EXPLORING POSTOPERATIVE RECOVERY IN SENIORS UNDERGOING ELECTIVE ABDOMINAL SURGERY

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ABSTRACT

Background:

Elderly patients aged 65 years and older represent a significant portion of individuals undergoing elective abdominal surgery (1). This type of surgery has been shown to impact physiological function and patient autonomy in elderly patients (2). Most surgical recovery studies focus on hospitalization outcomes, such as length of stay (3), occurrence of postoperative complications (4, 5) and 30-day mortality (6). However, the short-term nature of hospitalization outcomes captures limited information on patient health, poorly reflects what is considered important to elderly patients, and incompletely describes their recovery process. Due to the challenges of measuring recovery by hospitalization outcomes, research has shown that patient-centered outcomes (PCO) measuring functional status, cognition, mental health, and quality of life, are better adapted to characterize the full spectrum of patient recovery and present a relevant framework for reporting surgical recovery in elderly patients (7, 8). The aim of this thesis is to improve our knowledge of surgical recovery measured by a comprehensive set of hospitalization and patient-centred outcomes in elderly patients and to identify potential preoperative factors that may impact their recovery post-surgery. To accomplish this, we designed and conducted a prospective cohort study that examined the relationship between preoperative factors (preoperative nutritional status and frailty) and postoperative recovery in elderly patients measured by multiple hospitalization and patient-centered outcomes.

Methods:

Patients aged 70 years or older undergoing elective abdominal general surgery were recruited for this study. Only patients requiring postoperative hospitalization were included in the study and were followed for a total of 6-months postoperatively. Further exclusion criteria included: surgeries within the previous six months, an inability to ambulate, a previous diagnosis

of dementia or a Mini-Mental State Examination (MMSE) score of less than 18 (9) and the inability to speak English or French. Patients who underwent subsequent surgeries within the 6-month follow-up period withdrew from the studies, and no further data were collected on them. All participants provided informed consent prior to enrolment. The study was approved by the Ethics Review Board at Jewish General Hospital and St. Mary's Hospital Center in Montreal, Quebec, Canada.

In the first part of this study, we prospectively assessed the impact of preoperative nutritional status on functional recovery. The preoperative nutritional status was determined by the Subjective Global Assessment (SGA) and the primary outcome for functional status was upper body strength measured by hand grip strength (HGS). In this primary analysis, surgical recovery was defined as return to or a surpassed level of preoperative hand grip strength over the 6-month follow-up period. Repeated measures analysis was used to determine whether SGA status affects the trajectory of postoperative HGS.

In the second part of this study, we investigated the association of frailty and recovery of multiple hospitalization and patient-centered outcomes (functional status, cognition, mental health and perception of quality of life) during the follow-up period. Preoperative frailty was assessed according to five frailty domains as outlined by Fried et al (10). Individuals exhibiting three or more frailty criteria were categorized as frail, one or two frailty criteria as pre-frail, and no criteria as non-frail (10). Recovery to preoperative functional status (activities of daily living (ADL) and instrumental activities of daily living (IADL)), cognition, quality of life, and mental health were assessed at 1, 3, and 6 months postoperatively. A repeated measures logistic regression was used to analyze the effect of frailty on recovery over time.

Results:

The results from the primary analysis demonstrated that mean postoperative hand grip strength (HGS) was higher in well-nourished patients compared to those categorized as mildly to moderately malnourished throughout the 6-month recovery period. Overall, 64% of well-nourished patients had recovered to their baseline HGS compared to 44% of mildly to moderately malnourished patients. After controlling for all relevant covariates, nutritional status was not a significant predictor of functional status (p=0.428). Moreover, the effect of nutritional status on the trajectory of postoperative HGS, estimated as the interaction between nutritional status and time, was not found to be statistically significant (p=0.455).

The results from the secondary analysis demonstrated that more frail patients experienced adverse hospitalization outcomes, and fewer had recovered to preoperative functional status. Recovery for cognition at 6 months was similar across frailty groups, ranging from 70% to 73%. We observed higher 6-month recovery for mental health measured by Geriatric Depression Scale (GDS) among frail patients (79%) compared to pre-frail (67%) and non-frail patients (52%), while pre-frail patients (77%) showed higher recovery for quality of life measured by EQ-5D-L than frail (60%) and non-frail (54%). Overall, adjusted models for trajectories of recovery showed no statistically significant differences across frailty groups for functional status, cognition and mental health. Only one significant difference was found in the trajectory of recovery for quality of life between pre-frail and non-frail patients (p = 0.02).

Conclusion:

In conclusion, our study is important as it characterizes postoperative recovery in elderly patients by evaluating a comprehensive set of hospitalization and patient-centered outcomes, at multiple time points over the recovery period. Overall, the study presented in this thesis suggests

that postoperative recovery among the elderly is protracted past 6 months. Moreover, we found no meaningful association between preoperative risk factors such as nutritional status or frailty and the trajectory of surgical recovery. Due to the rapidly growing number of elderly patients undergoing surgery, future studies should explore the possible benefits of surgical prehabilitation and optimization of perioperative care in this surgical population.

RÉSUMÉ

Contexte:

Les patients âgés de 65 ans et plus constituent une portion significative d'individus qui ont des chirurgies abdominales (1). Il a été démontré que ce type de chirurgie a un impact sur la fonction physiologique et sur l'autonomie des personnes âgées (2). La plupart des études sur le rétablissement postopératoire se concentrent sur la durée du séjour (3), l'apparition de complications postopératoires (4, 5) et la mortalité à 30 jours (6). Cependant, le peu de données recueillies pendant la courte période qu'est l'hospitalisation ne permet pas de relever assez d'informations sur les patients. Ces données reflètent peu ce qui est considéré comme important pour les personnes âgées et décrivent de manière incomplète leur rétablissement postopératoire. Il a été démontré que les indicateurs centrés sur le patient (PCO), incluant le statut fonctionnel, la cognition, la santé mentale et la qualité de vie, permettent de mieux caractériser le spectre entier de rétablissement du patient (7, 8). Les PCO fournissent un cadre de travail pertinent pour rapporter les résultats du rétablissement postopératoire chez les personnes âgées. Le but de cette thèse est d'améliorer notre connaissance du rétablissement postopératoire chez les personnes âgées mesuré par des indicateurs postopératoires et centrés sur le patient (PCO) et d'identifier les facteurs préopératoires qui peuvent influencer leur rétablissement postopératoire. Dans ce but, nous avons conçu et réalisé une étude prospective chez des personnes âgées pour examiner l'association entre les facteurs préopératoires (comme le statut nutritionnel préopératoire et la fragilité) et le rétablissement postopératoire mesuré par plusieurs indicateurs postopératoires et centrés sur le patient.

Méthodes:

Des patients âgés de 70 ans et plus devant subir une chirurgie générale abdominale ont été recrutés pour l'étude. Seuls les patients qui avaient besoin d'une hospitalisation à la suite de leur opération ont été inclus dans l'étude. Ils ont été suivis pour un total de six mois après l'opération. D'autres critères d'exclusion incluaient: une chirurgie dans les six derniers mois, l'incapacité à se déplacer, un diagnostic antérieur de démence ou un score de moins de 18 sur le *Mini-mental state examination* (MMSE) (9) et l'incapacité à parler en anglais ou en français. Les patients qui ont eu des chirurgies subséquentes pendant la période de six mois de suivis ont été retirés de l'étude et aucune autre donnée n'a été collectée à leur sujet. Tous les participants ont donné leur consentement libre et éclairé avant d'être recrutés dans l'étude. Cette étude a été approuvée par les comités d'éthique de l'Hôpital Général Juif et du Centre Hospitalier de St. Mary à Montréal, Québec, Canada.

Dans la première analyse de cette étude, nous avons évalué prospectivement l'impact du statut nutritionnel préopératoire sur le rétablissement fonctionnel. Le statut nutritionnel préopératoire a été déterminé par l'Évaluation globale subjective (ÉGS). Le résultat principal pour le statut fonctionnel était la force du haut du corps mesurée par la force de préhension (HGS). Ici, le rétablissement postopératoire a été défini comme le retour ou le dépassement des valeurs préopératoires de la force de préhension après une période de suivi de six mois. L'analyse de mesures répétées a été utilisée pour déterminer si le statut de l'ÉGS affecte la trajectoire de la force de préhension postopératoire.

Dans la deuxième analyse de cette étude, nous avons étudié l'association entre la fragilité et le rétablissement postopératoire mesuré par plusieurs indicateurs postopératoires et centrés sur le patient (PCO) (statut fonctionnel, la cognition, la santé mentale et la perception de la qualité de vie) pendant la période de suivi. La fragilité préopératoire a été évaluée en fonction des cinq

critères de la fragilité, comme décrits par Fried et al. (10). Les patients qui présentaient trois critères de fragilité ou plus ont été catégorisés comme fragiles; ceux qui remplissaient un ou deux critères de fragilité, comme pré-fragiles; et ceux qui ne remplissaient aucun critère, comme non fragiles (10). Le rétablissement du statut fonctionnel préopératoire (les activités de la vie quotidiennes (AVQ), les activités instrumentales de la vie quotidienne (AIVQ)), la cognition, la qualité de vie et la santé mentale ont été évaluées à un, trois et six mois après opération. Une régression logistique de mesures répétées a été utilisée pour analyser l'effet de la fragilité sur le rétablissement au fil du temps.

