine or cervical cancer, remains selective, particularly in ovarian cancer. Patients with extensive carcinomatosis, or with disease that would be difficult to resect via MIS, undergo a laparotomy. These limitations were addressed

by applying the average hospital costs of surgeries before and after the robotic system was employed, where the former were derived from historical cohorts prior to the start of our robotics program. While these costs may have changed over time, the primary driver of the reduced hospitalization costs in the robotic surgery cohorts was consistently the diminished length of stay following MIS compared to laparotomy [89, 99, 275], and it is reasonable to assume that patients undergoing MIS procedures would continue to be discharged from the hospital within a shorter time frame.

Although all costs to date, including the robots' upfront and service costs, are sunk costs that have already been spent, given the retrospective nature of the study they were included in the analyses to gain insight into the value of robotics from a capital budgeting standpoint. Certain hospital expenses associated with a robotics program were ignored including the costs of the robot's *real estate* footprint in the operating room and the training of surgical staff. Given that the hospital is publicly funded, the tax shield advantage of the equipment was ignored, though this should otherwise be taken into account. The way the capital and maintenance costs were attributed to gynecologic cancer surgeries on the basis of the number of surgeries as a proportion of all robotic procedures performed in the hospital may have also under- or overestimated the capital expenditures attributable to these surgeries.

Most importantly, the costs used in the current analysis are estimates; while the average surgery costs were taken from previous analyses conducted in our division, the application of these average costs across the board in the current study ignores the true marginal cost of each surgery and is therefore only a crude approximation. Methodological differences between the cited studies [89, 99, 275] may have also created discrepancies. Nevertheless, the fact that all figures come from the same source strengthens the study. Finally, the current study focuses solely on the use of robotics in gynecologic oncology from the hospital's perspective; the value of robotics in other

specialties was outside the scope of the current analysis. The quality-of-life benefits and the economic value of MIS to patients and their caregivers were also not taken into account in this study.

The costs of the robots and their annual maintenance used in the current study reflect their use among a single department within a high-volume academic center in Canada. The achievement of synergies by sharing the robotic systems with other specialties, or the potentially higher cost of robotic surgeries for other indications, was not taken into consideration in this study. Nevertheless, others have also advocated for the multidisciplinary and maximal use of the robot in order to make it cost-effective [283, 284]. One center has even reportedly been able to accomplish over a thousand surgeries using a single robot in one year alone (personal communication, Professor Liping Cai, First Affiliated Hospital of Nanchang University, China, June 2018). In addition to maximizing its use, the success of a robotics program is also dependent on—among other things—strategic planning, operating room design, leadership to "champion" (Mendivil et al., 2009, p. S29; Palmer et al., 2012, p. 13) the program, buy-in from colleagues, comprehensive training, and a continuous evaluation of data and outcomes [60, 284]. The decision to invest in a robotics platform is highly dependent on local factors (e.g., surgical volume, specialties involved, cost structure, etc.) and should be carefully evaluated accordingly.

Intuitive Surgical has undoubtedly generated the market for robotic surgery and has maintained a virtual monopoly over the industry [285-287]. With the expiry of relevant patents [285] and the entry of competing platforms [86, 285-287] as well as an active interest in the development of robotics on the part of other medical device manufacturers [86, 285, 287-290], the market is expected to shift towards a more competitive landscape [285-287]. It is thus conceivable that the costs of robotic systems could not only come down with time [283, 285-287] but further drive innovation [285-287].

Further to the direct effects of robotically-assisted surgery on patients and on the healthcare system today, the advent of robotic surgery, notwithstanding continued challenges to its adoption, has spawned an age of high-tech surgery. The use of computer assistance in the operating room has bolstered the potential for long-distance surgery [75-77], the miniaturization of robots (micro- or nanorobotics) [291, 292], the incorporation of imaging data in real-time to achieve augmented reality [77, 286, 292, 293], the integration of artificial intelligence and machine learning capabilities to enhance surgical performance [294, 295], and even the possibility of automating certain surgical tasks [76, 294, 296].

7.7 Conclusion

The findings from the current analysis illustrate the value of a robotics program in replacing conventional open surgeries and driving a seven-fold increase in the availability of MIS. The responsible use of robotics in the current setting allowed for financial savings from our division. In addition to improved perioperative outcomes, continued research and development in the field of surgical robotics could help further drive the evolution and digitization of surgery.

7.8 Funding

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7.9 Conflict of Interest

Walter Gotlieb and Susie Lau obtained partial travel support for proctoring robotic surgery.

7.10 Acknowledgments

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7.11 Tables

Table 1. Characteristics of patients operated on by laparotomy, laparoscopy, and robotically-assisted surgery

	Uterus				Cervix				Ovary			
	Laparotomy	Laparoscopy	Robotics	P value	Laparotomy	Laparoscopy	Robotics	P value	Laparotomy	Laparoscopy	Robotics	P value
N	209	65	625		26	1	85		194	3	113	
Age	65.5 (11.0)	58.8 (8.9)	64.9 (11.0)	0.20	47.6 (12.3)	41.0	48.4 (11.5)	0.80	60.6 (11.2)	60.3 (5.7)	61.6 (13.3)	0.50
Body Mass Index, BMI (kg/m^2)	29.6 (7.1)	27.0 (5.7)	32.0 (9.0)	0.0062	25.6 (5.1)	22.0	26.2 (5.6)	0.72	26.8 (6.6)	26.2 (5.8)	27.6 (6.8)	0.31
ASA score*	2.1 (0.7)	1.7 (0.6)	2.2 (0.6)	0.13	1.8 (0.6)	2.0	1.8 (0.6)	0.97	2.2 (0.7)	1.7 (0.6)	2.2 (0.6)	0.83
Grade												
Well differentiated	59 (28.2%)	44 (67.7%)	253 (40.5%)	<0.001	3 (11.5%)	0 (0%)	32 (37.7%)	0.008	16 (8.3%)	0 (0%)	8 (7.1%)	0.83
Moderately differentiated	72 (34.5%)	16 (24.6%)	170 (27.2%)	0.028	10 (38.5%)	0 (0%)	19 (22.4%)	0.21	16 (8.3%)	0 (0%)	6 (5.3%)	0.37
Poorly differentiated	74 (35.4%)	5 (7.7%)	200 (32.0%)	0.10	13 (50.0%)	0 (0%)	27 (31.8%)	0.17	162 (83.5%)	3 (100%)	99 (87.6%)	0.33
Unspecified	4 (1.9%)	0 (0%)	2 (0.3%)		0 (0%)	1 (100%)	7 (8.2%)		0 (0%)	0 (0%)	0 (0%)	
Stage												
1	142 (68.0%)	59 (90.8%)	474 (75.8%)	0.008	24 (92.3%)	1 (100%)	79 (92.9%)	1	26 (13.4%)	1 (33.3%)	19 (16.8%)	0.32
2	16 (7.7%)	1 (1.5%)	40 (6.4%)	0.42	2 (7.7%)	0 (0%)	4 (4.7%)	0.62	11 (5.7%)	0 (0%)	10 (8.9%)	0.35
3	40 (19.1%)	5 (7.7%)	94 (15.0%)	0.10	0 (0%)	0 (0%)	2 (2.4%)	1	133 (68.6%)	2 (66.7%)	62 (54.9%)	0.048
4	11 (5.3%)	0 (0%)	17 (2.7%)	0.065	0 (0%)	0 (0%)	0 (0%)		24 (12.4%)	0 (0%)	19 (16.8%)	0.31
Unstaged	0 (0%)	0 (0%)	0 (0%)		0 (0%)	0 (0%)	0 (0%)		0 (0%)	0 (0%)	3 (2.7)	
Procedure time (minutes) †	219 (66)	218 (69)	234 (57)	0.004	275 (69)	270.0	276 (64)	0.96	254 (107)	286 (101)	305 (81)	<0.0001
Estimated blood loss (mL)	377 (762)	101 (99)	60 (80)	<0.0001	513 (559)	400.0	76 (78)	<0.0001	530 (495)	110 (69)	148 (195)	<0.0001
Conversion to laparotomy, n (%)	n/a	3 (4.6%)	5 (0.9%)	n/a	n/a	0 (0%)	0 (0%)	n/a	n/a	0 (0%)	9 (8.0%)	n/a
Length of hospital stay, days	6.4 (4.5)	1.9 (3.0)	1.5 (2.4)	<0.0001	6.9 (4.9)	1	1.2 (0.7)	<0.0001	8.7 (6.9)	1	2.2 (2.5)	<0.0001

Data presented as mean (SD) unless stated otherwise

P values represent statistical significance between all minimally invasive procedures (laparoscopy and robotics combined) and laparotomy

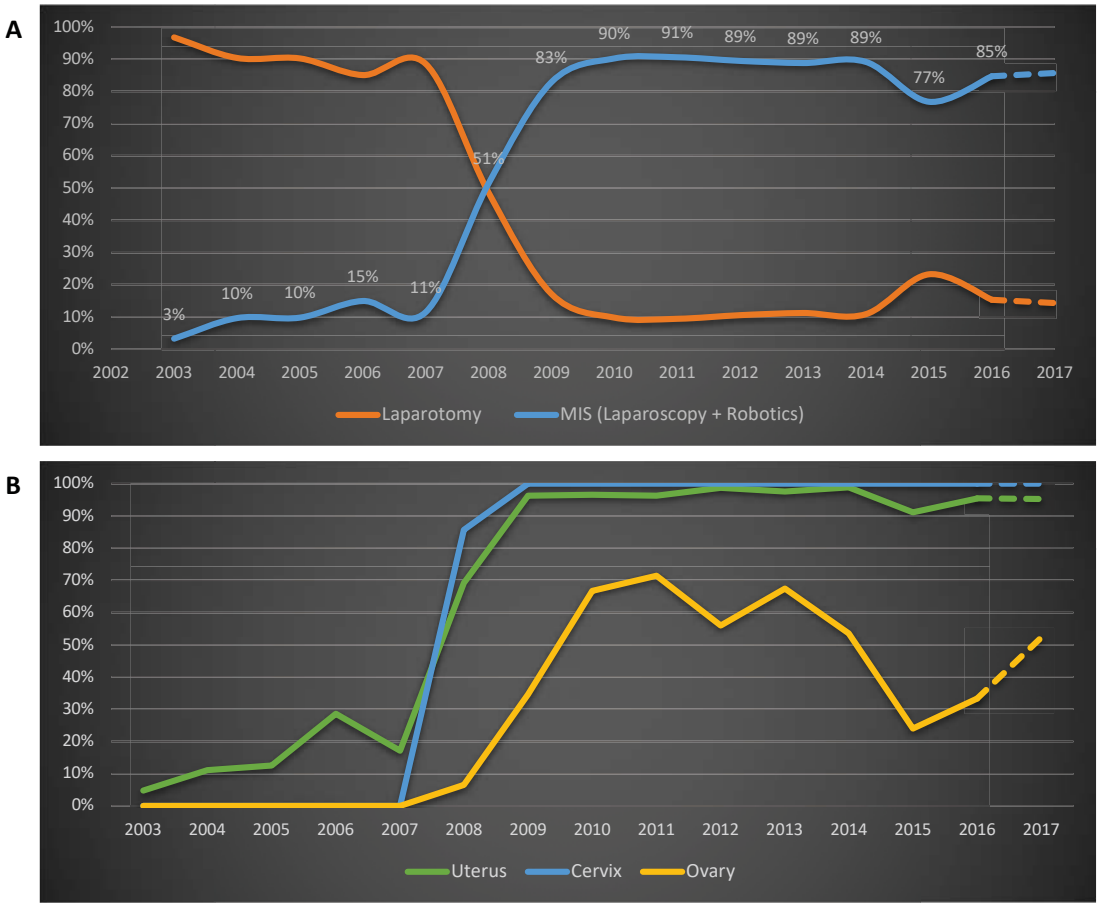
n/a: data not applicable or not relevant

* Average of scores from 1 to 4 from American Society of Anesthesiologists' physical status classification system

† Procedure time calculated from skin incision to closure

7.12 Figures

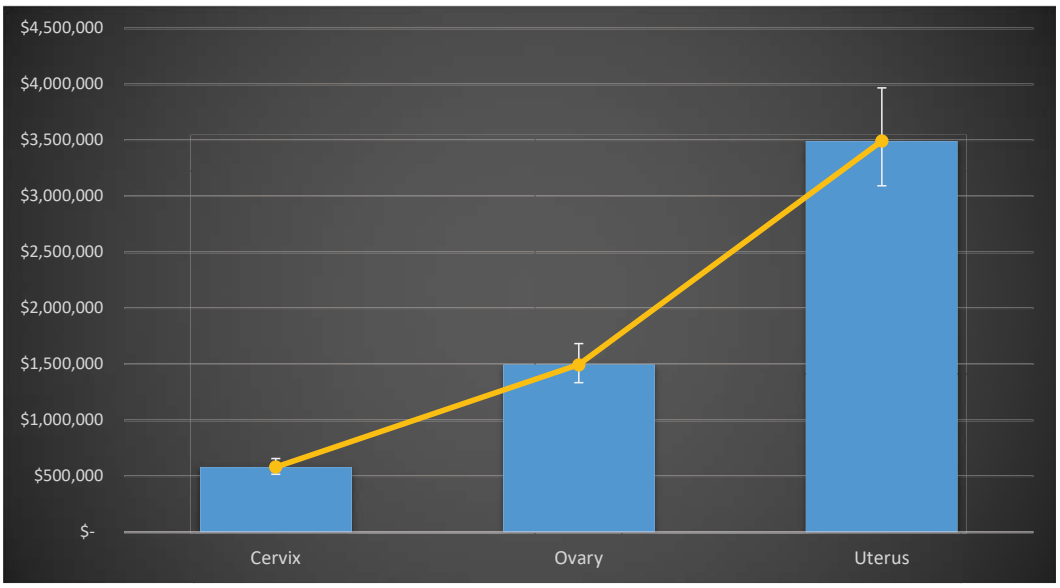
Figure 1. Shift in use of minimally invasive surgery following introduction of robotic surgery in gynecologic oncology



Graph A represents shift across all disease sites. Graph B represents shift in function of disease site.

2016 data ends August 31, 2016 (cutoff point of analysis). Dashed lines represent data beyond cutoff point between September 2016 and December 2017, inclusively.

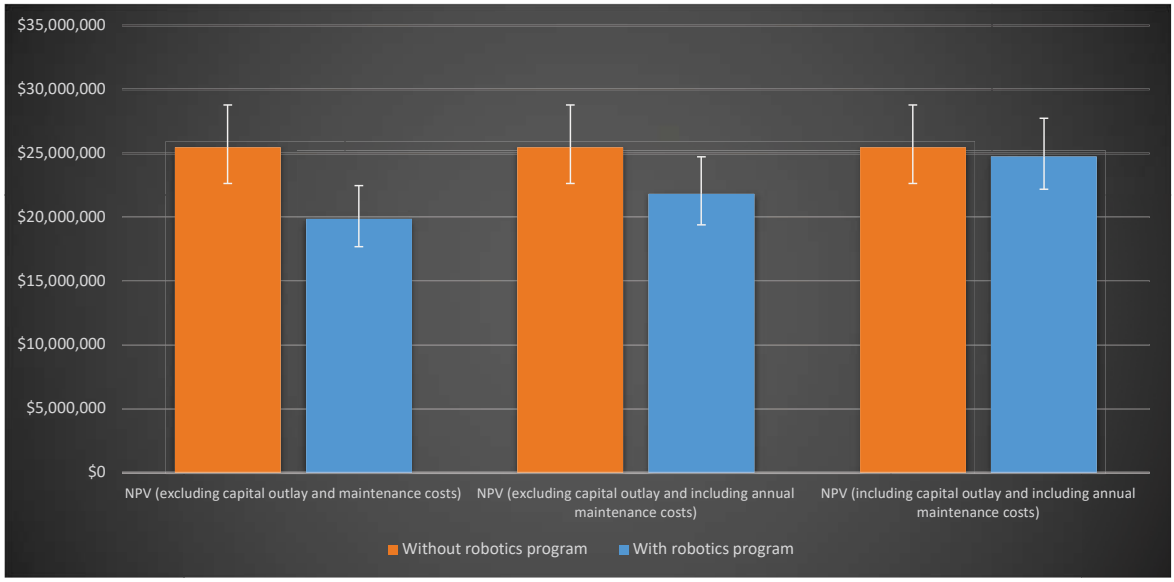
Figure 2. Estimated cost savings from a fifteen-year robotic surgery program, by disease site



Graph ignores costs of the machines and associated maintenance costs, representing actual scenario where capital expenditures are donated.

Costs are discounted at 1.5% discount rate in the base case. Error bars represent sensitivity analysis using discount rates of 0% (positive bars) and 3% (negative bars).

Figure 3. Estimated net present value (NPV) of surgical costs in gynecologic oncology



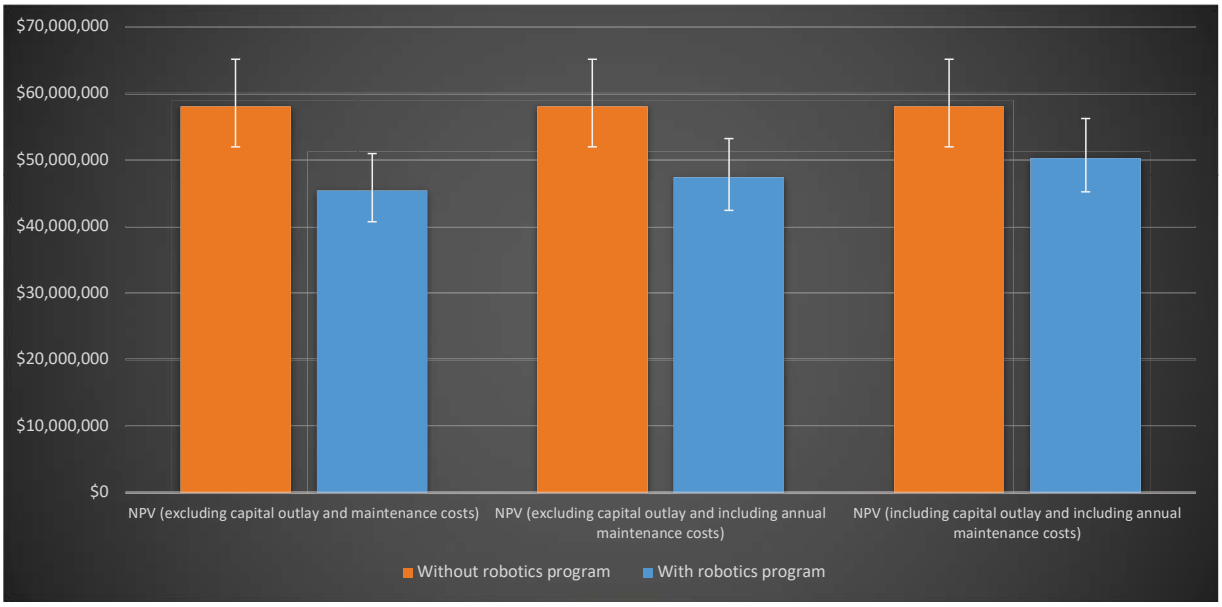
Blue columns represent costs of laparotomy and MIS (robotic and/or laparoscopy) during the period of the robotics program and forecasted to incorporate the remaining useful life of the robots (2008–2022); orange columns represent hypothetical scenario had all surgeries been performed via the same case-mix (laparotomy and laparoscopy) that was used prior to the introduction of robotics.

Costs are discounted at 1.5% discount rate in base case. Error bars represent sensitivity analysis using discount rates of 0% (positive bars) and 3% (negative bars).

Capital acquisition and maintenance costs of the robots were scaled down to reflect the number of gynecologic cancer surgeries in the current analysis as a proportion of all robotic procedures performed in the hospital.

