

The Effectiveness of Hand Massage on the Pain of Cardiac Surgery Critically Ill- A Randomized
Controlled Trial

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Abstract

Background

Postoperative pain is one of the most severe and distressful symptoms cardiac surgery patients experience in the intensive care unit. Opioids constitute the mainstay treatment for pain in the intensive care unit, yet pain continues to persist despite their administration. Massage is one of the non-pharmacological interventions suggested to maximize pain relief given its opioid-sparing and analgesia-enhancing potential. Some trials suggest that massage can be effective at reducing postoperative pain in acute care units; however, its effects on pain relief in the intensive care unit and when pain severity is highest remain unknown.

Objectives

This study aimed to evaluate the effectiveness of hand massage on the pain intensity (primary outcome), unpleasantness and interference, muscle tension, anxiety, and vital signs of critically ill patients after cardiac surgery. A complementary objective was added while conducting the study to evaluate the effects of hand massage on sleep in the intensive care unit.

Methods

A 3-arm randomized controlled trial was conducted in a medical-surgical intensive care unit in Canada. Patients were considered eligible if they were 18 years or older, able to speak French or English and self-report symptoms, underwent elective cardiac surgery, and did not have a high risk of postoperative complications and contraindications to having their hands massaged. Eligible patients were randomly allocated (1:1:1) to standard care plus either three 20-minute hand massages (experimental), three 20-minute hand holdings (active control), or three 20-minute rest periods (passive control). Pain intensity, pain unpleasantness, anxiety, muscle tension, and vital signs were evaluated before, immediately after, and 30 minutes later for each

intervention administered within 24 hours postoperatively. Pain-related interference with functioning and sleep was assessed on the second postoperative day.

The 0-10 numeric rating scale was used to assess pain intensity, pain unpleasantness and anxiety. Muscle tension was evaluated using the Critical-Care Pain Observation Tool, a behavioral pain scale for the assessment of pain in the critically ill. Vital signs were collected from the patients' bedside monitors. The Brief Pain Inventory was used to assess pain interference with functioning and the Richards Campbell Sleep Questionnaire was used to measure sleep quality.

Results

A total of 138 patients were screened, 95 were eligible and approached for participation in the study. From the 83 patients who agreed to participate, 60 were randomized (20 hand massage, 19 hand holding, 21 rest). After controlling for baseline scores, the hand massage group reported significantly lower pain intensity, pain unpleasantness and anxiety for the 1st data collection set compared to both hand holding and rest (ANCOVA, $p < 0.02$) with an average decrease of 2 points on a 0-10 scale. No statistically significant differences were noted between hand holding and rest for any of the symptoms.

For the 2nd data collection set ($n=43$), pain intensity was lowest for the hand massage (adjusted mean=1.80) group compared to both hand holding (adjusted mean=3.41) and rest (adjusted mean=3.94) after adjusting for baseline scores (ANCOVA, $F_{(2)}=3.68$, $p=0.034$). With a smaller sample size for the 2nd data collection set ($n=38$), decrease in pain unpleasantness was not significantly different across groups (ANCOVA, $F_{(2)}=1.59$, $p=0.218$). A tendency for significant differences was observed for the 2nd data collection set (ANCOVA, $F_{(2)}=2.64$, $p=0.084$) where the hand massage group reported the lowest anxiety scores post-intervention

(adjusted mean=0.89, SE=0.54) followed by the rest (adjusted mean=1.90, SE=0.55) and hand holding groups (adjusted mean=2.65, SE=0.54). Unfortunately, insufficient data was obtained for the 3rd data collection set to run statistical analyses.

A greater proportion of patients in the hand massage group had decreased muscle tension after the first hand massage (20/20) compared to hand holding (18/19) and rest (15/19) (Chi-Square =5.89, $p=0.053$). Muscle tension was similar across groups at all time points for the 2nd data collection set. Despite some fluctuations in vital signs, they did not differ significantly between groups for any of the data collection sets.

Although no significant differences were observed across groups at the follow-up interview on the second postoperative day, the hand massage group reported a maximum pain intensity throughout the first postoperative day (median=5.75, range: 2-10) that was lower than the hand holding (median=6.50, range: 1-10) and rest groups (median=6.25, range: 0-10). The hand massage group was more likely to reach 0 pain intensity throughout a 24-hour period (median=0, range: 0-7) compared to the hand holding (median=2, range: 0-5) and rest groups (median=1.75, range: 0-4.5). A tendency towards a higher proportion of patients in the hand massage group ($n=12$, 71%) reported none or mild (i.e., <4) pain interference with walking compared to hand holding ($n=6$, 40%) and rest ($n=8$, 67%) ($p=0.176$). Overall, patients in all groups reported predominantly light sleep (medians 68.75-91.88) and being awake roughly 50% of the night time (medians 47.50-71.88). Unfortunately, insufficient data on the quality of sleep could be collected to examine the effectiveness of hand massage on this outcome.

Conclusions

Findings suggest that a 20-minute hand massage in addition to routine postoperative pain management can concomitantly reduce pain intensity, pain unpleasantness and anxiety by 2

points on average on a 0-10 scale. Hand massage could help patients experience longer periods of time without pain and lower levels of maximum pain intensity. When coupled with recovery activities, hand massage could reduce pain interference with functioning. Future randomized controlled trials are needed to test the effectiveness of hand massage on the sleep of cardiac surgery critically ill patients.

Clinical Trial: [ClinicalTrials.gov NCT02679534](https://clinicaltrials.gov/ct2/show/study/NCT02679534)

Keywords: massage, pain, anxiety, muscle tension, vital signs, sleep, critical care, cardiac surgery

Abrégé

Toile de Fond

La douleur postopératoire compte parmi les symptômes les plus sévères et dérangeants expérimentés par les patients de soins intensifs ayant subi une chirurgie cardiaque. Les opioïdes constituent le traitement principal pour le soulagement de la douleur en soins intensifs, toutefois, la douleur persiste malgré leur administration. Le massage constitue une intervention non-pharmacologique pouvant maximiser le soulagement de la douleur étant donné son potentiel de limiter les doses d'opioïdes administrées et d'augmenter leur effet analgésique. Certains essais cliniques suggèrent que le massage peut être efficace pour réduire la douleur postopératoire dans des unités de soins aigus; par contre, ses effets sur la douleur en soins intensifs lorsque l'intensité de la douleur est la plus élevée sont peu connus.

Objectifs

Cette étude vise à évaluer l'efficacité du massage des mains sur l'intensité de la douleur (variable principale), l'aspect désagréable et l'interférence reliés à la douleur, la tension musculaire, l'anxiété, et les signes vitaux des patients post chirurgie cardiaque en soins intensifs. Un objectif complémentaire a été ajouté pendant le déroulement de l'étude afin d'évaluer les effets du massage des mains sur le sommeil en soins intensifs.

Méthode

Un essai contrôlé randomisé a été mené dans une unité de soins intensifs médicaux et chirurgicaux au Canada. Les patients étaient éligibles s'ils étaient âgés de 18 ans et plus, s'ils parlaient français ou anglais, s'ils pouvaient autoévaluer leurs symptômes, s'ils avaient subi une chirurgie cardiaque élective, et s'ils ne présentaient pas des complications postopératoires et des contre-indications au massage des mains. Les patients éligibles ont été alloués de façon aléatoire (1 :1 :1) aux soins usuels plus trois sessions de massage des mains de 20 minutes (groupe

expérimental) ou trois sessions de toucher des mains de 20 minutes (groupe contrôle actif) ou trois périodes de repos de 20 minutes (groupe contrôle passif). L'intensité, l'aspect désagréable et l'interférence de la douleur, la tension musculaire et les signes vitaux ont été évalués avant, après le massage des mains, le toucher des mains ou la période de repos, et 30 minutes plus tard pour chacune des interventions administrées dans les 24 heures après la chirurgie. L'interférence de la douleur et le sommeil ont été évalués lors du deuxième jour postopératoire.

L'échelle numérique de 0 à 10 a été utilisée pour l'évaluation de l'intensité, de l'aspect désagréable de la douleur et de l'anxiété. La tension musculaire a été évaluée à l'aide de l'item de tension musculaire de l'outil *Critical-Care Pain Observation Tool*, conçu pour l'évaluation de la douleur chez les patients en soins intensifs. Les signes vitaux ont été documentés via les moniteurs de chevet des patients. L'outil *Brief Pain Inventory* a été utilisé pour évaluer l'interférence de la douleur avec le fonctionnement, et le *Richards Campbell Sleep Questionnaire* a été utilisé pour évaluer la qualité du sommeil.

Résultats

Au total, les critères d'éligibilité ont été vérifiés pour 138 patients et parmi ceux-ci 95 étaient éligibles et ont été approchés pour participer à cette étude. Parmi les 83 patients qui ont accepté de participer, 60 ont été randomisés (20 au groupe massage des mains, 19 au groupe toucher des mains, 21 au groupe repos). Pour la première collecte de données et après avoir contrôlé l'effet des scores pré-intervention, le groupe du massage des mains a rapporté des scores d'intensité et de sensation désagréable de la douleur, et d'anxiété plus bas en comparaison aux groupes du toucher des mains et du repos (ANCOVA, $p < 0.02$), avec une baisse significative moyenne de 2 points sur une échelle de 0-10. Aucune différence significative n'a été observée pour aucun des symptômes entre les groupes du toucher des mains et du repos.

Pour la deuxième collecte de données (n=43), le groupe du massage des mains (moyenne ajustée=1.80) a rapporté une plus faible intensité de douleur en comparaison au groupe du toucher des mains (moyenne ajustée=3.41) et au groupe du repos (moyenne ajustée=3.94) après avoir contrôlé l'effet des scores pré-intervention (ANCOVA, $F_{(2)}=3.68$, $p=0.034$). Avec un échantillon plus petit pour la deuxième collecte de données (n=38), la sensation désagréable de la douleur n'a pas été différente entre les groupes (ANCOVA, $F_{(2)}=1.59$, $p=0.218$). Une tendance vers une différence significative a été observée lors de la deuxième collecte de données (ANCOVA, $F_{(2)}=2.64$, $p=0.084$) pour le groupe du massage des mains qui a rapporté des scores plus faibles d'anxiété post-intervention (moyenne ajustée =0.89, SE=0.54) suivi par le groupe de repos (moyenne ajustée =1.90, SE=0.55) et le groupe du toucher des mains (moyenne ajustée =2.65, SE=0.54). Malheureusement, lors de la troisième collecte, les données étaient insuffisantes pour effectuer des tests d'inférence statistiques.

Une diminution de la tension musculaire a été observée chez une plus grande proportion de patients du groupe du massage des mains après la première intervention (20/20) comparativement aux patients du groupe du toucher des mains (18/19) et de ceux du groupe repos (15/19) (Chi-Square =5.89, $p=0.053$). Aucune différence dans la tension musculaire n'a été observée entre les groupes et les temps de mesure lors de la deuxième collecte de données. Malgré certaines fluctuations des signes vitaux, celles-ci n'étaient pas significativement différentes entre les groupes et les temps de mesure.

Lors de l'entrevue de suivi au 2^e jour postopératoire, le groupe du massage des mains a rapporté une intensité maximale de douleur (médiane=5.75, écart: 2-10) plus basse que le groupe du toucher des mains (médiane=6.50, écart: 1-10) et le groupe du repos (médiane=6.25, écart :0-10), mais la différence n'était pas statistiquement significative. Le groupe du massage des mains

a été plus susceptible à atteindre une intensité de la douleur de 0 lors des dernières 24 heures (médiane=0, écart: 0-7) comparativement au groupe du toucher des mains (médiane=2, écart: 0-5) et au groupe du repos (médiane=1.75, écart: 0-4.5). Une plus grande proportion des patients du groupe du massage des mains (n=12, 71%) a rapporté aucune ou une légère interférence de la douleur avec la marche (i.e., <4) comparativement au groupe du toucher des mains (n=6, 40%) et du repos (n=8, 67%) (p=0.176). Dans l'ensemble, les patients de tous les groupes ont rapporté un sommeil léger (médianes 68.75-91.88) et être restés éveillés pendant approximativement 50% de la nuit (médianes 47.50-71.88). Malheureusement, les données collectées sur la qualité du sommeil ont été insuffisantes pour examiner l'efficacité du massage des mains sur cette variable.

Conclusions

Les résultats suggèrent que le massage des mains d'une durée de 20 minutes en plus du traitement pharmacologique usuel de la douleur postopératoire peut réduire l'intensité et la sensation désagréable de la douleur, et l'anxiété d'au moins 2 points sur une échelle de 0-10. Le massage des mains peut aider les patients à être sans douleur pendant de plus longues périodes et à expérimenter une intensité maximale de douleur plus faible. Lorsque jumelé aux activités de rétablissement, le massage des mains pourrait réduire l'interférence de la douleur avec le fonctionnement. D'autres essais contrôlés randomisés sont nécessaires pour tester l'efficacité du massage des mains sur le sommeil des patients en soins intensifs suite à une chirurgie cardiaque.

Clinical Trial: [ClinicalTrials.gov NCT02679534](https://clinicaltrials.gov/ct2/show/study/NCT02679534)

Mots-Clés: massage, douleur, anxiété, tension musculaire, signes vitaux, sommeil, soins critiques, chirurgie cardiaque

Preface

Thesis Format

In agreement with the thesis supervisor Dr. Céline Gélinas and thesis committee members (Dr. Andréa Maria Laizner, Dr. Christine Maheu and Dr. Géraldine Martorella), the candidate chose to submit a thesis by manuscript. This thesis comprises four manuscripts and six chapters.

The first chapter provides the background information on the prevalence of pain in the cardiac surgery critically ill despite the use of analgesia and the need for complementary interventions such as massage to maximize the pain relief in this patient population. The second chapter includes the first published manuscript: “*The Effect of Massage on Acute Postoperative Pain in Critically and Acutely Ill Adults Post-Thoracic Surgery: Systematic Review and Meta-analysis of Randomized Controlled Trials*”, which provides an overview of the potential of massage to reduce pain and highlights the gap in testing the effectiveness of massage in the intensive care unit.

The third chapter provides the theoretical framework that guided the selection of massage as a potential pain-relieving intervention and the selection of outcome variables. Based on the theoretical framework, research hypotheses were formulated. The fourth chapter includes the second published manuscript: “*The Effectiveness of Hand Massage on Pain in Critically Ill Patients After Cardiac Surgery: A Randomized Controlled Trial Protocol*”, which presents the methods and procedures of this randomized controlled trial.

The fifth chapter summarizes the results of this study in two manuscripts: manuscript 3 “*Effects of Massage in Reducing the Pain and Anxiety of the Cardiac Surgery Critically Ill- A Randomized Controlled Trial*” and manuscript 4 “*Does Hand Massage Have Sustained Effects on Pain Intensity and Pain-Related Interference in the Cardiac Surgery Critically Ill? – A*

Randomized Controlled Trial". The last chapter concludes with an overview of the main outcomes, study limitations, contributions and future directions.

Contributions of Authors

The candidate was involved in the design, recruitment, intervention administration, data collection and analysis, interpretation and writing of all manuscripts submitted with this thesis. The thesis supervisor and all thesis committee members were involved in the conception and design of this study, review of analyses, and critical revision of the manuscripts and this thesis.

Chapter 1. Problem Statement

Prevalence of Pain in the Intensive Care Unit

Pain is a common phenomenon in the intensive care unit (ICU) despite the multitude of efforts dedicated to promoting its effective relief. In the ICU, pain is generally the result of acute nociception from disease processes, surgical interventions or trauma that are aggravated by invasive medical procedures and routine bedside care (Azzam & Alam, 2013; Gélinas, 2016; Pasero, 2003). Mounting evidence shows that cardiac surgery ICU patients experience moderate to severe pain reaching proportions as high as 74% despite the use of analgesics (Gélinas, 2007b; Puntillo, 1994; Watt-Watson et al., 2004; Yorke, Wallis, & McLean, 2004). Pain at rest is compounded by routine ICU procedures such as turning, coughing, breathing and chest tube removal, which are perceived to be the most painful in the immediate postoperative period (Gélinas, 2007b; Puntillo et al., 2014; Yorke et al., 2004). Yet, even the continuous use of assistive devices such as mechanical ventilation represents a major source of pain and discomfort for patients in need of this compensatory measure (Chanques et al., 2006; Saadatmand et al., 2015; Yamashita, Yamasaki, Matsuyama, & Amaya, 2017). Moderate to severe pain has been shown to be experienced by 63% of patients during mechanical ventilation despite an unrestricted use of fentanyl and morphine (Chanques et al., 2006).