Résultats:

La première analyse présentée dans cette thèse a démontré que la force de préhension (HGS) postopératoire moyenne était supérieure chez les patients très bien nourris comparés à ceux qui étaient catégorisés comme étant légèrement à modérément mal nourris durant la période de rétablissement de six mois. Au total, 64% des patients bien nourris ont eu un bon rétablissement, atteignant des valeurs de HGS équivalentes à leurs valeurs initiales, comparativement à 44% des patients modérément mal nourris. Après avoir effectué un contrôle de toutes les covariables pertinentes, le statut nutritionnel n'était pas un indicateur significatif du statut fonctionnel ($p=0.428$). En plus, l'effet du statut nutritionnel sur la trajectoire de HGS postopératoire, estimé comme une interaction entre le statut nutritionnel et le temps, n'était pas statistiquement significatif ($p=0.455$).

La deuxième analyse présentée dans cette thèse a démontré que plus de patients fragiles ont eu des indicateurs postopératoires adverses et que peu ont récupéré leur statut fonctionnel préopératoire initial. Le rétablissement pour la cognition à six mois était similaire dans les groupes peu importe la fragilité, atteignant 70% à 73%. Nous avons observé un plus grand rétablissement

en six mois pour l'indicateur de santé mentale mesuré par l'Échelle de dépression gériatrique (GDS) parmi les patients fragiles (79%) comparés aux pré-fragiles (67%) et aux patients non fragiles (52%). De plus, les patients pré-fragiles avaient un meilleur rétablissement pour l'indicateur de qualité de vie mesuré par l'EQ-5D-L (77%) comparativement aux patients fragiles (60%) et non fragiles (54%). En somme, les modèles ajustés pour la trajectoire de rétablissement n'ont démontré aucune différence statistique significative entre les groupes pour le statut fonctionnel, la cognition et la santé mentale. Seule une différence significative a été observée dans la trajectoire de rétablissement pour la qualité de vie entre les patients pré-fragiles et non fragiles ($p=0.02$).

Conclusion:

En conclusion, notre étude est importante parce qu'elle caractérise le rétablissement postopératoire des personnes âgées en évaluant plusieurs PCO et indicateurs postopératoires à différents moments de la période de rétablissement. Dans l'ensemble, l'étude décrite dans cette thèse suggèrent que le rétablissement postopératoire chez les personnes âgées est prolongé à plus de six mois. De plus, nous n'avons trouvé aucune association significative entre les facteurs de risques préopératoires, comme le statut nutritionnel ou la fragilité, et la trajectoire de rétablissement postopératoire. En raison de la croissance rapide du nombre de patients âgés qui ont des chirurgies, plus de recherche est nécessaire pour explorer les bénéfices possibles de la préadaptation chirurgicale et l'optimisation de soins périopératoires dans cette population spécifique.

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-Tarifin Sikder

CONTRIBUTION TO ORIGINAL KNOWLEDGE

This thesis contributed to original knowledge by:

1. Characterizing postoperative recovery in older surgical populations from a multidimensional framework consisting of hospitalization and patient-centered outcomes.

2. Measuring the impact of preoperative factors such as nutritional status and frailty on the surgical recovery of elderly patients using validated outcome measures.

3. Identifying a need for future studies to examine the impact of surgical pre-habilitation or geriatric assessments on managing surgical care and postoperative recovery in elderly patients.

CONTRIBUTION OF AUTHORS

Ms. Tarifin Sikder contributed to the acquisition, analysis and interpretation of the data, drafting and revising both manuscripts.

Dr. Simon Bergman contributed to the conception/design of the research, interpretation of the data, drafting and revising of both manuscripts.

Ms. Nadia Sourial contributed to the conception/design of the study, interpretation of the data, drafting and revising of both manuscripts.

Ms. Geva Maimon contributed to the analysis and interpretation of the data and drafting and revising of both manuscripts.

Dr. Mehdi Tahiri contributed to the acquisition of the data for both manuscripts.

Ms. Debby Teasdale contributed to the acquisition of the data for both manuscripts.

Dr. Shannon A. Fraser critically revised both manuscripts.

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Ms. Paule Bernier critically revised the manuscript for Study I presented in Chapter 2.

Dr. Howard Bergman critically revised the manuscript for Study II presented in Chapter 3.

LIST OF ABBREVIATIONS

ADL Activities Daily Living

BMI Body Mass Index

CCI Charlson Comorbidities Index

CI Confidence Interval

IQR Interquartile Ratio

ED Emergency Department

EQ EQ-5D-3L

GDS Geriatric Depression Scale

HGS Handgrip Strength

IADL Instrumental Activities Daily Living

IRR Incidence Rate Ratios

LOS Length of Stay

MMSE Mini Mental Status Exam

MOCA Montreal Cognitive Assessment

OARS Older American Resources and Services

OR Odds Ratio

PCO Patient centered outcomes

SGA Subjective Global Assessment

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CHAPTER 1: INTRODUCTION

Elderly patients aged 65 years and older represent a significant portion of individuals undergoing elective abdominal surgery (1). This type of surgery has been shown to impact physiological function and patient autonomy in elderly patients' post-surgery and throughout the recovery process (2). Surgical recovery in elderly patients is complex due to lower physiological reserves (11, 12), a greater number of comorbidities (13) and potential cognitive impairment (14). Currently in the literature, the process of surgical recovery is increasingly studied by researchers, however, there is little consensus on how recovery should be measured or what factors impact the surgical recovery of elderly patients.

Most surgical studies characterize surgical recovery by measuring hospitalization outcomes, such as length of stay (3), the occurrence of postoperative complications (4, 5), and 30-day mortality (6). These outcomes are widely studied because they are highly objective and easy to measure. However, the short-term nature of hospitalization outcomes captures limited information on patient health, poorly reflects what is considered important to elderly patients, and incompletely describes their recovery process. Due to the challenges of measuring recovery by hospitalization outcomes, research has shown that patient-centered outcomes (PCO) measuring functional status, cognition, mental health, and quality of life, are better adapted to characterize the full spectrum of patient recovery and present a relevant framework for reporting surgical recovery in elderly patients (7, 8). It is important to understand the recovery process in this surgical population so that multidisciplinary institutional processes can be developed to optimize care for this patient population.

This thesis aims to improve our knowledge of surgical recovery measured by a comprehensive set of hospitalization and patient-centered outcomes in elderly patients and to

identify potential preoperative factors that may impact their recovery post-surgery. To accomplish this, we designed and conducted a prospective cohort study that examined the relationship between preoperative factors and postoperative recovery in elderly patients measured by multiple hospitalization and patient-centered outcomes. This thesis presents the prospective cohort study and its focused analyses on preoperative nutritional status, frailty, and postoperative recovery.

CHAPTER 2: STUDY I

Assessing the Effect of Preoperative Nutrition on Upper Body Function in Elderly Patients Undergoing Elective Abdominal Surgery

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CLINICAL RELEVANCY STATEMENT

The findings of this study demonstrate the importance of preoperative nutritional status on upper body function in elderly patients. This study is relevant to healthcare professionals aiming to develop multidisciplinary institutional processes for optimizing nutritional and functional status for this patient population.

ABSTRACT

Background: Malnutrition among elderly surgical patients has been associated with poor postoperative outcomes and reduced functional status. Although previous studies have shown that nutrition contributes to patient outcomes, its long-term impact on functional status requires better characterization. The objective of this study is to examine the effect of nutritional status on postoperative upper body function over time in elderly patients undergoing elective surgery.

Methods: This is a two-year prospective study of elderly patients (≥70) undergoing elective abdominal surgery. Preoperative nutritional status was determined using the Subjective Global Assessment (SGA). The primary outcome was hand grip strength (HGS) at 1, 4, 12 and 24-weeks post-surgery. Repeated measures analysis was used to determine whether SGA status affects the trajectory of postoperative HGS.

Results: The cohort included 144 patients with mean age of 77.8 ± 5.0 years, and mean BMI of 27.7 ± 5.1 kg/m^2. The median (IQR) CCI was 3 (2-6). Participants were categorized as well nourished (86%) and mildly to moderately malnourished (14%), with mean preoperative HGS of 25.8 ± 9.2 kg and 19.6 ± 7.0 kg, respectively. At 24-weeks, 64% of well-nourished patients had recovered to their baseline HGS compared to 44% of mildly to moderately malnourished patients. Controlling for all relevant covariates, SGA did not significantly affect the trajectory of postoperative HGS.

Conclusion: While HGS values over the 24 weeks were consistently higher in the well-nourished SGA group than the mildly to moderately malnourished SGA group, no difference in the trajectories of HGS was detected between the two groups.

INTRODUCTION

Twenty to twenty-five percent of surgical patients aged 65 and older are malnourished prior to elective abdominal surgery (1, 2). This is due to lower physiological reserves (3), greater number of comorbidities (4), potential cognitive impairment (5) and social isolation (6). Postoperatively, malnutrition is associated with longer hospital stays, increased susceptibility to complications, higher mortality, decreased quality of life, and reduced functional capacity (7-10).