7.13 Supplementary Material

S1. Hypothetical model of the estimated net present value (NPV) of surgical costs in gynecologic oncology using a more productive surgical caseload



Blue columns represent costs of laparotomy and MIS (robotic and/or laparoscopy) in a hypothetical scenario where six surgeries are performed per week, times fifty workweeks, across fifteen years (2008–2022) using the same proportions noted in the primary analysis; orange columns represent hypothetical scenario had all surgeries been performed via the same case-mix (laparotomy and laparoscopy) that was used prior to the introduction of robotics.

Costs are discounted at 1.5% discount rate in base case. Error bars represent sensitivity analysis using discount rates of 0% (positive bars) and 3% (negative bars).

Capital acquisition and maintenance costs of the robots were scaled down to reflect the number of gynecologic cancer surgeries in the current analysis as a proportion of all robotic procedures performed in the hospital.

CHAPTER 8 – DISCUSSION AND FUTURE DIRECTIONS

Amara's law states that "we tend to overestimate the effect of a technology in the short run and underestimate the effect in the long run" (Roy Amara) [297]. This is sometimes depicted using Gartner's technological "Hype Cycle" from its initial discovery or development, ascending to a peak of overestimated expectations, declining to a low of disappointment, and returning to a gradual "slope of enlightenment" (Gartner, Inc.) [298]. Though it may be difficult to predict the long-term impact of a technology, it is critical for organizations to monitor its effects.

Everett Rogers outlined the stages of the technological adoption process, the categorization of individuals based on their disposition towards innovation, and the consequences of innovations on social systems [299]. Donald Berwick applies Rogers' theory [299] to healthcare [300] and underscores three factors that could influence the dissemination of innovation: (1) how individuals perceive the innovation, including its potential benefits, risks, and complexity; (2) the behavior of individuals vis-à-vis innovation; and (3) organizational culture and social structures [300]. Berwick points out how innovation often diffuses slowly in healthcare, explaining that "in health care, invention is hard, but dissemination is even harder" (Donald M. Berwick, 2003, p. 1970) [300].

In the surgical field, technological adoption should be carefully evaluated and evidence-based [301]. The Donabedian model proposes a three-pronged approach to measuring the quality of medical care: outcomes (e.g., patient outcomes such as recovery, survival, satisfaction, etc.), process (i.e., the delivery of healthcare and its appropriateness), and structure (i.e., the setting in which healthcare is provided including its facilities, resources, the qualifications of providers, and administrative factors) [302]. Setting up a robotics program touches on each component of this framework, from structural requirements (administrative and financial commitments, resource use,

training, etc.), processes (changes in how surgical and postoperative care are delivered), and outcomes (adverse events, convalescence, quality of life, hospital costs, etc.).

The studies conducted demonstrated that robotics results in a relatively rapid return to baseline quality of life and pain, satisfaction with the surgery, and less use of analgesics in the perioperative period compared to laparotomy. For the treatment of ovarian cancer, where the role of MIS continues to be evaluated, robotics was shown to have satisfactory cytoreduction rates as well as overall and progression-free survival, and was associated with improved clinical outcomes and lower hospital costs due primarily to the reduced length of hospital stay. Furthermore, across all gynecologic cancers, the use of robotics was shown to permit a greater turnover on the inpatient ward by reducing the number of surgical bed-days required per patient. Finally, the use of robotics allowed for an exponential increase in the use of MIS over the life of the robotics program; this evolutionary shift from open to robotically-assisted surgery was tied to certain clinical and financial implications. Using a unique capital budgeting approach, albeit driven by many assumptions, the robotics program was found to be a worthwhile investment from the perspective of one division. While the absolute cost savings were difficult to ascertain, given that the robots were donated by the hospital's foundation, the gyn-oncology robotics program was estimated to at the least not be a 'white elephant.'

Since conducting or reporting these analyses, others have substantiated our findings or have described similar results. Some have reported a return to preoperative HRQOL within 6 weeks [303] or 5 weeks [304] of surgery though those were the first assessments since baseline and the first week post-surgery mark, respectively. Similar conclusions to ours were also reached as it pertains to drug use and its associated costs [305].

As described in the manuscripts, there are limitations to the studies conducted. The studies were non-randomized, generally retrospective in nature, and pre/post analyses (i.e., comparing the period before and after the implementation of the robotics program) were employed. Consequently, there are inherent biases as well as the possibility of confounding factors to explain some of the results obtained. Additionally, as in most cost analyses, there was a reliance on a set of assumptions. To control for some possible confounding variables and assumptions, sensitivity analyses and 'what if' scenarios were conducted throughout. The studies did not focus on the comparison of robotics to laparoscopy as very few patients were offered MIS at the time that robotics was first introduced in the division.

The data used to conduct these analyses came from a single setting that managed to scale the use of the robotic platforms over time. This limits the transferability of the findings due to variations in demographics, practice patterns, surgical and clinical experience, costs, healthcare resources, organizational factors, and healthcare systems [306]. At the same time, most cost studies on the topic have been carried out in the United States or Europe [88, 90, 96, 105, 115, 143-149], and the evaluation of robotics in a Canadian context may offer a different perspective. To date, Canadian health technology assessments on robotic surgery have been undertaken by the Canadian Agency for Drugs and Technologies in Health (CADTH) for multiple indications (prostatectomy, hysterectomy, nephrectomy, and cardiac surgery) [307] as well as in Ontario for radical prostatectomy [308] and in Alberta for radical prostatectomy [309], partial nephrectomy [310], and transoral robotic surgery [311].

In the current thesis, robotic surgery was shown to offer a range of clinical benefits to patients, improve aspects of operational efficiency for the hospital, and result in lower costs in comparison to open surgery from the perspective of the gyn-oncology division. While these findings may not necessarily be replicable at other institutions or in other specialties, the results,

the methodologies used to obtain them, and the commentaries provided, may offer some guidance for future studies evaluating the implementation of technology in a health care setting. Additional studies on robotic surgery and their implications for patients, hospitals, and other stakeholders, are necessary to paint a better picture on this subject.

In addition to the results described, there are numerous other possible effects to consider when introducing a robotics program. Other groups have described a relatively rapid learning curve for robotic surgery [84, 85, 94, 312, 313]. Furthermore, the robotic system may provide a more ideal environment for simulation-based training, which will likely continue to be enhanced by leveraging advancements in virtual reality (VR) [314, 315] and artificial intelligence [295, 316, 317]. The implications for trainees has also been documented both within the OR [87, 318-320] as well as outside of it (*manuscript ready for submission*, 2018) [321]. Additional intangible benefits of technological investments in devices like robotic surgery may include marketing for a hospital [48, 322] and a means of attracting talent [141] as well as patients [141, 323]. At the same time, the growth of robotic surgery in itself has also been influenced by early adopter "technophile surgeons" (Barbash and Glied, 2010, p. 704) [324] as well as patient demand [323, 324] due in part to marketing of the manufacturer of the robot [322]. Some have asserted that this may have even spurred the use of robotics for indications of prostate cancer that would have otherwise been managed non-surgically [324], raising the possibility of supplier-induced demand [325]. Then again, others have found evidence to the contrary in the treatment of kidney cancer, where the availability of robotics was associated with increased access to partial nephrectomies where appropriate—leading to improved clinical and economic outcomes compared to radical nephrectomies—without increasing its use in cases where it might be unsuitable [326].

It has been reiterated that the robotic platform may alleviate fatigue, pain, discomfort, and/or poor ergonomics associated with the performance of conventional laparoscopy [48-51, 141,

327-330]. Conversely, a 2012 survey of gynecologic oncologists suggested conflicting results by drawing a possible link between robotics and increased physical discomfort [331]. In addition to the effects on surgeons' experiences, the use of robotics has been purported to impact the dynamics of the OR team as a whole [332]. Just as autopilot systems have revolutionized aviation [333, 334] despite "separating the pilot from direct control and authority of the airplane . . . [and masking] the most basic feedback cues" (Manninghmam, 1997) [334], robotic systems—despite likewise physically distancing the surgeon from the patient and removing tactile cues—could very well push the boundaries of human capabilities with continued innovation [48, 335]. Certain avenues for technological advancement, including the possibility of remotely-operated surgeries [75-77] and the potential for augmented reality (AR) by integrating image-guidance into the platform [77, 286, 292, 293, 336], were described in the last manuscript (Chapter 7).

The robotics technology is thus a tool upon which additional features could potentially be built. This is perhaps analogous to the nature of the Internet and its ability to accommodate on new uses [337-340]. In the pre-Internet age, France Telecom developed Minitel to help digitalize the phone network in France [341-346]. The Minitel was a revolutionary system that allowed users to access an *online* telephone directory, use banking services, book travel arrangements, and access an abundance of information via a terminal connected to their phone line [341-345]. However, the eventual advent of the Internet and the ability of users from around the globe to access the World Wide Web rendered the Minitel obsolete [342-345]. In spite of this, some people rejected the Internet and remained devoted to the Minitel [342-344]; it was only taken offline in June 2012 [342, 343]. Just as the Internet was a natural advancement over Minitel's underlying technology [343, 344], so too is robotics vis-à-vis laparoscopy [19, 55], hence the commonly used term "robotic-assisted laparoscopy" [19, 51, 55, 67, 88, 105, 107, 131]. While some indicate that robotics is merely a more expensive form of laparoscopy [142], the conventional MIS technique

is limited in technological scope, whereas the architecture of robotic technology and computer-assisted surgery is such that continued innovation is envisioned [19, 48, 51, 77, 285, 286, 292, 335]. Moreover, just as the Internet required heavy expenses upfront (e.g., an extensive physical infrastructure, far-reaching fiber optic cabling, computers, network and Internet service providers, etc.) [337, 347], the hope is that the long-term developments of robotics will continue to change how surgeries are performed [19, 48, 51, 77, 285, 286, 292, 335] and that prices will come down with time, enabling the diffusion of MIS to accelerate further [283, 286]. Fittingly, some have compared new developments in surgical robotics to the evolution from expensive and bulky mainframe computers to the modern-day personal computer—anticipating a time where a robotics platform will be in every OR [348]. Though it is difficult to predict how technology will evolve over the long term [297], in the meantime, surgeons may employ open surgeries when necessary and laparoscopies when feasible.

The growing practice of understanding the effects of novel medical technologies is especially important in the current paradigm shift towards value-based care where the procurement of products, pricing, and reimbursements are tied to outcomes, quality of care, and patient value [349-353]. The current thesis focused on two aspects of robotic surgery: the impact of patient outcomes as well as the effect on a hospital division. The aim of many health economic and cost-effectiveness analyses is to provide information for decision makers to determine whether an intervention should be adopted (i.e., the added benefits are worth the extra costs) given a scarcity of resources [354-359]. Some preference-based HRQOL measures are sometimes used for the calculation of Quality-Adjusted Life-Years (QALYs) in cost-utility analyses [354, 357, 360], and although popular, ethical concerns have also been raised in this regard [358, 359, 361-363]. This approach was not a focus of the current thesis. The current thesis was not meant to make a normative judgement on whether robotics is *worth the costs* or whether it ought to be adopted from

a societal or resource allocation standpoint. Rather, the scope of the thesis focused on presenting a set of descriptive analyses on robotics from a single setting (using an institutional perspective) in a manner more consistent with a cost-consequences analysis; it is up to the reader to apply what may be relevant to their setting as well as to patients, hospital administrators, and healthcare providers to make informed decisions about robotic surgery and assess the value of the technology as they see fit.

CHAPTER 9 – REFERENCES

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CHAPTER 10 – APPENDICES

Appendix I. Publication on quality of life outcomes following robotic surgery (Chapter 2)

Source: Abitbol, J., et al., *Prospective quality of life outcomes following robotic surgery in gynecologic oncology.* Gynecol Oncol, 2014. **134**(1): p. 144-9.

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Prospective Quality of Life Outcomes Following Robotic Surgery in Gynecologic Oncology

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HIGHLIGHTS

- Quality of life and body image return to baseline by 3 weeks after robotic surgery.
- Social well being was not affected by robotic surgery.
- Emotional well being increased after robotic surgery.

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ABSTRACT

Purpose. To characterize the health-related quality of life (HRQL) of patients undergoing robotic surgery for the treatment of gynecologic cancers.

Methods. 211 patients completed a quality of life questionnaire before surgery. Postoperative questionnaires, consisting of the same assessment with the addition of postoperative questions, were given at 1 week, 3 weeks, 3, 6, and 12 months after surgery. The Functional Assessment of Cancer Therapy—General (FACT-G) and its subscales were used to evaluate HRQL. Patient-rated body image was evaluated using the Body Image Scale. Statistical significance was measured by the Wilcoxon signed-rank test. Minimally important difference (MID) values were analyzed to evaluate clinical significance.

Results. Overall HRQL and body image decreased at 1 week after surgery and returned to baseline by 3 weeks. Physical and functional well-being decreased at 1 week after surgery and returned to baseline by 3 months after surgery. However, using MID criteria, physical well-being returned to baseline by 3 weeks. Social well-being did not change significantly. Emotional well-being increased immediately by 1 week after surgery.

Conclusion. Patient reported HRQL outcomes following robotic surgery for the treatment of gynecologic cancers suggests a rapid return to pre-surgery values.

Introduction

There is a growing interest to integrate the assessment of health-related quality of life (HRQL) into clinical practice [1–3] as its measurement has become pivotal in patient care [4–6]. In oncology, the symptoms of cancer as well as side-effects from treatment have been associated with a decrease in HRQL [7–9], and HRQL has become an important indicator of the value of health care programs and new technologies.

Gynecologic cancers and their treatments not only affect the general well-being of patients, but can have specific impacts on femininity [10,11], self-esteem [11], and body image [10–12]. In addition, sexual health following gynecologic cancer surgery can be impacted by modification of genitalia and/or loss of childbearing capacity [10–15], decreased libido [10,14,15], and surgical menopause[12,13]. The introduction of minimally invasive surgery has corresponded with improved patient HRQL when compared with traditional laparotomy [16–18]. Though HRQL is a broad term which many have attempted to define, some have narrowed it down to four domains: physical, functional, mental/psychological, and social functioning [19].Following a pilot study showing good recovery at one post-operative evaluation [20], we initiated this prospective study comparing HRQL prior to and after surgery in an unselected consecutive series of patients following robotic surgery for gynecologic cancers.

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Methods

Recruitment of patients

Patients were recruited to this study from the gynecologic–oncology clinic of a publicly funded tertiary care hospital. All patients scheduled to undergo robotic surgery for the treatment of a gynecologic cancer (uterine, ovarian, cervical) were invited to participate in this study, and signed an informed consent which was approved by the institution's Research Ethics Committee. Three surgeons experienced with robotic surgery performed the surgeries. Between December 2009 and December 2012, there were 211 consecutive subjects included in the study. None of the patients were part of our previous pilot study [20]. A flow chart of the study process is shown in Supplementary Fig. S1. After giving written informed consent, participants were provided with the baseline questionnaire prior to surgery (provided in Supplementary Material S2). On the day of surgery, patients were given a follow-up questionnaire to be completed one week after surgery. Patients were then asked to complete the same follow-up questionnaire at their in-clinic visit three weeks after surgery. Subsequent questionnaires were mailed to patients at 3, 6, and 12 months after surgery. Completed questionnaires were transferred to an electronic database by a trained data manager, and none of the surgeons had access to the answers of the patients. Participants were eligible to participate in this study if they completed a baseline questionnaire, and were excluded if their surgery was converted to laparotomy (n = 11). Questionnaires (see Appendix, S2) were completed either in English or French.

Outcome measures

FACT-G

HRQL was measured using the validated cancer-specific FACT-G questionnaire. The FACT-G is a 27-item questionnaire that assesses HRQL across four domains: physical well-being, social well-being, emotional well-being, and functional well-being [21]. Higher FACT-G scores correspond to better HRQL [21]. Following established guidelines, FACT-G subscale scores were considered valid if more than 50% of the questions were answered; total FACT-G scores were considered valid if more than 80% of all 27 questions were answered and all comprising subscale scores were valid [21]. Participants with too many missing FACT-G answers were therefore excluded from the FACT-G analysis. If too many missing values were found in the baseline questionnaire, all subsequent subscale scores and/or total FACT-G scores were removed for that participant. This ensured that all follow-up questionnaires have a corresponding baseline questionnaire as a control.

Body image scale

Body image was measured using the Body Image Scale (BIS) designed for cancer patients by Hopwood et al. (2001) [22]. Scores on the 10-item questionnaire range from 0 to 30, with higher scores indicating a more negative self-image [22]. For consistency with the FACT-G, where higher scores reflect better HRQL, all BIS scores were subtracted from 30 so that higher scores correspond to better body image. Similarly to the FACT-G scoring methodology, BIS questionnaires with more than two missing answers were excluded from the body image analysis; if more than two missing answers were in the baseline questionnaire, all BIS data were excluded for that participant. Two missing items were considered acceptable to impute in accordance with what has been reported [22].

Statistical Analysis

Statistical analysis was performed using STATA 12 statistical software (StataCorp) and Microsoft Excel 2003. Some distributions of HRQL scores by visits were not normally distributed. We therefore performed non-parametric Wilcoxon signed-rank test to test for significant differences in questionnaire scores between different time points. To assess clinical differences, changes in questionnaire scores were also evaluated using minimally important difference (MID) values established for the questionnaires where applicable [21]. A difference of 3–7 points is suggested as a minimally important difference (MID) for the total FACT-G Score; 2–3 points for the physical and functional well-being subscales; 2 points for the emotional well-being subscale [21]; and 2 points for the social well-being subscale [23]. Kruskal Wallis analysis of variance was used to test differences in questionnaire scores by age and marital status.

A return to pre-surgery HRQL was considered if the difference between scores at post-operative time points were not significantly different from baseline. A significance level of $p < 0.05$ was used throughout the study.

Results

Patient characteristics

Patient demographics and lifestyle habits are shown in Table 1. The mean age was 61 years old (20–92). Most patients were treated for endometrial cancer (70.6%) and more than a third had a BMI greater than 30 (37%).

Quality of life

FACT-G subscale scores and overall FACT-G scores are tabulated in Table 2. Overall FACT-G scores are graphically represented by box plots in Fig. 1.

Table 3 shows changes in questionnaire scores, with Wilcoxon signed-rank test results, and minimally important difference (MID) values established for the questionnaires where applicable [21].

Overall HRQL, as measured by the total FACT-G score, decreased at 1 week follow-up ($p < 0.0001$, MID = −6.5) and returned to baseline by 3 weeks after surgery ($p = 0.1$, MID = −1.2). In the long-term 12-months after surgery, overall HRQL was significantly higher than HRQL measured before surgery ($p = 0.0005$, MID = 8.0).

The four domains of the FACT-G questionnaire were further evaluated separately. **Physical well-being** decreased at 1 week after surgery ($p < 0.0001$, MID = −5.0) and returned to baseline at 3-month follow-up ($p = 0.3$, MID = −0.6). By the recommended MID criteria, however, physical well-being returned close to baseline by the third week after surgery (MID = −1.5). **Functional well-being** decreased after surgery and returned to baseline at 3-month follow-up ($p = 0.4$, MID = 0.1). Mean **social well-being** increased from baseline after surgery though it was not significant and returned closer to baseline by 3 months after surgery. Changes in social well-being did not meet the minimally important difference values. **Emotional well-being** was found to increase significantly by 1 week after surgery ($p < 0.0001$, MID = 3.0) and remained significantly higher than baseline.

Body Image

Means and 95% confidence intervals of Body Image Scale scores are tabulated in Table 2 and box plots are illustrated in Fig. 2, underlining the median and outliers. Wilcoxon signed-rank test results are shown in Table 3. Patient-rated body image was found to decrease by the first week after surgery ($p = 0.002$) and return closer to baseline by the third week ($p = 0.9$).

One expected advantage of robotic surgery is the minimally invasive approach resulting in small scars. The specific question concerning scars from the Body Image Scale [22] revealed (Fig. 3) that at 1 week after surgery, 62% were "not at all dissatisfied with the appearance of their scar", and this increased to 82% by 3 weeks.