The International Association for the Study of Pain has defined pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (IASP, 1979). Pain typically involves a noxious stimulus that activates nociceptors in the body's tissues, which then convey signals to the sensory cortex by specialized afferent nerve tracts (Pasero & McCaffery, 2011). In the cerebral cortex, nociceptive signals are processed and generate multiple responses such as the "unpleasant sensory and emotional

experience” included in the IASP definition. Pain is influenced by many factors and is known to be a multidimensional experience encompassing sensory-discriminative, affective-motivational and cognitive-evaluative dimensions (Melzack, 1999a). The sensory-discriminative dimension is evaluated through self-reports of pain intensity, localization and quality of pain. The affective-motivational dimension includes the unpleasant affective quality of pain and the aversive responses initiated to relieve the respective pain (Melzack & Casey, 1968). Last, the cognitive-evaluative dimension encompasses people’s evaluation of the meaning and consequences of pain on daily activities also described as pain interference.

Cardiac Surgery, Postoperative Pain and its Consequences

Cardiac surgeries, such as coronary-artery bypass grafting (CABG) and valve replacement (VR), rank among the most frequently performed surgical interventions worldwide (Benjamin et al., 2017). The nature of cardiac surgery necessitates the routine admission of patients to the ICU for a determined period based on patients’ clinical condition and potential post-operative complications. While variability exists between hospital settings, the average length of ICU stay for cardiac surgery patients is one to three days.

Cardiac surgeries are commonly indicated to reduce anginal pain, but the surgical procedure itself can lead to the development of postoperative pain. The nature of postoperative pain after cardiac surgery is multifocal and multifactorial (Bigeleisen & Goehner, 2015). Surgeries involving median sternotomy are known to provoke somatic pain due to significant surgical soft tissue and bony injury occurring during the dissection phase. In addition, visceral pain is produced by the mediastinal and pleural drains as well as vein harvesting (Bigeleisen & Goehner, 2015). Thus, in the immediate postoperative period, patients are likely to suffer from complex acute pain of various origins. Moderate pain intensity is experienced in the first 24

hours post-surgery during movement (4-5/10) (Chapman, Zaslansky, Donaldson, & Shinfeld, 2012; Denault et al., 2014), common procedures such as turning (4.9/10) (Gélinas, 2007a, 2007b) and mediastinal tube removal (5.2/10) (Boitor, Fiola, & Gélinas, 2016), but also at rest (3.9/10) (Denault et al., 2014) despite the administration of analgesic medication, and is described mainly as burning or throbbing with common pain sites being the sternum and epigastric region (Gélinas, 2007b; Mueller et al., 2000). These pain intensity scores are above the cut-off for moderate pain (i.e., >3), and require the regular administration of opioids in addition to non-opioids and adjuvants (Gerbershagen, Rothaug, Kalkman, & Meissner, 2011; WHO, 2015). Very few patients are without pain on day one (< 30%), and this proportion increases gradually thereafter (Chapman et al., 2012; Choiniere et al., 2014; Denault et al., 2014; Lahtinen, Kokki, & Hynynen, 2006; Mueller et al., 2000).

Cardiac surgery patients are known to experience postoperative pain that can persist for extended periods of time after surgery (Guimaraes-Pereira, Reis, Abelha, Azevedo, & Castro-Lopes, 2017). In the first week postoperatively, moderate to severe pain during movement is present in over 65% of patients (n = 1110) (Choiniere et al., 2014). Specific to those undergoing sternotomy, pain of moderate to severe intensity is experienced for an average of five to 12 days postop (Lahtinen et al., 2006; Leegaard, Naden, & Fagermoen, 2008). However, pain can persist beyond the normal time for tissue healing, generally estimated at three months after the surgical intervention (Katz & Seltzer, 2009; Kehlet, Jensen, & Woolf, 2006; Macrae, 2008). An estimated 30-50% of patients experience pain beyond the critical time for tissue healing (Bruce et al., 2003; Choiniere et al., 2014; Kalso, Mennander, Tasmuth, & Nilsson, 2001), and some even at six (22.1%), 12 (16.5%) and 24 months postop (9.5%) (Choiniere et al., 2014).

Several studies investigated the risk factors associated with the development of persistent postoperative pain to guide interventions for its prevention. The intensity of acute postoperative pain immediately after surgery has been consistently reported to be a significant predictor of the presence and severity of persistent postoperative pain (Choiniere et al., 2014; Katz & Seltzer, 2009; Kehlet et al., 2006). This pain phenomenon is a serious and often unrecognized complication after cardiac surgery that may interfere with daily activities and long term health-related quality of life (Gjeilo, Stenseth, & Klepstad, 2014). Therefore, sustained efforts are warranted to relieve and prevent the acute pain post cardiac surgery to maximize patients' recovery and address this modifiable risk factor for the development of persistent postsurgical pain.

While most studies address the intensity of acute pain after cardiac surgery, little is known about patients' unpleasantness related to pain despite its overwhelming and disruptive nature (Melzack & Casey, 1968). A recent study highlighted the pain unpleasantness that cardiac surgery patients experience during routine ICU procedures, such as mediastinal tube removal, with a mean score of 4.22 on a 0-10 numeric rating scale (Boitor et al., 2016). Nonetheless, there has been a growing awareness of the short and long term adverse consequences of unrelieved pain in the critically ill, and its interference with patient functioning. Projections of the nociceptive tracts to the hypothalamus and pituitary gland contribute to the autonomic and neuroendocrine-mediated reactions to nociception such as tachycardia, elevated blood pressure, diaphoresis, skeletal muscle hypertonia, glycemic dysregulation, increased myocardial oxygen demand, and immune suppression (Azzam & Alam, 2013). Inadequate pain management can further interfere with patients' ability to cough and mobilize effectively, which predisposes them to postoperative complications such as atelectasis, pneumonia and deep vein thrombosis (Desai,

1999; Puntillo, 1994; Yorke et al., 2004). All of these may put the patient at risk for delayed recovery and a prolonged ICU and hospital stay (Chanques et al., 2006; Payen et al., 2009).

Limitations of Pharmacological Treatments and Innovative Complementary Approaches

Much research has been devoted to the testing and optimization of various pain management protocols in the ICU. Among the pharmacological approaches to pain control, opioids constitute the mainstay treatment in the ICU, with morphine, fentanyl and hydromorphone being the most commonly prescribed (Azzam & Alam, 2013; Barr et al., 2013). Despite the well documented potency of these drugs in bringing pain relief, pain has been shown to persist even during unrestricted use of these analgesic agents (Chanques et al., 2006; Denault et al., 2014). Even so, the use of opioid analgesics requires close monitoring and treatment of its incurred side effects. The most current adverse effects common to opioids include nausea, constipation, sedation, respiratory depression and urinary retention (Erstad et al., 2009; Pasero, Portenoy, & McCaffery, 1999), which represent potential threats to patients' recovery but also to patients' comfort and well-being. Of great concern is also the risk for the development of opioid induced neurotoxicity manifested as hallucinations, delirium, myoclonus/seizures and hyperalgesia¹ more commonly occurring with high-dose opioid administration (Daeninck & Bruera, 1999). Overall, the use of opioid analgesia can carry significant risks for patients, calling forth the need for additional pain relief measures.

The use of non-opioids in the ICU has been proposed in clinical practice recommendations to decrease the amount of opioids administered and to decrease opioid-related side effects (Barr et al., 2013), but their use is limited by potential for drug-drug interactions, side effects complicating the critical illness, severity of pain states, and limited routes of

¹ Increased pain from a stimulus that normally provokes pain. Hyperalgesia is a consequences of perturbation of the nociceptive system with peripheral and/or central sensitization (IASP, 1994).

administration (Azzam & Alam, 2013; Erstad et al., 2009). In light of these limitations, a multimodal approach to pain management in ICU patients has been recommended that incorporates the use of complementary non-pharmacologic interventions given their opioid-sparing and analgesia-enhancing potential (Barr et al., 2013). The combined use of pharmacologic and non-pharmacologic interventions has the potential to provide patients more effective pain control than when each is used alone by lowering the doses of opioids required and their related side effects (Erstad et al., 2009; Puntillo & Naidu, 2016), and to prevent the development of chronic pain in those with severe and persistent pain (Macrae, 2008).

Interventions are labelled as non-pharmacological if they do not involve the use of medications, and fall in two categories: cognitive-behavioral or physical (sensory). Non-pharmacological interventions include psychotherapy, behavioral interventions, surgery, technical procedures, devices, rehabilitation, and complementary and alternative therapies (Boutron et al., 2008). Massage is one of the non-pharmacological interventions repeatedly suggested for use in the ICU in light of its opioid-sparing and analgesia-enhancing potential, safety of delivery and ease of implementation at the bedside by clinicians with little resources (Azzam & Alam, 2013; Barr et al., 2013; Erstad et al., 2009). However, at present, insufficient research evidence is available to support the effectiveness of massage in promoting pain relief in the ICU and to recommend its broad implementation in critical care settings.

Chapter 2. Literature Review

Definition and Types of Massage

Massage is gaining increasing popularity, and emerging as one of the most commonly used types of complementary non-pharmacological interventions. Massage has been defined as the manual manipulation of muscles and soft tissues of the body through the application of various systematic and rhythmic hand movements (Dunn, Sleep, & Collett, 1995; Richards, Gibson, & Overton-McCoy, 2000). There are many forms of massage such as reflexology, sports massage, shiatsu and Swedish massage used alone or in combination with other therapies (e.g., aromatherapy) (Bush, 2001), which share the common element of interpersonal touch in the form of soft tissue manipulation (Moyer, Rounds, & Hannum, 2004). With classic types of massage, effleurage (stroking), petrissage (compression), tapotement (percussion), vibration, and friction are applied. The duration of massage, the specific techniques of touch administered, the material resources used to facilitate the treatment, the body areas targeted and the place of delivery can all vary considerably (Moyer et al., 2004), making comparisons of massage effectiveness difficult to pursue.

Massage Effects with Postoperative Cardiac Surgery Patients

Physical and psychological signs and symptoms persist in the early recovery phase in the form of surgery-related pain (Mueller et al., 2000), mild state anxiety (Asilioglu & Celik, 2004; Vingerhoets, 1998; Young et al., 2005), tension (Eaker, Sullivan, Kelly-Hayes, D'Agostino, & Benjamin, 2005) and even occurrences of atrial fibrillation (Eaker et al., 2005; Mitchell, Crystal, Heilbron, & Page, 2005). The important, although insufficient, effect of pharmacological treatments in responding to these signs and symptoms has been a precursor to the search for complementary non-pharmacological interventions. Researchers have demonstrated growing

interest in introducing massage in the care of postoperative cardiac surgery adults and conducted pilot and randomized controlled trials (RCTs) to test its effect on various outcome variables, of which pain, anxiety, muscle tension, and vital signs are the most commonly studied. The next sections will present the results of these RCTs on the effects of massage on the following outcomes:

1. Pain Intensity
2. Anxiety
3. Muscle Tension
4. Vital Signs
5. Sleep

1. *Massage Effects on the Pain Intensity of Cardiac Surgery Adults*

A systematic review and meta-analysis of RCTs was conducted to assess the effect of massage on acute pain in critically and acutely ill adults post-thoracic surgery, and is presented at the end of this section as **Manuscript 1** (Boitor, Gélinas, Richard-Lalonde, & Thombs, 2017). Although the review aimed to include RCTs targeting both pulmonary and cardiac surgery patients, only RCTs with cardiac surgery patients were eligible and included in the meta-analysis. The review concluded that a single massage of 10-30 minutes duration administered in addition to standard pharmacological analgesia reduced acute post-cardiac surgery pain intensity by almost 1 point on a 0-10 numeric rating scale, however more RCTs are needed to evaluate its effect specifically on the acute pain of the critically ill patients.

In our previous pilot RCT conducted with 40 patients (21 experimental, and 19 control) (Boitor, Martorella, Arbour, Michaud, & Gélinas, 2015), massage therapy of moderate pressure using effleurage and petrissage (Kolcaba, Schirm, & Steiner, 2006) was administered for 15

minutes by a trained nurse on patients' hands using lavender cream followed by a 30 minute supervised rest period. This was repeated between two to three times within the first 24 hours postop. Meanwhile, the control group received 15-minute hand holding by the same nurse using lavender cream, but without any massage. The pilot RCT showed that patients receiving two sessions of 15-minute hand massage (n=21) reported a trend towards statistical significance for decrease in pain intensity ($p=0.088$) compared to hand holding (n=19) (Boitor et al., 2015). Yet, those receiving three hand massages reported a significantly greater decrease in pain intensity ($p=0.008$) and a trend towards statistical significance for muscle tension ($p=0.079$). Conversely, the administration of a single massage did not yield any significant decrease in pain intensity or muscle tension, suggesting that repeated administration is necessary in this patient population to achieve the desired pain relief and muscle relaxant effect.

In this pilot study, pain intensity was evaluated using the 0-10 Faces Pain Thermometer (FPT), which has been validated with ICU patients after cardiac surgery (Gélinas, 2007a). Muscle tension was evaluated by performing passive flexion-extension of patient's arm and assessing the resistance felt in response to these passive movements on a 0-2 ordinal scale, which is part of the Critical-Care Pain Observation Tool (CPOT) (Gélinas, 2010). This pilot study did not include a standard care control group, making the differential beneficial effect inconclusive. Future RCTs are needed that compare massage with a control exposure and with standard care to unravel both the relative and absolute efficacy of massage.

2. *Massage Effects on the Anxiety of Cardiac Surgery Adults*

Mixed findings have been reported as three RCTs supported significant improvements in anxiety levels (i.e., 1-2 points reduction on the visual analog scale) with massage compared to control (Bauer et al., 2010; Braun et al., 2012; Cutshall et al., 2010) versus two RCTs where

group differences were not significant (Albert et al., 2009; Hattan, King, & Griffiths, 2002). Interestingly, the same studies that failed to show benefits of massage in decreasing pain also failed to show any improvements in anxiety levels. Moderate pressure massage was administered for 20 minutes over the body areas selected by patients after the second postoperative day, and repeated twice over the course of two days (Bauer et al., 2010; Braun et al., 2012). Both RCTs involved large sample sizes, 113 (62 experimental and 51 control) and 146 (75 experimental and 71 control), respectively with equivalent groups at baseline. Yet, even a single 20 minute massage therapy, delivered between the second and fifth postoperative day to body sites chosen by patients, appeared to be sufficient to significantly reduce anxiety in a pilot RCT (30 experimental and 28 control) (Cutshall et al., 2010).

Conversely, in a RCT with 252 cardiac surgery patients (126 experimental and 126 usual care), anxiety levels were not significantly different between the massage and usual care group (Albert et al., 2009). Two sessions of 30-minute massage were offered on the back, arms and legs after the second postoperative day. The repositioning required for back massage and the anticipated fear of pain associated with turning on a side might explain the lack of improvements in anxiety in the RCT. Similarly, no significant difference was observed in anxiety between a single session of 20 minute foot massage, guided relaxation and standard care when administered 48 hours postop in a RCT with comparable groups (Hattan et al., 2002). The lack of significance might be the result of an underpowered analysis with a total of only 25 participants, of which nine received foot massage, nine guided relaxation and seven standard care.

Anxiety levels of cardiac surgery ICU patients measured using the State-Trait Anxiety Inventory Form Y (STAI-Y) seem to significantly decrease after a 60 minute massage using neutral oil with a large effect size (0.60) (Lindgren et al., 2013).

3. *Massage Effects on the Muscle Tension of Cardiac Surgery Adults*

The following studies evaluated muscle tension using the self-report Visual Analog Scale (VAS). Three RCTs conducted with patients having undergone cardiac surgery (e.g., CABG, VR) via median sternotomy showed that patients receiving massage had significantly decreased muscle tension (Bauer et al., 2010; Braun et al., 2012; Cutshall et al., 2010) compared to control (i.e., rest). In two of these RCTs massage was administered twice (Bauer et al., 2010; Braun et al., 2012), however, even a single 20 minute massage session significantly reduced muscle tension (mean decrease of 3.1 points on a 0-10 scale, SD=2.77) (Cutshall et al., 2010).

No significant difference was observed in self-reported muscle tension between a single session of 20 minute foot massage (n=9), guided relaxation (n=9) and standard care (n=7) when administered 48 hours postop (Hattan et al., 2002). In the ICU, our pilot RCT (Boitor et al., 2015) indicated a trend for statistical significance for muscle tension after the third intervention with the hand massage group experiencing more relaxed muscles compared to hand holding ($X^2[1]=3.09$, $p=0.079$)

4. *Massage Effects on the Vital Signs of Cardiac Surgery Adults*

There has been a long recognition of the dangers of imbalanced vital signs on patients' recovery after cardiac surgery. Of great concern has been the occurrence of hypertension and tachycardia that increase the myocardial oxygen demand, which heightens the risk of myocardial ischemia if insufficiently compensated by the oxygenated blood supply (Ardehali & Ports, 1990). The same RCTs discussed above also measured changes in vital signs with the administration of massage. Systolic and diastolic blood pressures (SBP and DBP) were observed to be 3.7 and 1.8 mm Hg lower after the first 30 minutes of limb and back massage as compared to control, but not after the second massage (Albert et al., 2009), and the respiratory rate (RR) was significantly

lower after each session of 20-minute massage compared to control (Bauer et al., 2010).