Most studies investigating the impact of malnutrition on functional capacity group together surgical and medical patients (11), have only short-term follow-up assessments (12, 13), often merge emergent and elective surgeries (13), and lack key baseline measures (14). Medical and surgical populations should not be combined as higher prevalence of malnutrition has been reported among medical populations (15, 16). The short-term nature of most investigations provides an incomplete picture of how malnutrition impacts functional status. To better characterize this impact on functional capacity throughout recovery, consistent functional measures must be obtained at time points throughout an extended postoperative period.

Studies combining emergent and elective surgeries may result in an overestimation of the influence of malnutrition on functional capacity, as higher rates of malnutrition and functional decline are associated with patients undergoing emergent procedures (17).

The objective of this study was to describe the effect of preoperative nutritional status on functional capacity, as measured by hand grip strength (HGS) in elderly patients undergoing elective abdominal surgery over a 24-week follow-up period.

METHODS

This prospective study was conducted from July 2012 to December 2014 at two institutions in Montreal, Canada.

Study Population

Patients aged 70 years or older undergoing elective abdominal general surgery were recruited for the study. Only patients requiring postoperative hospitalization were included in the study, and were followed for a total of 24 weeks after surgery. Further exclusion criteria included: surgeries within the previous six months, an inability to ambulate, a previous diagnosis of dementia or a Mini-Mental State Examination (MMSE) score of less than 18 (18) and the inability to speak English or French. Patients who underwent subsequent surgeries within the 24-week follow-up period withdrew from the study, and no further data were collected on them. All participants provided informed consent prior to enrolment. The study was approved by the Ethics Review Board at both institutions.

Patient Characteristics

The following patient characteristics were recorded preoperatively: age, sex, height, weight, the presence of cancer, comorbidities and nutritional status. Nutritional status was measured using the Subjective Global Assessment (SGA),a validated tool which categorizes participants as well nourished, mildly to moderately malnourished or severely malnourished, by evaluating weight change and dietary intake and performing a physical exam (19). In the context of this study, a modified validated version of the SGA, excluding functional capacity and gastro-intestinal symptoms, was used, allowing for a shorter questionnaire without affecting the resulting

classifications (19). Comorbidity was measured by the Charlson Comorbidity Index (CCI) and derived based on the number and severity of the observed comorbidities (20).

Hospitalization Data

Data pertaining to perioperative factors such as wound class (clean, clean-contaminated, contaminated, or dirty) and surgical approach (laparoscopic or open) were collected to control for the type of surgery patients underwent. Other hospitalization data such as length of stay and occurrence of postoperative complications were also recorded. All postoperative complications were retrieved from patient charts in accordance with the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) definitions (21, 22). Each complication was scored on a scale of 0 to 100 using the Comprehensive Complication Index (23), which captures a wide range of complications and their varying severities; a score of 0 represents no complications and a score of 100 represents death. In the case of multiple complications, severe complications are accorded more weight on the Comprehensive Complication Index score compared to complications of lesser severity (24).

Primary Outcome

The primary outcome was postoperative upper body strength as measured by handgrip strength (HGS). Studies have shown that grip strength is a validated measure of upper body capacity in elderly persons (25). Additionally, lower HGS has been associated with surgical outcomes, such as higher incidence of complications (26) and longer length of stay(4). HGS was measured in kilograms using a Jamar hand dynamometer from a seated upright position with feet in contact with the floor and knees bent at ninety degrees (27, 28). The dynamometer was held in the dominant hand with the arm positioned at ninety degrees from the body (27-29). HGS was

measured preoperatively and postoperatively at 1, 4, 12, and 24 weeks. At each time point, the participant was given 3 trials and the best score was recorded. Measurements were taken either at the hospital or at the home of the participants.

Secondary Outcomes

The secondary outcomes were length of stay, postoperative complications, recovery to preoperative upper body strength, and walking speed. Patients were considered recovered if postoperative HGS values returned to or surpassed baseline measures. Furthermore, once a patient was deemed recovered, the patient was considered to be recovered at all subsequent time points regardless of a drop in their HGS.

Statistical Analysis

Descriptive statistics were conducted on baseline and postoperative data. Wounds were categorized as class I (clean), class II (clean-contaminated), class III (contaminated) and class IV (dirty). Wound classes II and III were combined due to low numbers in class III.

A repeated measures linear regression model was used to assess the effect of preoperative nutritional status on the trajectory of postoperative HGS over the 24-week follow-up period. A spatial power correlation structure was used to estimate the degree of correlation between HGS values over time within each patient. The interaction between SGA and time was tested to determine if the trajectories of HGS over time differ between SGA groups. To account for possible sources of confounding, the model was adjusted for: sex, age, BMI, comorbidities (CCI), surgical approach, preoperative HGS and the presence of cancer. Secondary analyses included: a regression model to evaluate the effect of preoperative nutrition on the presence of postoperative complications, a Negative Binomial model for length of stay, a repeated measures logistic model

for recovery of HGS, and a repeated measures model for walking speed. For all models, estimates of the effects were obtained along with their associated 95% confidence intervals.

Lastly, the baseline characteristics and postoperative outcomes of subjects in the final analysis and subjects that voluntary withdrew from the study were compared to assess potential bias due to loss to follow-up.

All analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Across both hospital institutions, 351 patients were identified and screened to participate in the study. Seventy-one patients did not meet the inclusion criteria, 88 patients refused to participate, and 21 patients were unable to be reached by the research assistants. Overall, 280 patients were eligible for the study, of which 171 patients agreed to participate, resulting in a participation rate of 61.1 %. Following enrollment, 27 patients were excluded from the analysis, most often because their surgery had been cancelled. Thirty-eight patients (26.4 %) voluntarily withdrew from the study during the 24-week follow up period due to subsequent surgeries, lack of motivation, fatigue or travel. For these patients, evaluation data up until their withdrawal from the study were included in the analysis. No clinically, nor statistically significant differences in patient baseline characteristics and postoperative outcomes were observed between patients who withdrew from the study and those who remained in the study until completion (results not shown).

Baseline Characteristics and Postoperative outcomes

One-hundred and forty-four patients were included in the study; 54.9% were male and the mean age was 77.8 ± 5.0 years (Table 1). The mean BMI was 27.7 ± 5.1 kg/m^2, the median CCI was 3 (IQR 2-6) and 68.1 % of the patients had cancer. The mean preoperative grip strength was 24.9 ± 9.2 kg. Using the FNIH Sarcopenia cutoffs of less than 26 kg for males and less than 16 kg for females (30), preoperatively none of the male study participants had low handgrip strength and 26% of the female participants did. The mean preoperative walking speed was 0.85 ± 0.22 m/s. The most common surgeries included colorectal procedures (n=81, 56.3 %), hernia repair (n=22, 15.3%) and hepatobiliary surgeries (n=20, 13.9%). Hiatal hernia repairs, gastric surgery, splenectomy, small bowel resection, and retroperitoneal sarcoma resection represented the remaining 14.6 % (n=21). Overall, 72.2 % of patients underwent open procedures. Seventy-seven percent (n=111) of wounds were categorized as wound class II (clean-contaminated) or class III (contaminated) and there were no class IV (dirty) wounds. Thirty-five percent (n=50) of patients had one or more complications with a mean Comprehensive Complication Index score of 26.2 ± 24.1. The mean length of hospitalization was 7.6 ± 5.3 days. The mortality rate of this cohort was 2.1 % (n=3).

Impact of Preoperative Nutritional Status on the Trajectory of Postoperative Handgrip Strength

One-hundred and twenty-four patients (86.1%) were categorized as well-nourished, 20 patients (13.9%) were categorized as mildly to moderately malnourished and none of the study patients were determined to be severely malnourished. Male patients made up 57% of the well-nourished group and 40% of the mildly to moderately malnourished group. The preoperative mean grip strengths were 25.8 ± 9.2 kg and 19.6 ± 7.0 kg for the well-nourished group and mildly to moderately malnourished group, respectively. The trajectory of postoperative HGS for each SGA

group is depicted in Figure 1. The percent of patients recovered per SGA group over the 24-week follow-up period is shown in Figure 2. The mean postoperative HGS for the well-nourished group is higher than the mildly to moderately malnourished group throughout the 24-week recovery period.

Table 2 shows the unadjusted and adjusted effect estimates for nutritional status, time and other covariates. In the unadjusted model, nutritional status was associated with postoperative HGS ($p=0.001$). However, when adjusting for all other confounders, nutritional status was not a significant predictor of postoperative HGS ($p=0.428$). Moreover, the effect of nutritional status on the trajectory of postoperative HGS, estimated as the interaction between nutritional status and time, was not found to be statistically significant ($p=0.455$). Other predictors in the adjusted model such as gender ($p=0.001$) and preoperative grip strength ($p<0.0001$) were statistically significant for determining postoperative grip strength.

Additional Exploratory Analyses

Additional post-hoc analyses were conducted to study the effect of SGA status on secondary outcomes including recovery to preoperative upper body strength, length of stay, postoperative complications and walking speed. Nutritional status was not found to be a predictor for these secondary outcomes.