Kruskal–Wallis analysis of variance was used to evaluate the impact of age and marital status on HRQL. Age was dichotomized into two

Table 1
Patient demographics and lifestyle habits.

	N = 211	(%)
Diagnosis		
Endometrial cancer	**149**	**(70.6)**
Ovarian cancer	**43**	**(20.4)**
Cervical cancer	**19**	**(9.0)**
BMI		
<30	**132**	**(62.6)**
30.0–39.9	**57**	**(27.0)**
≥40	**20**	**(9.5)**
No answer	**2**	**(0.9)**
Ethnicity		
White/Caucasian/Canadian	**160**	**(75.8)**
Other	**27**	**(12.8)**
No answer	**24**	**(11.4)**
Highest education level*		
Elementary	**19**	**(9.0)**
Secondary	**63**	**(29.9)**
College/University	**120**	**(56.9)**
No answer	**9**	**(4.3)**
Language†		
English	**167**	**(79.1)**
French	**152**	**(72.0)**
Other language(s)	**82**	**(38.9)**
No answer	**12**	**(5.7)**
Work status		
Working	**92**	**(43.6)**
Not working or retired	**116**	**(55.0)**
No answer	**3**	**(1.4)**
Current relationship status		
Married	**123**	**(58.3)**
Cohabitating	**15**	**(7.1)**
Dating	**6**	**(2.8)**
Single, widowed, divorced	**61**	**(28.9)**
No answer	**6**	**(2.8)**
Children		
Yes	**167**	**(79.1)**
No	**15**	**(7.1)**
No answer	**29**	**(13.7)**
Alcohol drinking habits		
None	**72**	**(34.1)**
Occasionally	**47**	**(22.3)**
1–3/week	**41**	**(19.4)**
≥4/week	**40**	**(19.)**
No answer	**11**	**(5.2)**
Cigarette consumption		
None	**184**	**(87.2)**
Very few or rarely	**1**	**(0.5)**
3–5/day	**2**	**(0.9)**
6–10/day	**6**	**(2.8)**
>10/day	**9**	**(4.3)**
No answer	**9**	**(4.3)**
Exercising habits		
Never	**76**	**(36.0)**
≤5 times per month	**5**	**(2.4)**
1–4 times per week	**76**	**(36.0)**
≥5 times per week	**39**	**(18.5)**
No answer	**15**	**(7.1)**

* Subjects who only reported years of schooling were categorized accordingly.
† Knowledge of language includes any or all of the following: speaking, reading, and/or writing.

Table 2
Mean and 95% confidence interval values for FACT-G, FACT-G subscales, and Body Image Scale.

Questionnaire	N	Mean (95% confidence interval)
Physical Well-Being, FACT-G		
Baseline	193	23.9 (23.2–24.7)
1 week after surgery	121	18.9 (17.9–20.0)
3 weeks after surgery	92	22.4 (21.6–23.3)
3 months after surgery	114	23.3 (22.4–24.3)
6 months after surgery	81	23.8 (22.8–24.8)
12 months after surgery	67	25.3 (24.5–26.1)
Social Well-Being, FACT-G		
Baseline	184	22.9 (22.1–23.7)
1 week after surgery	116	23.7 (22.9–24.5)
3 weeks after surgery	85	23.8 (22.7–24.9)
3 months after surgery	111	22.3 (21.2–23.5)
6 months after surgery	81	22.2 (20.8–23.5)
12 months after surgery	68	23.1 (22.0–24.3)
Emotional Well-Being, FACT-G		
Baseline	185	15.2 (14.5–16.0)
1 week after surgery	114	18.2 (17.3–19.1)
3 weeks after surgery	85	18.4 (17.5–19.3)
3 months after surgery	108	19.6 (18.9–20.3)
6 months after surgery	77	18.1 (17.1–19.2)
12 months after surgery	63	19.2 (17.9–20.4)
Functional Well-Being, FACT-G		
Baseline	191	19.9 (19.0–20.8)
1 week after surgery	119	15.1 (14.0–16.3)
3 weeks after surgery	89	16.2 (14.9–17.6)
3 months after surgery	115	20.0 (18.9–21.1)
6 months after surgery	82	19.8 (18.3–21.2)
12 months after surgery	69	22.6 (21.4–23.8)
Overall HRQL, FACT-G		
Baseline	177	82.1 (79.8–84.4)
1 week after surgery	107	75.5 (72.4–78.6)
3 weeks after surgery	79	80.9 (77.6–84.2)
3 months after surgery	106	85.6 (82.8–88.5)
6 months after surgery	76	83.5 (79.9–87.1)
12 months after surgery	63	90.0 (86.6–93.5)
Body Image Scale		
Baseline	172	25.9 (25.0–26.8)
1 week after surgery	103	23.7 (22.4–25.1)
3 weeks after surgery	79	26.1 (25.0–27.3)
3 months after surgery	104	24.9 (23.8–26.0)
6 months after surgery	71	24.6 (23.1–26.0)
12 months after surgery	60	26.5 (25.3–27.7)

Note: Higher scores correspond to better HRQL and Body Image.

groups: below 70 years old and greater than or equal to 70. Patients younger than 70 displayed significantly higher emotional well-being ($p = 0.02$) and functional well-being ($p = 0.01$), while patients 70 years or older had higher body image ($p = 0.0001$). We chose 70 years of age as a clinical definition of elderly, though to mitigate the potential sample size bias, we repeated the analysis by dividing the sample into tertiles of age and found similar results with the highest age group reporting lower emotional and functional well-being, and the lowest age group reporting lower body image. We also repeated the analysis by splitting the sample at the median age, 62, and found significance only with body image ($p = 0.0001$), again with older patients reporting better body image.

We found a significant difference by marital status for social well-being ($p = 0.0001$), functional well-being ($p = 0.048$), and overall FACT-G score ($p = 0.025$), with single/divorced/widowed patients having the lowest scores. Body image scores were not influenced by marital status ($p = 0.6$). However, physical well-being ($p = 0.0002$) and body image ($p = 0.0001$) were significantly worse in patients who completed any form of adjuvant therapy, either chemotherapy (33% of patients) and/or radiation (28% of patients).

Discussion

The aim of this study was to prospectively characterize the HRQL outcomes following robotic surgery in patients with gynecologic cancers. Results showed a decrease in overall HRQL at 1 week after surgery, and a return to baseline by 3 weeks. The total FACT-G score was then broken down into its component subscales. The results for physical well-being depended on the test used, e.g. using the MID values, there was a return to baseline by 3 weeks after surgery but using the Wilcoxon signed-rank test, it returned to baseline by 3 months after surgery. This discrepancy may be due to the different methodologies of each test. Whereas the Wilcoxon signed-rank test evaluates the sign of the ranked score differences between time points, the MID

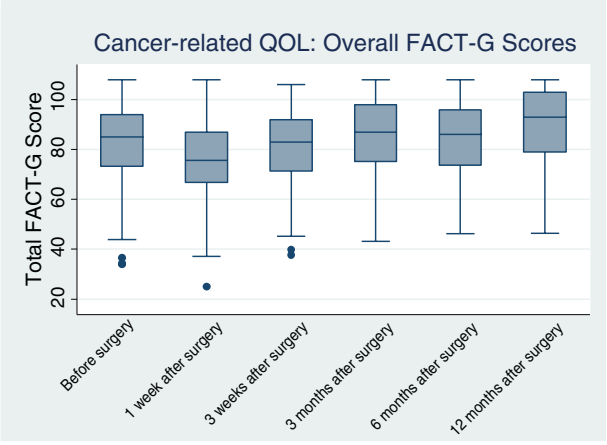

Fig. 1. Cancer-related HRQL before and after robotic surgery. Box and whisker plots of FACT-G scores over time. The middle bar represents the median. Outer edges of the box represent the 25th and 75th percentiles. Whiskers represent the lower and upper adjacent values. Dots represent outliers.

values were used as a reference point when comparing average scores between time points. The latter is therefore more sensitive to outlier scores. The time gap between the 3-week and 3-month evaluation makes it difficult to ascertain at which point within that time interval patients can be expected to recuperate physically and functionally. Adding an intermediate follow-up would be more appropriate for future studies. There was a non-significant increase in mean social well-being in the short term after surgery. The minimal impact on social well-being could be related to the additional social support usually provided to cancer patients [23,24] in the intermediate term after surgery. The social well-being subscale evaluates how close individuals feel with their friends, family, and partner, which may be expected to be higher during times of illness. Social support has also been associated with a decrease in depressive symptoms in cancer patients [25], which may account in part for the improvement in emotional well-being after surgery. This improvement may also be attributed to an emotional distress at baseline after being diagnosed with cancer, as well as a heightened sense of emotional relief following surgery, perhaps encompassing the minimal impact of the surgery or the rapid rate of recovery.

The progression of HRQL and FACT-G domains following surgery in our study reminds us of what has been reported previously [16,17] in laparoscopy trials. In the multicenter Gynecology Oncology Group study LAP2 [16] comparing laparoscopy to laparotomy, the FACT-G was used to assess overall HRQL. Although the authors did not report data on the FACT-G subscales or the significance of changes in postoperative HRQL relative to baseline, their laparoscopy data seem comparable to ours [16]. Using a different validated instrument, the generic Short-Form SF-36, they also reported a decrease in mean physical functioning scores 1 week after surgery, gradually returning to baseline by 6 months after surgery [16]. Mean body image scores increased by one week after surgery in both their laparoscopy and laparotomy

Table 3
Minimally important differences and Wilcoxon Signed-Rank Test results between HRQL scores at different post-operative time points relative to baseline.

Questionnaire	z-score	*p*-value	difference between mean score and baseline	*MID*
Physical Well-Being, FACT-G				
1 week after surgery*	7.841	<0.0001	−5.0	Y
3 weeks after surgery*	4.125	<0.0001	−1.5	N
3 months after surgery	1.079	0.2807	−0.6	N
6 months after surgery**	1.694	0.0902	−0.2	N
12 months after surgery	−1.083	0.2789	1.3	N
Social Well-Being, FACT-G				
1 week after surgery	−1.199	0.2303	0.8	N
3 weeks after surgery	−0.803	0.4221	0.9	N
3 months after surgery	1.185	0.2361	−0.5	N
6 months after surgery	0.542	0.5877	−0.7	N
12 months after surgery	0.848	0.3967	0.3	N
Emotional Well-Being, FACT-G				
1 week after surgery*	−6.591	<0.0001	3.0	Y
3 weeks after surgery*	−5.227	<0.0001	3.2	Y
3 months after surgery*	−7.637	<0.0001	4.4	Y
6 months after surgery*	−5.175	<0.0001	2.9	Y
12 months after surgery*	−5.076	<0.0001	3.9	Y
Functional Well-Being, FACT-G				
1 week after surgery*	6.974	<0.0001	−4.7	Y
3 weeks after surgery*	5.161	<0.0001	−3.7	Y
3 months after surgery	0.912	0.3616	0.1	N
6 months after surgery	0.998	0.3184	−0.1	N
12 months after surgery*	−2.830	0.0047	2.7	Y
Overall HRQL, FACT-G				
1 week after surgery*	4.791	<0.0001	−6.5	Y
3 weeks after surgery**	1.649	0.0990	−1.2	N
3 months after surgery**	−1.754	0.0794	3.6	Y
6 months after surgery	−0.383	0.7016	1.4	N
12 months after surgery*	−3.495	0.0005	8.0	Y
BIS				
1 week after surgery*	3.094	0.0020		n/a
3 weeks after surgery	−0.109	0.9135		n/a
3 months after surgery	1.512	0.1304		n/a
6 months after surgery	0.620	0.5352		n/a
12 months after surgery	−1.502	0.1331		n/a

All postoperative questionnaire scores were compared to baseline scores using non-parametric Wilcoxon Signed-Rank Test. HRQL was considered to have returned to baseline if differences with baseline were insignificant.
Note: Similar significance results were obtained by the Mann–Whitney–Wilcoxon Rank Sum Test.
MID: Minimally important difference. A minimally important difference (Y) was reached if the difference in mean scores at baseline and at postoperative time points was greater than or equal to the referenced MID.
* Significance at $p < 0.05$.

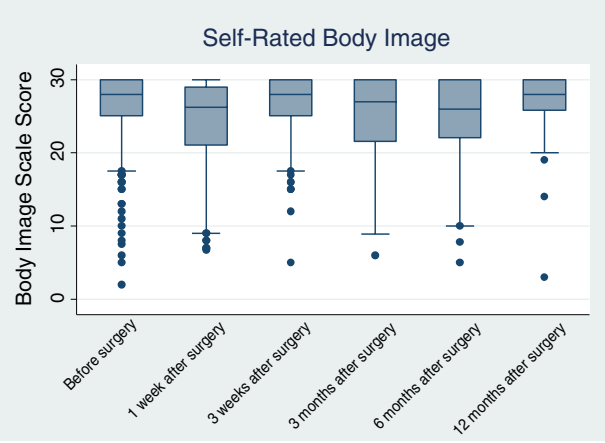

Fig. 2. Self-rated body image before and after robotic surgery. Box and whisker plots of body image scores over time. Body Image Scale (BIS) scores were subtracted from 30 so that higher scores correspond to better body image. The middle bar represents the median. Outer edges of the box represent the 25th and 75th percentiles. Whiskers represent the lower and upper adjacent values. Dots represent outliers.

groups [16] though the use of a different questionnaire to assess body image again makes it difficult to compare with our data.

Three diagnoses were included in this study: endometrial, ovarian, and cervical cancer. We performed Kruskal Wallis analysis of variance to test any differences between the three groups at baseline and found a significant difference only for functional well-being with median baseline scores of 21, 21.5, and 24 for endometrial, ovarian, and cervical cancer patients, respectively ($p = 0.0261$). Compared to studies that have assessed HRQL following laparoscopy [16–18], we did not exclude patients at high risk, such as those with advanced stage cancer, poor performance status, and/or other major medical conditions: 95% of all operable patients with endometrial cancer, uterine sarcoma, or cervical cancer underwent robotic surgery in our center. Over a third of the patients (38%) in our study were at higher risk for complications or poor quality of life, either because of age (22% were 70 years old or older) and/or obesity (37% obese: 16% with BMI between 30.0 and 34.9; 11% with BMI between 35.0 and 39.9 kg/m^2, and 10% with BMI ≥ 40). The feasibility of robotics in the elderly and obese populations reflects the findings of our previous studies [20,26].

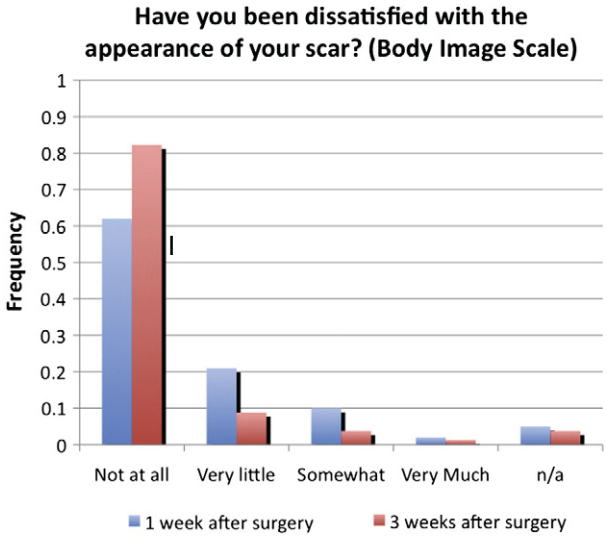

Fig. 3. Patient-rated satisfaction with scarring after robotic surgery.

When we dichotomized our sample at 70 years of age, older patients were found to have lower emotional and functional well-being though higher body image. Dichotomized at the median age of 62, only body image was significantly different, with older patients reporting better body image. Others have also found older age to be associated with higher body image [22] and lower functional wellbeing [3] in cancer patients. In contrast, some have reported emotional wellbeing [3] and depressive symptoms [25] to be worse in younger patients. Gil et al. (2007) [24] looked for factors that influence baseline HRQL in patients planned to undergo gynecologic oncology surgery. The group found age to be positively correlated with the physical and emotional wellbeing domains of the FACT-G questionnaire. In contrast to our findings that marital status influences the FACT-G scores, they found no differences in pre-operative FACT-G scores between women who were married and not married though their analysis was not intended to evaluate the course of treatment [24]. We noted a significant difference in overall FACT-G scores as well as social and functional well-being by marital status, with single/divorced/widowed women having the lowest scores. These same domains have similarly been shown to be significantly lower in patients who have help no at home [3].

One limitation with our study is the missing response data and the decrease in questionnaire response over time, especially at 3 weeks after surgery as shown in Table 2. Based on questionnaire guidelines, we excluded questionnaires with too many missing responses. In addition, subjects who had not completed a valid baseline questionnaire were excluded to ensure that every patient at follow-up was her own control. To evaluate this potential bias, we re-calculated all our data by including the invalid questionnaires. Mean and median scores were graphically compared and showed similar results in FACT-G subscales, overall FACT-G, and Body Image Scale scores over time.

While a decrease in questionnaire response is usually observed over time in this type of study, we evaluated the association between HRQL with completion of questionnaires at 12 months. Patients who completed the 12-month questionnaire had an overall worse body image ($p = 0.0047$), but better physical well-being ($p = 0.040$), emotional well-being ($p = 0.011$), functional well-being ($p = 0.0079$), and total FACT-G score ($p = 0.016$). This may be explained by the fact that patients who completed the 12-month follow-up were also more likely to have completed the 3-month (Odds Ratio = 2.2, $p = 0.001$) and 6-month (Odds Ratio = 2.9, $p < 0.001$) follow-up questionnaires, which were associated with a higher HRQL. We therefore repeated the analysis by looking at the HRQL at 3-months and 6-months after surgery and comparing HRQL scores in participants who completed the 12-month questionnaire to those who did not. We found no significant difference at either follow-up. We then used Pearson's chi-squared test and simple logistic regression in order to characterize the cohort that responded at 12-months compared to the one with missing responses. Ovarian cancer patients were less likely to complete the 12-month follow-up questionnaires in comparison to endometrial cancer patients (Odds Ratio = 0.7, $p = 0.048$). Whether or not participants completed the 12-month questionnaire was not significantly affected by age (less than versus greater than 70 years old), marital status, or whether patients had received chemotherapy and/or radiotherapy at any point during the course of the study.

Results from this study demonstrated a decrease in HRQL and body image 1 week after surgery. Between 1 week and 3 weeks, HRQL and body image returned close to baseline, providing evidence that robotic surgery for the treatment of gynecologic cancers results in a rapid return to pre-surgery quality of life.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ygyno.2014.04.052.

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Conflict of interest statement

Walter Gotlieb and Susie Lau obtained partial travel support for proctoring robotic surgery.

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Appendix II. Publication on patient-rated pain and satisfaction following robotic surgery

Source: Abitbol, J., et al., *Evaluating postoperative pain and satisfaction among women treated by robotic surgery for gynecologic cancer.* Gynecology and Pelvic Medicine, 2019. **2**.

Original Article

Evaluating postoperative pain and satisfaction among women treated by robotic surgery for gynecologic cancer

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Background: Postoperative pain is frequently undermanaged in spite of advancements in pharmacologic and non-pharmacologic therapies for pain. Minimally invasive surgery is a promising surgical technique associated with reduced postoperative pain. The current study evaluates satisfaction following robotically-assisted surgery and its impact on short-term and long-term patient-rated pain.

Methods: Prospective study on all consecutive patients (n=367) undergoing robotic surgery in the division of gynecologic oncology from December 2009 to December 2012. Patients were invited to complete questionnaires before surgery and at 1 week, 3 weeks, 3, 6, and 12 months after surgery. The brief pain inventory (BPI) was used to evaluate patient-rated pain severity, interference of pain with daily life, and treatments taken for pain.