Conversely, no differences were noted in BP, heart rate (HR) and RR between groups in two other RCTs (Braun et al., 2012; Hattan et al., 2002). This high heterogeneity of findings might stem from the differing pharmacological treatments prescribed for participant patients after cardiac surgery, which can influence their vital signs; the timing of massage administrations and data collection.

Within the critical care context, researchers have shown a great interest in the effects of massage therapy on vital signs, mainly on BP, HR and RR. Statistically significant differences were seen in the RR immediately after a 20 minute foot massage using plain oil (n=25) or aromatherapy (neroli oil) (n=25) compared to the two controls (i.e., standard care, n=25 and chat with nurse without tactile input, n=25) of cardiac surgery patients (Stevensen, 1994).

Conversely, no significant differences were seen in BP, HR and RR between a 60 minute massage (n=10) and rest group (n=10) of cardiac surgery ICU patients (Lindgren et al., 2013). In our pilot RCT, vital signs were not statistically different before and after intervention except for diastolic pressure (second intervention) ($F_{(3, 108)}=32.07$; $p=.039$), which increased in the experimental group (pre: 54.96 SD 8.10; 30 minutes post: 57.11 SD 8.43) and decreased in the control group (pre: 56.03 SD 8.36; 30 minutes post: 54.81 SD 6.71) (Boitor et al., 2015). Such findings could suggest that extraneous factors beyond the use of massage can influence significantly the fluctuation of vital signs in the ICU. Overall, these research studies conducted in the ICU report mixed findings of the potential effect of massage therapy on BP, HR and RR, making the evidence inconclusive in this regard.

5. *Massage Effects on the Sleep of Cardiac Surgery Adults*

One randomized controlled trial (RCT) including critically ill men with cardiovascular illness compared a six-minute back massage versus relaxation intervention plus relaxing music (combined muscle relaxation, mental imagery, and audiotape) and versus usual care (Richards, 1998). Participants in the back-massage group (mean=319.82 minutes of sleep, SD=48.45) slept more than one hour longer than those in the usual care group (mean=257.33 minutes of sleep, SD=108.22; p value not reported). In another RCT, cardiac surgery patients receiving massage after ICU discharge reported an increased sleep effectiveness (mean=33.8, SD=6.6) compared to control (mean=28.0, SD=7.9) ($p=0.019$) (Nerbass, Feltrim, de Souza, Ykeda, & Lorenzi, 2010), thereby supporting the potential benefit of massage in this surgical patient population. To date, the effect of massage on sleep in the ICU is largely unexamined (Hu et al., 2015), and more research is awaited to verify its potential to improve the much needed quantity and quality of sleep in the critically ill post-cardiac surgery.

Overview of Studies

A great limitation of these studies is the lack of standardization of massage techniques (e.g., effleurage, petrissage, friction, Swedish), duration of massage, body areas massaged and timing of massage administrations (from the second postoperative day onward), which make recommendations for their application in clinical practice hard to formulate. Nonetheless, 20 minutes of moderate pressure massage (Bauer et al., 2010; Braun et al., 2012; Cutshall et al., 2010) seem to be sufficient for positive effects on symptoms such as pain, anxiety and muscle tension after the second postoperative day, and repetition seems to enhance its beneficial effects. Also, the positioning required during massage is warranted careful consideration not to induce discomfort in participants, especially after open heart surgery.

Overall, there is a paucity of high-level evidence on which to base massage therapy decisions in the management of pain of post-cardiac surgery ICU patients. Extrapolations of evidence from other patient populations and clinical settings are flawed by the differing health status and symptom severity of this specific subgroup of ICU patients. Future rigorous RCTs that are conducted in the context of the ICU with cardiac surgery adults in their immediate postoperative period are essential to make recommendations for the use of massage in clinical practice including the minimal effective dose, body area massaged and techniques employed.

Manuscript 1**TITLE PAGE**

Title: The Effect of Massage on Acute Postoperative Pain in Critically and Acutely Ill Adults Post-Thoracic Surgery: Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

Critical care practice guidelines identify a lack of clear evidence on the effectiveness of massage for pain control. To assess the effect of massage on acute pain in critically and acutely ill adults post-thoracic surgery. Medline, Embase, CINAHL, PsychInfo, Web of Science, Scopus and Cochrane Library databases were searched. Eligible studies were randomized controlled trials (RCTs) evaluating the effect of massage compared to attention control/sham massage or standard care alone on acute pain intensity post-thoracic surgery. Twelve RCTs were included. Of these, nine evaluated massage in addition to standard analgesia, including 2 that compared massage to attention control/sham massage in the intensive care unit (ICU), 6 that compared massage to standard analgesia alone early post-ICU discharge, and 1 that compared massage to both attention control and standard care in the ICU. Patients receiving massage with analgesia reported less pain (0-10 scale) compared to attention control/sham massage (3 RCTs; N=462; mean difference -0.80, 95% confidence interval [CI] -1.25 to -0.35; $p < 0.001$; $I^2=13\%$) and standard care (7 RCTs; N=1087; mean difference -0.85, 95% CI -1.28 to -0.42; $p < 0.001$; $I^2=70\%$). Massage, in addition to pharmacological analgesia, reduces acute post-cardiac surgery pain intensity.

Introduction

Thoracic surgery, which includes cardiac and pulmonary surgeries, is performed more frequently than any other surgery.^{1,2} Cardiac surgeries require admission to an intensive care unit (ICU), whereas patients undergoing pulmonary surgery may be admitted to an ICU, postanesthesia care unit, or to a dedicated intermediate care or step-down unit.³ Following discharge, recovery is supported on acute care wards.

Thoracic surgery patients often experience severe acute postoperative pain that can originate from a range of sources, including deep tissue injuries, thoracostomy tubes, costovertebral joint disruption, and fractures of the sternum or ribs.⁴⁻¹¹ Unrelieved postoperative pain can interfere with patients' ability to cough and mobilize effectively, which predisposes them to postoperative complications, such as atelectasis, pneumonia and deep vein thrombosis.^{4,6,12} Moreover, uncontrolled acute postoperative pain is a significant predictor of the persistence and severity of long-term pain.¹³⁻¹⁶

Opioids are routinely provided for severe postoperative pain, but the use of complementary non-pharmacologic interventions may reduce the need for opioids and enhance analgesic effects.¹⁷ Massage therapy has been identified by patients and nurses as an acceptable, feasible, and potentially effective method to maximize pain relief in the ICU.¹⁸ In a recent study, researchers found that administering massage in the ICU to patients after undergoing cardiac surgery was feasible and perceived to be an acceptable complementary therapy for pain relief.¹⁹ It has been shown to reduce postoperative pain in several randomized controlled trials (RCTs).^{20,21} Current practice guidelines from the Society of Critical Care Medicine¹⁷ suggested that massage may be used to improve pain control, but noted that the lack of clear evidence on effectiveness precluded recommending the routine use of massage.

A recent meta-analysis found that massage therapy was effective for treating pain in surgical populations,²¹ however it is unclear if massage can have the same beneficial effect in the critical care setting where pain intensity is highest and continues to persist even during unrestricted use of opioids.^{6,9,22,23} A 2015 systematic review of massage therapy post-cardiac surgery²⁰ evaluated six RCTs²⁴⁻²⁹ and one non-randomized trial,³⁰ but did not synthesize results quantitatively and only included comparisons to usual care alone, but not to sham massage or attention control. Additionally, the systematic review did not focus on the effects of massage in critical care and did not include several key studies conducted in this highly acute clinical setting.

Objective

The objective of the present study was to conduct a systematic review and meta-analysis to evaluate the effects of massage therapy on acute postoperative pain among adult thoracic surgery patients in the ICU and early post-ICU discharge compared to usual care or compared to sham massage or attention control.

Methods

Protocol and registration

The protocol for this meta-analysis was registered in PROSPERO (CRD42015026931). The meta-analysis was reported per the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement.³¹

Eligibility criteria

Included studies were RCTs that assessed the effect of massage on acute postoperative pain among adult inpatients in the ICU or acute care wards post-thoracic surgery, excluding laparoscopic surgery. Eligible interventions included massage administered to any body part

within one week of surgery. Eligible comparisons included usual care alone, sham massage that involved the use of touch (e.g., hand holding), or attention controls (e.g., therapeutic presence without the use of touch). Massage could be administered alone or in combination with analgesics or other non-specific interventions (e.g., aromatherapy). To be eligible, patients in the massage and comparator trial arms had to receive similar analgesics protocols. Eligible studies had to report the assessment of pain intensity, measured within 24 h of massage administration, using either a numerical rating scale (e.g., 0-10) or visual analog scale (e.g., 0-100). There were no restrictions based on language, publication status, or year of publication.

Additionally, eligible studies were sought by scanning the reference lists of included articles and relevant reviews. Also, in November 2015, we searched the Current Controlled Trials, Clinicaltrials.Gov, the ISRCTN Register, the National Centre for Complementary and Alternative Medicine database, and the WHO International Clinical Trials Registry Platform. The search was further updated on April 1st, 2017. Authors of included trials were contacted to attempt to identify any unpublished trials.

Study selection

Study selection was done independently by two investigators. First, titles and abstracts were screened, and if either reviewer indicated that the trial was potentially eligible, the full text was reviewed independently by both reviewers. Any disagreements at the full-text level were resolved via consensus by consulting a third reviewer.

Data extraction and risk of bias assessment

Data were extracted independently by two investigators using a pre-defined data extraction form in DistillerSR. The data extraction form was pilot-tested on two randomly selected studies and subsequently refined. Data were extracted on patient population, sample

size, study setting, type of massage therapy and comparator (including duration, frequency, technique, body area, interventionist), pain assessment tool, pain intensity pre- and post-intervention, and adverse events. If otherwise eligible studies did not report pain intensity data within 24 h of the massage, authors were contacted for these data. Risk of bias was evaluated independently by two reviewers using the Cochrane Risk of Bias Tool.³² Disagreements were resolved via consensus, including consultation with a third reviewer.

Statistical analysis

Statistical analyses were performed using Review Manager 5.3 software.³³ Effect estimates for all analyses were estimated using DerSimonian-Laird random effects models. Pain intensity effect sizes were calculated using mean pre-post changes and SDs based on the first post-massage assessment. If change scores were not available, we used post-massage means and SDs. If scores were reported on a 0-100 VAS, they were converted to 0-10 scores for the purpose of data analysis. Given the high correlations observed across studies between the VAS and NRS, the VAS scores were converted to NRS ratings.³⁴ Between-study variability was evaluated with I^2 .³² Subgroup analyses were planned by comparator (standard care versus sham massage or attention control) and to explore other possible reasons for heterogeneity. Possible publication bias was assessed using visual inspection of funnel plot asymmetry. Although not anticipated pre-review, markedly different pain management protocols required that trials of massage done in the context of standard analgesic therapy be evaluated separately from trials of massage applied without these therapies.

Results

Study selection

The database and registry searches and manual searches of reference lists retrieved 194 total citations, including 165 unique citations. Of these, 25 underwent full-text review, and 12 were determined to be eligible and were included. See Fig. 1 and Supplemental Digital Content 2. Excluded Articles post full-text Review. Four of the seven massage studies from a previous systematic review²⁰ were included. Three were excluded either because they did not randomize patients,³⁰ did not assess pain close to the time of the massage,²⁶ or did not report pain outcomes²⁷ (see Supplemental Digital Content 3. Comparison with Previous Systematic Review).

Study characteristics

The characteristics of the 12 included RCTs are summarized in Table 1. Trials were conducted mainly in the USA (n=6) and Iran (n=3), but also in the UK (n=1), Canada (n=1), and Australia (n=1). Despite our attempt to include all types of thoracic surgeries, only studies evaluating massage in the context of cardiac surgery were eligible. Eleven studies included only patients who underwent cardiac surgery, and one study included patients who underwent cardiac surgery (64% of patients) or who had abdominal surgery with an incision greater than 8 cm and entering the peritoneal cavity (36%).³⁵ Mean age was 63 years old; 69% of patients were males, and, in the five studies that reported race/ethnicity data, more than 85% were White. The first massage in each trial was administered between the first and third day post-surgery when patients were either in the ICU (n=4) or acute care wards (n=8). Commonly used massage techniques included Swedish massage, effleurage, petrissage and the application of moderate pressure over different body areas, including the feet, back, and hands. Four trials compared

massage to sham massage or attention control,^{29,36-38} seven to usual care,^{24,25,28,39-42} and one to both attention control and standard care.³⁵

Trials from the USA, Canada, UK and Australia all evaluated the effects of massage applied in conjunction with standard analgesic treatments with opioids as the mainstay treatment in all cases. Conversely, in studies conducted in Iran, acetaminophen was the routine analgesic with morphine for breakthrough pain in one study,³⁶ patients who had severe pain and needed analgesics were excluded in another study,²⁹ and massage was administered at least 3 h post-analgesics in two studies.^{36,42} Because of the differences in pain management protocols, trials from the USA, Canada, UK and Australia that evaluated the effects of massage in addition to standard analgesia were evaluated separately from trials from Iran that were done in the context of substantially different pain management protocols. Two studies had the full-text published in Persian,^{36,42} and were translated in English.

Massage versus sham massage or attention control

Study characteristics

Three RCTs that compared massage with standard analgesia to sham massage or attention control included a total of 462 patients (233 who received massage therapy).^{35,37,38} The mean number of participants per study was 154 (median=40; range 20-402), and the first massage was administered in the ICU in all trials. Patients received between 10 and 20 min of massage per session, and massage was administered either by a massage therapist³⁵ or nurses.^{37,38}

Two RCTs conducted in Iran compared the effect of massage without analgesia to sham massage or attention control. In these studies massage was given for 20 min by nurses³⁶ or for 30 min by family members trained by a nurse.²⁹

Risk of bias within studies

See Supplemental Digital Content 4 for detailed risk of bias assessments. The three RCTs that evaluated massage in the context of standard analgesia^{35,37,38} had low risk of bias for all domains with the exception of blinding. Risk of blinding was low for outcome reporting and unclear for study personnel in one study where massage was compared to sham,³⁸ but high for both in two studies where massage was compared to attention control.^{35,37}

For the two trials of massage without analgesia, risk of bias was unclear or high for most domains.

*Massage versus standard care**Study characteristics*

Seven RCTs that compared massage with analgesia to standard care included a total of 1087 patients (551 who received massage).^{24,25,28,35,39-41} The mean number of participants per study was 155 (median=113; range 16-403). Patients received between 20 and 30 min of massage per session, administered by massage therapists,^{24,25,28,35,39,41} or healing coaches.⁴⁰ The first massage was administered in the ICU in one study³⁵ and early post-ICU discharge in the other 6 trials.^{24,25,28,39-41} Standard care consisted of routine care of the study setting and, in some studies, was accompanied by solitary rest periods.^{25,28,39-41}

One RCT from Iran evaluated the effect of 30 min of massage administered by nurses in the ICU, 3 h post analgesia administration.⁴²

Risk of bias within studies

In the context of standard analgesia, except for those with a poor description of the random sequence generation^{39,41} and procedures for allocation concealment^{28,39,41} (unclear risk of bias), all studies had low risk of bias (Supplemental Digital Content 5. Risk of Bias Summary). All the

studies were rated as high risk of bias due to lack of blinding of participants and personnel. Five studies had a low risk of attrition bias either because they had no missing primary outcome data or because missing data were minimal and balanced across groups.^{24,28,35,40,41} Although some trials were not registered,^{24,25,39-41} the risk for selective reporting was low as data on pain scores were reported.

The effect of massage on pain intensity

Massage versus sham massage or attention control

The pain intensity scores pre- and post-interventions are summarized in Supplemental Digital Content 6 and 7. In three studies^{35,37,38} where massage was administered in conjunction with analgesics in the ICU, massage significantly reduced pain intensity compared to active control (MD -0.80, 95% CI -1.25 to -0.35; $p < 0.001$) ($I^2 = 13\%$) (Fig. 2). In the two studies conducted in Iran where massage was administered in the absence of analgesia,^{29,36} there was a greater reduction in pain intensity (MD -2.47, 95% CI -4.88 to -0.06; $p = 0.04$) ($I^2 = 91\%$).