DISCUSSION

In this study of elderly patients undergoing elective abdominal surgery, 14% of the cohort was identified as being mild to moderately malnourished using the SGA. This is similar to values in the literature, which report malnutrition for 8.5% to 25% of patients undergoing elective surgery

(1, 2, 31). In this study, grip strength was lower among malnourished patients compared to well-nourished individuals both preoperatively and during the recovery period. Our findings are consistent with previous research conducted on medical and surgical elderly populations (4), although we found no significant association between nutritional status and the trajectory of functional status over time when controlling for all other confounders. In our study, 64% of well-nourished patients had recovered their HGS at 24 weeks compared to 44% of mildly to moderately malnourished patients. This is consistent with previous findings looking at short-term recovery at time of discharge and long-term recovery over a 24-week postoperative period, which suggests well-nourished patients may recover faster than malnourished individuals postoperatively (32, 33). Overall, for this cohort only 61% of patients had recovered to baseline HGS values at 24 weeks post-surgery. The fact that a significant number of patients had not recovered at 24 weeks is not surprising and similar to previous research that has reported that recovery of HGS among the elderly is protracted past 24 weeks (34).

Our findings show that preoperative malnutrition was associated independently with suboptimal preoperative and postoperative functional status. This suggests that well-nourished individuals maintain higher functioning capacity throughout the recovery process. Bastow et al. showed that malnutrition negatively impacted recovery of functional capacity of elderly patients after surgery (32). Similarly, Lawrence et al. reported that nutritional status was a predictor of functional status, measured with activities of daily living for elderly patients (34). Others have shown that functional capacity is reduced postoperatively in hospitalized malnourished patients (35-37). Furthermore, previous research has demonstrated that malnutrition is related to prolonged length of stay and increased complication risk (26, 38, 39). This study did not find significant associations between malnutrition and these outcomes.

Functional status in the elderly holds significant clinical relevance as it is one of the factors that takes the longest to return to baseline during the recovery period (34, 40). Moreover, functional status is of crucial importance to patients themselves as many would forgo lifesaving medical interventions if it meant significantly impaired functional capacity and dependency (29). In this study, HGS was the measure used to evaluate functional status. HGS has been used to assess functional status in both medical and surgical patient populations (41, 42), and has also been shown to be both reliable and sensitive in detecting changes in functional capacity of elderly persons (25, 43, 44). In this study, being male and having higher preoperative functional capacity were both associated with a higher postoperative grip strength. Although this is consistent with previous findings(11, 13, 45, 46), some have demonstrated that preoperative grip strength failed to predict the rate of recovery to baseline grip strength among elderly surgical patients (12). Wound class and surgical approach were used to control for type of surgery but were not found to be significant predictors of functional status. Malnutrition has also been related with prolonged length of stay and higher risk of postoperative complications (7, 38, 46, 47), although this was not demonstrated in this study.

There are several potential limitations to our study. First, the study participation rate was 61.1%. Although, our participation rate was in the range (49% to 84%) reported among studies focusing on the elderly, selection bias is possible (2, 14, 44). Second, due to the inclusion/exclusion criteria, those with dementia, wheel chair bound or undergoing emergent surgery were not included in the study and thus the functional recovery of these patients was not characterized. Next, standard reference values for grip strength for the elderly surgical population are lacking in the literature and thus determining minimal clinically significant differences between SGA groups was difficult. In our study population, the number of patients with inadequate nutritional status was relatively

low, limiting the power in this study to detect differences in the primary outcome. Moreover, none of the patients in our study were categorized as severely malnourished. Thus, our study can only demonstrate the impact of mild to moderate malnutrition on HGS; we can make no inference on the effects of severe malnutrition on grip strength for the elderly, surgical population. Lastly, at the end of the follow up period 39% of the patients had not recovered to baseline grip strength measures, therefore only a partial recovery of grip strength was captured in this study.

This study suggests that elderly patients who have superior preoperative nutritional status have higher functional capacity, before surgery and during the recovery period. Among all the possible predictors of functional recovery analyzed in this study, preoperative grip strength was a modifiable factor. A positive impact of long term recovery may be observed by implementing institutional processes or establishing pre-habilitation programs to identify and support elderly patients at risk of suffering from reduced functional status prior to surgery (48-50). Programs providing an early-interdisciplinary approach through strength conditioning and optimization of nutritional status may be a key to optimizing functional recovery post-surgery (48-50). Due to the rapidly growing number of elderly patients undergoing surgery, further investigations are needed to understand how to best prepare and manage the complexities associated with their surgical recovery.

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APPENDIX

Table 1. Patient Characteristics

Baseline Characteristics & Postoperative Outcomes	Total Sample (n=144)
Age, mean (SD)	77.8(5.0)
Male gender, n (%)	79 (54.9)
Body Mass Index, mean (SD)	27.7 (5.1)
Nutritional Status, Well-nourished, n (%)	124 (86.1)
Charlson comorbidity index, median (IQR)	3 (2-6)
Preoperative Grip Strength, mean (SD)	24.9 (9.2)
Cancer Diagnosis, n (%)	98 (68.1)
Wound Class II or III, n (%)	111 (77.1)
Laparoscopic surgery, n (%)	40 (27.8)
Type of Surgery, n (%)	
Colorectal	81 (56.3)
Hernia Repair	22 (15.3)
Hepatobiliary	20 (13.9
Other	21 (14.6)
Postoperative Outcomes	
Mortality, n (%)	3 (2.1)
Length of Stay, mean (SD)	7.6 (5.3)
Comprehensive Complication Index for Patients with Complications, mean (SD)	26.2 (24.1)

Table 2. Repeated Measures Linear Mixed Models, Predictors of Postoperative Grip Strength (n=153)

	Unadjusted Models			Adjusted Models		
Variable	Estimate	95% CI	*P*-value	Estimate	95% CI	*P*-value
Age	-0.71	(-0.98, -0.44)	<0.0001*	-0.07	(-0.19, 0.05)	0.254
Gender [a]	-9.23	(-11.73, -6.73)	<0.0001*	-2.16	(-3.40, -0.92)	0.001*
Body Mass Index	0.19	(-0.10, 0.47)	0.204	0.03	(-0.08, 0.15)	0.561
Charlson comorbidity index	0.40	(-0.11, 0.91)	0.126	0.05	(-0.16, 0.26)	0.637
Preoperative Grip Strength	0.90	(0.84, 0.96)	<0.0001*	0.81	(0.73, 0.88)	<0.0001*
Nutritional Status [b]	-7.07	(-11.16, -2.98)	0.0008*	-0.90	(-3.14, 1.34)	0.428
Cancer Diagnosis [c]	-0.60	(-3.71, 2.50)	0.702	0.26	(-1.23, 1.75)	0.731
Wound Class [d]	-1.20	(-4.65, 2.25)	0.494	-0.55	(-2.16, 1.05)	0.499
Surgical Approach [e]	-1.69	(-4.91, 1.53)	0.301	-0.44	(-1.64, 0.76)	0.471
Time	0.004	(-0.003, 0.011)	0.280	0.003	(-0.003, 0.009)	0.359
Interaction between Nutritional Status and Time [b]	-0.007	(-0.027, 0.0137)	0.526	-0.006	(-0.022, 0.010)	0.455

[a] Female compared to male, [b] SGA mildly to moderately malnourished compared to well-nourished, [c] No cancer diagnosis compared to cancer diagnosis, [d] Wound class 1 versus 2 and 3, [e] Open surgery compared to laparoscopy.

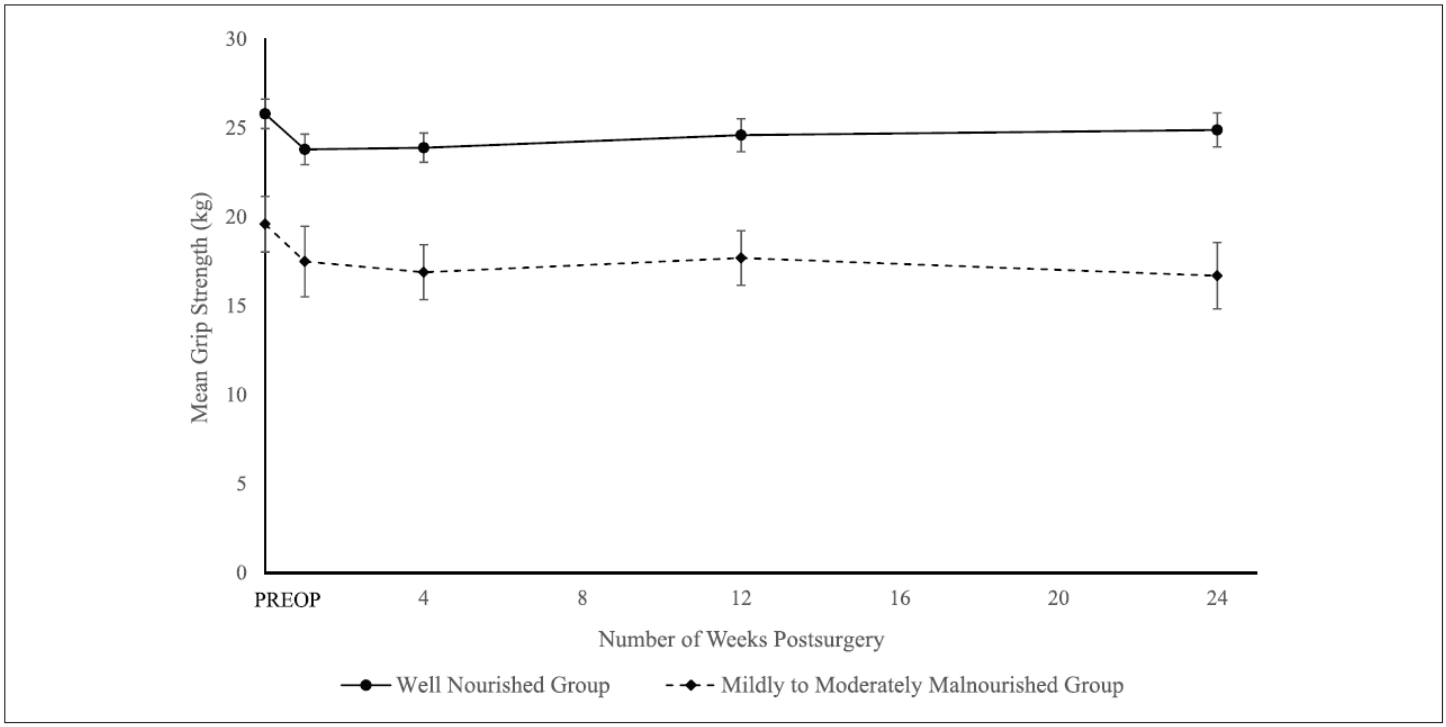

Figure 1. Postoperative handgrip strength by nutrition status over a follow-up period of 24 weeks ($P = .455$). The P value is based on the interaction of Subjective Global Assessment and time on handgrip strength. PREOP, preoperative.