Results: After controlling for preoperative factors, both pain severity and pain interference with daily life returned to pre-surgery levels within three weeks of surgery. Patients using opioids for pain relief remained very low, varying from 2% at baseline to 11% during the first week, returning to 5% by the third week. By the first week post-surgery, the vast majority of patients expressed high satisfaction with an average score of 91%.

Conclusions: Robotic surgery for the treatment of gynecologic cancers results in a minimal impact on short- and long-term patient-rated pain. The majority of patients (~90%) did not require the use of opioids and were very satisfied with their surgery.

Keywords: Robotic surgery; pain; satisfaction; quality of life

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Introduction

Pain has been described as among the worst and most prevalent symptoms of cancer and its treatments (1-4). Pain has also been associated with longer recovery time (5), higher postoperative readmission rates (6), and interference with patients' daily activities, wellbeing, and enjoyment of life (3,7,8), as well as their social surroundings including family and caregivers (3,8).

Pain is a subjective feeling that may result from the activation of nociceptors by noxious stimuli such as tissue damage (e.g., surgery), and is often followed by hyperalgesia (a heightened response to noxious stimuli) and/or allodynia (a feeling of pain induced by normally

non-noxious stimuli) (9). Acute pain may also have the potential to become chronic (10), sometimes persisting long after surgery and adding to the long-term morbidity and interference with daily life (9,11-15).

In spite of advancements in the field of pain management and the availability of tools to alleviate this distressing symptom, pain continues to be undermanaged in cancer patients (3,4,7,8,16,17). In many of these individuals, pain intensity is often moderate to severe (1,3,4,7).

In gynecology and gynecologic oncology, the introduction of laparoscopy has significantly reduced postoperative pain in patients in whom the technique is feasible (18,19). Robotically-assisted surgery has facilitated the practice of minimally invasive surgery, allowing an increasing number of patients to benefit from the procedure. Some groups have shown similar benefits for robotic surgery with respect to postoperative pain reduction (20,21), though studies have mostly focused on the immediate postoperative period without assessing preoperative pain or the long-term impact of surgery.

Results from our pilot study demonstrated that two thirds of patients reported feeling no pain by the first postoperative visit after robotic surgery (at three to four weeks) for the treatment of endometrial cancer (22). Limitations of our pilot study included the lack of a preoperative baseline questionnaire and the use of a questionnaire that had not been validated (22). In the current study, we address these limitations to better describe the short- and long-term impact of robotic surgery on pain and its interference with daily life in women treated for gynecologic cancer. The secondary objective is to describe patients' satisfaction with their surgery.

Methods

All consecutive patients planning to undergo robotic surgery for the treatment of a suspected gynecologic cancer between December 2009 and December 2012 were invited to participate in this prospective study (23). During the preoperative clinic visit, participants were given an informed consent form and a questionnaire assessing baseline self-reported outcomes including levels of pain. Postoperative questionnaires were handed or mailed to participants in the short term (one week and three weeks) and long term (three, six, and twelve months) after surgery. Patients were excluded if their surgery was converted to laparotomy (n=14) or if they were re-operated by laparotomy prior to being discharged from the hospital (n=1).

Pain was evaluated using the brief pain inventory (BPI) (24,25). This validated questionnaire asks if participants feel pain "other than everyday kinds of pain" and if they are taking any treatments for their pain. Treatments for pain were categorized as no treatments, NSAIDs or Acetaminophen, opioids or opioid-containing medications (e.g., codeine, morphine, acetaminophen-codeine combination, etc.), physical therapy (e.g., massage, physiotherapy, etc.), alternative medicine (naturopathy, homeopathy, acupuncture), and/or other. The BPI asks participants to rate the pain they felt in the last 24 hours at their worst, least, on the average, and in that moment on a scale of 0 to 10 from no pain to worst imaginable pain. The four answers are averaged to give a pain severity score (24), and can be reported as mild (scores 1–4), moderate (scores 5–6), or severe (scores 7–10) (26). The BPI assesses how pain interfered, on a scale of 0 to 10, with different aspects of life: general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life. Scores are averaged to give an overall pain interference score (24). Based on the guidelines (24), pain severity scores were only calculated if all four component questions were answered, and pain interference scores were only calculated if more than half of the questions were answered. To remain conservative, if participants circled more than one answer or were between two values on any of the numerical rating scales, only the worst score was counted.

Included in the postoperative questionnaires were a series of questions related to patients' satisfaction with the surgery. Patients were asked to rate their satisfaction with their recovery time as well as with their surgery overall on a scale of 0 to 10 from not at all to completely satisfied. In addition, participants were asked to rate, on a scale of 1 to 4 from not at all to very much, to what extent the surgery met their expectations and whether they would recommend the surgery to someone in similar circumstances.

The study was approved by the Jewish General Hospital's Research Ethics Office (protocol #09-123) and informed consent was obtained from all patients.

Statistical analysis

Responses to questionnaires were recorded on Microsoft Excel 2003, statistical analysis was performed using STATA 13 (StataCorp), and figures were produced in Excel. Pain outcomes were regressed against the timing of the questionnaires using univariate logistic and linear models

Table 1 Patient demographic and lifestyle habits

Characters	n (N=367) (%)
Suspected or confirmed tumor site	
Uterus	245 (67%)
Ovaries, fallopian tubes, peritoneum	79 (22%)
Cervix	43 (12%)
BMI	
<30	210 (57%)
30.0–39.9	105 (29%)
≥40	52 (14%)
Highest education level*	
Elementary	27 (7%)
Secondary	112 (31%)
College/university	205 (56%)
No answer	23 (6%)
Current relationship status	
Married	198 (54%)
Cohabitating	26 (7%)
Dating	12 (3%)
Single, widowed, divorced	118 (32%)
No answer	13 (4%)
Children	
Yes	287 (78%)
No	27 (7%)
No answer	53 (14%)
Alcohol drinking habits	
None	154 (42%)
Occasionally	69 (19%)
1–3/week	57 (16%)
≥4/week	62 (17%)
No answer	25 (7%)
Cigarette consumption	
None	316 (86%)
Very few or rarely	1 (0%)
1–5/day	7 (2%)
6–10/day	8 (2%)
>10/day	14 (4%)
No answer	21 (6%)
Exercising habits	
Never	135 (37%)
≤5 times per month	8 (2%)
1–4 times per week	124 (34%)
≥5 times per week	68 (19%)
No answer	32 (9%)

*, subjects who only reported years of schooling were categorized accordingly.

as well as stepwise multiple logistic and linear regression models to control for the timing of the questionnaires, primary suspected tumor site, age (<70 *vs.* ≥70 years old), body mass index (BMI), marital status, and highest education level attained. For logistic regressions, odds ratios were shown as OR [95% confidence interval (CI)], and for linear regressions, beta coefficients were shown as β (95% CI). The Wilcoxon Sign Rank test and the McNemar test were used, where appropriate, to compare postoperative pain responses to baseline scores. Statistical significance was defined as $P<0.05$ throughout the study.

Results

Baseline characteristics

Patient demographics and lifestyle habits are shown in *Table 1*. Two thirds of patients (n=245, 67%) were treated for a suspected endometrial cancer on endometrial biopsy. Beginning one year after the start of our robotics program, patients with an ovarian tumor were carefully selected for robotic surgery, representing 22% of subjects in the current analysis. One hundred fifty-seven patients (43%) were obese. The mean age was 61 years old (±13 years) and 23% were elderly (70 years or older). More than half of patients (56%) reported a college or university degree. Most patients reported being in a relationship (64%), and the majority (78%) had children.

General pain & treatments for pain

The first item on the BPI asks whether patients have any pain other than "everyday kinds of pain". More patients reported pain at the one-week follow-up compared to

baseline (42% at baseline *vs.* 58% by the first week, P=0.002), and this returned to baseline within three weeks after surgery (40%, P=0.7), and remained statistically non-significant for the remaining follow-ups.

Whether or not patients reported pain was regressed against the time since surgery in a univariate analysis. At the one-week follow-up, patients were close to twice as likely to report pain [OR =1.9 (1.3–2.8), P=0.002]. By the three-week follow-up, the likelihood of patients reporting pain had already returned to baseline [OR =0.9 (0.6–1.4), P=0.6], and this was sustained until one year after surgery. As shown in *Table 2*, similar results were obtained after controlling for demographic and clinical factors (diagnosis, elderly status, obesity, educational status, and marital status): the likelihood of reporting pain increased by the first week [OR =2.18 (1.54–3.08), P<0.001] and returned to baseline by the second follow-up three weeks after surgery (P=0.81).

Patients who had more than a high school education were less likely to report pain other than everyday kinds of pain [OR =0.61 (0.45–0.82), P=0.001] and patients undergoing surgery for the diagnosis of cervical cancer were more likely to do so than those with a diagnosis of endometrial cancer [OR =1.92 (1.25–2.95), P=0.003]. The remaining factors in the model were not significant.

When asked whether or not they were taking treatments for their pain, more patients reported taking pain medications at their one-week follow up compared to baseline (73% at one week compared to 31% at baseline, P<0.0001), again returning to baseline by the three-week follow-up (33%, P=0.3).

In the univariate analysis, the use of treatments for pain was associated with the one-week follow-up [OR =5.92 (4.12–8.50), P<0.001], returning to baseline within three weeks of surgery [OR =1.1 (0.6–1.8), P=0.8]. Similar results were obtained after controlling for the aforementioned baseline variables, and none were significantly associated with whether treatments were taken for pain.

Figure 1 illustrates the types of treatments patients reported taking for pain across time points. Treatments were divided into none, NSAIDs and/or acetaminophen, and opioids. Before surgery, 69% of patients were not taking treatments for pain, 29% were using NSAIDs, and 2% took opioid-containing medications. By one week, these changed to 27%, 70%, and 11%, respectively, and returned close to baseline by three weeks: 67%, 30%, and 5%, respectively. Percentages sum up to over 100% due to overlap between those taking both NSAIDs and opioid-containing medications. Few patients (<4% at each time point) also described employing physical therapy, alternative medicine, or other means of pain management.

Pain severity & pain interference

Pain severity and interference were higher at the one-week follow-up [β =0.56 (0.23–0.90), P=0.001, and β =1.27 (0.90–1.65), P<0.001, respectively] but returned to baseline by three weeks [β =–0.2 (–0.7–0.3), P=0.21, and β =–0.3 (–0.8–0.3), P=0.65, respectively].

The stepwise linear regression analyses for pain severity and interference are tabulated in *Table 2*. Similar results were obtained after controlling for baseline factors: higher pain severity and interference were significantly associated with the one-week follow-up (P=0.001 for pain severity; P<0.001 for pain interference), returning to baseline by the three-week follow-up. Educational status was also a significant factor, with higher education associated with less pain severity (P<0.001) and interference (P=0.003). Patients treated for a cervical cancer were also associated with higher pain severity scores (P=0.009) while patients with morbid obesity (BMI greater than or equal to 40 kg/m^2) were associated with greater pain interference (P=0.04).

Figure 2 shows the change in mean pain severity scores over time as well as the proportions of patients reporting the different levels of pain severity (no pain, mild, moderate, or severe pain). Pain severity and pain interference scores at each postoperative time point were compared to baseline using the Wilcoxon signed rank test. Both pain severity and interference increased by the one-week follow-up (P=0.02 and P=0.0001, respectively) but returned to baseline within three weeks (P=0.6 and P=0.2).

Pain severity and pain interference were found to be strongly correlated (r=0.67, P<0.001).

Satisfaction with surgery

Patients' overall satisfaction with their surgery at one week and at three weeks after surgery is illustrated in *Figure 3*. By the first week, the mean overall satisfaction score was 9.1 out of 10 (median and modal score of 10 or completely satisfied) and patients reported being satisfied with their recovery time following their surgery (mean score of 8.3; median of 9; mode of 10). By week three, the mean scores were 9.5 and 8.9, respectively, and 95% of respondents rated their overall satisfaction at 8 or higher.

Regarding whether the surgery met their expectations by the one-week follow-up, the mean score was 3.7 out

Table 2 Step-wise multiple regression models of patient-reported pain before and after robotic surgery

Predictor variables	Pain other than everyday pain*			Treatments for pain*			Pain severity†			Pain interference†		
	OR (95% CI)	SE	P value	OR (95% CI)	SE	P value	β (95% CI)	SE	P value	β (95% CI)	SE	P value
Visit												
Before surgery												
1 week after surgery	2.18 (1.54–3.08)[&]	0.39[&]	<0.001[&]	5.92 (4.12–8.50)[&]	1.09[&]	<0.001[&]	0.56 (0.23–0.90)[&]	0.17[&]	0.001[&]	1.27 (0.90–1.65)[&]	0.19[&]	<0.001[&]
3 weeks after surgery			0.81			0.69			0.21			0.65
3 months after surgery	0.77 (0.54–1.09)	0.14	0.14			0.27			0.75			0.30
6 months after surgery			0.69			0.44			0.99			0.90
12 months after surgery	0.66 (0.41–1.06)	0.16	0.086			0.80			0.73			0.86
Diagnosis												
Endometrial												
Ovarian			0.85			0.97			0.41			0.42
Cervical	1.92 (1.25–2.95)[&]	0.42[&]	0.003[&]			0.18	0.57 (0.15–1.00)[&]	0.22[&]	0.009[&]	0.39 (–0.10–0.88)	0.25	0.12
Age (years)												
<70												
≥70	0.72 (0.50–1.03)	0.13	0.071			0.80			0.78			0.50
BMI												
<30.0												
30.0–39.9			0.34			0.61			0.69			0.16
≥40			0.57			0.41	0.35 (–0.075–0.78)	0.22	0.11	0.53 (0.038–1.02)[&]	0.25[&]	0.035[&]
Marital status												
Single/divorced/widowed												
Married/dating/cohabitating	0.76 (0.56–1.04)	0.12	0.083			0.60			0.58			0.27
Education												
Up to high school												
More than high school	0.61 (0.45–0.82)[&]	0.092[&]	0.001[&]	0.80 (0.59–1.08)	0.12	0.15	–0.84 (–1.13––0.55)[&]	0.15[&]	<0.001[&]	–0.51 (–0.83––0.18)[&]	0.17[&]	0.003[&]

*, multiple logistic regression model showing odds ratio (OR) with 95% confidence interval (CI) and standard error (SE); †, multiple linear regression model showing beta coefficient (β) with 95% confidence interval (CI) and standard error (SE); &, significant results (P<0.05) are presented.

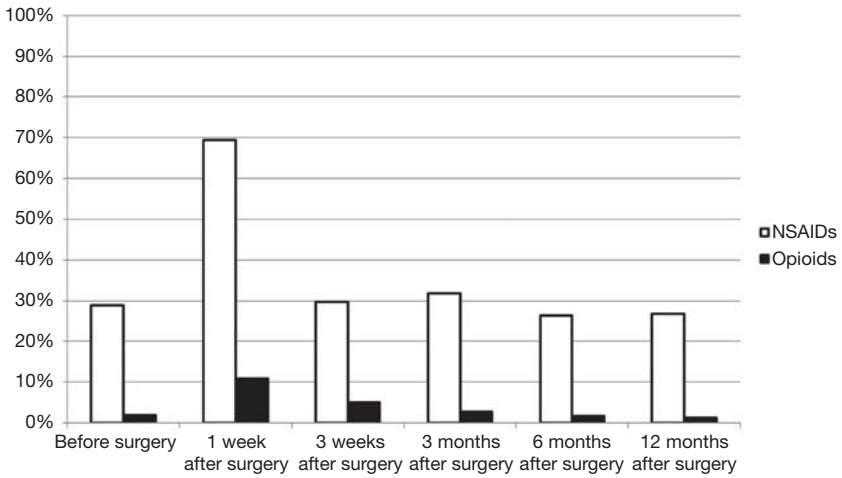

Figure 1 Treatments for pain over time following robotic surgery.

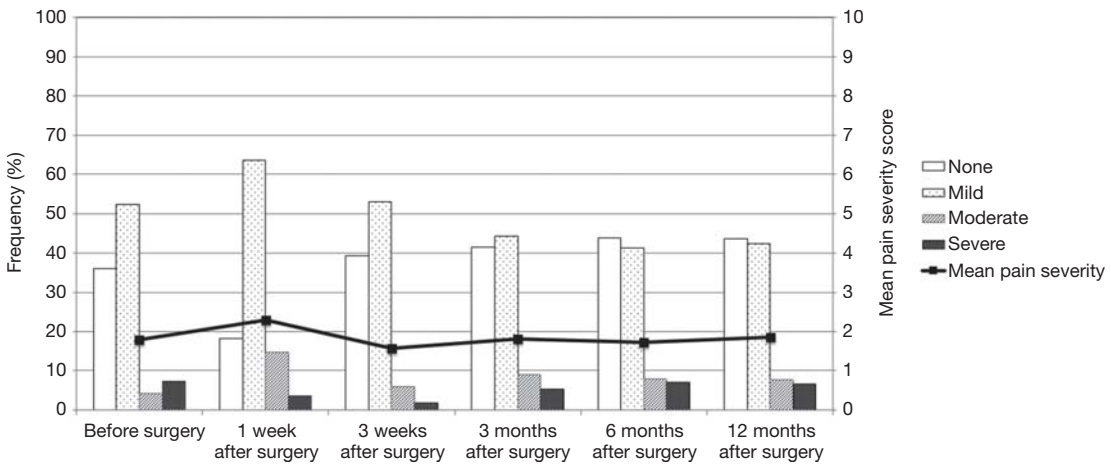

Figure 2 Mean pain severity and pain severity rating following robotic surgery. Pain severity scores from the brief pain inventory (BPI) were grouped as follows: 0 (none), 1–4 (mild), 5–6 (moderate), 7–10 (severe). *, P<0.05 (mean pain severity score compared to baseline).

of 4 (median and mode of 4 or very much). Most patients would also recommend the surgery to someone in similar circumstances with a mean score of 3.9 (median and mode of 4).

Following the first week, the median scores on the above dimensions of satisfaction were the maximum value (i.e., 10 or 4 depending on the question) for all subsequent follow-ups.

Sensitivity analysis

In order to control for variability in surgical procedures and the presence of malignancy on final pathology, the analysis was repeated after removing patients with no cancer (n=66, 18%) and/or those who did not have a hysterectomy (n=35, 10%). Similar results were obtained with pain scores returning to baseline by three weeks after surgery. Of note is that across the multivariable regression models, a diagnosis of ovarian cancer became significantly associated with increased pain scores.

Discussion

Our findings show that pain outcomes tended to increase at the first follow-up one week after robotic surgery but returned to baseline within three weeks of surgery. Even in

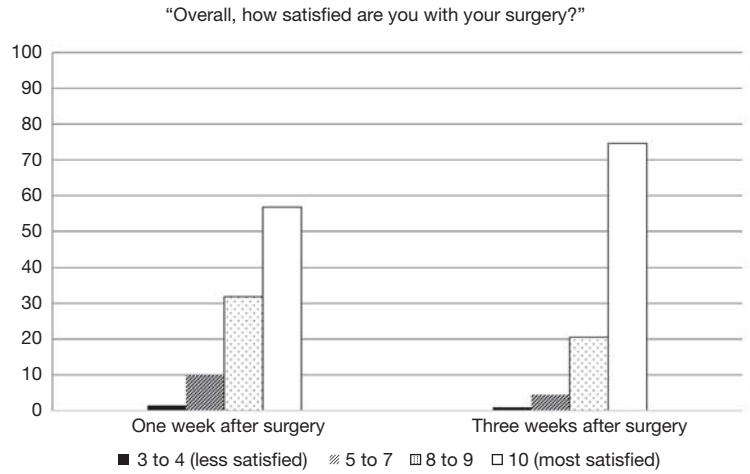

Figure 3 Overall satisfaction with surgery at one week and three weeks postoperatively.

the short term after surgery, the majority of patients were satisfied with the surgery, and did not require narcotics (89%); NSAIDs and/or acetaminophen seemed sufficient for pain control. This is consistent with our previous publication on a matched historical cohort of patients treated for endometrial cancer by laparotomy, showing that patients who underwent robotic surgery used less analgesics, including significantly less opioids, and were much less likely to be given patient-controlled analgesia in the immediate postoperative period (27).