Massage versus standard care

In the seven^{24,25,28,35,39-41} studies conducted in conjunction with analgesia, there was a significant decrease in pain intensity (MD -0.85, 95% CI, -1.28 to -0.42; $p < 0.001$), although there was potentially substantial heterogeneity ($I^2 = 70\%$). See Fig. 3. When considering only the 6 studies that administered massage in the context of analgesia early post-ICU discharge,^{24,25,28,39-41} massage was associated with a decrease in pain intensity of 0.89 points compared to standard care (MD -0.89, 95% CI -1.45 to -0.33; $p = 0.002$) ($I^2 = 75\%$).

In the RCT conducted in Iran where massage was administered 3 h post analgesia administration,⁴² pain was 1.65 points lower in the massage group compared to standard care (95% CI, -2.72 to -0.58).

Risk of bias across studies-publication bias

Funnel plots suggested possible publication bias, but the small number of trials did not allow conclusions to be drawn (Supplemental Digital Content 8).

Adverse effects of massage

No adverse events related to massage were reported in the four studies that documented and reported adverse events.^{28,35,40,41}

Discussion*Summary of main results*

Massage reduced the intensity of acute postoperative pain of critically and acutely ill patients post-cardiac surgery compared to sham massage or attention control and compared to standard care alone. In three studies from North America, massage, added to standard analgesic treatment, reduced pain intensity in the ICU by 0.80 points on a scale from 0 to 10 when compared to sham or attention control. In seven trials from the USA, UK, or Australia, massage added to analgesic care reduced pain by 0.85 points compared to standard care in the ICU and early post-ICU discharge, however there was high heterogeneity. These findings are similar to the largest RCT (n=605)³⁵ where a 0.70 reduction in pain was observed in the ICU when compared to attention control, and a 0.80 reduction in pain when compared to standard care. Substantially higher reductions in pain were observed in studies conducted in Iran, which could be due to higher baseline pain scores, limited or no analgesia administration prior to massage, or high risk of bias.

Comparison with other meta-analyses

This is the first meta-analysis to estimate the effect of massage on the pain intensity of critically and acutely ill cardiac surgery adults. In the general surgical pain populations, massage

therapy appears to reduce pain intensity by 0.79 points compared to control (7 trials; N=1101; SMD -0.79, 95% CI -1.36 to -0.23), however there is high heterogeneity ($I^2=94.35\%$) within the time of administration (i.e., pre-, during, or post-surgical procedure) and type of comparator used (e.g., guided relaxation, individualized attention, usual care, rest).²¹ Other meta-analyses have reported large effects of massage on acute pain during first stage of labor regardless of the use of analgesia (4 trials; N=225; standardized mean difference [SMD]-0.82, 95% CI -1.17 to -0.47),⁴³ and for low back pain when compared to sham therapy (2 trials; N=91; SMD -0.92, 95% CI -1.35 to -0.48) and relaxation (2 trials; N=54; MD on scale of 0-10: -1.27, 95% CI -2.46 to -0.08).⁴⁴

Implications for practice

Massage can complement pharmacological analgesia in reducing postoperative pain by almost 1 point on a 0-10 scale in both critically and acutely ill cardiac surgery patients. Although this does not reach the clinically significant 2-point reduction in acute pain intensity,⁴⁵ it appears to be safe and may have the potential to concomitantly improve other symptoms such as pain distress and anxiety. Moreover, it appears to be an easy-to-deliver intervention that could be easily implemented at bedside by staff nurses following a short training. In one of the included RCTs,²⁹ family members could be successfully trained on the administration of massage in 60-90 min.

Implications for research

Although there is evidence to support the pain relieving effects of massage in cardiac surgery patients, very few studies were conducted in the ICU, when pain intensity is highest.^{9,23} Given the complexity and severity of pain in the ICU, future rigorously conducted RCTs are needed to evaluate the effect of massage on the pain intensity of critically ill adults. Furthermore,

research studies are still needed to evaluate the effect of massage on other dimensions of pain such as pain distress and pain interference, and the use of opioids during hospitalization. A decrease in the use of opioids could improve patients' recovery by reducing opioid-related side effects.

Limitations

This meta-analysis combined data from 12 studies to estimate the effects of massage compared to sham, attention control and standard care. Limitations to consider in interpreting results relate to the relatively small number of trials that could be included, and that massage therapy, although of similar duration and techniques, was not the same across all studies. There were also other differences across studies, including differences in the method for assessing pain intensity. In addition, the quality of included trials varied and blinding of participants and personnel was unlikely in the majority of studies. Ten of the RCTs included in the meta-analysis did not explicitly state following an intention-to-treat approach to data analysis, thereby potentially leading to overestimation of the effects of massage in decreasing acute postoperative pain. Few of the included RCTs were registered, and publication bias could not be ruled out. Our search strategy included 7 databases, but it is possible that inclusion of additional databases could have identified one or more trials that were not included in our systematic review.

Conclusions

This is the first meta-analysis to estimate the effect of massage therapy on the pain intensity of cardiac surgery patients. Our findings suggest that massage therapy can be of benefit to patients post-cardiac surgery, however more RCTs are needed to evaluate its effect specifically on the acute pain of critically ill patients.

Acknowledgments

Ms. Boitor and Dr. Gélinas report a potential conflict of interest related to their authorship of a randomized controlled trial that was included in the present meta-analysis. Dr. Thombs declares that he has no competing interests. There was no direct funding for this study. Ms. Boitor is supported by doctoral bursaries from the Quebec Nursing Intervention Research Network (QNIRN), Fonds de Recherche du Québec - Santé (FRQS), Ministère de l'Enseignement Supérieur de la Recherche et de la Science (MESRS), and McGill Nursing Collaborative Fellowship. Dr. Gélinas receives support from a Research Career Award from FRQS. Dr. Thombs receives support from an Investigator Award from the Arthritis Society.

Supplementary data

Supplementary data related to this article can be found at:

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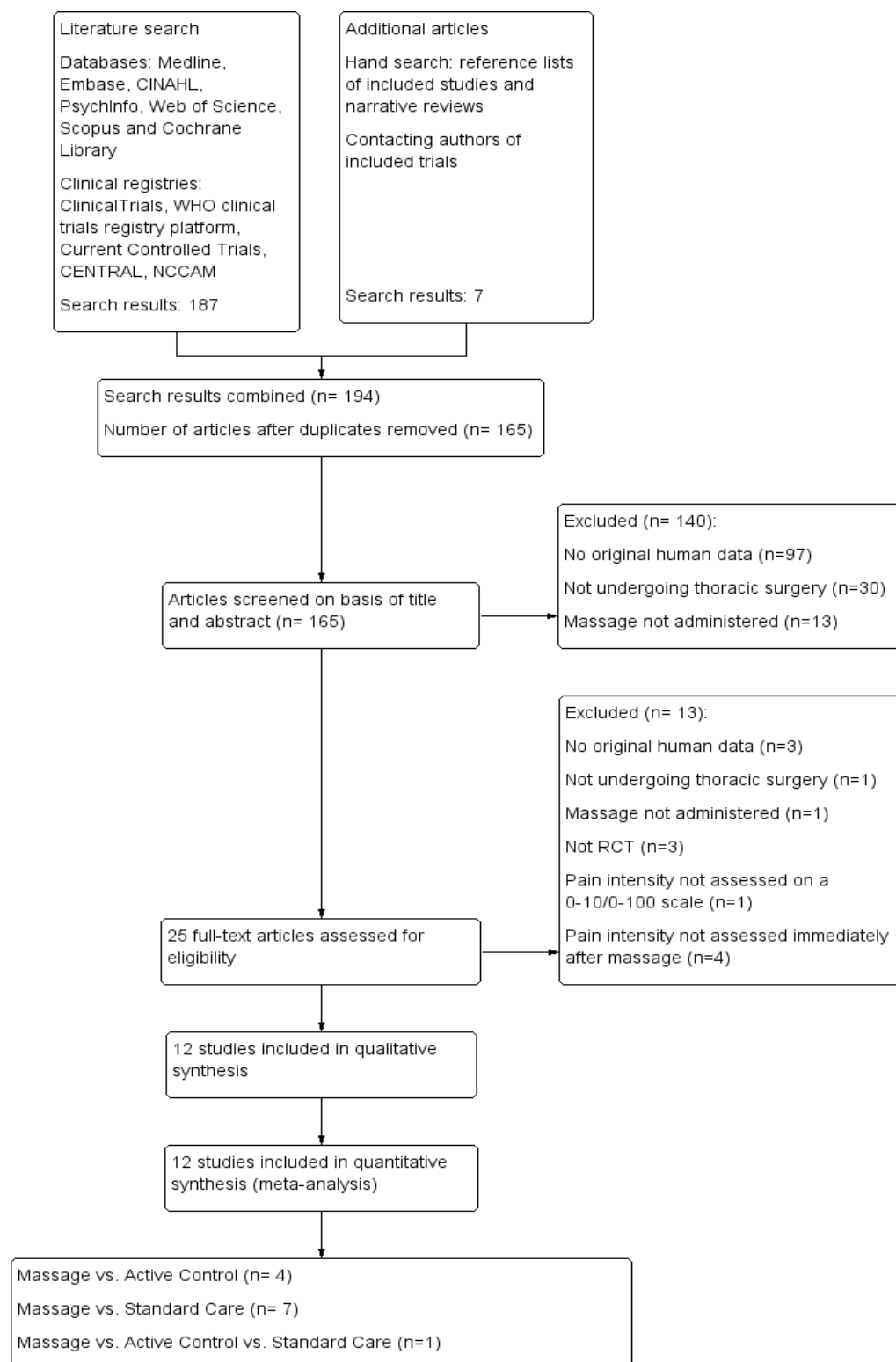
Figure 1. Literature search and study selection

Figure 2. Analyses of mean difference in pain intensity for massage and sham/attention control in addition to pharmacological analgesia in the intensive care unit using a random effects model

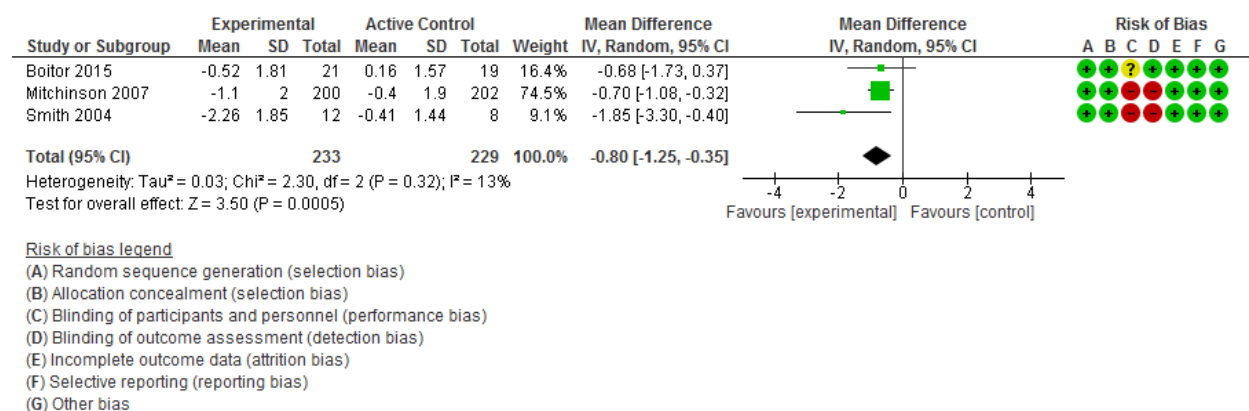


Figure 3. Analyses of mean difference in pain intensity for massage and standard care in addition to pharmacological analgesia in the intensive care unit and early post-intensive care unit discharge using a random effects model

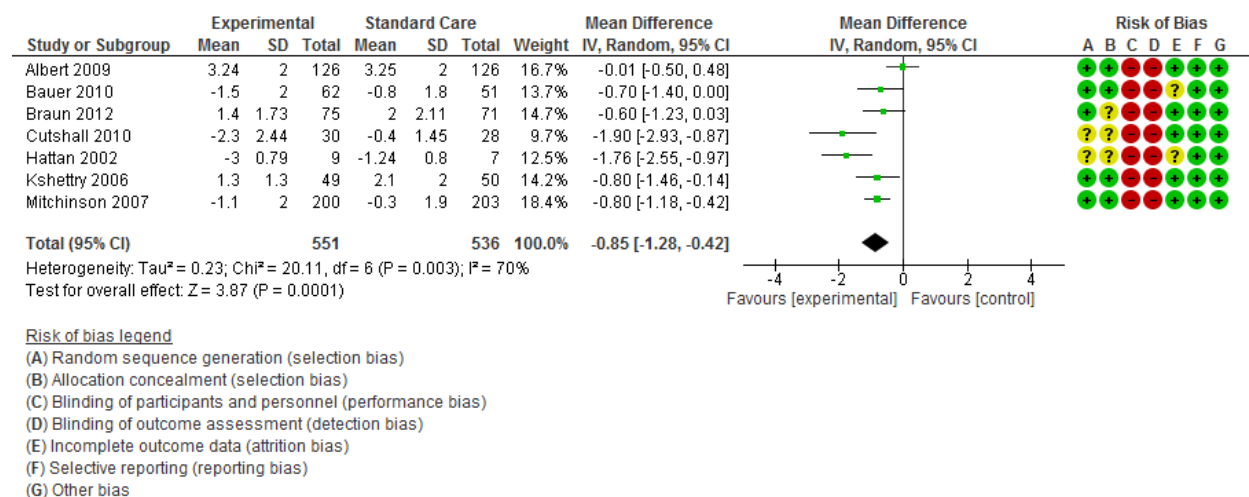


Table 1. Descriptive Characteristics of the 12 Eligible Studies

| Study | Year | Country | Clinical setting | Population | Type of surgery | Nr days since surgery at 1 st administration | Massage | Comparator | Pain Assessment Tool |
|----------------------------|------|---------|------------------|---|---------------------|---|--|---|----------------------|
| Albert et al. [24] | 2009 | USA | Acute care | Age ^a : 65 (12) Male: 73% Sample size: 252 | CABG, VR, CABG & VR | 2 or 3 | Duration: 30 Frequency/day: 1 Sessions: 2 Protocol: specific (back, arms, legs) | Duration: - Frequency**: - Sessions: - Type: standard care | VAS 0-10 |
| Bagheri-Nesami et al. [36] | 2012 | Iran | Acute care | Age ^a : 59 (9) Male: 50% Sample size: 80 | CABG | 2 | Duration: 20 mins Frequency/day: 1 Sessions: 4 Protocol: specific (feet) | Duration: 20 mins Frequency**: 1 Sessions: 4 Type: attention control | VAS 0-10 |
| Bauer et al. [25] | 2010 | USA | NR | Age ^a : 66 (13) Male: 69% Sample size: 113 | CABG, VR, CABG & VR | 2 | Duration: 20 mins Frequency/day: 1 Sessions: 2 Protocol: specific (hands, feet, back, arms, | Duration: 20 mins Frequency**: 1 Sessions: 2 Type: standard care with quiet relaxation | VAS 0-10 |

| | | | | | | | | | |
|----------------------|------|-----------|-----------------|---|---------------------|----------------------------|---|---|----------|
| | | | | | | | legs, neck, shoulders, head, pt preference) | | |
| Boitor et al. [38] | 2015 | Canada | ICU | Age ^a : 67 (11) Male: 78% Sample size: 40 | CABG, VR, CABG & VR | The day of surgery (POD 0) | Duration: 15 mins Frequency/day: 2-3 Sessions: 2-3 Protocol: specific (hands) | Duration: 15 mins Frequency**: 2-3 Sessions: 2-3 Type: sham massage | FPT 0-10 |
| Braun et al. [28] | 2012 | Australia | Acute care ward | Age ^a : 67 (12) Male: 75% Sample size: 146 | CABG, VR or both | 3-4 | Duration: 20 mins Frequency/day: 1 Sessions: 2 Protocol: unclear (hands, feet, back, legs, neck, shoulders, head, pt preference) | Duration: 20 mins Frequency**: 1 Sessions: 1 Type: standard care (relaxing quietly in a chair/bed – rest time) | VAS 0-10 |
| Cutshall et al. [41] | 2010 | USA | NR | Age ^a : 66 (16) Male: 75% Sample size: 58 | CABG, VR, CABG & VR | Between POD2-5 | Duration: 20 mins Frequency/day: 1 Sessions: 1 Protocol: unclear (back, arms, legs, neck, shoulders, head, pt preference) | Duration: 20 mins Frequency**: 1 Sessions: 1 Type: standard care with quiet time | VAS 0-10 |

| | | | | | | | | | |
|------------------------|------|------|-----------------------|---|--|------------|---|---|-----------|
| Hattan et al. [39] | 2002 | UK | NR | Age ^a : 63 (9) Male: 80% Sample size: 25 | CABG | 2 | Duration: 20 mins Frequency/day: 1 Sessions: 1 Protocol: unclear (feet) | Duration: - Frequency**: - Sessions: - Type: standard care (reading or resting while in bed) | VAS 0-100 |
| Kshetry et al. [40] | 2006 | USA | Acute care | Age ^a : 63 (14) Male: 72% Sample size: 115 | CABG, VR, CABG & VR | Day 2 or 3 | Duration: 30 mins Frequency/day: 1 Sessions: 1 Protocol: unclear | Duration: 20 mins Frequency**: 1 Sessions: 1 Type: standard care with rest period | NRS 0-10 |
| Mitchinson et al. [35] | 2007 | USA | ICU and surgical ward | Age ^a : 64 (10) Male: 99% Sample size: 605 | 64% cardiac surgery requiring sternal incision & 36% abdominal surgery | 1 | Duration: 20 mins Frequency/day: 1 Sessions: up to 5 Protocol: specific (back) | Duration: 20 mins Frequency**: 1 Sessions: up to 5 Type: attention control Comparator 2: standard care | VAS 0-10 |
| Najafi et al. [29] | 2014 | Iran | Acute care | Age ^a : 60 (7) Male: 54% | CABG | 3 | Duration: 30 mins Frequency/day: 1 | Duration: 30 mins Frequency**: 1 | VAS 0-10 |