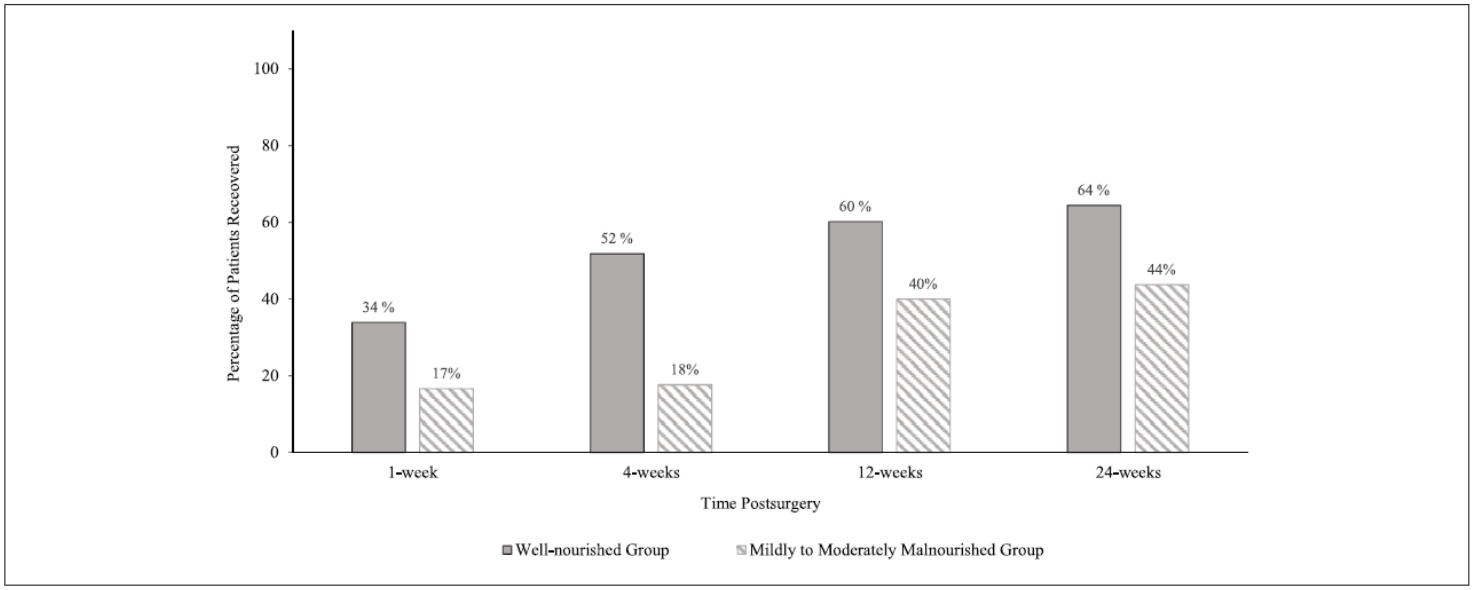

Figure 2. Percentage of patients recovered to preoperative handgrip strength over a follow-up period of 24 weeks ($P = .503$). The P value is based on the interaction of Subjective Global Assessment and time on handgrip strength.

CHAPTER 3: STUDY II

Postoperative Recovery in Frail, Pre-Frail, and Non-Frail Elderly Patients Following Abdominal Surgery

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ABSTRACT

Background: The objective of this study is to explore the association between frailty and surgical recovery over a 6-month period, in elderly patients undergoing elective abdominal surgery.

Methods: 144 patients were categorized as frail, pre-frail and non-frail based on five criteria: weight loss, exhaustion, weakness, slowness, and low activity. Recovery to preoperative functional status (activities of daily living (ADL) and instrumental activities of daily living (IADL)), cognition, quality of life, and mental health was assessed at 1, 3, and 6 months postoperatively. A repeated measures logistic regression was used to analyze the effect of frailty on recovery over time. The effect of frailty on hospitalization outcomes was also evaluated.

Results: Mean age was 78 ± 5 years with 17.4% of patients categorized as frail, 60.4% pre-frail, and 22.2% non-frail. At 6-months, the percent of patients who had recovered to preoperative values were: ADL 90%; IADL 76%; cognition 75.5%; mental health 66%; and quality of life 70%. While more frail patients experienced adverse hospitalization outcomes and fewer had recovered to preoperative functional status, these differences were not found to be statistically significant. Overall, frailty status was not significantly associated with the trajectory of recovery or hospitalization outcomes.

Conclusion: Strong, institutional commitment to quality surgical care, as well as appropriate strategies for older patients, may have mitigated the impact of frailty on recovery. Further research is needed to examine the role of frailty in the surgical recovery process.

INTRODUCTION

Elderly patients aged 65 years and older represent a significant portion of individuals undergoing elective abdominal surgery (1). This type of surgery has been shown to impact physiological function and patient autonomy in elderly patients (2). These patients are often classified as frail, defined as "a biological syndrome with decreased physiological reserves across multi-organ systems which consequently reduces the ability to withstand stressors and increases the likelihood of poor outcomes" (3). This syndrome has been associated with increased hospital length of stay (LOS), higher morbidity and mortality, greater risk for postoperative complications, and increased likelihood for readmission (4-7).

Most surgical studies investigating frailty focus on hospitalization outcomes, such as length of stay, occurrence of postoperative complications and 30-day mortality (8-10). However, the short-term nature of hospitalization outcomes captures limited information on patient health, poorly reflects what is considered important to elderly patients, and incompletely describes their recovery process. Recovery assessed by patient-centered outcomes, including functional status, cognition, mental health and quality of life, have been shown to better characterize the full spectrum of patient recovery and present a relevant framework for reporting surgical recovery in elderly patients (11, 12). The relationship between frailty and such recovery outcomes has been described mostly in the cardiac surgery population (13-16). Among the few non-cardiac studies, only a limited subset of recovery outcomes has been examined (17-19).

The objective of this study is to explore the association of frailty and recovery of functional status, cognition, mental health and perception of quality of life over the course of a 6-month follow-up period, in elderly patients undergoing elective abdominal surgery.

METHODS

This study is a secondary analysis of data collected for a larger prospective study assessing the relationship between perioperative process-based quality indicators and recovery in elderly patients undergoing elective abdominal surgery at two university hospitals. Patient characteristics and hospitalization outcomes were collected retrospectively through chart review and data pertaining to frailty criteria were determined by clinical assessments. The inclusion criteria were i) aged 70 years or older, ii) undergoing elective abdominal general surgery and iii) requiring a postoperative hospitalization stay of at least one night. The exclusion criteria were i) inability to speak English or French, ii) surgery in the previous 6 months, iii) inability to ambulate, and iv) cognitive impairment or a Mini Mental State Examination (MMSE) (20) score of less than 18. All patients were assessed preoperatively and at 1 month, 3 months, and 6 months postoperatively at home or in hospital. The research team discontinued clinical assessments for patients who underwent subsequent surgeries within the 6-month follow-up period. Study data were collected in person at the hospital sites or at patient homes by three evaluators (a research nurse (DT), a surgical resident (MT) and a research assistant (TS) using a data management software on a laptop. Data were then transferred to a secure server within the hospital sites.

Patient Characteristics

Age, sex, height, weight, the presence of cancer, and other comorbidities including chronic heart failure, chronic obstructive pulmonary disease, diabetes and stroke were retrieved from the hospital charts of all patients. Comorbidity was measured by the Charlson Comorbidity Index (CCI), a weighted score ranging from 0 (no comorbidities) to 6 (death) including age and the following chronic conditions: myocardial infraction, congestive heart failure, peripheral vascular

disease, cerebrovascular disease, dementia, chronic pulmonary disease, ulcers, liver disease, diabetes, hemiplegia, presence of tumors (nonmetastatic or metastatic), cancer and AIDS (21). High CCI scores have been associated with increased likelihood of adverse outcomes. Body mass index (BMI) was calculated using height and weight.