The landmark trial LAP2 compared outcomes between laparotomy and laparoscopy for the staging of early endometrial cancer (18). The study set a precedent for laparoscopy as a less invasive approach to reduce postoperative pain, as measured using items from the BPI, with pain severity measured using worst and least pain (18). While differences in pain scores between treatment arms were compared for statistical significance, pain scores over time were not compared to baseline to measure the impact of surgery over time. Still, the magnitude of the changes in pain scores is noteworthy. We recalculated pain severity and interference scores among patients who were diagnosed with a confirmed endometrial cancer, using the same methodology as in the LAP2 study. Caution should be taken in interpreting these differences in pain scores across two different studies and study populations, however the robotic cohort presented in this manuscript exhibited an increase in pain severity of 24% from baseline to the one-week follow-up, and, by three weeks, pain severity scores were already less than pre-surgery levels (13% decrease). In contrast, pain severity more than doubled in the laparoscopy and laparotomy arms in LAP2's intention-to-treat analysis (150% increase from baseline to one week after surgery), and were still higher at three weeks (close to 50% increase from baseline) (18). Similarly so for pain interference, our robotic cohort noted a 58% increase in pain interference from baseline to one week after surgery, reaching lower than pre-surgery levels by three weeks (6% decrease). In the LAP2 cohorts, those assigned to laparoscopy and laparotomy reported an over 200% increase in pain interference by one week after surgery, and by three weeks, pain interference scores were still over double pre-surgery levels (18).

Using the SF-36 bodily pain subscale, another study indicated worse mean bodily pain scores by the six-week follow-up in comparison to baseline in both the laparotomy and laparoscopy groups, though these were not compared to baseline for statistical significance (28). In a study combining both benign and malignant gynecologic cases (20), and in a study on benign gynecologic cases only (29), no significant differences in pain scores were observed between laparoscopy and robotic surgery.

In our sample, patients with more than a high school education were significantly less likely to report pain other than everyday kinds of pain (P=0.001) and were associated with significantly less pain severity (P<0.001) and interference with daily life (P=0.003). van den Beuken-van Everdingen *et al.* [2007] reported on the prevalence, severity, and adequacy of treatment for pain among patients with cancer (4). In accordance with our findings, age and marital status were not significantly associated with the prevalence of pain, while patients with lower education

levels were associated with a higher risk of pain (4).

BMI was not significantly associated with patients' reporting of pain, use of treatments for pain, or pain severity. This supports findings from our pilot study where we reported no impact of BMI on analgesic use (22). However, in the current study, a BMI of 40 kg/m^2 or higher was associated with greater interference of pain with daily life. Our pilot study also demonstrated a significant impact of age on the reporting of pain after surgery with a greater proportion of younger patients reporting no pain (22). With the introduction of a baseline questionnaire in the current study, we found that elderly status was not significantly associated with any of the pain outcomes. Additionally, as in the current study, participants in our pilot analysis also reported high levels of satisfaction with the surgery (22).

Limitations of the current study include incomplete as well as missing questionnaires, a challenge of many survey-based studies (*Table S1*). While only few patients who completed the pain questionnaires did not provide valid assessments, the pain severity and interference analyses were repeated without excluding patients with incomplete data, and this yielded similar results. Moreover, while a validated and reliable instrument was used for the pain assessment, the satisfaction survey was not a validated questionnaire and respondents' satisfaction could have been influenced by other aspects of their care apart from the robotic surgery. However, while capturing the patient experience has its challenges (30), we included the questions to generate feedback and to incorporate broader measures of the quality of surgical care from the patients' perspectives. In addition, the current study focuses on patient-reported outcomes following robotic surgery; patients treated via laparotomy or laparoscopy were not included. At the time robotics was being rolled out in our division, up to 15% of all hysterectomies for a gynecologic cancer were done by laparoscopy (manuscript in submission, January 2019). Since then, rates of minimally invasive surgery reached over 90% due to the use of the robotics platform (manuscript in submission, January 2019). Another limitation is that this study was limited to a single tertiary hospital in Canada and some have reported on differences in patient-reported pain and pain management across different countries as well as ethnicities (31,32). For example, in comparison to Australian patients evaluated for post-surgical pain and opioid requirements after major abdominal surgeries, Chinese patients in Hong Kong were found to be associated with higher pain severity yet lower opioid consumption, which the authors attributed in part to potential differences in susceptibility to opioid-induced side effects (31) as well as the possibility that patients may appear to be more stoic and less likely to complain about pain in Chinese culture (31,33). Coupled with an increasing incidence of gynecologic cancers over time (34) as well as a booming use of surgical robotics in China (35,36), the methodological approach and implications of the study's results may be relevant to other settings.

The findings from the current study support results from a previous study demonstrating a return to overall health-related quality of life within the three-week follow-up after robotic surgery (23). Future studies evaluating quality of life and pain following robotic surgery could consider assessing patient-reported outcomes sooner than three weeks after surgery.

Patients have ranked pain as among the worst postoperative outcomes they would hope to avoid (37,38), and the results from the current study could help aleviate some of the worry patients experience with regard to postoperative pain expectations following robotic surgery.

In conclusion, the current study shows that robotic surgery for the treatment of gynecologic cancers results in a minimal impact on patient-rated pain, little narcotic use, and positive satisfaction in the short and long term after surgery.

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Footnote

Conflicts of Interest: WH Gotlieb and S Lau obtained partial travel support for proctoring robotic surgery. R Kessous obtained a grant from Intuitive Surgical. The other authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the Jewish General Hospital's Research Ethics Office (protocol #09-123) and informed consent was obtained from all patients.

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Table S1 Valid responses to brief pain inventory (BPI) and satisfaction questions before and after robotic surgery

Time point	Pain other than everyday kinds of pain		Taking treatment(s) for pain		Pain severity [0–10]		Pain interference [0–10]		Satisfaction with recovery time [0–10]		Satisfaction with surgery overall [0–10]		Surgery met expectations [1–4]		Would recommend surgery to others [1–4]	
	n	(%)	n	(%)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
Before surgery	193	42.5	156	31.4	164	1.8 (2.1)	149	1.8 (2.5)	NA		NA		NA		NA	
1 week after surgery	203	58.1	200	73	198	2.3 (2.0)	202	2.9 (2.7)	210	8.3 (1.8)	213	9.1 (1.4)	208	3.7 (0.5)	210	3.8 (0.5)
3 weeks after surgery	126	39.7	121	33.1	117	1.6 (1.9)	128	1.5 (2.0)	137	8.9 (1.7)	137	9.5 (1.1)	133	3.8 (0.5)	137	3.9 (0.3)
3 months after surgery	205	34.2	179	35.8	190	1.8 (2.3)	187	1.8 (2.4)	222	8.9 (1.8)	222	9.4 (1.3)	215	3.7 (0.5)	220	3.9 (0.3)
6 months after surgery	142	39.4	121	28.9	128	1.7 (2.3)	130	1.6 (2.3)	151	9.0 (1.8)	149	9.3 (1.7)	146	3.7 (0.6)	150	3.9 (0.4)
12 months after surgery	103	31.1	82	30.5	92	1.9 (2.3)	89	1.6 (2.2)	110	9.1 (1.5)	109	9.5 (1.1)	107	3.8 (0.5)	108	3.9 (0.4)

Appendix III. Publication on pain medication use following robotic surgery (Chapter 3)

Source: Abitbol, J., et al., *Minimizing pain medication use and its associated costs following robotic surgery.* Gynecologic Oncology, 2017. **144**(1): p. 187-192.

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Minimizing pain medication use and its associated costs following robotic surgery

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HIGHLIGHTS

- Robotic surgery is associated with less use of pain medications post-operatively.
- The reduction in pain medications is associated with a decrease in analgesia-related costs.
- The routine use of patient-controlled analgesia is not required after robotic surgery.

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ABSTRACT

Introduction. Minimally invasive surgery (MIS) has been associated with diminished postoperative pain and analgesia requirements. The objective of the current study was to evaluate the use of analgesia in the post-operative period following robotic surgery for endometrial cancer.

Methods. All consecutive patients who underwent robotic surgery for the treatment of endometrial cancer were included in this study. The timing, dose, and type of analgesics administered postoperatively were recorded from patients' electronic medical record. Data was compared to a matched historical cohort of patients who underwent laparotomy before the introduction of the robotic program.

Results. Only eight patients (2.4%, 5 during the first 25 cases and 3 following mini-laparotomy) received patient-controlled analgesia (PCA) following robotic surgery. Most patients' pain was alleviated by over-the-counter analgesics (acetaminophen, non-steroidal anti-inflammatories). In comparison to laparotomy, patients who underwent robotic surgery required significantly less opioids (71 mg vs. 12 mg IV morphine, $p < 0.0001$) and non-opioids (4810 mg vs. 2151 mg acetaminophen, 1892 vs. 377 mg ibuprofen, and 1470 mg vs. 393 mg naproxen; all $p < 0.0001$).

Conclusion. Patients require less analgesics (opioids and non-opioids) following robotic surgery in comparison to conventional laparotomy, including the elderly and the obese. The diminished pain medication use is associated with some cost savings.

1. Background

In 1986 and again in 1996, the World Health Organization (WHO) developed guidelines to alleviate pain resulting from cancer and its treatments [1,2], yet to this day pain in cancer patients continues to be undertreated [3,4]. To further diminish post-surgical pain and limit the use of opioids, minimally invasive laparoscopic surgery (MIS) has been championed as a less traumatic approach to surgery. Since the introduction of robotically assisted surgery, more patients have been able to benefit from the minimally invasive technique [5].

Recently, we reported that 40% of patients did not take any analgesics for pain at the time of their first post-op visit [6]. Using validated psychometric instruments, we demonstrated that pain severity, pain interference with daily life, and use of treatments for pain returned to pre-surgery levels within 3 weeks of surgery [manuscript submitted for publication]. In the current study, we evaluate the use of pain

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0090-8258/

medications during the post-operative hospital stay following surgery for endometrial cancer.

2. Methods

All consecutive patients who underwent robotic surgery for endometrial cancer were included in this study. A trained research assistant extracted medications, doses, routes of administration, and time of administration for every patient in the post-operative period, from every chart on the hospital's electronic medical record system. Time of administration was described as having been given after surgery on postoperative day 0 (POD0), POD1, and every day thereafter (POD2+). Patient characteristics and clinical data were obtained from a prospective computerized departmental database. Direct costs associated with the administration of pain medications were gathered from the hospital's pharmacy and purchasing departments. The following costs were included: medications, needles, syringes, Patient Controlled Analgesia (PCA)-associated costs (PCA syringe, catheter, tubing, dressing, and labor costs for preparations by pharmacy personnel), epidural-associated costs (epidural kits, bags, tubing, labor costs for preparations, and anesthetist's fees for epidural injection and follow-up). All costs were expressed in 2015 Canadian dollars.

Since 2009, over 95% of patients with endometrial cancer undergo robotic surgery in our center, virtually eliminating laparotomy for this indication. We therefore evaluated pain medication usage in a cohort of consecutive patients treated by laparotomy for endometrial cancer, just prior to the introduction of the robotic platform. Electronic medical records were reviewed for both cohorts. Due to the greater number of patients in the robotic cohort, patients from the historical cohort were matched by stage (as a proxy for extent of disease) and age (as it can affect a drug's pharmacokinetics) in a 1:3 ratio to those treated by robotic surgery. Institutional IRB approval was obtained for this study. Outcomes were compared for statistical differences between the two cohorts using the Mann–Whitney *U* test, the chi-squared test, or Fisher's exact test, where applicable, using the STATA statistical software (StataCorp). A significance level of $p < 0.05$ was used throughout the study.

3. Results

A total of 356 patients were treated for endometrial cancer by robotically assisted surgery since the introduction of the robotics program in December 2007 until April 2013, the time at which this study was designed. No differences in procedures occurred since that time. Sixteen patients were excluded because the final pathology demonstrated non-cancerous or benign disease (n = 4), the presence of multiple malignancies (n = 6), re-operation within the same admission (n = 3), incomplete pain medication chart (n = 1), or conversion to laparotomy for intolerance to Trendelenburg (n = 2). Patients who underwent a mini-laparotomy for the removal of large uteri (n = 6) remained included in the robotic cohort, leaving 340 robotic cases for analysis.

The mean age was 65 years, and 34% were ≥70 years old (Table 1). The mean body mass index (BMI) was 32 kg/m^2, 51% were obese and 19% morbidly obese (BMI > 40). Most patients had stage IA disease (62%) and most tumors were of endometrioid histology (74%).

The average surgical time (skin incision to closure) was 240 min (95%CI 234 to 245 min) with a mean estimated blood loss (EBL) of 70 mL (95%CI 60 to 80 mL). Patients stayed in the hospital, on average, 1.6 days (95%CI 1.4 to 1.7 days, median 1 day).

Pain medication use is tabulated in Table 2. Most patients' pain was alleviated by acetaminophen (mean 2294 mg) and NSAIDs (mean 461 mg ibuprofen, 375 mg naproxen). As part of the anesthesia protocol for minimally invasive procedures, patients were administered intravenous fentanyl (mean 53 mcg) in the Post-Anesthesia Care Unit. The average dose of morphine administered was 1.3 mg intravenously, 3.1 mg subcutaneously, and 1.2 mg orally. Only eight (2.4%) patients were on Patient Controlled Analgesia (PCA), six on IV morphine and two on IV fentanyl. No patients required continuous epidural analgesia. Five of

Table 1
Baseline characteristics of all patients with robotic surgery.

	Robotic (n = 340)
Age, mean (SD)	64.8 (11.5)
BMI, mean (SD)	31.9 (8.7)
ASA	
1	10.3%
2	62.1%
3	27.1%
4	0.6%
Final histology	
Endometrioid	73.8%
Serous	10.9%
Clear cell	5.0%
Carcinosarcoma	4.1%
Adenosquamous	3.5%
Mucinous	1.2%
Sarcoma	1.2%
Unclassified	0.3%
Grade	
1	42.1%
2	23.8%
3	34.1%
Surgical stage	
IA	61.5%
IB	16.2%
II	5.0%
IIIA	3.5%
IIIB	0.6%
IIIC	10.9%
IVA	0.6%
IVB	1.8%

Table 2
Pain medication use following robotic surgery.

Medication	Full robotic sample (n = 340)			
	n	Mean	SD	Median
Acetaminopen				
Acetaminopen	300	2294.0	2293.4	1650
NSAIDS				
Ibuprofen	145	461.2	702.0	0
Toradol	34	1.0	3.0	0
Naproxen	122	375.4	655.7	0
Diclofenac (PO/PR)	20	7.1	32.0	0
Meloxicam	2	0.1	1.1	0
Ketoprofen	0	0.0	0.0	0
Rofecoxib	0	0.0	0.0	0
Indomethacin	0	0.0	0.0	0
Celecoxib	1	0.6	10.8	0
Oral opioids				
Codeine	20	3.2	15.1	0
Oxycodone	4	0.1	1.1	0
Hydromorphone (PO)	24	0.3	1.9	0
Morphine				
Morphine (IV)	48	1.3	4.2	0
Morphine (SC)	69	3.1	10.0	0
Morphine (PO)	43	1.2	3.8	0
Other				
Fentanyl (IV)	177	0.05	0.07	0.03
Neurontin (PO)	2	3.5	45.9	0
Demerol (IV/IM)	4	0.3	2.7	0
Hydromorphone (IV/SC)	17	0.1	0.4	0
Empracet (PO)	10	1.3	8.4	0
Patient-controlled analgesia				
# on PCA	8			
Morphine (IV PCA)	6	0.83	7.19	0
Fentanyl (IV PCA)	2	0.002	0.04	0
Continuous epidural analgesia				
# on CEA	0			
Morphine IV equivalence				
Including PCA/CEA	280	12.8	17.1	7.8

Note: All doses presented are in milligrams (mg).

those on PCA were during the learning curve in the first 25 cases and three had a mini-laparotomy for retrieval of a large uterus. All opioids were converted into a morphine IV scale to estimate the total narcotic use. Including patients on PCA, on average 12.8 mg of morphine were administered.

3.1. Comparing to matched laparotomy group

59 non-selected patients in the historical laparotomy group had available electronic records containing data on pain medications administered after surgery.

Patients in the laparotomy group were then matched in a 1:3 ratio (for n = 177 robotic cases) by stage and age to those in the robotics group.

Patient and oncologic characteristics for the matched cohorts are shown in Table 3. There was no significant difference in the mean age (67 years old in both groups, p = 1.0), BMI (29 vs. 30 in the laparotomy and robotic groups, respectively; p = 0.3), and ASA scores (58% vs. 62% had an ASA level of 2, p = 0.6). Most tumors were of endometrioid histology (75% vs. 66%, p = 0.3), most patients had Stage I disease (68% in both cohorts), and one fifth of patients in both cohorts had Stage III disease.

The robotic cohort tended to have longer mean surgical times (247 vs. 202 min, p < 0.0001) though significantly lower estimated blood loss (76 vs 314 mL, p < 0.0001) and length of stay (1.5 vs. 6.1 days, p < 0.0001).

Table 4 shows pain medication use comparing the laparotomy and robotic cohorts. There are standard order sheets but no protocol per se for patients undergoing laparotomy. Overall, patients who had a laparotomy tended to require significantly more narcotic and non-narcotic analgesics. The laparotomy cohort required more acetaminophen (4810 mg vs. 2151 mg, p < 0.0001), ibuprofen (1892 vs. 377 mg, p < 0.0001), and naproxen (1470 mg vs. 393 mg, p < 0.0001). In addition, all but one patient in the laparotomy cohort were either on PCA (90%) or continuous epidural analgesia (9%). In contrast, only three (2%) patients in the matched robotics cohort were on PCA (p < 0.0001): two with morphine and one with fentanyl and no patients were on continuous epidural analgesia (p < 0.0001). Among those who were on PCA, there was no difference in the doses administered via PCA (57.9 mg morphine and 611 mcg fentanyl in the laparotomy group; 53.4 mg morphine and 720 mcg fentanyl in the robotic group).

Taking into account all opioids on a morphine IV equivalent scale, patients who had a robotic surgery were administered significantly less opioids than those who were operated by laparotomy (12 vs 71 mg, p < 0.0001).

Neither BMI nor age were associated with a difference in the use of the NSAIDs (acetaminophen, ibuprofen, naproxen) or opioids (morphine IV equivalent), but both obese and elderly patients used significantly less of these analgesics following robotic surgery compared to laparotomy (p < 0.01).

Due to the difference in length of stay between the two cohorts, the use of analgesics is represented on the basis of daily use (Figs. 1 and 2).

While patients were matched between the laparotomy and robotic cohorts, to control for a selection bias, the statistical analysis was run again between the laparotomy cohort and the entire robotic sample (n = 340), and yielded similar results.

Table 3
Baseline characteristics in matched laparotomy and robotic sample.

	Laparotomy (n = 59)	Robotic (n = 177)	p-Value
Age, mean (SD)	67.4 (10.2)	67.3 (10.3)	0.95
BMI, mean (SD)	29.3 (6.5)	30.2 (6.6)	0.29
ASA			
1	16.9%	11.9%	0.32
2	57.6%	61.6%	0.59
3	23.7%	26%	0.73
4	1.7%	0.6%	0.44[†]
Final histology[a]			
Endometrioid	74.6%	66.1%	0.26
Serous	8.5%	15.3%	0.27
Clear cell	6.8%	6.2%	1.0
Carcinosarcoma	6.8%	5.6%	0.75
Adenosquamous	3.4%	4.5%	1.0
Mucinous	0%	1.1%	1.0
Sarcoma	0%	0.6%	1.0
Unclassified	0%	0.6%	1.0
Grade			
1	25.4%	33.9%	0.23
2	40.7%	21.5%	0.004
3	33.9%	44.6%	0.15
Surgical stage[a]			
IA	54.2%	54.2%	1
IB	13.6%	13.6%	1
II	6.8%	6.8%	1
IIIA	1.7%	1.7%	1
IIIB	0%	0%	
IIIC	20.3%	20.3%	1
IVA	0%	0%	
IVB	3.4%	3.4$	1

[a] Significance tested using Fisher's exact test.