Sample
size: 70

Sessions: 1

Protocol: unclear (hands,
feet, back, arms, legs,
neck, shoulders, pt
preference)

Sessions: 1

Type: attention
control

| | | | | | | | | | |
|----------------------|------|------|---|--|------|----------------------------------|--|---|-----------|
| Rigi et al. [42] | 2015 | Iran | ICU | Age ^a : 56 (8) Male: 86% Sample size: 52 | CABG | 2 | Duration: 30 Frequency/day: 1 Sessions: 1 Protocol: specific (feet) | Duration: - Frequency**: - Sessions: - Type: standard care | NRS 0-10 |
| Smith et al. [37] | 2004 | USA | ICU & cardiac observati on unit | Age ^a : 62 (10) Male: 75% Sample size: 20 | CABG | Between 30-45 hours postop | Duration: 10 Frequency/day: 1 Sessions: 1 Protocol: specific (back) | Duration: 10 Frequency**: 1 Sessions: 1 Type: attention control | VAS 0-100 |

CABG = Coronary Artery Bypass Graft, FPT = Faces Pain Thermometer, NR = Not Reported, NRS = Numeric Rating Scale, POD = postoperative day, VAS = Visual Analog Scale, VR = valve replacement

^a Mean (SD)

Purpose and Study Questions

This research study aims to test the effectiveness of hand massage administrations at three different times on the pain, anxiety, muscle tension, and vital signs of adult ICU patients after cardiac surgery. More specifically, this study aims to answer the following research questions:

1. What is the effect of three 20-minute hand massage administrations within 24 hours postop on the pain intensity of adult ICU patients post cardiac surgery versus hand holding and rest?
2. What is the effect of three 20-minute hand massage administrations within 24 hours postop on the pain unpleasantness, anxiety, muscle tension and pain interference of adult ICU patients post cardiac surgery versus hand holding and rest?
3. What is the effect of three 20-minute hand massage administrations within 24 hours postop on the vital signs (BP, HR, RR) of adult ICU patients post cardiac surgery versus hand holding and rest?

Based on preliminary observations and patients' reports, a complementary research question was added during the conduct of this RCT:

4. What is the effect of three 20-minute hand massage administrations within 24 hours postop on the sleep of adult ICU patients post cardiac surgery versus hand holding and rest?

Chapter 3. Theoretical Framework

The theoretical foundation of this thesis was built on the neuromatrix theory of pain proposed by Melzack (1999a), which provides a model for the mechanisms underlying nociception, pain perception and the stress systems related to pain. This theory is renowned for changing the way in which pain is conceptualized so that pain is no longer described simply as a sensation produced by injury, inflammation or other tissue pathology, but recognized to be a multidimensional experience produced by multiple influences acting on the brain's neural network. The neuromatrix theory of pain acknowledges the mechanisms of nociception and the essential role of the central nervous system in pain processes such that pain can no longer be explained exclusively in terms of peripheral factors.

Nociception

Nociception represents the neural processes of encoding and processing noxious stimuli that are generated by the activation of nociceptors (Loeser & Treede, 2008). Nociception has been distinguished from pain as each can occur without the presence of the other. Pain is a product of higher brain center processing, and for nociception to evoke pain, an intact transmission of nociceptive signals is necessary from the periphery and up to the higher centers of the brain. Yet, pain can also exist in the absence of peripheral nociception such as the pain originating in thalamic structures (Loeser & Treede, 2008).

Four major processes are involved in the neural mechanisms of nociception, namely, transduction, transmission, perception and modulation (Pasero & McCaffery, 2011).

Transduction. First, noxious stimuli that induce mechanical (e.g., surgical incision, pressure from swelling), thermal (e.g., sunburn) or chemical (e.g., toxic) tissue damage cause the release of numerous excitatory neurotransmitters (e.g., substance P, prostaglandins, histamine)

that activate the nearby primary afferent nociceptors. These nociceptors will fire an action potential to the spinal cord and initiate the transmission of nociceptive signals from the peripheral to the central nervous system. This initial step of converting the noxious stimuli into neuronal action potentials represents the first process of nociception also referred to as transduction.

Transmission. Then, the nociceptive signal is transmitted from the site of transduction to the brain in three segments: 1) along the nociceptive fibers to the level of the spinal cord, 2) dorsal horn processing, and 3) transmission to the thalamus and cortex. The afferent nerve fibers A delta ($A\delta$) and C transmit pain impulses from the peripheral nociceptors in the skin, muscle, joints and viscera to the dorsal horn of the spinal cord (Guirimand & Le Bars, 1996). $A\delta$ fibers are small, myelinated and medium-conducting fibers that transmit pain sensation described as pricking, sharp, well localized and short in duration. C fibers are small, unmyelinated and slow-conducting fibers that transmit pain sensation that is dull, aching, burning, diffuse and of a relatively long duration. These afferent nociceptive fibers release neurotransmitters (e.g., substance P) into the synaptic cleft of the dorsal horn and activate the second-order neurons. These neurons stimulate the spinal reflex response such as muscle tension or spasm, and activate the ascending tracts which transmit the nociceptive signal to the third order neurons in the thalamus and other regions of the brain where pain perception occurs.

Pain perception. In the brain, the nociceptive signal is perceived as pain. Although pain has been long recognized as a purely sensory phenomenon perceived in the somatosensory brain region, several other brain structures are now known to be equally involved in pain perception. The neuromatrix theory of pain (Melzack, 1999a, 1999b) proposes that the brain possesses a neural network, referred to as the body-self neuromatrix, which integrates multiple inputs to

produce the output pattern that evokes pain (see Figure 1. for an adapted diagram of the Neuromatrix Theory of Pain). The body-self neuromatrix comprises a widely distributed neural network that includes parallel somatosensory, limbic and thalamocortical components. The somatosensory system is responsible for the localization and characterisation of pain (i.e., intensity, pattern and quality); the limbic system is responsible for the emotional (i.e., pain unpleasantness) and behavioral responses to pain; and the thalamocortical component is thought to be crucial in constructing the meaning and the possible consequences of pain (i.e., beliefs, attitudes, evaluations and goals). The output of the neuromatrix produces the sensory-discriminative, affective-motivational and evaluative-cognitive dimensions of pain experience and behavior.

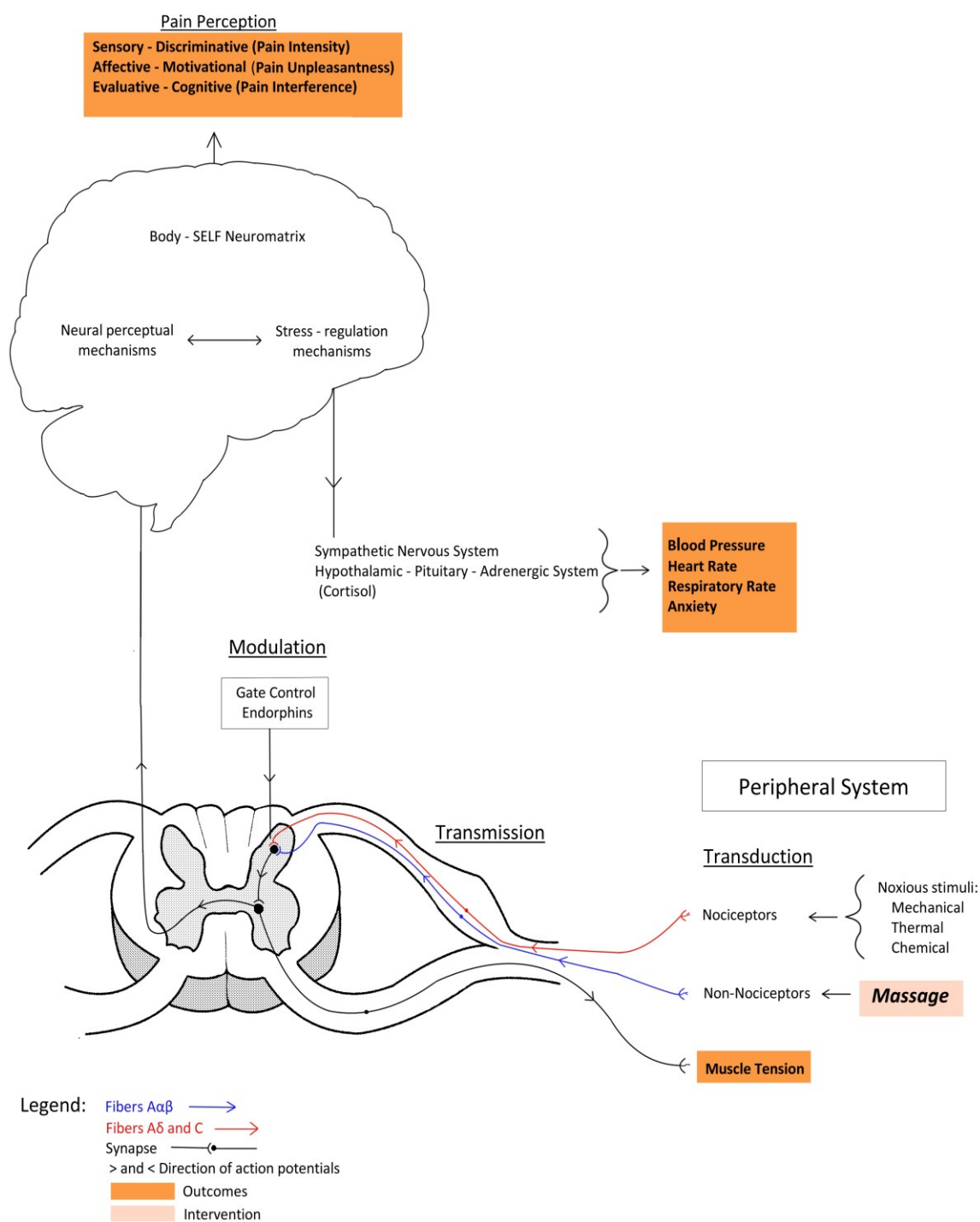


Figure 1. The adapted diagram of the Neuromatrix Theory of Pain

Modulation. Finally, modulation involves the activation of descending pathways that exert inhibitory or excitatory effects on the transmission of nociceptive signals. The neuromatrix theory of pain supports the active role of the central nervous system in modulating nociceptive impulses perceived as painful, and highlights the dynamic sites of dorsal horns and brain where inhibition, excitation and modulation occur.

At the level of the dorsal horns, the Gate Control Theory of Pain proposes a mechanism for the modulation of nociceptive signals (Melzack & Wall, 1965). The theory posits that the stimulation of the skin evokes nerve impulses that are transmitted to the cells of the substantia gelatinosa (SG) in the dorsal horn (see Appendix A for a diagram of the Gate Control Theory of Pain). The large non-nociceptive afferent fibers A alpha ($A \alpha$) and A beta ($A \beta$) that are responsible for the rapid transmission of impulses initiated by tactile sensations and proprioception in the muscles ($A \alpha$) and skin ($A \beta$) (Guirimand & Le Bars, 1996), and the small nociceptive afferent fibers A δ and C project to the SG. The SG is said to function as a gate control system that modulates the synaptic transmission of nerve impulses from afferent peripheral fibers to central cells before being projected and transmitted to the brain. Large diameter fibers $A \alpha$ and $A \beta$ increase the inhibitory effect exerted by the SG on the afferent fiber terminals and close the gate to nociceptive stimuli transmission. Conversely, small diameter fibers $A \delta$ and C decrease this inhibitory effect, the gate is open and painful sensations are perceived by the brain. Large diameter fibers are known to be stimulated by massage, rubbing, application of heat and several other types of skin stimulations.

Pain and Stress

In addition to the role of the brain's neural network in pain perception is the stress regulation system which is thought to play an important role in pain processes. The body-self

neuromatrix is said to comprise both neural perceptual mechanisms and the stress-regulation system. When injury occurs, sensory information alerts the brain, which activates the stress-regulation system to reinstate homeostasis. The noradrenergic system is one of the programs activated for this purpose. Adrenalin is released in the blood stream and the locus coeruleus/norepinephrine (LC/NE) system in the brain stem stimulates the sympathetic nervous system that prepares the heart, blood vessels and other viscera to restore homeostasis as observed with increases in vital signs (i.e., blood pressure, heart and respiratory rates).

Massage and its Mechanisms of Action

Massage and Pain. The neuromatrix theory of pain supports the potential benefit of massage in promoting pain relief, and provides the underlying mechanisms between massage administration and ultimate pain perception. First, massage can have an impact on the perception of pain by modulating the transmission of nociceptive stimuli in the dorsal horn of the spinal cord. Massage therapies that consist of the application of touch to skin surfaces and of moderate pressure to muscle tissue can stimulate the peripheral non-nociceptive receptors. Hands, for example, have abundant mechanoreceptors that can be activated by the touch, pressure and cutaneous tension involved with massage administration (Purves, Augustine, & Fitzpatrick, 2001; Wang & Keck, 2004). The non-nociceptive receptors activated by the touch of skin stimulate the large diameter non-painful A β fibers, and those activated by the application of pressure to muscles stimulate the large diameter non-painful A α fibers (Guirimand & Le Bars, 1996). These large diameter non-painful fibers project to the SG in the dorsal horn where they inhibit the nociceptive stimuli transmitted by smaller nerve fibers (A δ and C) in the spinal cord. Ultimately, transmission of nociceptive impulses is blocked before they reach the body-self neuromatrix where pain perception occurs.

Second, massage can decrease pain by acting on the release of endogenous opioids. The manipulation involved with the administration of massage such as rubbing and applying pressure is thought to stimulate the release of beta-endorphins² in the bloodstream (Andersson & Lundeberg, 1995; Degenhardt et al., 2007; Kaada & Torsteinbo, 1989). These endogenous opioids can modulate the first synapses of the nociceptive afferent fibers with the second-order neurons in the dorsal horn. Endorphins bind to opioid receptors and block the release of neurotransmitters from the nociceptive fibers (especially substance P), which are required to activate spinal neurons and the firing of nociceptive impulses along the ascending tract to the brain (Girimand & Le Bars, 1996).

Overall, massage is an input applied peripherally and projected to the body-self neuromatrix to influence the output pattern, which produces the sensory, affective and cognitive dimensions of pain for which outcome measures have already been defined. The sensory dimension comprises the sensory aspects of pain such as pain intensity, localization and quality, which are evaluated using self-report scales (e.g., 0-10 NRS), body maps, and open-ended questions (e.g., describe the quality of pain), respectively. The affective dimension reflects the emotional and aversive aspects of pain, which are commonly assessed using a pain unpleasantness self-report scale. Last, the cognitive dimension further reflects the patient's evaluation of the possible consequences of pain, and could be captured by tools measuring the interference of pain in the patient's life such as the Brief Pain Inventory (Cleeland & Ryan, 1994).

² Beta-endorphins are neuropeptides involved in pain management. In the Peripheral Nervous System (PNS), they produce analgesia by binding to opioid receptors at pre- and post-synaptic nerve terminals where they inhibit the release of tachykinins (particularly substance P) involved in the transmission of pain. In the Central Nervous System (CNS), they bind to opioid receptors and inhibit the release of GABA, which results in excess dopamine production, also associated with pleasure (Sprouse-Blum, Smith, Sugai, & Parsa, 2010).

Massage and Muscle Tension. Analogous to the gate-control mechanism of massage in decreasing pain is the mechanism underlying reductions in muscle tension. By activating large diameter non-nociceptive nerve fibers and closing the gate to the transmission of nociceptive stimuli in the dorsal horn, massage is also interfering with the spinal reflex response. Afferent nociceptive fibers are no longer synapsing with interneurons or effector neurons in the spinal cord, thereby failing to stimulate the contraction of skeletal muscles, which could explain the potential effects of massage in decreasing muscle tension.