Frailty Assessment

Preoperative frailty was assessed according to five frailty domains as outlined by Fried et al (3). Individuals exhibiting three or more frailty criteria were categorized as frail, one or two frailty criteria as pre-frail, and no criteria as non-frail (3).

i) Weight loss and nutritional status: Unintentional weight loss of 5% or more (3), mild to severe malnourishment, or a BMI less than 22 (22, 23).

ii) Exhaustion: Self-reported usual energy level of the past month (24, 25).

iii) Weakness: For women: BMI $\leq$ 23 and hand grip strength (HGS) $\leq$ 17 kg, 23 < BMI $\leq$ 26 and HGS $\leq$ 17.3 kg, 26 < BMI $\leq$ 29 and HGS $\leq$ 18 kg, or 29 < BMI and HGS $\leq$ 21 kg. For men: BMI $\leq$ 24 and HGS $\leq$ 29 kg, 24 < BMI $\leq$ 26 and HGS $\leq$ 30 kg, 26 < BMI $\leq$ 28 and HGS $\leq$ 30 kg, or 28 < BMI and HGS $\leq$ 32 kg (3). The Jamar dynamometer was used for all HGS measurements (26).

iv) Slowness: A gait speed less than 0.6 m/s (27).

v) Self-reported frequency and intensity of physical activity (28, 29).

Hospitalization Outcomes

Patient charts were reviewed to obtain the following perioperative and postoperative (over 6-month follow-up period) information: surgery type (colorectal, hernia,

hepatopancreaticobiliary, esophagogastric and small bowel); surgical approach (open or laparoscopic); length of hospital stay; discharge destination; mortality; readmission; occurrence of emergency department (ED) visit; number of postoperative outpatient clinic visits; and occurrence and type of postoperative complications (30, 31). The Comprehensive Complication Index was used to score the extent of a patient's complications on a scale of 0 (no complications) to 100 (death). (32)

Recovery Outcomes

Recovery for functional status, cognition, mental health, and quality of life was assessed at each visit during the follow-up period. Patients were categorized at each study visit as having recovered for an outcome if their current status was at, or better than, their preoperative value.

Activities of daily living (ADL) (bathing, dressing, toileting, transferring, continence, and feeding) and instrumental activities of daily living (IADL) (shopping, meal preparation, housekeeping, laundry, transportation, telephone use, medication use, and finances), measured by the Katz Index (33) and the Older American Resources and Services (OARS) scale (46), respectively, validated tools for measuring functional status in the geriatric population (33, 34). We defined two measures of functional status that were used to determine recovery: the percentage of ADL tasks each patient was able to perform, and the percentage of applicable IADL tasks each patient was able to perform.

Cognitive status was evaluated using the Montreal Cognitive Assessment (MoCA) (35), a validated tool for detecting mild cognitive impairment in the elderly. The score was adjusted for educational level (35).

Mental health was assessed with the Geriatric Depression Scale (GDS) (36), which has high reliability and validity for identifying depression in elderly patients.

Quality of life was measured using the EQ-5D-3L (EQ) (37), a composite score ranging from 0 (death) to 1 (perfect health) including five descriptive domains (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression) and a measure of overall self-reported health (38).

The study was approved by the Ethics Review Board of two hospitals affiliated with the McGill University Health Center, in Montreal, Canada.

Statistical Analysis

For the recovery outcomes measured at multiple time points, the trajectory of recovery was modeled using a repeated measures multivariate logistic regression, which adjusted for possibly confounding variables such as, age, gender, BMI, comorbidities (CCI), a cancer diagnosis, surgical approach, type of surgery, and the preoperative outcome value used in determining recovery. Time was included as a continuous covariate in the model. Both the main effect of frailty status and its interaction with time were included in the model, in order to estimate the impact of frailty both on average recovery and on the trajectory of recovery over the 6-month follow-up period.

The hospitalization outcomes were modeled to determine the effect of frailty, adjusting for all previously mentioned covariates. LOS and the number of outpatient visits were modeled using a negative binomial distribution; the occurrence of a complication, readmission and visit to the ED were modeled with a logistic regression. The Comprehensive Complication Index was modeled for those with a postoperative complication using a normal distribution. Effect estimates for the

logistic models are presented as odds ratios (OR), and for the negative binomial models, as incidence rate ratios (IRR).

Finally, preoperative patient and surgical characteristics, as well as postoperative outcomes of subjects who completed the 6-month follow-up and subjects who voluntary withdrew from the study were compared to assess potential bias due to loss of follow-up.

All analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

A total of 351 patients were identified and screened to participate in the study across both institutions; 71 patients did not meet the inclusion criteria, 88 patients refused to participate in the study, and 21 patients were unable to be reached by the research assistants. Overall, 280 patients were eligible for the study, of which 171 patients agreed to participate, resulting in a recruitment rate of 61.1 %. Following enrollment, 27 patients were excluded from the analysis, most often due to the cancellation of their surgery, leading to a final study size of 144 patients. During the follow-up period, 125 patients were assessed at 1 month, 113 patients at 3 months and 106 patients at 6 months. Thirty-eight patients (26.4 %) withdrew from the study during the 6-month follow-up period, due to subsequent surgeries (n=5), lack of motivation (n=10), fatigue (n=8), unavailable due to travelling (n=4), loss to follow-up (n=6) and death (n=5). Data that were collected on these patients until their withdrawal remained in the analysis. No differences were observed between patients who withdrew or remained in the study.

Preoperative and Surgical Characteristics

The preoperative and surgical characteristics of 144 patients is provided in Table 1. At the preoperative visit, 17.4% were classified as frail, 60.4 % as pre-frail, and the remaining 22.2% as non-frail (Table 1). Patients characterized as frail were older, less capable of performing instrumental activities of daily living, had a lower proportion of laparoscopic surgery, higher depression scores and lower quality of life scores, compared to patients who were characterized as pre-frail or non-frail.

Descriptive Statistics on Hospitalization Procedures and Outcomes

Patients underwent the following general surgery procedures: 81 with colorectal procedures (colon resection (n=64, 44.4%), rectal resection (n=14, 9.7%), Hartman's reversal (n= 2, 1.4%), rectopexy (n=1, 0.69%)); 20 with hepatobiliary procedures (Whipple (n=8, 5.5%), hepatectomy (n=4, 2.8%), distal pancreatectomy (n=6, 4.2%), radiofrequency ablation of liver lesion (n=1, 0.69%), ampullary resection (n=1, 0.69%)); 22 (15.3%) with incisional hernias; 13 with esophagogastric procedures (hiatal hernia repair (n=10, 6.9%), gastrectomy (n=3, 2.1%)); 5 with small bowel procedures (small bowel resection (n=3, 2.1%) and ileostomy reversal (n=2, 1.4%)); 2 (1.4%) with splenectomy and 1 (0.7%) with sarcoma resection (Table 1). Thirty-five percent (n=50) of patients had one or more complication, with a median Comprehensive Complication Index score of 22.6 (IQR 8.7-26.2) (Table 2). The median length of hospital stay was 7.0 (IQR 4.0-9.0) days, and 93.1% (n=134) were discharged to their home. Within the 6-month follow up period, 18.8% (n=27) of patients were readmitted to the hospital, 32.6% (n=47) visited the ED and the median number of outpatient visits was 5.5 (IQR 2.0-13.0) visits. Frail and pre-frail patients had a 2-day longer median LOS compared to non-frail patients. A greater proportion of frail patients had postoperative complications (36% vs. 25%), readmissions (20%

vs. 9%), occurrence of ED visits (36% vs. 25%), and fewer discharges to home (84.0% vs. 93.8%) compared to non-frail patients.

Descriptive Statistics on Recovery at 6 months

At the end of 6-month postoperative period, 90% of all patients had recovered to preoperative ADL status, 76% had recovered to preoperative IADL status, 75.5% had recovered to preoperative MOCA scores, 66% had recovered to preoperative GDS scores and 70% had recovered to preoperative EQ scores. When comparing the rate of recovery by frailty group, we found that only 70% of frail patients had recovered to preoperative ADL status compared to 92% among pre-frail and 100% among non-frail (Figure 1). In terms of IADL status, a similar trend was observed with 65% of frail patients having recovered to preoperative IADL status compared to 78% among pre-frail and 81% among non-frail. Recovery for MoCA at 6 months was similar across frailty groups, ranging from 70% to 73%. We observed, however, higher 6-month recovery for GDS among frail patients (79%) compared to pre-frail (67%) and non-frail patients (52%), while pre-frail patients showed higher recovery for EQ (77%) than frail (60%) and non-frail (54%).

Statistical Modeling Results

Overall, adjusted models for trajectories of recovery showed no statistically significant differences across frailty groups for ADL, IADL, MoCA, or GDS (Table 3). Only one significant difference was found in the trajectory of recovery for EQ between pre-frail and non-frail patients ($p = 0.02$). No association was observed between frailty and the hospitalization outcomes: postoperative complications, readmissions, occurrence of ED visits, number of outpatient visits and discharged to somewhere other than home (Table 4).

DISCUSSION

This study found that six months after surgery, a significant number of patients had not yet fully recovered to their preoperative levels. Frail patients demonstrated trends towards greater complications, longer length of stay, and higher postoperative readmissions and ED visits. Nevertheless, across frail, pre-frail, and non-frail individuals, the majority of the recovery trajectories did not show any statistically significant differences.