3.2. Cost analysis

The average direct costs associated with post-operative analgesia in the laparotomy cohort were higher than that of the robotic cohort ($47.57 vs. $6.39, p < 0.0001). The most expensive costs were attributed to the epidural analgesia, though even when these were excluded, costs were still higher in the laparotomy cohort ($29.31 vs. $6.39, p < 0.0001). To control for the longer hospitalization among laparotomy patients, total analgesia costs per day were calculated and were still significantly higher in the laparotomy cohort ($7.89 vs. $2.52, p < 0.0001).

4. Discussion

The current study demonstrates reduced pain medication utilization in the immediate post-operative period following robotic surgery in comparison to laparotomy. Overall, patients who underwent robotic surgery used, on average, significantly less non-opioids (acetaminophen, ibuprofen, and naproxen; all p < 0.0001), opioids (p < 0.0001), PCA or continuous epidural analgesia (p < 0.0001).

Incision size has been found to be an important predictor for severe postoperative pain in the first hour after surgery [7]. Some mathematical models also suggest that wound tension is not linearly but exponentially related to the length of an incision, suggesting that multiple small incisions result in less morbidity than a single large open incision [8].

Indeed, compared to laparotomy, minimally invasive laparoscopic surgery is associated with reduced patient-rated pain [9] and analgesic requirement [10,11]. In comparison to laparoscopy, robotic surgery has been shown to be associated with significantly less use of opioids following surgery for cervical [12] and endometrial cancer [13]. The latter study reported high rates of intravenous PCA use (86% in the robotic cohort and 88% in the laparoscopy cohort), though the authors describe having ceased the routine administration of PCA in their robotic surgery patients [13]. With only eight (2%) patients on IV PCA in our robotic cohort (three of whom required a mini-laparotomy), the current study is evidence that the routine use of PCA is not required in patients undergoing robotic surgery. While patients with a mini-laparotomy might be expected to experience greater pain, these were included in the robotic cohort as these were not considered full conversions. These patients were excluded in a sensitivity analysis yielding similar results. All eligible consecutive patients surgically treated for endometrial cancer by laparotomy and robotic surgery were included in the analysis. Three patients in the matched robotic cohort had a previous hysterectomy (one subtotal) and salpingo-oophorectomy and we're re-operated robotically for completion staging. One patient with stage 4 disease had biopsies and a pelvic lymphadenectomy but complete debulking was abandoned

Table 4
Comparing pain medication use following laparotomy and robotic surgery.

Medications	Laparotomy (n = 59)				Robotic (n = 177)				p-Value
	n	Mean	SD	Median	n	Mean	SD	Median	
Acetaminopen									
Acetaminopen	57	4810.2	2194.6	4875	153	2151.1	2216.5	1650	<0.0001
NSAIDS									
Ibuprofen	48	1891.5	1498.2	1600	68	377.4	593.5	0	<0.0001
Toradol	2	1.4	7.5	0	21	1.2	3.2	0	0.071
Naproxen	34	1470.3	2716.5	1000	67	393.4	704.6	0	<0.0001
Diclofenac (PO/PR)	6	11.9	37.5	0	13	9.0	37.4	0	0.49
Meloxicam	0	0.0	0.0	0	1	0.1	1.1	0	0.56
Ketoprofen	1	13.6	104.2	0	0	0.0	0.0	0	0.083
Rofecoxib	1	1.7	13.0	0	0	0.0	0.0	0	0.083
Indomethacin	2	4.7	25.2	0	0	0.0	0.0	0	0.014
Celecoxib	0	0.0	0.0	0	1	1.1	15.0	0	0.56
Oral opioids									
Codeine	0	0.0	0.0	0	13	4.1	17.3	0	0.033
Oxycodone	1	0.1	1.0	0	1	0.1	1.1	0	0.42
Hydromorphone (PO)	0	0.0	0.0	0	14	0.4	2.6	0	0.026
Morphine									
Morphine (IV)	2	0.3	1.4	0	23	1.2	4.0	0	0.039
Morphine (SC)	38	14.8	22.4	5	37	3.0	8.8	0	<0.0001
Morphine (PO)	0	0.0	0.0	0	18	1.0	3.7	0	0.011
Other									
Fentanyl (IV)	1	1.0	7.8	0	85	46.5	64.6	0	<0.0001
Neurontin (PO)	1	81.4	624.9	0	1	3.4	45.1	0	0.41
Demerol (IV/IM)	1	1.7	13.0	0	2	0.3	2.6	0	0.73
Hydromorphone (IV/SC)	1	0.1	0.9	0	11	0.1	0.5	0	0.18
Empracet (PO)	6	15.8	60.9	0	6	1.5	9.2	0	0.034
Patient-controlled analgesia									
# on PCA	53				3				<0.001[a]
Morphine (IV PCA)	51	50.0	39.2	42.9	2	0.6	6.4	0	<0.0001
Fentanyl (IV PCA)	4	0.04	0.2	0	1	0.004	0.054	0	0.0043
Continuous epidural analgesia									
# on CEA	5				0				0.001[a]
Bupivacaine (IV CEA)	5	23.5	79.0	0	0				0.0001
Morphine (IV CEA)	3	1.0	4.5	0	0				0.0026
Sufentanil (IV CEA)	3	0.003	0.01	0	0				0.0026
Morphine IV equivalence									
Including PCA/CEA	59	71.0	47.2	59	144	12.2	17.1	7.5	<0.0001

Note: All doses presented are in milligrams (mg).
[a] Significance tested using Fisher's exact test.

due to diffuse metastases. All other patients had full staging with hysterectomy, salpingo-oophorectomy, and pelvic lymphadenectomy. Some also had peri-aortic lymph nodes removed (78 in the matched robotic cohort, 37 in the laparotomy cohort), omentectomy or omental biopsy (41 robotic, 37 laparotomy), appendectomy (1 in each matched cohort), and hernioplasty (1 in each matched cohort).

To account for the quicker discharge of patients after robotic surgery, the daily use of analgesics was evaluated, further reflecting the

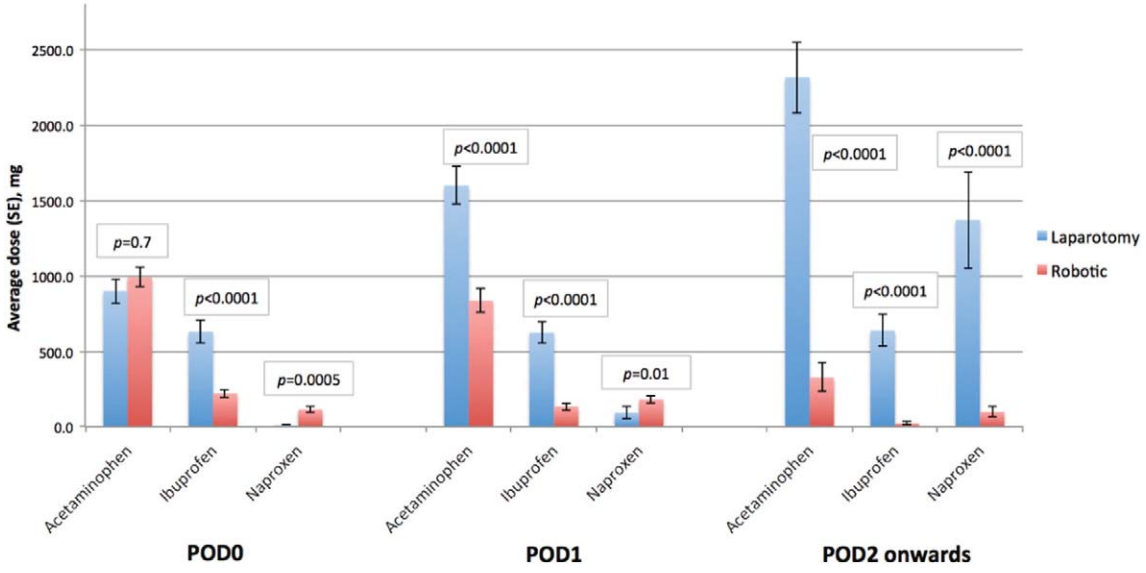

Fig. 1. Daily use of non-opioids following laparotomy and robotic surgery for endometrial cancer.

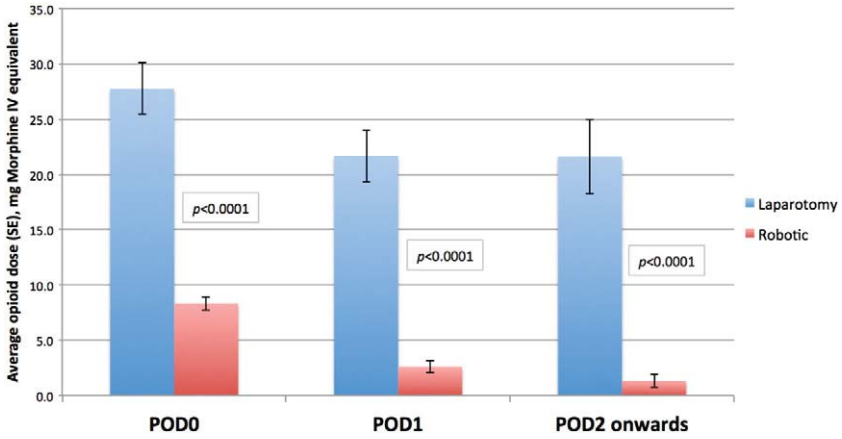

Fig. 2. Daily use of opioids following laparotomy and robotic surgery for endometrial cancer.

significantly reduced need for opioids in the robotic cohort ($p < 0.0001$ on POD0, POD1, and POD2 onwards).

The benefits of robotic surgery remained regardless of body habitus or age. The total use of opioids among the elderly was significantly reduced in the robotic cohort compared to the laparotomy cohort (67 mg vs. 10 mg, $p < 0.0001$). This is particularly relevant considering the increased risk of adverse events associated with the use of opiates in the geriatric population [14].

The decrease in the use of post-operative pain medications following the introduction of robotic surgery was associated with a 70% decrease in pain medication costs per day. While these costs take into account the costs of medications and supplies for the injection of parenteral medications, they underestimate cost savings attributed to the reduced nursing hours required to tend to patients for the alleviation of pain. Robotic surgery has similarly been found to decrease pain medication costs compared to laparoscopy [15].

In addition to decreased analgesic use, robotically-assisted surgeries were associated with longer surgical times but less blood loss and shorter hospital stay. A recent study by Bogani et al. similarly noted significantly longer surgical times but shorter hospitalizations in endometrial cancer patients undergoing robotic surgery compared to open surgery [16]. Similar trends were previously described following the introduction of laparoscopy for apparent early stage gynecologic cancers, noting a significant growth in the use of laparoscopy relative to open surgery, and associated with decreased blood loss and shortening of hospital stay [17].

There are some limitations in the current study. First, data was gathered retrospectively. For the most part, the availability of medications was similar between the two eras, with only few exceptions (e.g. Rofecoxib was withdrawn from the market in 2004 but was only used once by a single laparotomy patient). Prior to the introduction of robotics in our department, only up to 17% of patients were operated by MIS [18]. In the first year of our robotics program, 66% of endometrial cancer patients underwent robotic surgery though this was only due to limited access to the robotic system [19]. From 2009 and onwards, over 95% of operable endometrial cancer patients underwent robotic surgery [18, 19].

The analysis was also limited to post-operative use of pain medications only. Intra-operatively, all robotic trocar sites are routinely infiltrated with bupivacaine 0.5% without epinephrine before skin incision and at the conclusion of surgery to diminish pain. This procedure is not done for patients undergoing laparotomy. Pre-operative use of chronic pain medications were also not taken into account when calculating equianalgesic values. However, the differences in opioid usage in the robotic and laparotomy cohorts were so apparent that it is unlikely to have made a difference. Opioids were prescribed "as needed" in the routine post-op orders and were therefore available to all patients. Due to the rapid onset and excretion of fentanyl, intravenous fentanyl is administered to patients in the PACU following minimally invasive procedures as part of a standard recovery room protocol.

Our previous studies on outcomes following robotic surgery have demonstrated a rapid return to pre-operative patient-reported pain scores [manuscript submitted]. The current study supports these findings by demonstrating the low use of both opioid and non-opioid pain medications, and although the absolute cost reduction is not abundant, there were some cost savings attributed to the reduction in the use of analgesia.

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Conflicts of interest

Walter Gotlieb and Susie Lau obtained partial travel support for proctoring robotic surgery. Dr. Kessous obtained a grant from Intuitive Surgical

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Appendix IV. Publication of mini-review presenting key results on robotic surgery from our division

Source: Abitbol J and Gotlieb WH. *Robotic surgery in gynecologic oncology: where do we stand?* In ³Reproductive Geneeskunde, Gynaecologie en Obstetrie² (2015) DCHG Med. Comm, Haarlem (The Netherland) E. Slager Editor, p. 1142-50.

Robotic surgery in gynecologic oncology: where do we stand?

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Key words: robotic surgery; clinical outcome; minimal invasive surgery; gynecologic cancer; economics

Introduction

Surgery has been defined as a 'medical treatment in which a doctor cuts into someone's body in order to repair or remove damaged or diseased parts'. [1] Comparably, a *stab* is defined as 'a wound made by a pointed weapon (such as a knife)'. [2] The difference between the two, lays in the intent of the one holding the blade; one can therefore think of the act of surgery as a form of 'controlled aggression' in the best interest of the patient. Up to the 1970's the archetype in complex surgery was 'the bigger the scar, the bigger the surgeon'. More recently with the availability of minimally invasive surgery (MIS) and improved molecular treatments, the paradigm is evolving towards 'the smaller the scar, the bigger the surgeon'. In gynecologic oncology, where the mainstay surgical management involves laparotomy, the aggressiveness of surgery has been greatly diminished by MIS. In spite of the well-established benefits offered to patients [3-5], use of laparoscopy has remained scarce among gynecologic oncologists performing complex surgeries [6,7] due to the inherent difficulties of the technique, mainly related to the strait instruments and fulcrum effect, leading to long learning curves. [8,9] Robotics has been a natural evolution of the strait stick laparoscopic instruments. With improved ergonomics, dexterity, visualization, and instrumentation, robotically assisted MIS allows for an easier adoption of the minimally invasive technique on the part of the surgeon. Outcomes following robotic surgery continue to be evaluated across different fields.

The current study is a review of our institution's experience with robotic surgery (presently reaching one thousand cases) for the treatment of the major gynecologic cancers, namely endometrial, cervical, and pelvic epithelial cancers.

Endometrial cancer

The Gynecologic Oncology Group (GOG)'s randomized controlled trial, LAP-2, paved the way for laparoscopy as a superior alternative to laparotomy for the treatment of early stage endometrial cancer. [3] Without impacting the survival of endometrial cancer patients [10],

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numerous studies have demonstrated the benefits of laparoscopy over laparotomy including decreased blood loss [5], postoperative complications, [3], hospital stay [3,5], and postoperative pain. [4] Studies evaluating robotic surgery for endometrial cancer staging have found similar benefits. [11-13] Compared to the outcomes of patients undergoing laparotomy or laparoscopy in the LAP-2 study [3], surgical management of endometrial cancer by robotic surgery in our institution provided favourable results (Table 1). We reported a lower length of stay (4 days vs. 3 days vs. 1 day for laparotomy, laparoscopy, and robotic surgery, respectively), lower complication (8% vs. 10% vs. 2.8%), conversion (25.8% laparoscopy vs. 4.2% robotic), and blood transfusion rates (7% vs. 9% vs. 1.4%) [3,14], a decrease in post-operative pain 3 weeks after surgery as opposed to an increase (46% vs. 52% vs. 15% [unpublished data]) [4], and a milder decrease in overall health-related quality of life (6.5% vs. 3.6% vs. 1.4%). [4,15]

Table 1. Clinical and Quality of Life outcomes following robotic surgery for the treatment of endometrial cancer at our center in comparison to results from the LAP-2 study.

	Laparotomy* (n=920)	Laparoscopy* (n=1682)	Robotics (n=486)
Length of stay (median # days)	4	3	1†
Intra-operative complications	8%	10%	2.8%†
Conversion	-	25.8%	4.2%†
Blood transfusion	7%	9%	1.4%†
Change in pain severity (brief pain questionnaire: preop to 3 weeks postop)**	+46%‡	+52%‡	-15%§
HRQOL decrease (FACT-G at 3 wk)***	6.5%‡	3.6%‡	1.4%††

LAP-2 quality of life results retrieved from Kornblith et al. (2009) [4]

Retrieved from unpublished data and adjusted for comparison to LAP-2 (added pain at its worst and at its least for all endometrial cancer patients)

Retrieved from Abitbol et al. (2014) [15] and adjusted for comparison to LAP-2 (calculated as per version 3 of FACT-G for all endometrial cancer patients)

Change in pain severity from before surgery to 3 weeks after surgery using Brief Pain Inventory.

Decrease in Health-Related Quality of Life (HRQOL) from before surgery to 3 weeks after surgery using FACT-G questionnaire.

While laparoscopy affords better outcomes compared to laparotomy, the approach could be particularly challenging in obese patients, preventing many from benefiting from MIS. [3] The introduction of robotic surgery in our department has mitigated that barrier. The heaviest patient who successfully underwent robotic surgery in our department had a BMI of 85. Stratified by non-obese (BMI <30 kg/m^2), obese (BMI 30-39.9), and morbidly obese (BMI ≥40), patients undergoing robotic surgery for endometrial cancer had similar outcomes (Table 2). [16] Between the three groups, we reported no significant difference in console time (168 vs. 174 vs. 183 minutes in the non-obese, obese, and morbidly obese, respectively; p=0.2), median length of stay (1 vs. 2 vs. 2 days; p=0.2), or major complications (0, 1, 0; p=0.5). [16] It appears as though the robotic platform neutralizes the surgical risk factors associated with obesity.

Table 2. Characteristics and clinical outcomes following robotic surgery for the treatment of endometrial cancer at our center, stratified by Body Mass Index (BMI, kg/m^2). [16]

	BMI <30	BMI 30-39.9	BMI ≥40	P-value
Mean BMI	25	34	46	p<0.0001
Age (mean)	69.3	66.9	54.7	p<0.0001
ASA score (mean)*	1.7	2	2.3	p<0.01
Diabetes (%)	16%	27%	30%	p=0.3
Hypertension (%)	58%	70%	80%	p=0.2
Console time (min)	168	174	183	p=0.2
Conversions (n)†	3	1	2	p=0.6
Estimated Blood Loss (mL)	64	96	94	p<0.05
Hemoglobin (g/L, pre-op - post-op)	135-116	138-118	130-116	p=0.08 preop, p=0.8 postop
Median hospitalization (days)	1	2	2	p=0.2
Major complications (n)	0	1	0	p=0.5
Time to resume physical activities (d)	21	11	18	P=NS

Data retrieved from Lau et al. (2011). [16]

ASA score: American Society of Anesthesiologists classification system

† All were mini-laparotomies for uterus extraction

With an aging patient population, the elderly are another important high-risk group to consider when deciding on a surgical approach. Our first 100 robotic surgeries for endometrial cancer were divided into patients less than 70 years old and compared to those 70 or older. [17] The two groups had similar outcomes with no statistically significant differences in estimated blood loss (81 vs. 83 mL in the younger compared to the older group, respectively), console time (175 vs. 171 min), or median hospital stay (1 vs. 2 days). [17] Postoperative quality of life was also assessed, with no significant differences except for the time to resume chore activities, which was sooner in the older group (16.1 vs. 9.7 days, p=0.02). [17] Comparing our elderly patients (70 years of age or older) undergoing robotic surgery to a matched historical cohort of elderly patients who underwent laparotomy, we further reported that the introduction of robotic surgery decreased mean estimated blood loss (74.8 vs. 334 mL in the robotic and open surgery cohorts, respectively; p<0.0001), minor post-operative complications (17% vs. 60%; p<0.0001), and mean hospital stay (3.1 vs. 8.0; p<0.0001).