Massage, Anxiety and Vital Signs. The activation of peripheral afferent nociceptors, the transmission of nociceptive signals via the nociceptive nerve fibers (A δ and C) to the spinal cord and their projection to the body-self neuromatrix in the brain results in the activation of the stress response (Melzack, 1999a). Massage can block the transmission of nociceptive signals in the dorsal horn through the gate-control mechanism and release of beta-endorphins, and subsequently, inhibit the stimulation of the stress-regulation system responsible for the activation of the noradrenergic and sympathetic nervous system. The resultant lack of up-regulation of adrenaline and noradrenaline could explain the potential effects of massage in decreasing blood pressure, heart and respiratory rates, and the subjective sensations of anxiety (Bremner, Krystal, Southwick, & Charney, 1996; Goddard et al., 2010; Moyer et al., 2004).

Research Hypotheses

Based on the theoretical framework presented and previous studies conducted in this area, this study has three research hypotheses for the primary (pain intensity), secondary (pain unpleasantness, anxiety, muscle tension and pain interference), and tertiary outcomes (vital signs):

1. Primary research hypothesis: Adult cardiac surgery ICU patients receiving three 20-minute hand massages within 24 hours postop by the trained nurse will demonstrate lower pain intensity compared to those receiving three 20-minute hand holding by the same nurse and those in the rest group.
2. Secondary research hypothesis: Adult cardiac surgery ICU patients receiving three 20-minute hand massages within 24 hours postop by the trained nurse will demonstrate lower pain unpleasantness, anxiety, muscle tension and pain interference compared to those receiving three 20-minute hand holding by the same nurse and those in the rest group.
3. Tertiary research hypothesis: Adult cardiac surgery ICU patients receiving three 20-minute hand massages within 24 hours postop by the trained nurse will demonstrate lower vital signs (i.e., BP, HR, RR) compared to those receiving three 20-minute hand holding by the same nurse and those in the rest group.

No research hypothesis was formulated with regards to sleep at the beginning of the study, yet preliminary observations and patients' reports suggested that hand massage could enhance sleep in cardiac surgery critically ill:

4. Complementary research hypothesis: Adult cardiac surgery ICU patients receiving three 20-minute hand massages within 24 hours postop by the trained nurse will

demonstrate better sleep quality compared to those receiving three 20-minute hand holding by the same nurse and those in the rest group.

Chapter 4. Methods

The RCT was registered with ClinicalTrials.gov (NCT02679534) and the protocol was published in the JMIR Research Protocols (JMIR Res Protoc 2016;5(4):e203). The second manuscript presents the published protocol. The data collection forms are presented in Appendices B-E.

Manuscript 2**TITLE PAGE**

Title: The Effectiveness of Hand Massage on Pain in Critically Ill Patients After Cardiac Surgery: A Randomized Controlled Trial Protocol

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Abstract

Background: Postoperative pain is common in the intensive care unit despite the administration of analgesia. Some trials suggest that massage can be effective at reducing postoperative pain in acute care units; however, its effects on pain relief in the intensive care unit and when pain severity is highest remain unknown.

Objective: The objective is to evaluate the effectiveness of hand massage on the pain intensity (primary outcome), unpleasantness and interference, muscle tension, anxiety, and vital signs of critically ill patients after cardiac surgery.

Methods: A 3-arm randomized controlled trial will be conducted. A total of 79 patients who are 18 years or older, able to speak French or English and self-report symptoms, have undergone elective cardiac surgery, and do not have a high risk of postoperative complications and contraindications to hand massage will be recruited. They will be randomly allocated (1:1:1) to standard care plus either 3 20-minute hand massages (experimental), 3 20-minute hand holdings (active control), or 3 20-minute rest periods (passive control). Pain intensity, unpleasantness, anxiety, muscle tension, and vital signs will be evaluated before, immediately after, and 30 minutes later for each intervention administered within 24 hours postoperatively. Peer-reviewed competitive funding was received from the Quebec Nursing Intervention Research Network and McGill University in December 2015, and research ethics approval was obtained February 2016.

Results: Recruitment started in April 2016, and data collection is expected to be complete by January 2017. To date, 24 patients were randomized and had data collection done.

Conclusions: This study will be one of the first randomized controlled trials to examine the effect of hand massage on the pain levels of critically ill patients after cardiac surgery and to provide empirical evidence for the use of massage among this population.

ClinicalTrial: ClinicalTrials.gov NCT02679534;

<https://clinicaltrials.gov/ct2/show/NCT02679534> (Archived by WebCite at

<http://www.webcitation.org/6l8Ly5eHS>)

KEYWORDS

massage; pain; critical care; randomized controlled trial; anxiety; muscle tension; vital signs;
clinical protocol; complementary therapies; thoracic surgery

Introduction

Overview

Undergoing cardiac surgery constitutes a major event for patients that is accompanied by physical and psychological symptoms such as postoperative pain [1-5] and anxiety [6-8]. Recent studies reveal that massage could complement pharmacological treatments and have positive effects in reducing these symptoms in acute care units [9-11], yet empirical evidence is lacking to support the same effects early in the postoperative phase when patients are in the intensive care unit (ICU) and pain is at its highest.

In the ICU, postoperative pain can be compounded by routine ICU procedures such as turning, coughing, breathing, and chest tube removal, activities which are perceived to be the most painful in the immediate postoperative period [3,5]. Given the higher severity and complexity of pain in the ICU, findings from massage studies conducted on acute care wards cannot be extrapolated to the unique context of the ICU and the early recovery phase after cardiac surgery. Further evidence is needed to unravel the potential role of massage in relieving the pain of cardiac surgery in ICU patients and guide international clinical practice guidelines with regard to the use of this complementary nonpharmacological intervention in this patient population.

Background

Cardiac surgeries, such as coronary artery bypass grafting and valve replacement, rank among the most frequently performed surgical interventions worldwide [12] and necessitate the routine admission of patients to the ICU. Cardiac surgeries are commonly indicated to reduce anginal pain, but the surgical procedure itself can lead to the development of postoperative pain. Mounting evidence shows that cardiac surgery ICU patients experience moderate-to-severe pain

reaching proportions as high as 74% despite the use of analgesics [2-5], with the highest pain intensity commonly experienced in the first 24 hours post surgery [13].

Unrelieved postoperative pain can interfere with patients' ability to cough and mobilize effectively, which predisposes them to postoperative complications such as atelectasis, pneumonia, and deep vein thrombosis [2,5,14], thereby delaying recovery and ICU discharge. Moreover, the intensity of acute postoperative pain immediately after surgery is a significant predictor of the presence and severity of persistent postoperative pain up to 2 years post surgery [15-17], a serious and often unrecognized complication after cardiac surgery that may interfere with daily activities and quality of life [18].

Among the pharmacological approaches to pain control, opioids constitute the mainstay of treatment in the ICU [19,20], yet pain has been shown to persist even during unrestricted use of these analgesic agents [13,21]. The use of complementary nonpharmacologic interventions such as massage has been suggested in the clinical practice guidelines of the Society of Critical Care Medicine given their opioid-sparing and analgesia-enhancing potential [20]. Massage has been defined as the manual manipulation of muscles and soft tissues of the body through the application of various systematic and rhythmic hand movements [22,23].

A recent systematic review exploring the effectiveness of massage on postoperative outcomes among patients undergoing cardiac surgery [24] indicated that out of the 7 eligible studies (N=40-252/study), 6 reported that massage therapy ranging from 20 to 30 minutes in duration improved postoperative outcomes such as pain, anxiety, and muscle tension [9,10,25-28], while only one study reported no positive results [29]. The latter study evaluated the effectiveness of a 30-minute massage therapy involving each limb for 5 minutes followed by a 10-minute back massage while patients were lying on the left side. The positioning required for

the back massage might have obscured or minimized the potential benefit of massage in relieving pain, anxiety, and muscle tension given that side-lying may exert traction on the sternotomy site, causing pain [3] and increasing muscle tension and possibly anxiety as turning on one side could be perceived as a painful procedure. Of note, only one of these studies was conducted in the ICU [25], and it lacked random assignment.

One pilot randomized controlled trial (RCT) conducted with 40 ICU patients post–cardiac surgery [30] showed promising pain relief and muscle relaxant effects of up to 3 15-minute hand massages, whereas the administration of a single massage therapy did not yield any significant decrease in pain intensity or muscle tension, suggesting that repeated administration of hand massage is necessary in this patient population. Overall, there is a paucity of high-level evidence on which to base massage therapy decisions in the management of pain in post–cardiac surgery ICU patients. Extrapolations of evidence from other patient populations and clinical settings are flawed by the differing health status and symptom severity of this specific subgroup of ICU patients. Future rigorous RCTs conducted in the context of the ICU and with cardiac surgery adults in their immediate postoperative period are essential to make recommendations for the use of massage in clinical practice including the minimal effective dose, body area massaged, and techniques employed.

Theoretical Framework

The protocol is based on the neuromatrix theory of pain [31] where the brain’s neural network, the body-self neuromatrix, integrates multiple inputs such as sensory (eg, cutaneous) and opioid systems (ie, endogenous opioids) to influence the sensory (intensity, localization, and quality), affective (unpleasantness), and cognitive dimensions (interference with daily functioning) of pain (Figure 1). The sensory stimulation of nonnociceptive fibers in the skin and

muscles involved in massage could block the transmission of nociceptive impulses in the dorsal horns and may increase the release of beta-endorphins in the bloodstream [32,33], which block the release of neurotransmitters from the nociceptive fibers (especially substance P) [34], thereby blocking the transmission of nociceptive impulses from reaching the body-self neuromatrix where pain perception occurs. Similarly, by blocking the transmission of nociceptive signals, the stimulation of the stress-regulation system responsible for the activation of the noradrenergic and sympathetic nervous system could be inhibited. The resultant lack of up-regulation of adrenaline and noradrenaline could explain the potential effects of massage in decreasing blood pressure, heart and respiratory rates, and the subjective sensations of anxiety [35-37].

Aim

The primary aim of this research study is to compare the effect of 3 20-minute hand massage administrations by a trained nurse within 24 hours after cardiac surgery versus hand-holding (ie, simple touch) and standard care on the postoperative pain intensity of adult ICU patients.

Methods

Trial Design

This research study is designed as a randomized, controlled, patient-blinded, single-center superiority trial with 3 parallel groups and a 1:1:1 allocation ratio. A modified Consolidated Standards of Reporting Trials flow diagram for individual RCTs of nonpharmacologic treatments will be used to document recruitment and retention of participants (see Multimedia Appendix 1) [43].

Participants

This RCT targets adults admitted to the ICU after undergoing cardiac surgery in a university-affiliated hospital in Canada. A single setting was selected for this study because of standardized pain management practices and surgical techniques and single patient rooms. Patients will be screened for inclusion using the eligibility criteria seen in Textbox 1. Patients at higher risk of postoperative complications and those with contradictions to having their hands massaged will be excluded.

Sample Size and Sampling Procedure

A power analysis was conducted using the G*Power 3 program [38] to estimate the sample size required to capture the potential effects of massage to decrease the primary outcome (pain intensity) and to strengthen the statistical conclusion validity. The mean treatment difference was observed to be greater than 1.5 in several RCTs [11,26,39,40] and approximates the clinically significant difference of 2 points on the 0 to 10 Numeric Rating Scale (NRS) [41]. This trial is powered to be able to detect a difference in the pain intensity score of 1.5 between the hand massage and standard care group. The standard deviation of pain intensity scores is approximately a 2.0 value, which was selected for the sample size calculation. To detect a mean difference in pain intensity scores of 1.5 points (SD 2.0) immediately after the third massage with a 2-sided significance level of .05 and power of .80 with equal allocation to 3 arms and a repeated measures between factors context with 3 measurements would require a minimum of 72 patients. Given the low attrition rates observed with this patient population (0% [9,10,30] and 35/287 (12.2%) [29]), a 10% drop-out rate is considered in the calculation of the total sample size. Therefore, the final size required for this RCT is 79, and it will be reached using convenience sampling.

Randomization

Before the study begins, permuted-block randomization will be generated for 85 patients by a statistician using SAS computer software (SAS Institute) and block sizes of 3, an allocation ratio of 1:1:1, and one strata to minimize the imbalance in the number allocated to each group. Then, the randomization schedule will be transcribed in sequentially numbered and opaque sealed envelopes by a research coordinator not involved in assignment allocation to ensure allocation concealment. The allocation list will be stored in a locked filing cabinet of the principal investigator and will not be made accessible to the interventionist involved in enrollment and treatment allocation.

Recruitment of Participants

Patient recruitment will begin preoperatively when eligibility criteria such as age and language spoken will be verified (Table 1). The remaining eligibility criteria (eg, blood loss, peripheral intravenous lines) will be evaluated post-cardiac surgery and ICU admission. After the collection of baseline data, patients meeting all the inclusion criteria will be randomly assigned to either hand massage, hand-holding, or rest. As each participant enters the study, he or she receives the next envelope in the sequence, thereby concealing the interventionist's and trial participants' knowledge of the upcoming group assignment.

The interventionist will then administer the assigned intervention (hand massage, hand-holding) without informing participants of their group assignment until the end of data collection. Nurses and other ICU clinicians will also be masked to patients' group assignment. The similarity of the hand massage and hand-holding therapy characteristics serves to mask study participants and clinicians with regard to the specific intervention received as observed in a feasibility and acceptability study where patients receiving hand-holding referred to the

intervention as massage [42]. Conversely, patients in the rest group are less likely to be masked to the group assigned.

A modified Consolidated Standards of Reporting Trials flow diagram for individual RCTs of nonpharmacologic treatments will be used to document recruitment and retention of participants [43].

Choice of Comparators

The majority of massage studies include standard care control groups to examine the absolute efficacy of massage in improving outcome variables. While this is important in attributing benefits to the massage therapy itself, studies that involve the administration of massage by a trained therapist, as recommended in Cochrane Systematic Reviews [44], should equally include a touch control group to verify if the additional manipulation included in massage is superior to touch only. Some studies suggest that touch, a free and easily administered intervention not requiring training, can have potential pain relief effects [45] and should, thus, be included as an active control group in future RCT designs to additionally examine the relative efficacy of massage. Furthermore, the touch control group can help mask patients with regard to the group assigned through its resemblance with actual massage, thereby controlling for placebo effects [44].

Interventions

Training of Interventionist and Timing of Interventions

Eligible patients will be randomized in equal proportions among hand massage, hand-holding, and rest. One interventionist will deliver the hand massage and hand-holding interventions, which will be standardized across participants. The interventionist is a registered nurse with no previous experience in massage therapy who will be trained by a professional

massage therapist through an accredited workshop of 6 hours including practical exercises and verification of competency, as was done in the pilot RCT [30].

The first intervention (hand massage or hand-holding) will be delivered in the evening of the day of surgery and the remaining two interventions the day after when patients are still in the ICU. Overall, three interventions will be administered within 24 hours postoperatively over the course of two days.

Experimental Group

Patients assigned to the experimental group will receive a 20-minute hand massage by the interventionist in addition to the standard ICU care. Before administering the massage, a favorable environment will be created that promotes calmness such as dampening the light, reducing the alarm intensity, closing the curtains and door, and posting a “do not disturb” notice, and a comfortable positioning of the patient will be ensured [9,30,46]. After performing hand hygiene and explaining the procedure to the patient, the interventionist will hold each hand for 5-10 seconds and apply 5-10 mL of unscented hypoallergenic cream to both hands and wrists. The cream will be supplied by the interventionist and reserved for use within the research context only. The interventionist will then perform massage using moderate pressure and stroking and kneading techniques during 10 minutes on the palm and back of each hand as inspired by the procedure by Kolcaba et al [47] and developed with the support of an experienced massage therapist (Textbox 2).

Active Control Group

The active control group will receive hand-holding by the same interventionist in addition to standard ICU care. The same hand hygiene and environmental adjustments will be made as for those receiving massage. Patients will have their hands held for 5-10 seconds and unscented

hypoallergenic cream applied to both hands. Then, the interventionist will hold each of the patients' hand in her hand for ten minutes with occasional stroking for a total of 20 minutes.

Passive Control Group

The passive control group will receive the standard care administered in the ICU including a 20-minute rest period including the environmental adjustments of the experimental and active control groups. The interventionist will be outside of the patient room and have no contact with the patient throughout the 20 minutes. The standard care includes the pharmacological and nonpharmacological treatments (eg, repositioning) used to promote recovery and pain relief. In the study ICU, cardiac surgery patients are automatically prescribed a pain management protocol that includes the regular administration of morphine and breakthrough doses of analgesia as needed.

Criteria for Modifying Interventions

The allocated interventions will be discontinued upon the participant's withdrawal of consent or if skin irritation is suspected or patient comfort is disrupted due to the intervention itself, both of which will be reported as adverse events. Consenting participants will be retained in the trial whenever possible in spite of the discontinuation of the assigned intervention to allow remaining data collection and limit missing data.