The cohort of patients in this study (significant comorbidity and 17% frail) is comparable to those found in other studies on surgical recovery in elderly patients (19, 39-41). In our study, at 6 months, recovery of ADL and IADL was observed in 90% and 76% of patients, respectively. Recovery for cognition, mental health, and quality of life was seen in 66-76% of patients. In comparison, others have reported 76-90% ADL recovery and 81% IADL recovery at 6 to 12 months (42-44). In addition, recovery for cognition has been reported in 73-92% of patients, in 70% for quality of life, and in 50-90% for mental health (41, 45, 46).

This study demonstrated a numerical trend consisting of frail and pre-frail individuals having higher lengths of stay, postoperative complications, readmissions, and visits to the ED, when compared to non-frail individuals. Similarly, less frail patients were discharged home when compared to the pre-frail and non-frail groups. Nevertheless, these observed differences were not statistically significant. Several surgical studies have demonstrated an association of frailty with increased length of stay (10), mortality (40, 47), readmissions (48), postoperative complications (10, 49), and decreased likelihood of being discharged home (19). Many of these studies have looked only at a subset of outcomes or at the evolution of outcomes over a shorter timeframe.

For patient-centered recovery outcomes at 6 months, there was no statistically significant difference in trajectories of recovery between frailty groups for functional status, cognition, and mental health. These finding are similar to a recent study of elderly patients undergoing colorectal surgery (41). Finally, while others have shown that frailty is associated with a postoperative decline in cognition (50, 51), the data on postoperative cognitive impairment after non-cardiac surgery are inconsistent and difficult to interpret.

While the results did not reach statistical significance, we did observe consistent trends showing slower recovery among frail subjects. Specifically, for functional status, we observed the lowest proportion of recovery among individuals categorized as frail compared to pre-frail and non-frail groups. Recovery to preoperative functional status is clinically relevant in re-establishing autonomy following surgery (44). Furthermore, this is one aspect of recovery that can be potentially optimized, as demonstrated by a study showing that pre-rehabilitation programs with physical conditioning improved functional recovery in frail patients undergoing colorectal surgery compared to elderly patients who were provided conventional surgical care (52).

Contrary to the limited surgical literature on the impact of frailty on surgical outcomes and recovery, we found no association between frailty and surgical recovery in our study (17-19). Several reasons may explain this contradictory finding including differences in the operational definitions of frailty, specific outcomes and the surgical population studied. The small portion of patients categorized as frail may have limited the statistical power to detect differences in the trajectories of recovery across outcomes. On the other hand, it may be that strong institutional commitment to quality surgical and geriatric care in the two study hospitals has limited the impact of frailty on surgical recovery. Proactive, preoperative preparation of elderly patients, sensitive to the needs and expectations of older persons, with referrals to comprehensive geriatric assessments

for the most vulnerable, may help minimize adverse outcomes. Engagement of a multidisciplinary team of healthcare professionals, including social workers, physiotherapists, occupational therapists, and pharmacists, as well as education strategies, thorough discharge planning, and appropriate home support, has been crucial in addressing the variety of medical and psychosocial issues encountered by this population.

This study is not without limitations. Patient withdrawals during the follow-up due to reasons of fatigue or inability to travel may have been linked to poor functional status which would create a selection bias in the analysis of ADL/IADL outcomes. The study may have been under powered for some outcomes. For hospitalization outcomes, the confidence intervals were generally wide and may include clinically meaningful effects that could have been detected with a larger sample. Confidence intervals for the recovery outcomes, on the other hand, were very narrow, implying that power was not a limitation for these outcomes. While we included an overall index of comorbidity, data on individual comorbidities were not available.

In conclusion, this study is important in its effort to characterize postoperative recovery in frail, pre-frail, and non-frail patients by evaluating a comprehensive set of hospitalization and patient-centered outcomes, at multiple time points over the recovery period. Overall, it demonstrated that many elderly patients had still not fully recovered 6 months after surgery and that this trajectory did not statistically differ across frailty groups. Therefore, we suggest that frailty should not be considered a contra-indication for surgery. Future studies should explore the possible benefits of surgical prehabilitation and optimization of perioperative care in the older surgical population.

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APPENDIX

Table 1. Preoperative Patient Characteristics by Frailty Group

	Total Sample (N=144)	Frail (n=25)	Pre-Frail (n=87)	Non-Frail (n=32)
Age, mean (SD)	77.8 (5.0)	81.3 (6.0)	77.4 (4.7)	76.2 (3.4)
Male gender, n (%)	79 (54.9)	15 (60.0)	47 (54.0)	17 (53.1)
Body mass index mean (SD)	27.7 (5.1)	26.4 (5.6)	28.0 (5.1)	27.6 (4.7)
Frailty markers, n (%)				
Weight Loss	38 (26.4)	15 (60.0)	23 (26.4)	0 (0)
Exhaustion	23 (16.0)	16 (64.0)	7 (8.1)	0 (0)
Weakness	81 (56.3)	24 (96.0)	57 (65.5)	0 (0)
Slowness	14 (9.8)	9 (36.0)	5 (5.8)	0 (0)
Low physical activity	47 (32.9)	19 (79.2)	28 (32.2)	0 (0)
Living alone at home, n (%)	45 (31.3)	10 (40.0)	29 (33.3)	6 (18.8)
Charlson comorbidity index, median (IQR)	3.0 (2.0-6.0)	3.0 (2.0-6.0)	4.0 (2.0-6.0)	3.0 (2.0-6.0)
Cancer diagnosis, n (%)	98 (68.1)	18 (72.0)	57 (65.5)	23 (71.9)
Laparoscopic surgery, n (%)	40 (27.8)	5 (20.0)	24 (27.6)	11 (34.4)
Procedure Type, n (%)				
Colorectal	81 (56.3)	16 (64.0)	44 (50.6)	21 (65.6)
Hernia	22 (15.3)	3 (12.0)	16 (18.4)	3 (9.4)
Hepatopancreaticobiliary	20 (13.9)	2 (8.0)	13 (14.9)	5 (15.6)
Esophagogastric	13 (9.0)	2 (8.0)	9 (10.3)	2 (6.25)
Small Bowel	5 (3.5)	1 (4.0)	3 (3.5)	1 (3.1)
Other	3 (2.1)	1 (0.04)	2 (2.3)	0 (0.0)
Preoperative percentage of ADL[a] tasks performed, mean (SD)	99.3 (3.3)	99.3 (3.3)	99.0 (3.9)	100 (0)
Preoperative percentage of IADL[b] tasks performed, mean (SD)	92.1 (15.1)	83.2 (19.8)	93.3 (13.4)	96.0 (13.2)
Preoperative MoCA[c] score, mean (SD)	23.0 (3.5)	22.1 (3.9)	22.9 (3.6)	23.9 (3.0)
Preoperative GDS[d] score, mean (SD)	3.0 (2.6)	4.4 (3.2)	2.9 (2.3)	2.3 (2.3)
Preoperative EQ[e] score, mean (SD)	0.84 (0.14)	0.75 (0.15)	0.85 (0.13)	0.89 (0.11)

[a]Activities of daily living, [b]Instrumental activities of daily living, [c]Montreal Cognitive Assessment, [d]Geriatric Depression Scale, [e]EQ-5D-3L for quality of life perception

Table 2. Postoperative Outcomes by Frailty Group

	Total Sample (N=144)	**Frail (n=25)**	**Pre-Frail (n=87)**	**Non-Frail (n=32)**
Length of Stay, median (IQR)	7.0 (4.0-9.0)	7.0 (6.0-12.0)	7.0 (4.0-9.0)	5.0 (4.0-8.5)
Postoperative Complications, n (%)	50 (34.7)	9 (36.0)	33 (37.9)	8 (25.0)
Comprehensive Complication Index [a], median (IQR)	22.6 (8.7-26.2)	20.1 (8.7-22.6)	22.6 (8.7-29.6)	23.2 (8.7-36.8)
Discharged to home [b], n (%)	134 (93.1)	21 (84.0)	83 (95.4)	30 (93.8)
Mortality, n (%)	5 (3.5)	1 (4.0)	3 (3.4)	1 (3.1)
Readmission [c], n (%)	27 (18.8)	5 (20.0)	19 (21.8)	3 (9.4)
ED visits [c], n (%)	47 (32.6)	9 (36.0)	30 (34.5)	8 (25.0)
Number of outpatient visits, median (IQR)	5.50 (2.0-13.0)	4.0 (2.0-11.0)	5.0 (2.0-12.0)	4.0 (2.0-11.0)

[a]Comprehensive Complication Index Score of those with postoperative complications, [b]Number of patients admitted from home and discharged to their home, [c]Number of patients with at least one or more visit to the emergency department

Table 3. Association between frailty and the trajectory of recovery[#]

	ADL[a]			IADL[b]			MoCA[c]			GDS[d]			EQ[e]		
	OR	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Interaction between time and pre-frail vs non-frail status[f]	1.00	(0.98, 1.01)	0.67	1.00	(0.99, 1.01)	0.52	1.00	(1.00, 1.01)	0.51	1.00	(0.99, 1.00)	0.47	1.01	(1.00, 1.02)	0.02*
Interaction between time and frail vs non-frail status[g]	0.99	(0.97, 1.00)	0.07	0.99	(0.98, 1.00)	0.19	1.00	(0.99, 1.01)	0.77	1.00	(0.99, 1.01)	0.71	1.00	(0.99, 1.01)	0.85
Time	1.01	(1.00, 1.02)	0.12	1.01	(1.01, 1.02)	<0.01*	1.00	(0.99, 1.01)	0.98	1.00	(1.00, 1.01)	0.08	1.00	(0.99, 1.01)	0.82
Pre-Frail vs Non-Frail status[h]	0.38	(0.06, 2.21)	0.28	0.79	(0.30, 2.04)	0.62	0.42	(0.17, 1.05)	0.06	2.97	(0.95, 9.34)	0.06	0.516	(0.18, 1.45)	0.22
Frail vs Non-Frail status[i]	0.70	(0.08, 5.84)	0.74	1.15	(0.32, 4.08)	0.83	0.42	(0.14, 1.29)	0.13	1.64	(0.32, 8.43)	0.56	0.67	(0.16, 2.84)	0.59

[#]Model estimates adjusted for age, gender, body mass index, comorbidities, cancer diagnosis and the preoperative outcome value.