Overall, for the treatment of endometrial cancer, the introduction of robotic surgery into our department has significantly improved operative, clinical, and economic outcomes. Comparing a historical series of patients treated by laparotomy and/or laparoscopy between April 2003 and November 2007 to patients treated by robotic surgery between December 2007 and May 2010, we've reported decreases in complication rates by close to 70%, wound complications by close to 80%, estimated blood loss by over 70%, and hospital stay by 80%. [14] At the time of analysis, we also reported a significantly lower 2-year recurrence rate in the robotic cohort compared to the historic cohort (p<0.001). [14] While cost remains a barrier to acquiring the robotic platform in many institutions, the benefits of robotic surgery we reported further translated into a significant reduction in overall cost per surgery from C$10,368 (95% CI $8,236-$12,500) to C$8,370 (95% CI $7,090-$9,651), including amortization of the robotic system and its maintenance fees over a period of 10 years and based on two cases per day. [14]

Some suggest that appropriate staging of endometrial cancer requires lymphadenectomy to evaluate the extent of disease and assess the need for adjuvant therapy. [18] Lymphadenectomy, however, is associated with lymphocyst formation, prolonged surgery, and increased risk of injury. [18] Sentinel lymph node (SLN) mapping has been suggested as a means of properly staging the cancer while reducing the risk of possible complications. [18,19] Robotic surgery has facilitated the detection of SLN's in our endometrial cancer patients. [19] Out of the first 100 endometrial cancer patients on our SLN protocol, we had a SLN detection rate of 92% with a specificity of 100%, sensitivity of 89% (eight out of nine patients with positive lymph nodes also had positive SLNs), and a negative predictive value of 99% (only 1 false negative SLN). [19] More recently, real-time fluorescence imaging on the newer da Vinci Si surgical platform has further enhanced SLN mapping in our endometrial and cervical cancer patients (submitted for publication).

Cervical cancer

In an updated survey sent to members of the Society of Gynecologic Oncology (SGO) in 2007, only 38% of respondents considered laparoscopy appropriate for the treatment of cervical cancer. [20] Similarly, prior to the introduction of robotics in our department in 2007, no patients were treated by MIS for cervical cancer. Since 2009, all cervical cancers and over 95% of uterine cancers, including endometrial cancers and sarcomas, are managed by robotically assisted MIS (Figure 1).

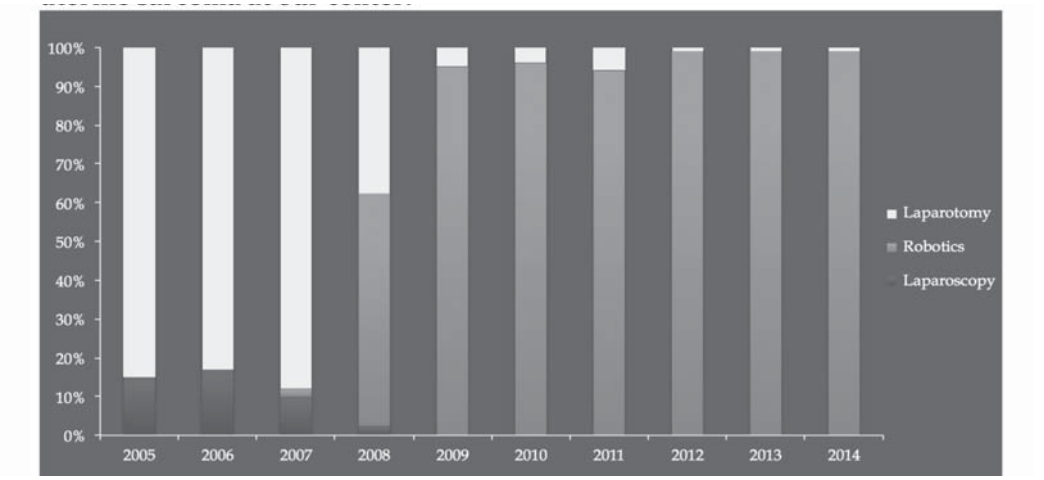

Figure 1. Annual proportion of surgical approaches for the treatment of endometrial cancer, cervival cancer, and uterine sarcoma at our center (zie voor kleurillustratie nummer xxx op pagina xxx)..

Since the introduction of robotics in our department, patient- and hospital-centered outcomes have been prospectively collected. Despite the fact that we had never offered laparoscopy to perform radical hysterectomies, patients who underwent robotic radical hysterectomy during the learning curve, between January 2008 and December 2009, for the treatment of cervical cancer were compared to a historical cohort of patients treated by open radical hysterectomy between March 2003 and December 2007. [21] Baseline patient demographics and histologic characteristics were not significantly different between the groups. Patients who had robotic radical hysterectomy had significantly less blood loss (546 vs. 106 mL for open and robotic hysterectomy, respectively; $p<0.0001$), less opioid use (4% vs. 50% used opioids for one day or less, $p=0.0026$; 67% vs. 0% used for three or more days, $p=0.0001$), required less time to diet (3.5 vs. 1.2 days, $p<0.0001$), and a shorter stay hospital stay (7.2 vs. 1.9 days, $p<0.0001$). [21] Complication rates were not significantly different with the exception of wound complications (29% vs. 0% for open and robotic hysterectomy, respectively; $p<0.03$) and minor complications (63% vs. 19%, $p=0.003$) in favour of robotic surgery. [21] Average perioperative costs were calculated for both cohorts. After amortizing the cost of the robot and maintenance fees over a period of seven years with an average of five robotic cases per week, there was a trend towards decreased cost of robotics for open and robotic radical hysterectomy, respectively). If the hospital already owns a robotic platform, the average perioperative cost is significantly less for robotic cases ($11,764 vs. $9,613, $p=0.002$). [21]

Table 3 presents results from our experience with robotic surgery as well as results from published studies comparing robotics, laparotomy, and laparoscopy for the treatment of cervical cancer. Results from the literature were weighted by the sample sizes of the referenced studies. [21-33] The data suggests that MIS cases tend to have longer operating time, less blood loss, fewer complications, and shorter hospital stay.

Table 3. Clinical outcomes following robotic surgery for the treatment of cervix cancer

	N	BMI	Age	OR time (min)	Estimated blood loss (ml)	Conversions	Complications	Length of stay (d)
Departmental data (21)	70	26	49	290	71	0	19%	1.5
Published literature[†]								
ROBOTICS	422	27	46	248	101	0.6%	27%	2.1
Laparotomy	273	26	46	204	488	-	42%	5.1
Laparoscopy	88	27	49	259	195	n/a	23%	4.2

[†] Data from the published literature, weighed by the reported sample sizes of the referenced studies. [22-33]

Pelvic epithelial cancer

Pelvic epithelial cancers (also known as ovarian, fallopian tube, or primary peritoneal cancers) are most often found at a late stage, requiring aggressive surgical debulking by midline laparotomy followed by adjuvant chemotherapy. [34] The use of laparoscopy for the management of these cancers has generally been limited to diagnostic and prognostic purposes (i.e. exploratory laparoscopy, second look procedures, and assessment of chemo-responsiveness). In 1994, Querleu and Leblanc (1994) first reported on the feasibility of complete laparoscopic staging for apparent early stage ovarian cancer including infrarenal perioartic lymphadenectomy. [35] More recently, the feasibility of surgical debulking by MIS for advanced disease has been described for select patients. [36,37]

The use of neoadjuvant chemotherapy prior to surgery has been proposed as
an alternative to aggressive upfront cytoreductive surgery, without compromising oncologic outcomes. [26] The decrease in tumor burden at the time of surgery from the use of neoadjuvant chemotherapy has allowed our group to explore the use of robotic surgery for the management of pelvic epithelial cancers.

We are currently evaluating outcomes from the first 65 cases of robotic surgery (31 primary debulking, 34 interval debulking following neoadjuvant chemotherapy) for the treatment of pelvic epithelial cancer, after a median time of follow-up of 3 years. Recurrence and survival data is being compared to a historical cohort of 89 patients treated by laparotomy (63 primary debulking, 26 interval debulking). Preliminary analyses suggest no significant differences between laparotomy and robotic groups matched by stage and use of neoadjuvant chemotherapy, with the exception of overall survival following interval debulking for Stage IIIC patients, in favour of robotic surgery (p=0.047) [manuscript in preparation].

Conclusion

Given the present cost of the robotic surgical system, it would undoubtedly not be cost-effective to replace laparoscopy for cases that could be done laparoscopically. However, the lack of diffusion of laparoscopy in gynecologic oncology in the past 20 years suggests a lack of interest, ability, or will for surgeons to perform major cancer surgeries by the minimally invasive technique. This lack of growth in the use of laparoscopy has hindered many patients from benefiting from MIS, especially the obese. The introduction of a robotic platform into our department has resulted in substantial growth (over 500% increase) in the use of MIS for patients with endometrial cancer, cervical cancer, and uterine sarcoma. The robotic platform has also improved SLN mapping and has further expanded the scope of surgeries that could be done by MIS such as for advanced disease, for the treatment of pelvic epithelial cancers, and in high-risk patient populations. The addition of robotic surgery to the surgical repertoire is therefore not to replace laparoscopy but to facilitate its use and avoid laparotomies, their induced morbidities, and, with adequate use over time, achieve substantial cost savings.

Disclosures: WG has obtained partial travel support for proctoring robotic surgery.

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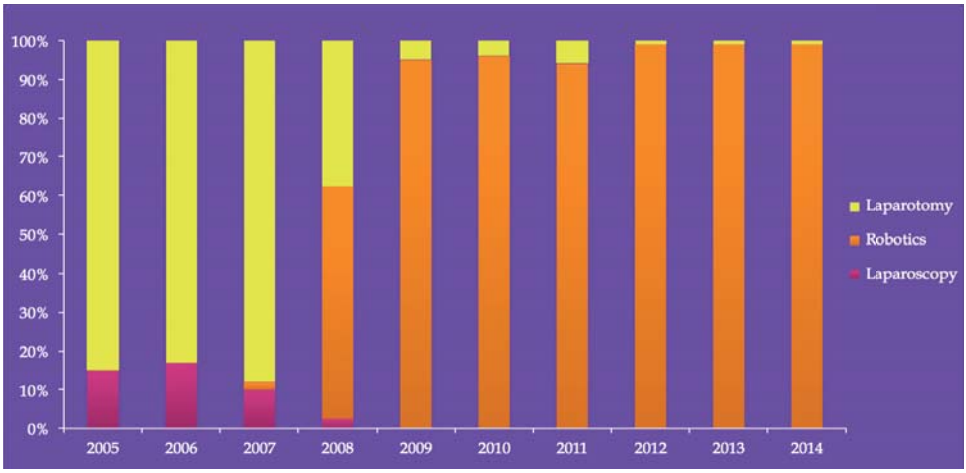
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Laparotomy
Robotics
Laparoscopy

Appendix V. Publication on changing patterns and resource use on the inpatient ward (Chapter 6)

Source: Leung, A., Abitbol, J., et al., *Outside the operating room: How a robotics program changed resource utilization on the inpatient ward.* Gynecol Oncol, 2017. **145**(1): p. 102-107.

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Outside the operating room: How a robotics program changed resource utilization on the inpatient Ward

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HIGHLIGHTS

- Introducing robotics decreased inpatients for elective surgery.
- Robotics is associated with admitting a higher proportion of patients with complex medical issues.
- Number of surgeries increased while liberating beds and decreasing overall inpatient costs.

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ABSTRACT

Objective. To analyze the changes in the composition of the gynecologic oncology inpatient ward following the implementation of a robotic surgery program and its impact on inpatient resource utilization and costs.

Methods. Retrospective review of the medical charts of patients admitted onto the gynecologic oncology ward the year prior to and five years after the implementation of robotics. The following variables were collected: patient characteristics, hospitalization details (reason for admission and length of hospital stay), and resource utilization (number of hospitalization days, consultations, and imaging).

Results. Following the introduction of robotic surgery, there were more admissions for elective surgery yet these accounted for only 21% of the inpatient ward in terms of number of hospital days, compared to 36% prior to the robotic program. This coincided with a sharp increase in the overall number of patients operated on by a minimally invasive approach (15% to 76%, $p < 0.0001$). The cost per surgical admission on the inpatient ward decreased by 59% ($9827 vs. $4058) in the robotics era. The robotics program contributed to a ward with higher proportion of patients with complex comorbidities (Charlson ≥ 5: RR 1.06), Stage IV disease (RR 1.30), and recurrent disease (RR 1.99).

Conclusion. Introduction of robotic surgery allowed for more patients to be treated surgically while simultaneously decreasing inpatient resource use. With more patients with non-surgical oncological issues and greater medical complexity, the gynecologic oncology ward functions more like a medical rather than surgical ward after the introduction of robotics, which has implications for hospital-wide resource planning.

1. Introduction

The assessment of new technology in healthcare generally involves evaluating its safety, clinical effectiveness, economic impact, as well as effects on a local organizational level [1]. In order to fully capitalize on the introduction of a new technology in a hospital setting, changes in organizational processes and work flow need to also be measured and adapted accordingly [2].

The introduction of robotic surgery in gynecologic oncology is a prime example of a practice-changing technological conversion, allowing for an accelerated transition from laparotomy to minimally invasive surgery (MIS), especially for patients with endometrial and cervical cancers [3]. Since the introduction of the da Vinci Surgical System at

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our institution in December 2007, all the patients with cancer of the cervix undergoing surgery went from being operated on by laparotomy to robotics [4] and the rate of MIS for the treatment of endometrial cancer rose from 17% by laparoscopy to over 95% using robotics by 2012 [5]. The use of robotic surgery for ovarian cancer at our institution is also steadily increasing (66% in 2013).

Systematic reviews have demonstrated the safety and effectiveness of robotic surgery for endometrial and cervical cancer [6] with similar oncological outcomes [7,8] when compared to laparoscopy and laparotomy. The high initial equipment and ongoing maintenance costs of robotic surgery are offset by the decreased length of hospitalization and decreased morbidity [4,5,9–11], and its potential to convert cases to outpatient same-day surgeries [12,13]. From a hospital administration and resource allocation perspective however, there is a paucity of data evaluating the organizational impact of introducing a robotic surgery program in gynecologic oncology. The objective of this study was to analyze the changes in the demographics of hospitalized gynecologic oncology patients (i.e., the composition on the inpatient ward) with the introduction of robotic surgery and its impact on resource utilization and implications for the management of the inpatient ward.

2. Methods

A retrospective chart review was conducted on patients admitted onto the gynecologic oncology ward at a university-affiliated tertiary care hospital, the year prior to (2007) and 5 years after the implementation of the robotic surgery program (2013), at the time when a learning curve plateau and a steady state had been reached with the robotics program. Admissions data from January to December of 2007 and 2013 were collected from the hospital's database following approval from the hospital institutional review board.

The design of the study was a non-experimental pre-test/post-test study. With robotic surgery as the intervention, the variables were analyzed before (pre-test) and after (post-test) the introduction of robotic surgery. The selected unit of analysis was the absolute number of hospitalization days rather than the number of admissions because patients could be admitted once for a prolonged period on the ward or have multiple admissions in that year for short periods of time. In order to capture a snapshot of the inpatient ward in the pre-robotic and robotic era, the relative risk (RR) of being on the ward with a particular clinical characteristic was calculated by comparing the proportion of total days spent on the ward by patients with those characteristics in both eras. For example, if 20% of the hospitalization days were spent by patients admitted for bowel obstruction in 2007 and 40% in 2013, one would be twice as likely to see a patient on the ward for bowel obstruction in 2013. Since the length of stay is often shorter for robotic surgeries, we hypothesized that the introduction of a robotic surgery program would affect the length of stay for patients hospitalized for elective surgeries to a relatively greater extent compared to those hospitalized for non-surgical reasons. Thus, the analysis was divided to those who were admitted for elective surgery, “surgical”, and those admitted for any other reason, “non-surgical”. Patients who were discharged post-operatively and at any point re-admitted for surgical complications (e.g., wound infection) were included in the latter non-surgical group to create the distinction with patients admitted for the elective surgery itself. In addition, a decrease in post-operative complications following robotics [5], might have further decreased the overall yearly inpatient population and cost, by avoiding re-admissions for surgical complications.

Patient charts (both electronic and paper) from all admissions were reviewed for patient characteristics (e.g., age, cancer type and stage, comorbidities), hospitalization details (e.g., reason for admission, length of hospitalization, complications), and resources used. Cancer type and stage were retrieved post-hoc, after a final diagnosis could be made, rather than at time of admission where these are often not yet available. The Charlson comorbidity score [14–16] was used as a measure of comorbidities in our population; a score equal to or >5 was chosen as the dividing point for analysis because of the associated exponential increase in the risk of mortality. Moreover, while medical issues may arise during hospitalizations and diagnoses may change, the initial admitting diagnosis was used as the reason for admission, and although most ascites and pleural effusions are managed in an outpatient setting, some required admission for placement of a permanent drain or for pleurodesis.

Variables pertaining to inpatient resource utilization included number of hospitalization days (e.g., cost for room, nursing, pharmacy, laboratory, and overhead costs), specialty consultations (e.g., Internal Medicine, Surgical subspecialties, Palliative Care, Geriatrics, etc.), inpatient imaging studies (e.g., X-ray, MRI, CT, Ultrasound, PET), and inpatient procedures (e.g., drain insertion by interventional radiology or rectal stent insertion by gastroenterology). Resources used intra-operatively (e.g., the robot, surgical instrumentation, anesthesia, etc.) were excluded to focus on the inpatient ward. Average direct and indirect costs of each of the above-mentioned tests were obtained from hospital and departmental administrative databases, including MedGPS (Logibec Inc., Montreal, Canada), a data warehouse which archives patient-level administrative and clinical data on health care utilization and calculates the costs of resources used in the hospital. Capital costs of imaging machines were depreciated over the expected life of the machines and the average number of hospital-wide exams per year, and included in imaging costs. Physician remuneration fees were obtained from the provincial health insurance board (*Regie de l'assurance maladie du Quebec*). All cost estimates in this study were adjusted for inflation to 2016 Canadian dollars.

Statistically significant differences were also calculated for categorical and continuous variables using the Chi-squared test and the Wilcoxon rank-sum test, respectively. Statistical analysis was performed using commercially available statistical software, STATA 14 (StataCorp, Texas). A two tailed p-value < 0.05 was considered statistically significant throughout the study.

3. Results

3.1. Description of admissions: surgical vs. non-surgical

There were more individuals admitted in 2013 than 2007 (291 vs. 246 patients admitted at least once) and among these patients, some were admitted multiple times during the year and there were overall more admissions to the gynecologic oncology service in 2013 than 2007 (395 vs. 356). Despite more admissions, the overall total number of hospitalization days decreased by 12% (2964 vs. 3358 in 2013 and 2007 respectively).

There were 207 admissions for elective surgery (52% of total admissions) in 2013 compared to 163 (46%) in 2007. Of these, the number of elective surgeries performed with a minimally invasive approach increased to 76% (94.3% of which were performed robotically) in 2013 from 15% (all by laparoscopy) in 2007 ($p < 0.0001$).

Fig. 1 illustrates the total number of bed days on the gynecologic oncology ward by reason for admission in 2007 and 2013. Despite performing more surgeries in 2013, only 21% of the inpatient bed days were dedicated to patients admitted for surgery, compared to 36% in 2007, saving 585 bed-days for surgery. This is likely due to the increase in number of patients who underwent robotic surgery resulting in a decrease in the median length of stay for surgical patients to 1 day in 2013 from 6 days in 2007 ($p < 0.0001$). Thus, patients were less likely to be on the ward for elective surgery in 2013 (RR 0.58; 95%CI 0.54 to 0.64). Moreover, of the patients admitted for surgical reasons in 2013, 50% of the days on the ward were dedicated to post-laparotomy patients even though only 17% of surgeries were done by laparotomy.