Concomitant Care

Concomitant interventions may be received by patients while participating in this trial. Consenting patients will be permitted to receive any of the pharmacological treatments prescribed by their treating physician and any of the nonpharmacological interventions offered in the ICU (eg, back rub), and such data will be recorded. It is not prohibited that patients

participate concomitantly in other research studies unless it involves any form of complementary therapy.

Outcomes

Primary Outcome

Pain intensity is the primary outcome and will be captured using the 0 to 10 NRS score. The analysis metric will be the change in pain intensity from baseline (preintervention) to immediately after each intervention and 30 minutes later.

Secondary Outcomes

Pain unpleasantness, pain interference, muscle tension, anxiety, and vital signs will also be assessed in relation to each intervention, and means and standard deviations will be reported and used for data analysis.

Instrumentation

Pain Intensity

The NRS will be used to assess pain intensity. The NRS is an 11-point unidimensional self-report scale recommended for the assessment of pain intensity where 0 is no pain and 10 the worst possible pain. Details about the NRS and other assessment tools are summarized in Table 2.

Pain Unpleasantness

The NRS will be used to assess the pain unpleasantness of patients. The unpleasantness dimension of symptom experience refers to the degree to which the person is bothered by the unpleasant symptom [58]. The pain unpleasantness NRS is scored on a scale from 0 to 10 with the anchors “not at all unpleasant” for 0 and “most unpleasant feeling possible” for 10.

Pain Interference

An adapted version of the Brief Pain Inventory (BPI) will be used. The BPI is a short pain assessment scale developed to measure the intensity of pain during the last 24 hours (sensory dimension) and the interference of the pain in the patient's life (cognitive dimension) [59,60]. The pain severity items are rated individually on an NRS with 0 assigned to "no pain" and 10 to "worst possible pain." Patients are asked to rate their pain severity at the time of interview (pain now) and the worst pain, the least pain, and average pain during the last 24 hours. The 7 items of pain interference evaluate the impact of pain on general activity, mood, walking/mobilization, work, relationships, sleep, and enjoyment of life. The item work is not considered relevant in the context of cardiac surgery patients who are hospitalized in the ICU or acute care units and will not be administered. Instead, additional items about coughing, deep breathing, appetite, and concentration will be included; these have been observed to have moderate-to-severe pain interference in postoperative cardiac surgery patients [4,15,61].

Muscle Tension

The assessment of muscle tension will be based on an ordinal scale derived from the behavioral pain scale Critical-Care Pain Observation Tool (CPOT), which was developed and tested for the assessment of pain in critically ill patients after cardiac surgery [53]. Evaluation of muscle tension is done by performing passive flexion and extension of the upper limbs of patients at rest with a score of 0 being assigned for "no resistance to passive movements," 1 for "resistance to passive movements," and 2 for "strong resistance to passive movements or incapacity to complete them."

Anxiety

For consistency and because intensity of anxiety is of interest in this study, the NRS will also be used to assess patients' anxiety levels.

Vital Signs

Means of blood pressure (ie, systolic, diastolic, mean arterial pressure) and heart and respiratory rates will be collected from the ICU bedside monitors for 1 minute at each assessment point.

Data Collection

Sociodemographic (e.g., age, gender) and medical-surgical data (e.g., type of cardiac surgery, analgesia) will be collected using standardized data collection sheets. Prior to the delivery of each intervention (hand massage or hand-holding) and before the first data collection for the rest group, patients will complete a self-administered data collection sheet with 5 short questions using the NRS for the self-report of pain intensity, pain unpleasantness, and anxiety, a body map for identifying the site of pain, and an open-ended question for a description of the quality of pain. The interventionist will be masked to patients' self-reports, which will be accessed only at the end of data collection to verify for missing data. The form will be completed before, immediately after the intervention (hand massage or hand-holding), and 30 minutes later, for a total of 3 data collection points per intervention. Those assigned to rest will complete the form at similar times. This bundle of assessments will be repeated for each of the 3 interventions. Muscle tension and vital signs will also be evaluated at the same assessment points.

Finally, pain interference will be evaluated using a structured interview using the BPI on the second postoperative day to examine any carry-over effects.

Data Analysis

The data will be entered in the SPSS software version 22.0 (IBM Corp), and a random subset of data will be used to identify missing or erroneous values. This study aims to use intention-to-treat analysis by including every participant who has been randomized, regardless of group assignment, study withdrawal, or protocol deviations.

Descriptive statistics will be calculated for sociodemographic and medical-surgical data and the baseline scores on all the outcome variables. Group differentiation in sociodemographic and medical-surgical characteristics for participant patients will be investigated using chi-square tests of independence for nominal level variables and one-way analyses of variance (ANOVA) for interval and ratio level variables. If group differences exist, the respective variable will be included as a covariate in the subsequent analyses. Frequencies and percentages of the location and descriptors of pain (ie, sensory dimension of pain) will be calculated for each group and assessment point and used to describe the pain characteristics of participants. Data on pain location and quality will be compared over time.

Repeated measures between ANOVA factors will be used to test for treatment (hand massage, hand-holding, rest), time (before, immediately after, and 30 minutes later), and interaction effect for pain intensity, pain unpleasantness, muscle tension, anxiety, and means of vital signs. This will be run for each intervention and each of these outcome variables. One ANOVA test will be performed for pain interference with the independent variable being group assignment (hand massage, hand-holding, rest). The main comparison of interest is between the hand massage and rest group and the difference in means pre- and immediately post-treatment.

Ethical Considerations

Ethical approval has been granted by the Research Ethics Committee of the study setting in February 2016. This protocol has been independently peer reviewed by McGill University and the Quebec Nursing Intervention Research Network, who funded the study (F242710).

Informed and written consent will be obtained from participants. The study's aim and procedure, risks and benefits, right to refuse participation and withdraw at any time without any repercussions on the care provided, confidentiality of data, randomization process, and lack of financial incentives for participation in the study will be explained to patients. They will be equally informed that there is no guarantee that they will benefit from this study. While there are no known risks associated with hand massage and hand-holding, any harmful effects during these interventions will be noted and reported to the Research Ethics Committee.

Validity and Reliability

This study follows the most recent Consolidated Standards of Reporting Trials guidelines for nonpharmacological treatments and randomized controlled trials [62] and the Standard Protocol Items: Recommendations for Interventional Trials statement for clinical trial protocols [63].

The tools to be used for the assessment of the study outcomes have established validity and reliability in the population of interest in this study (Table 2). Data collection errors in vital signs will be minimized by extracting their means from the bedside ICU monitors, which offer a continuous recording of vital signs. Additionally, the interventionist will be trained on the assessment of muscle tension. To enhance rigor, standardized hand massage and hand-holding will be ensured by training the interventionist on the administration of these therapies and by

using a camera to monitor the consistency and fidelity with which each of these interventions is delivered [42].

Results

Recruitment started the end of April 2016, and to date 34 patients have already been recruited. Of these, 24 patients were randomized and had data collection done as several were medically unstable postoperatively or had their surgery cancelled/postponed. Data collection is expected to be complete by January 2017.

Discussion

Interpretation

Pain is one of the most common and severe symptoms cardiac surgery patients experience during their ICU stay. The adverse effects of unrelieved acute postoperative pain are numerous and can be taxing to cardiac surgery patients during their recovery but worryingly also on the long term. There is a general agreement in practice guidelines that multimodal approaches to pain management should be implemented in the ICU [20]. Massage, a complementary nonpharmacological intervention, could play an important role in enhancing pharmacological analgesia and maximizing pain relief in the cardiac surgery patients, and providing rigorous empirical evidence for its use in the ICU is strongly awaited to inform practice guidelines.

In the proposed RCT, eligible and consenting patients will be randomly assigned to either the massage (ie, experimental), hand-holding (ie, active control) or rest (ie, passive control). While the administration of pleasant and potentially beneficial interventions [42] can help minimize attrition rates in the experimental and active control groups, the use of standard care with rest only could cause higher withdrawals in this group and subsequently increase the risk of attrition bias. In order to counter such bias and as an incentive to make participation in the study

more attractive, patients will be informed that hand massage can be offered to those assigned to the active or passive control groups at the end of data collection, if desired.

A strength of this RCT is the administration of massage in the actual ICU environment and the clinical context of the first 24 hours post–cardiac surgery when monitoring is accrued, thus enabling an evaluation of the effectiveness of this intervention on the patient’s pain and related signs and symptoms. However, the same ICU environment could interfere with the delivery of some of the planned hand massages and hand-holding in the selected mode (eg, quiet environment) and dose (ie, 3 times for 20 minutes). In order to monitor these interferences and consider them in the interpretation of study findings, a camera will be used to videorecord the interventions. Nonetheless, even if these interventions can no longer be administered (eg, use of invasive equipment on hands post randomization), attempts to continue collecting patients’ self-reports of symptoms will be prioritized over imputation for missing data.

Limitations

One of the anticipated limitations of this RCT is the lack of blinding of patients in the standard care group and the respective clinical personnel responsible for their care. Although environmental adjustments will be made, these patients will have already been informed of the 3 trial arms and their implications and could easily recognize their group assignment. Equally, it is expected that the ICU personnel will notice the absence of an active intervention and assume patient assignment to standard care. Given the unlikelihood of blinding related to the standard care group, patients could modify their self-report while the personnel could practice differently compared to when they see hand massage/hand-holding administrations, thereby increasing the risk of performance bias.

Only the cardiac surgery ICU patient population will be included in this RCT, which will limit the generalizability of the findings to other ICU patients. Even so, this study will reveal the effectiveness of massage in this group of ICU patients suffering from intense pain and should be a trigger for further research internationally on the use of this intervention in the ICU in addition to the locally established standard care.

Conclusion

This funded RCT will unravel the potential benefits to reduce ICU postsurgery pain by the use of massage therapy in cardiac surgery ICU patients compared to hand-holding and standard care. The results of this study will serve to inform clinical practice guidelines with regard to the dose, timing, and technique of massage administration for the relief of acute postoperative pain in the ICU in addition to analgesia. If effective, massage could be easily implemented in ICU practice with little resources to maximize pain relief in the acute postoperative period and prevent the serious adverse consequences of unrelieved pain.

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Conflicts of Interest

None declared.

Multimedia Appendix 1

Modified Consolidated Standards of Reporting Trials flow diagram. CONSORT E-HEALTH

(V1.6). [PDF File (Adobe PDF File), 975KB - resprot_v5i4e203_app1.pdf]

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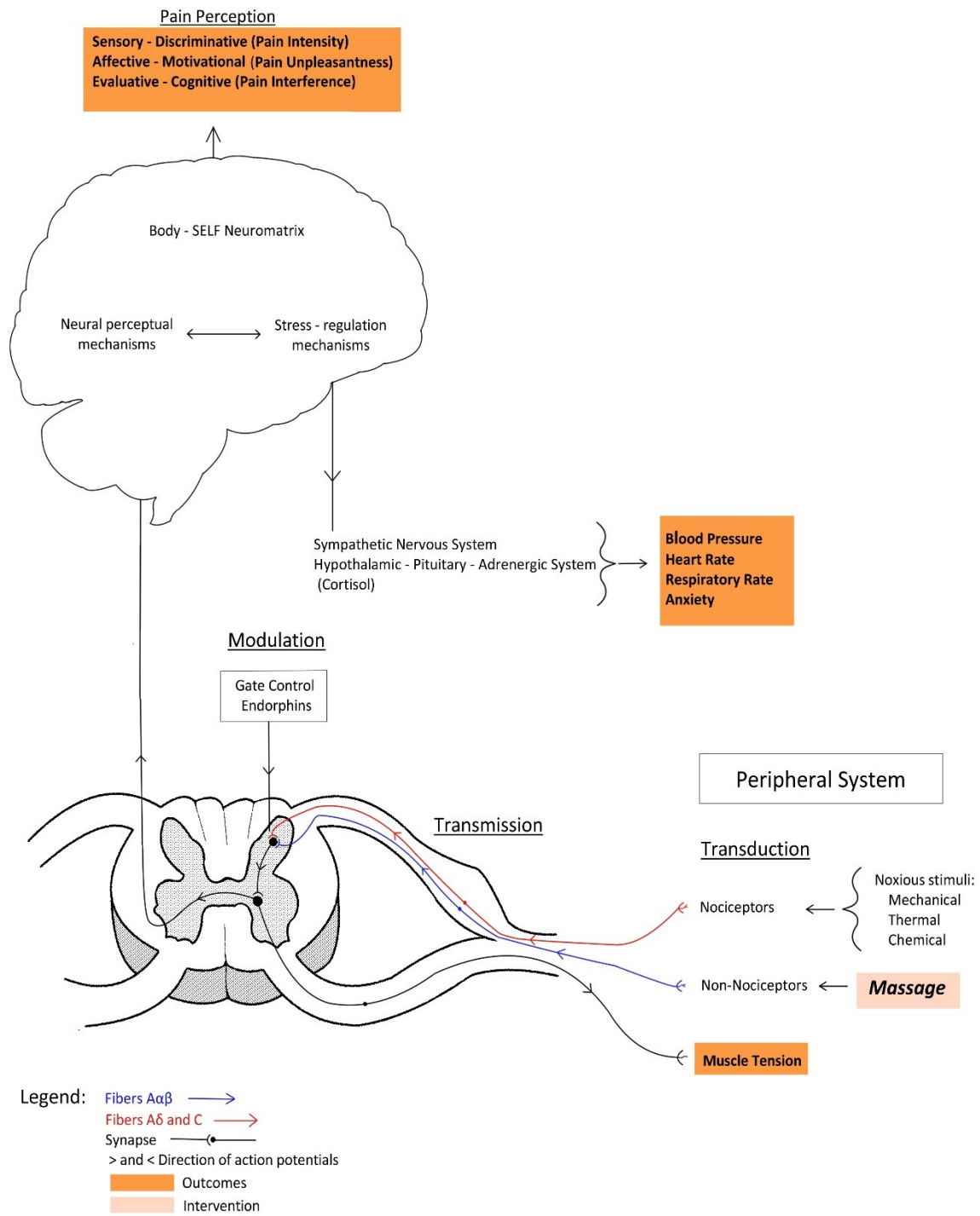
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Figure 1. The Adapted Diagram of the Neuromatrix Theory of Pain



Textbox 1. Eligibility criteria

| Inclusion criteria | Exclusion criteria |
|--|---|
| <ul style="list-style-type: none"> • 18 years of age and older • Able to speak French/English • Elective cardiac surgery • Able to answer questions and self-report symptoms | <ul style="list-style-type: none"> • Previous cardiac surgery • diagnostic of cognitive or psychiatric disorder • pulmonary artery pressure >50 mmHg • right ventricular failure • systolic left ventricular dysfunction (ejection fraction 35% or less) • body mass index > 30 • prolonged bleeding from the chest drainage tubes (i.e., >200 ml/h) • having mechanical blood pressure support (e.g., intra-aortic balloon pump) • receiving cardiac pacing with complete control of HR • peripheral intravenous line in the hands • suppurating/infective/inflammatory skin condition of the hands • hypersensitivity to touch |

Table 1. Study Timeline

| Procedures | Pre-op | POD 0 evening | POD 1 early evening | POD 1 late evening | POD 2 |
|-------------------------------|--------|------------------|---------------------------|--------------------------|-------|
| Enrolment | | | | | |
| First eligibility screen | X | | | | |
| Informed consent | X | | | | |
| Second eligibility screen | | X | | | |
| Randomization | | X | | | |
| Interventions | | | | | |
| Hand massage | | X | X | X | |
| Hand holding | | X | X | X | |
| Rest period | | X | X | X | |
| Standard care | X | X | X | X | X |
| Data collection | | | | | |
| Demographics questionnaire | X | X | | | |
| Pain intensity | | X | X | X | |
| Pain unpleasantness | | X | X | X | |
| Pain interference | | | | | X |
| Pain location and quality | | X | X | X | |
| Anxiety | | X | X | X | |
| Muscle tension | | X | X | X | |
| Vital signs | | X | X | X | |