[a]Activities of daily living, [b]Instrumental activities of daily living, [c]Montreal Cognitive Assessment, [d]Geriatric Depression Scale, [e]EQ-5D-3L for quality of life perception.
[f]Difference in trajectory of recovery of pre-frail group compared to non-frail group over 6-months, [g]Difference in trajectory of recovery of frail group compared to non-frail group over 6-months, [h] Average recovery of pre-frail group compared to non-frail, [i]Average recovery frail group compared to non-frail group.

Table 4. Association between frailty and hospitalization outcomes[#]

	Length of Stay			Occurrence of Complications			Severity of Complications		
	IRR	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**	**Effect Estimate**	**95% CI**	**p-value**
Pre-Frail vs Non-Frail status[a]	1.17	(0.94, 1.46)	0.16	1.63	(0.62, 4.27)	0.32	-2.63	(-17.25, 12.00)	0.72
Frail vs Non-Frail status[b]	1.31	(0.98, 1.74)	0.07	0.99	(0.28, 3.58)	0.99	-7.58	(-27.46, 12.30)	0.45
	Occurrence of Readmissions			**Occurrence of ED Visits**			**Number of Outpatient Visits**		
	OR	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**	**IRR**	**95% CI**	**p-value**
Pre-Frail vs Non-Frail status[a]	4.05	(0.48, 34.30)	0.20	2.03	(0.77, 5.37)	0.15	1.07	(0.71, 1.61)	0.76
Frail vs Non-Frail status[b]	4.06	(0.36, 46.00)	0.26	2.10	(0.57, 7.67)	0.26	1.08	(0.64, 1.83)	0.78

[#] Model estimates adjusted for age, gender, body mass index, comorbidities and cancer diagnosis

[a] Postoperative outcomes of pre-frail group compared to non-frail, [b] Postoperative outcomes of frail group compared to non-frail group.

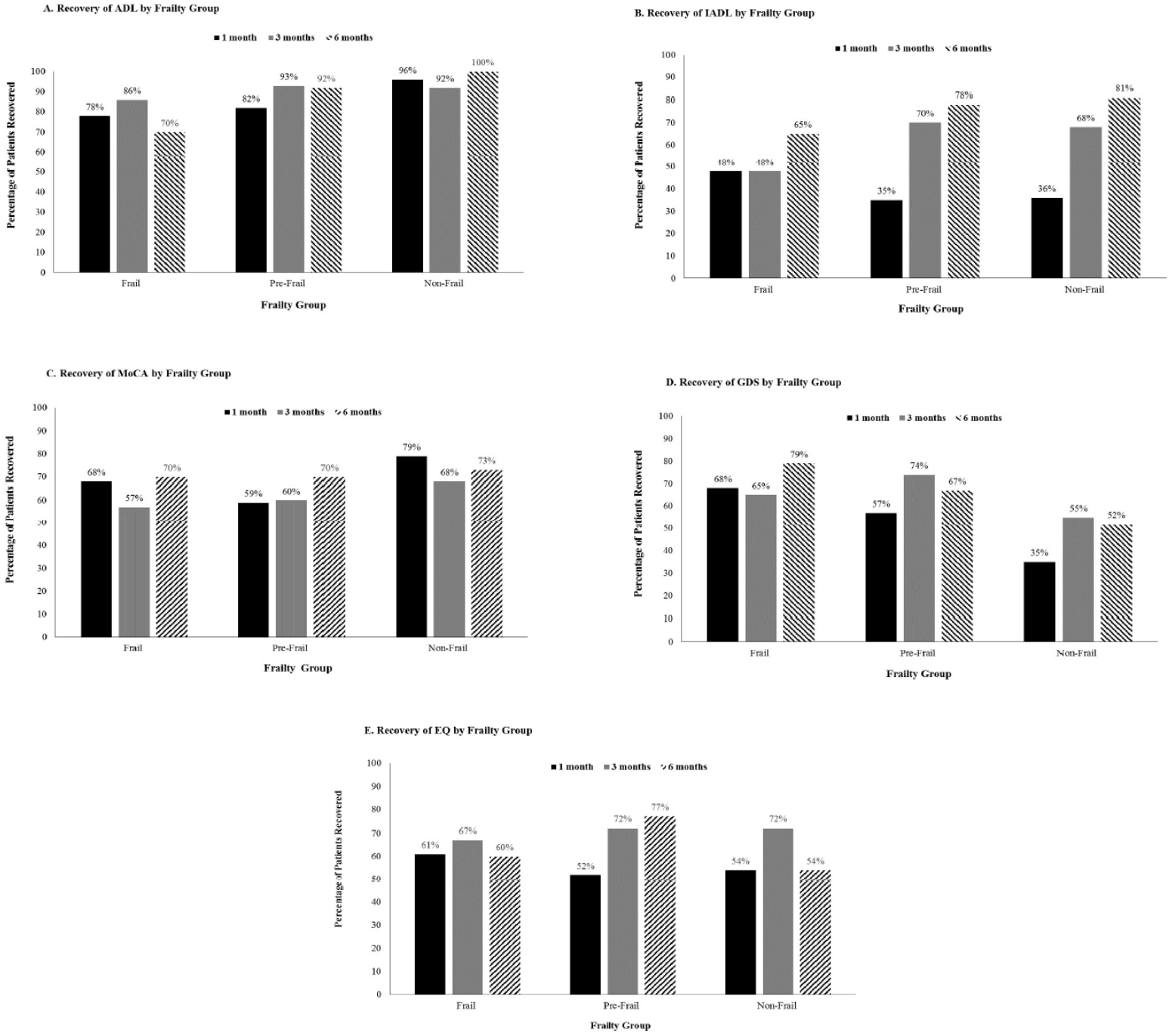

Figure 1. Recovery of ADL[a], IADL[b], MoCA[c], GDS[d] and EQ[e] by frailty group.

*Sample sizes varied across the follow-up period. At pre-op: Overall N= 144, Frail n=25, Pre-Frail n=87, Non-frail n=32;at 1 month: Overall N=125, Frail n=23, Pre-Frail n=74, Non-Frail n=28; at 3 months: Overall N=113, Frail n=21, Pre-Frail n=67, Non-Frail n=25; at 6 months: Overall N=106, Frail n=20, Pre-Frail n=60, Non-Frail n=26. Reported statistics are based on the respective sample sizes at each time point. [a]Activities of daily living, [b]Instrumental activities of daily living, [c]Montreal Cognitive Assessment, [d]Geriatric Depression Scale, [e]EQ-5D-3L for quality of life perception

CHAPTER 4: SUMMARY AND CONCLUSION

The focus of this thesis was to characterize the surgical recovery of elderly patients at multiple time points measured by a comprehensive set of hospitalization and patient-centered outcomes. The objective of evaluating a wide range of outcomes was to propose a multidimensional framework for describing postoperative recovery in the older surgical population. For this study, tools validated in the elderly were used to assess preoperative risk factors and measure postoperative recovery.

This thesis demonstrated that recovery to preoperative levels of functional status, cognition, mental health, and quality of life was protracted past 6 months for elderly patients. The findings in this thesis showed that individuals with higher preoperative risk factors were more likely to experience adverse hospitalization outcomes such as increased lengths of stay, postoperative complications, readmissions, and visits to the emergency department. However, our study found no statistically relevant association between preoperative risk factors such as frailty or preoperative nutritional status and surgical recovery in this patient population.

Future studies should explore the possible benefits of surgical pre-habilitation and optimization of perioperative care in the older surgical population. A positive impact of long-term recovery may be observed by implementing institutional processes or establishing pre-habilitation programs to identify and support elderly patients at risk of reduced functional status, cognition, mental health, or quality of life before surgery. Programs providing an early-interdisciplinary approach and proactive preoperative geriatric assessment may be key to optimizing recovery post-surgery for this patient population. Due to the rapidly growing number of elderly patients undergoing surgery, further investigations are needed to understand how to best prepare and manage the complexities associated with their surgical recovery.

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APPENDICES

APPENDIX 1 – **Rights and Permission for Publication:** *Assessing the Effect of Preoperative Nutrition on Upper Body Function in Elderly Patients Undergoing Elective Abdominal Surgery*

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