For non-surgical admissions, the number of hospitalization days increased (79% vs. 64% of the inpatient bed days in 2013 and 2007; $p < 0.0001$) for an additional 191 days, without a significant change in median length of stay (5 vs. 6 days, $p = 0.1$). Among these patients,

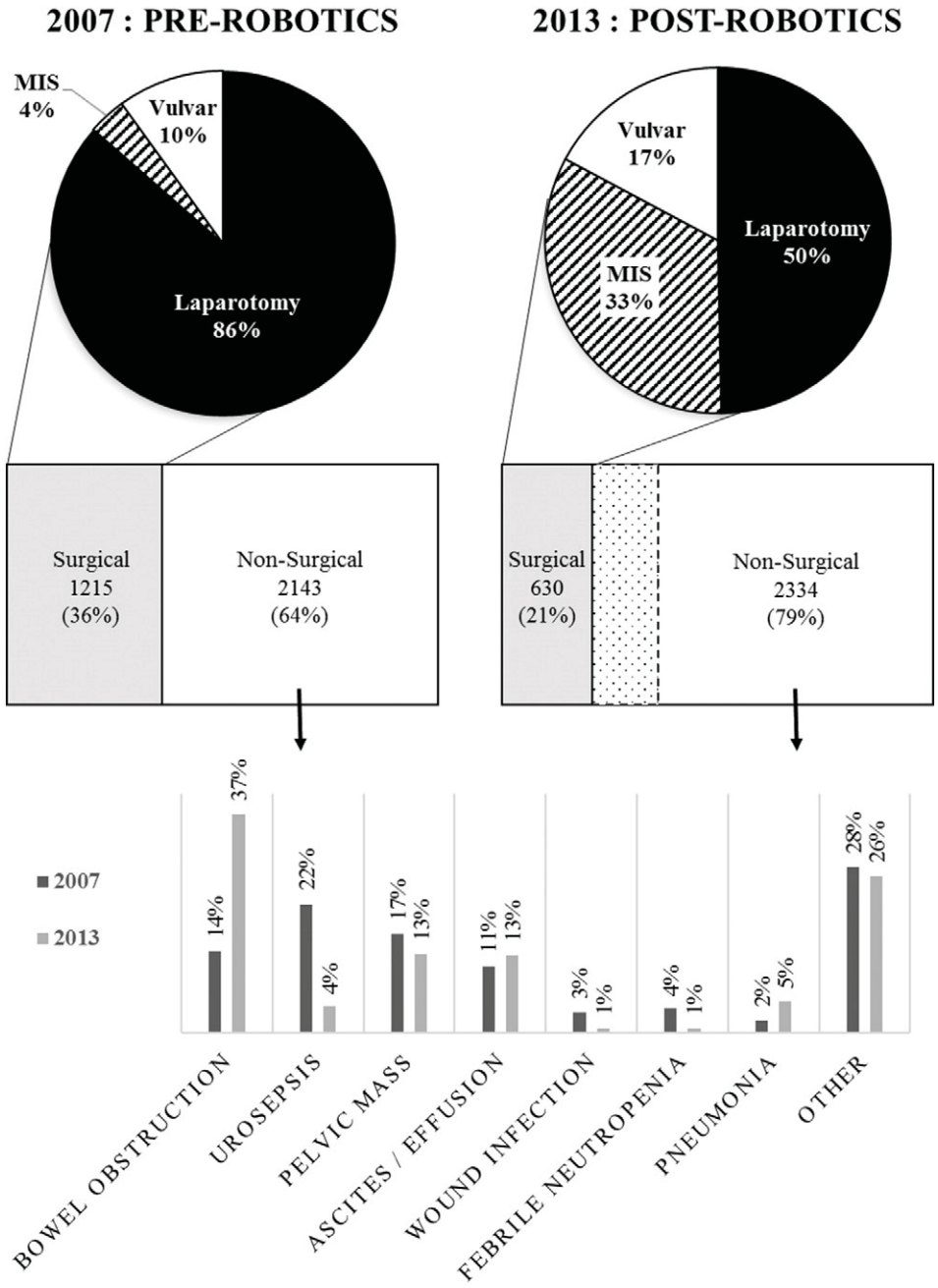

Fig. 1. Proportion of total hospital days spent on the inpatient ward in 2007 and 2013 based on reason for admission.

there was an increase in admissions for bowel obstruction, symptomatic ascites or pleural effusion, and pneumonia, and a decrease in admissions for urosepsis, wound infection, pelvic mass, and febrile neutropenia (all statistically significant, $p < 0.05$) (Fig. 1).

3.2. Changes in cancer diagnoses

The total number of hospitalization days was analyzed based on admitting diagnosis (Table 1). In 2013, there were fewer hospital bed days on the inpatient ward for patients with endometrial (RR 0.74; 95%CI 0.68 to 0.81) and cervical cancer (RR 0.51; 95%CI 0.42 to 0.62), and a greater number of hospital days for patients with ovarian/fallopian/peritoneal (RR 1.36; 95%CI 1.29 to 1.44) and vulvar cancer (RR 2.28; 95%CI 1.87 to 2.78). This is consistent with the decreased length of stay following robotic surgery and that majority of robotic cases were performed for endometrial and cervical cancers. This trend was also seen when the analysis was subdivided into surgical and non-surgical groups.

3.3. Changes in medical complexity of patients

The average age of patients did not differ between the two cohorts (59.8 ± 14.3 vs. 59.7 ± 15.1; $p = 0.9$). In the robotics era, inpatients were more likely to have stage IV disease (RR 1.30; 95%CI 1.21 to 1.39), twice as likely to have recurrence of disease at the time of admission (RR 1.99; 95%CI 1.86 to 2.13), and more likely to have a Charlson score ≥ 5 (RR 1.06, 95%CI 1.04 to 1.08), indicating an overall increase

Table 1
Total hospitalization days based on cancer type, cancer stage, recurrence, and Charlson score.

	Surgical			Non-surgical			overall		
	2007	2013	Relative risk	2007	2013	Relative risk	2007	2013	Relative risk
Cancer type									
Endometrial	348	134	0.71 (0.62–0.88)**	638	511	0.75 (0.67–0.81)**	986	645	0.74 (0.68–0.81)**
Ovarian	430	200	0.90 (0.78–1.03)	867	1359	1.44 (1.35–1.53)**	1297	1559	1.36 (1.29–1.44)**
Cervical	92	23	0.48 (0.31–0.75)*	221	118	0.49 (0.40–0.61)**	313	141	0.51 (0.42–0.62)**
Uterine sarcoma	29	63	4.19 (2.73–6.44)**	160	80	0.46 (0.53–0.60)**	189	143	0.86 (0.69–1.06)
Vulvar	111	160	2.78 (2.23–3.47)**	28	120	3.94 (2.62–5.91)**	139	280	2.28 (1.87–2.78)**
GTN	3	2	1.29 (0.22–7.67)	15	4	0.24 (0.08–0.74)*	18	6	0.38 (0.15–0.95)*
Vaginal	26	22	1.63 (0.93–2.86)	90	12	0.12 (0.07–0.22)**	116	34	0.33 (0.23–0.48)**
Benign	55	3	0.11 (0.03–0.33)*	15	0	0.03 (0.00–0.49)*	70	3	0.05 (0.02–0.15)**
Other	121	23	0.37 (0.24–0.57)**	109	130	1.10 (0.85–1.40)	230	153	0.75 (0.62–0.92)*
Stage									
Benign	161	35	0.42 (0.29–0.60)**	63	50	0.73 (0.51–1.05)	224	85	0.43 (0.34–0.55)**
Pre-malignant	25	10	0.77 (0.37–1.60)	7	0	0.06 (0.00–1.07)	32	10	0.35 (0.17–0.72)*
I	343	229	1.29 (1.12–1.48)*	125	116	0.85 (0.67–1.09)	468	345	0.84 (0.73–0.95)*
II	101	33	0.63 (0.43–0.92)*	84	130	1.42 (1.09–1.86)*	185	163	1.00 (0.81–1.22)
III	430	230	1.03 (0.91–1.17)	714	824	1.06 (0.98–1.15)	1144	1054	1.04 (0.98–1.12)
IV	69	30	0.84 (0.55–1.27)	986	1178	1.10 (1.03–1.17)*	1055	1208	1.30 (1.21–1.39)**
Unclassified	86	63	1.41 (1.04–1.93)*	164	36	0.20 (0.14–0.29)**	250	99	0.45 (0.36–0.56)**
Recurrence									
No Recurrence	1197	483	15.75 (9.75–25.45)**	1291	954	1.49 (1.40–1.58)**	2488	1437	1.99 (1.86–2.13)**
Recurrence	18	147		852	1380		870	1527	
Charlson score									
Charlson 0–4	294	113	1.08 (1.03–1.14)*	115	90	1.02 (1.00–1.03)*	409	203	1.06 (1.04–1.08)**
Charlson >= 5	921	517		2028	2244		2949	2761	
Total	1215	630		2143	2334		3358	2964	

Statistically significance: *$p < 0.05$, **$p < 0.0001$.
GTN = Gestational Trophoblastic Neoplasia. Ovarian includes primary peritoneal and fallopian carcinoma. "Other" cancer types include non-Mullerian carcinomas (e.g. gastrointestinal primary) and synchronous carcinomas (e.g., ovarian and endometrial together).

in the medical complexity and disease severity of patients found on the ward in the robotic era.

3.4. Resource utilization: Imaging tests and consults

As shown in Table 2, in 2013 there were less X-rays (−14.7%), ultrasounds (−34.2%), and nuclear imaging (−45.5%) studies requested, but an increase in the number of computed tomography (CT) (+18.1%) and magnetic resonance imaging (MRI) studies (+41.7%). The number of interventional radiology (IR) procedures doubled and the number of gastroenterology (GI) procedures remained unchanged. The number of consults decreased to 665 from 703 in 2007 (−5.4%) and there were less consults for post-operative issues such as pain management (5 vs. 27), general surgery (13 vs. 29), urology (14 vs. 22), and wound care (9 vs. 16). Among admissions for elective surgery only, there were fewer consults to other specialties and fewer imaging tests across the board with less X-rays, ultrasounds, CT, MRI, PET, although more IR and GI procedures.

3.5. Inpatient costs

Despite a greater number of admissions for surgery (207 in 2013 vs. 163 in 2007), the amount of time spent on the ward by post-operative patients decreased substantially from 1215 days to 630 days, with less use of resources for radiology, nuclear medicine, and consultations to other services, representing an estimated cost savings of $5833 on the inpatient ward per surgical admission at our institution, a 59% decrease

Table 2
Cost of hospitalization for surgical, non-surgical, and all admissions.

Number of admissions	*Surgical*				*Non-surgical*				*Overall*			
	2007		2013		2007		2013		2007		2013	
	163		207		193		188		356		395	
	Units	Cost ($)	Units	Cost ($)	Units	Cost ($)	Units	Cost ($)	Units	Cost ($)	Units	Cost ($)
Hospitalization ($1288)	1215	$1,564,920	630	$811,440	2143	$2,760,184	2334	$3,006,192	3358	$4,325,104	2964	$3,817,632
X-ray ($76)	113	$8588	51	$3876	357	$27,132	350	$26,600	470	$35,720	401	$30,476
US ($98)	13	$1274	8	$784	69	$6762	46	$4508	82	$8036	54	$5292
CT ($187)	37	$6919	19	$3553	151	$28,237	203	$37,961	188	$35,156	222	$41,514
MRI ($400)	4	$1600	0	$0	8	$3200	17	$6800	12	$4800	17	$6800
PET ($747)	5	$3735	1	$747	17	$12,699	11	$8217	22	$16,434	12	$8964
IR ($746)	0	$0	3[a]	$2238	52	$38,792	106	$79,076	52	$38,792	109	$81,314
GI ($409)	0	$0	2[b]	$818	12	$4908	10	$4090	12	$4908	12	$4908
Consults ($168)	151	$25,368	99	$16,632	552	$92,736	566	$95,088	703	$118,104	665	$111,720
Total cost ($)		$1,612,404		$840,088		$2,974,650		$3,268,532		$4,587,054		$4,108,620
Cost/admission ($)		$9892		$4058		$15,413		$17,386		$12,885		$10,402

[a] One patient required one PICC line insertion under ultrasound guidance for total parenteral nutrition as well as transgluteal pigtail draining for a postoperative pelvic abscess. A second patient required pleural tapping by interventional radiology for pleural effusion.
[b] One patient underwent surgery for a suspected ovarian carcinoma and postoperatively had two GI procedures (colonoscopy and gastroscopy) to confirm suspicion that the cancer was of gastrointestinal tract origin.

in surgical admission costs ($4058 vs $9892) in the robotics era (Table 2).

If the unit cost per admission of surgical patients from 2007 is extrapolated to the increased volume seen in 2013 (44 additional surgical admissions), the additional cost incurred if the robotics program were not implemented would have been $435,250, assuming all these patients would have been suitable candidates for robotic surgery and rates of MIS remained the same.

The unit cost per non-surgical admission increased by 13% ($17,386 vs. $15,413). This is likely in part due to the increased medical complexity of the non-surgical patients as described, with the associated greater demand for imaging investigations and consults. Despite the increased cost of non-surgical patients, the overall estimated cost savings obtained following the introduction of the robotics program from the inpatient ward perspective was $478,434 (Table 2).

4. Discussion

The current study demonstrates the changes in the makeup of the inpatient ward before and after the introduction of robotic surgery, with the later era representing a ward that is more medically complex, more likely to have patients with greater comorbidities, advance stage, recurrent disease, and with ovarian and vulvar cancer, as opposed to endometrial and cervical cancer who tend to undergo robotic surgery. The inpatient ward also consisted of patients less likely to be present for elective surgery following the introduction of robotics due to the shortened post-operative in-hospital convalescence following robotic surgery. The changes in the makeup of the inpatient ward following the expansion of our MIS program were associated with changes in the resource use and the day-to-day operation of the inpatient ward.

The faster turnover of patients admitted for surgery and the associated decreased cost is consistent with previous studies comparing laparotomy to laparoscopy [17–19] and robotic surgery [4,5,9,20,21]. Since the volume of surgeries performed at a centre is not only limited by availability of operating room time but also availability of beds on the ward, the robotics program allows for an increase in the number of elective surgeries as hospital bed availability is less of a limiting factor. At our centre, the introduction of robotic surgery allowed for an increase of 27% in the number of elective surgeries performed (from 163 to 207) while simultaneously decreased resource use and reduced the total number of bed-days required by 585 days. It should be noted that we have in the last two years begun discharging some patients following robotic surgery on the same day, where appropriate, potentially making this effect even more pronounced.

On the other hand, the proportion of non-surgical patients in the ward has simultaneously increased (79% in 2013 compared to 64% in 2007, increase of 191 bed-days). This may also reflect the evolution of any oncology department where more patients accumulate over time with prolonged survival due to treatment advances over the five-year period of the study. These non-surgical patients are more medically complex, demanding greater resource use with an increased cost per admission ($17,386 in 2013 compared to $15,413 in 2007, increase of 13%). What the robotics program has enabled the inpatient ward to do is to liberate beds for non-surgical patients, thus accommodating their increased demand. This was possible while decreasing the overall cost of the inpatient ward by $478,434 in our cohort.

Hence, following the introduction of a robotic program, surgeons, nurses, and administrators could expect a greater turnover of surgical patients on the inpatient ward with some of them becoming outpatient procedures and hospital beds becoming available more frequently. With the focus shifting from fewer post-operative to greater medical issues, there are several implications in terms of resource planning. Firstly, nursing and allied healthcare expertise need to be adapted. Nursing expertise should include comfort with managing issues such as chemotherapy side effects, pain management, and end-of-life care. Allied healthcare expertise should be expanded with more resources for services such as physiotherapy, nutrition, social work, and palliative care. Secondly, our data suggests that this growing population of non-surgical patients require more resources such as imaging and consultations, which should be accounted for in ward resource planning. Thus, the contrast in care pathways between surgical and non-surgical patients appears more pronounced with the introduction of robotic surgery. This suggests that perhaps a ward structure of post-robotic surgery "fast track" care separate from a "gynecology oncology" ward might be more efficient from a resource-planning perspective, similar to how "centres of excellence" developed standardized care maps and clinical pathways [22,23].

Understanding the implications of implementing a robotic surgery program on the inpatient ward is important in preparing the organization's "readiness for change" [24] in anticipating how it could change nursing tasks, work flows, and resource requirements. It should be noted that the data in the robotics era is derived from a time period when the robotics program was already well-established at our institution in order to allow for the analysis of the inpatient ward at a plateau steady-state. One might expect a transitional period with a steeper learning-curve for personnel on the ward and associated costs in the short term after implementing such a program. In this study, we did not evaluate the pattern of transition in the early phase of introducing a robotics program, prior to reaching stability. Implications for changes outside of the inpatient ward, such as intraoperative costs, outfitting of operating room suites, changes in pre-surgical admission testing units, and impact on the emergency room, were not considered in the current study, and were addressed in a previous study [5]. Moreover, within the inpatient ward, the amount of time on the ward may not correlate fully with time spent on nursing tasks at the patient-level. For instance, while patients may be spending less time on the ward, they may require certain nursing tasks such as patient education and discharge planning to occur in a more compressed manner, especially in "extended recovery beds". The impact on community resources used outside of the hospital was also not examined and might be a point of interest for future studies. Nonetheless, the unique methodology of taking a snapshot of a year in the inpatient ward offers a new dimension for assessing the impact of robotic surgery.

There are several limitations to our study. This was a non-experimental study design and lacks a control group of two groups during the same time period, thus it is difficult to determine what would have happened in the absence of the robotics program. A comparable laparotomy group was not possible as the robotics program was offered to every operable patient with endometrial, cervical, or uterine cancer. The observed changes in resource use could have also been confounded by new developments in treatments and other administrative changes within our institution. For instance, the use of neoadjuvant chemotherapy at our center, while mostly relevant to ovarian cancers, coincided with the introduction of robotics, also contributing to a trend away from aggressive primary debulking surgeries to more conservative surgical management and allowing for robotically-assisted interval debulking surgeries. In addition, administrative pushes for cost containment strategies across the board may have also resulted in some diminished resource use in the robotic era. However, while not technically a control group, given that the cost of non-surgical admissions did not experience a parallel dramatic decrease, this acts as an indicator to suggest that the robotics program was likely a dominant driver of decreasing surgical admission costs. The cost variables chosen might not account for all costs incurred by the hospitalization. The unit cost of a hospitalization day ($1011) was meant to capture some of the overhead, nursing staff, and ancillary costs associated with an average admission to the gynecologic oncology ward. Costs incurred intraoperatively, in the outpatient setting, and in emergency room visits that did not lead to admission to the hospital were omitted to focus on the impact on the inpatient ward. Lastly, the cost estimates are for a single institution in one Canadian province and therefore may limit the study's generalizability. It remains however difficult to reconcile a decrease in hospital

utilization and cost, with a decrease in physician reimbursement in certain jurisdictions.

A decade after its introduction, the debate on robotic technology is ongoing in the literature. Organizations are beginning to recognize that the economic implications of introducing a robotics program extend beyond the operating room. Regardless of whether a robotics program is sensible in a given local context, it is timely to evaluate the broader ripple effect robotics has on hospital departments outside of the operating room (i.e., inpatient ward, radiology, etc.). The methodology presented here provides a unique, intuitive, and pragmatic approach which may be used to evaluate changes in the hospital setting. The results of this study could help inform administrators in hospitals with an established robotics program as well as those evaluating the cost-benefit of incorporating robotics into their surgical program.

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Conflicts of interest

Roy Kessous obtained a fellowship training grant from Intuitive Surgical.

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