Textbox 2. Hand massage routine protocol

| |
|---|
| 1. Hygiene: Wash hands with warm water. |
| 2. Hold/Connect/Breathe: initial contact with patient, embrace hand, take a deep breath, place feet on floor |
| 3. Apply cream to entire hand, dorsal and palmer, including phalanges |
| 4. Spreading (5x) dorsal aspect of hand, using thumbs like opening a book. Repeat 5x on palmer aspect, using the other 4 fingers to grip and glide. Spread again 5x dorsal aspect of hand and 5x palmer aspect. |
| 5. Gentle shaking of bottom hand- vibration to help the patient relax and let go of any tension |
| 6. Rotations of the wrist 3x in each direction. Hold wrist with one hand while the other holds the patients hand and facilitates the passive rotation |
| 7. Stretch the carpal ridge 3x along wrist crease |
| 8. Zoning – caterpillar walk dorsal aspect, between the bones |
| 9. Pinching (dorsal/palmer) aspect of the hand in between the metacarpals |
| 10. Gently pull the webs of fingers |
| 11. Kneading (rock n roll): making a fist on the palmer aspect of patient's hand, gently rotate using the knuckles to apply pressure x 5. |
| 12. Zoning palm – caterpillar walk all areas of the palm, working proximal (towards the body) (if patient less comfortable with palm upwards continue with hand in a neutral position- palm down) |
| 13. Small circles along the 5 zones of the palmer surface of the hand (proximal to distal) |
| 14. Target key reflex areas – PRESS AND RELEASE 2x in each area: <ul style="list-style-type: none"> a. Shoulder-neck ridge (base of fingers) b. Solar Plexus (center of palm, just below the knuckle) PRESS and SPREAD (diaphragm line- moving outwards in both directions) x 5. c. Lateral aspect of palm d. Medial aspect of palm e. Pad of thumb |
| 15. Pinching lateral aspect of hand 3x |
| 16. Zoning Spine – caterpillar walk medial border of thumb 3x |
| 17. Zoning Fingers – <ul style="list-style-type: none"> a. Caterpillar walk proximal making sure to cover all surface areas b. Rotate knuckles gently 3x in each direction (proximal to distal) c. Gently pull fingers |
| 18. Finishing touches: SWEEP entire hand. HOLD. Switch to other side |
| 19. Hygiene: once both hands are massaged, wash hands with cold water |

Table 2. Description and psychometrics of the instruments used for outcome data collection

| Outcome | Instrument | Scoring | Psychometrics | |
|---------------------|------------|--|--|--|
| | | | Reliability | Validity |
| Pain intensity | NRS (0-10) | 0: no pain 10: worst possible pain | High test-retest reliability observed in cancer patients when measuring pain exacerbations (k=0.86) and background pain (k=0.80) [48]. | High concurrent validation with the VAS (r=0.84 to 0.94, p<0.001) [2,49]. Good discriminatory capability between background and peak intensity pain in the oncology population with only 14% of the 240 patients giving inconsistent evaluations [48]. |
| Pain unpleasantness | NRS (0-10) | 0: not at all unpleasant 10: most unpleasant feeling possible | | Good convergent validation with the Facial Affective Scale (r=0.71, p<0.01). Discriminant validation: correlated with the Functional Disability Inventory |

| | | | | |
|-------------------|--|--|--|--|
| | | | | ($r=0.28$, $p<0.05$). Good sensitivity to change over a 2-week period (mean change 1.89, $t_{68}=5.30$, $p<0.001$) in children and adolescents after surgery (Page et al., 2012). |
| Pain interference | Adapted BPI: Pain intensity index (4 NRS 0-10 subscales); Pain interference index (7 NRS 0-10 subscales) | Pain intensity: 0: no pain 10: pain as bad as you can imagine Pain interference: 0: no interference 10: interferes completely | Internal consistency was also supported for this patient population with Cronbach's alpha coefficients between 0.84-0.89 for the severity scale, and 0.91-0.94 for the interference scale. | Factor analysis revealed two distinct factors (i.e., pain intensity and interference) accounting for 66% and 75% of total variance, respectively [51]. Scores on both scales declined significantly from baseline to follow-up, thus testifying to the responsiveness of the BPI for detecting changes [51]. |
| Muscle tension | CPOT muscle tension subscale (0-2) | 0: no resistance 1: resistance 2: strong resistance | Moderate to high interrater reliability of CPOT scores between trained raters with ICCs 0.30-0.86 [52] and kappa | Discriminant validation: significant increases in CPOT scores during painful compared to non-painful |

| | | | | |
|---------|------------|---|---|--|
| | | | 0.52-0.88 [53,54]. | procedures [52-55]. Criterion validation: moderate correlation with patient self-report of pain intensity ($r=0.40-0.69$, $p<0.05$) [52,53]. Convergent validation: moderate correlation with pain unpleasantness ($r=0.31$, $p<0.01$) [52]. Sensitivity of 86% and a specificity of 78% for the presence of pain during turning procedures were shown for a CPOT cut-off score >2 [56]. |
| Anxiety | NRS (0-10) | 0: no anxiety 10: worst possible anxiety | Individual validity and reliability tests were not conducted to date with the NRS for anxiety, but it has been included in the Edmonton Symptom Assessment System whose validity and reliability received support over the past two decades [57]. | |

*NRS: Numeric Rating Scale; BPI: Brief Pain Inventory; CPOT: Critical-Care Pain Observation Tool

Chapter 5. Results

A total of 138 patients who were scheduled to undergo cardiac surgery at a medical-surgical ICU in Canada were screened for inclusion in this study. Ninety-five patients met the inclusion criteria and were approached to participate in this RCT. Some of them (n=6) refused to participate because of feeling overwhelmed with the upcoming surgery and/or experiencing multiple cancellations, and one refused as he did not expect postoperative pain. Three patients were unable to sign the consent form as they did not understand the study and two wanted to decide after the surgery.

Overall, 83 patients provided written consent and completed the preoperative socio-demographic data collection form. Postoperatively, baseline scores could be obtained for only 60 patients who were then randomized to one of the three groups. Main reasons for postoperative drop-out were not being able to self-report on a 0-10 NRS (n=8) due to sedation or postoperative delirium based on a positive Confusion Assessment Method for the ICU (CAM-ICU) (Ely et al., 2001), cancelled or postponed surgery (n=8), and being medically unstable (n=6). One patient withdrew his consent after surgery. Twenty patients were randomized to the hand massage, 19 to the hand holding and 21 to the rest group.

The results of this RCT are presented in two manuscripts (one accepted and one considered for publication in peer-reviewed journals) and a descriptive section with additional data not included in these manuscripts. The first manuscript presents the results of the immediate effects of the first and second hand massages on the pain intensity and unpleasantness, anxiety, muscle tension and vital signs of the cardiac surgery critically ill: *Effects of Massage in Reducing the Pain and Anxiety of the Cardiac Surgery Critically Ill- A Randomized Controlled Trial*. In

this manuscript, results regarding vital signs are briefly presented in text and the corresponding tables are included in Appendix F.

The second manuscript presents the results of the sustained effects of hand massage on pain intensity and pain-related interference of cardiac surgery patients, and descriptive results on the quality and quantity of sleep in the ICU: *Does Hand Massage Have Sustained Effects on Pain Intensity and Pain-Related Interference in the Cardiac Surgery Critically Ill? - A Randomized Controlled Trial.*

The subsequent section provides descriptive data on pain intensity and unpleasantness, anxiety, muscle tension and vital signs related to the third administration of hand massage and hand holding, as well as the third data collection set for the rest group. The results section concludes with the field notes and video recordings regarding the fidelity of hand massage administration in the critical care context.

Of note, we aimed to use the repeated measures between ANOVA factors to test for treatment (hand massage, hand holding, rest), time (before, immediately after, and 30 minutes later), and interaction effect for pain intensity, pain unpleasantness, anxiety, muscle tension, and means of vital signs. Unfortunately, not all patients provided their self-reports of pain intensity, pain unpleasantness and anxiety 30 minutes after each intervention, thereby decreasing the sample size and violating the assumptions for conducting the repeated measures between ANOVA factors test. Moreover, baseline scores in these symptoms were significantly different across groups, and to correct for this known confounder, ANCOVA was used to test post-intervention group differences with baseline scores as covariates. In the process of randomization, it is possible that groups differ in some prognostic factors (e.g., baseline scores) especially in trials with less than 200 participants. Similarly, given that no patient had a score of

2 on the 0-2 scale for muscle tension and that results were dichotomous (i.e., 0 or 1), the Pearson Chi-Square test was performed for evaluating differences across groups.

We also aimed to use the one-way ANOVA test to evaluate group differences in pain interference, however due to the non-normally distributed variables and imbalanced groups who provided data on pain interference on POD2, the non-parametric Kruskal-Wallis test was used.

Manuscript 3**TITLE PAGE**

Title: Effects of Massage in Reducing the Pain and Anxiety of the Cardiac Surgery Critically Ill-
A Randomized Controlled Trial

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Ill-a Randomized Controlled Trial. Pain Med. doi: 10.1093/pm/pny055

ABSTRACT

Objective: To evaluate the effectiveness of hand massage on the pain and anxiety of the cardiac surgery critically ill.

Design: A three-arm randomized controlled trial.

Setting: This study was conducted in a medical-surgical intensive care unit in Canada.

Subjects: Adult patients who underwent elective cardiac surgery, able to speak French/English and to self-report symptoms, without a high risk of postoperative complications were eligible.

Methods: Patients were randomly allocated to standard care plus either two 20-minute hand massages (experimental), two 20-minute hand holdings (active control) or two 20-minute rest periods (passive control). Pain intensity, pain unpleasantness, anxiety, muscle tension and vital signs were evaluated before, after, and 30 minutes later for each intervention.

Results: From the 83 patients recruited, 60 were randomized (20 massage, 19 hand holding, 21 rest). After controlling for baseline scores, the massage group reported significantly lower pain intensity, pain unpleasantness and anxiety for the 1st data collection set compared to both hand holding and rest (ANCOVA, $p < 0.02$) with an average decrease of 2 points on a 0-10 scale. No statistically significant differences were noted between hand holding and rest for any of the symptoms. Similar results were observed for the 2nd data collection set ($n=43$). Patients had decreased muscle tension post-massage. Vital signs did not differ significantly between groups.

Conclusion: Findings suggest that a 20-minute hand massage in addition to routine postoperative pain management can concomitantly reduce pain intensity, pain unpleasantness and anxiety by 2 points on average on a 0-10 scale.

Keywords: massage; pain; anxiety; critical care; cardiac surgery; randomized controlled trial

INTRODUCTION

Coronary-artery bypass grafting (CABG) and valve replacement (VR) are cardiac surgeries commonly performed across the globe (Benjamin et al., 2017). Patients undergoing cardiac surgery frequently experience symptoms such as pain (Gélinas, 2007b; Mueller et al., 2000; Puntillo, 1994; Watt-Watson et al., 2004; Yorke et al., 2004) and anxiety (Asilioglu & Celik, 2004; Vingerhoets, 1998; Young et al., 2005), which could interfere with postoperative recovery. With the International Association for the Study of Pain declaring 2017 as the global year against pain after surgery (IASP, 2017), relieving pain after cardiac surgery is an issue of major importance. Recent studies indicate that massage administered in the context of standard treatments can be beneficial in managing pain and anxiety in acute care units (Bauer et al., 2010; Braun et al., 2012; Cutshall et al., 2010), yet the evidence is inconclusive with regards to these positive effects early after surgery when pain intensity is high (Denault et al., 2014) and patients are admitted in the intensive care unit (ICU).

Specific to critical care, postoperative pain can be aggravated by painful procedures that are commonly performed in the ICU such as chest tube removal, turning/repositioning, breathing and coughing exercises (Gélinas, 2007b; Yorke et al., 2004). Owing to the unique context of the ICU and the recovery post cardiac surgery as well as the high intensity and complex nature of pain in this clinical setting, further research is needed to evaluate the effect of massage on the pain of cardiac surgery ICU patients.

Background

Every patient undergoing cardiac surgery is admitted to the ICU for 24-48 hours and then, transferred to acute care wards for support with recovery for an average total hospital stay of five days. While cardiac surgeries serve to reduce pain related to the cardiac condition, they

can provoke postoperative pain due to significant soft tissue and bone injury, and the visceral pain produced by mediastinal and pleural drains (Bigeleisen & Goehner, 2015). Over the past decade, cumulating evidence shows that ICU patients experience moderate to severe pain post cardiac surgery even though pain management protocols exist to maximize pain relief in this patient population (Gélinas, 2007b; Puntillo, 1994; Watt-Watson et al., 2004; Yorke et al., 2004).

Unrelieved postoperative pain is not benign and can have repercussions on patients' mobilisation, breathing exercises and cough, thereby making patients prone to complications including deep vein thrombosis, atelectasis and pneumonia (Desai, 1999; Puntillo, 1994; Yorke et al., 2004). Not only is the intensity of acute postoperative pain a potential barrier to uneventful recovery and ICU discharge, but it is also a strong predictor of both the presence and severity of persistent postoperative pain for up to two years post surgery (Choiniere et al., 2014; Katz & Seltzer, 2009; Kehlet et al., 2006). Persistent postoperative pain is a deleterious complication post cardiac surgery with negative impacts on activities of daily living and quality of life (Gjeilo et al., 2014).

Presently, opioids are the mainstay treatment for severe postoperative pain in the ICU (Azzam & Alam, 2013; Barr et al., 2013), yet pain continues to persist despite the regular use of these pharmacologic agents (Chanques et al., 2006; Denault et al., 2014). To maximize pain relief in the ICU, the clinical practice guidelines of the Society of Critical Care Medicine (SCCM) suggested the use of complementary non-pharmacological interventions, such as massage, given their potential to enhance the potential of analgesia and reduce the amount of opioids administered (Barr et al., 2013). Massage can take multiple forms and involves the manipulation of soft tissues of the body through various systematic and rhythmic movements of the hands (Dunn et al., 1995; Richards, Gibson, et al., 2000).

Several systematic reviews and meta-analyses were conducted to evaluate the potential of massage in treating pain, function- and health-related quality of life outcomes in the general (Crawford et al., 2016), cancer (Boyd et al., 2016a), and surgical pain populations (Boitor et al., 2017; Boyd et al., 2016b). Results revealed that massage was effective at reducing pain and anxiety in all three patient populations, including cardiac surgery, however, several research gaps need to be addressed before recommendations can be made with regards to its use including adherence to CONSORT guidelines, and use of equally credible and seemingly identical controls to massage. Moreover, more studies are needed to evaluate the effect of massage administered in the ICU and on other dimensions of pain such as pain unpleasantness (Boitor et al., 2017). One pilot RCT conducted by some members of this research team with 40 critically ill patients post-cardiac surgery (Boitor et al., 2015), showed that administering three 15-minute hand massages had the potential to bring pain relief compared to a single hand massage, which did not yield a significant decrease in pain intensity. In the context of the same study, the use of hand massage with ICU patients was observed to be feasible and perceived by patients to be an acceptable complementary method for pain relief (Martorella, Boitor, Michaud, & Gélinas, 2014).

Overall, there is still insufficient evidence on which to base massage decisions in the management of acute postoperative pain in the ICU. Future rigorous RCTs that are conducted in the ICU and with cardiac surgery adults in their immediate postoperative period are needed to determine the minimal effective dose to produce clinically significant reductions in pain intensity, the massaging techniques employed, and required training.

Aim

The main aim of this experimental study is to compare the effect of standard care plus two 20-minute hand massage interventions by a trained nurse within 24 hours post cardiac

surgery versus hand holding with occasional stroking (i.e., active control) in addition to standard care, and standard care with rest on the pain intensity of postoperative adult ICU patients.

METHODS

Trial design

This research study is designed as a randomized controlled trial with three parallel groups, and 1:1:1 allocation ratio. This study follows the most recent CONSORT guidelines for non-pharmacological treatments and randomized controlled trials (Boutron et al., 2008), and the SPIRIT statement for clinical trial protocols (Chan et al., 2013).

Trial registration

This study is registered with ClinicalTrials.gov (NCT02679534), and the protocol is published in JMIR (Boitor, Martorella, Laizner, Maheu, & G  linas, 2016).

Participants

This RCT included postoperative cardiac surgery adults admitted to the ICU in a university-affiliated hospital in Montreal, Canada. A single ICU was selected for this RCT in favor of standardized pain management practices and surgical techniques, and the single patient room design. Patients were eligible if they met the following criteria: a) ≥ 18 years of age, b) French or English speaking, c) underwent elective cardiac surgery (e.g., CAGB, VR), and d) could self-report. Patients who were more prone to develop postoperative complications and who could not have their hands massaged were not eligible (Boitor, Martorella, et al., 2016).

Sample size and sampling

The G*Power 3 program (Faul, Erdfelder, Lang, & Buchner, 2007) was used to estimate the required sample size to detect the potential effects of hand massage in decreasing pain intensity, the primary outcome. A total sample size of 79 patients was needed to detect a mean difference in pain intensity scores of 1.5 points (SD=2.0) (Boitor et al., 2015; Cepeda, Africano,

Polo, Alcala, & Carr, 2003) immediately after the massage with a two-sided significance level of .05, power of .80 with equal allocation to three arms, a repeated-measures between factors context, and a 10% drop out rate.

Randomization

Permuted-block randomization was generated by a data analyst using a computer software (e.g., SAS) and block sizes of three, an allocation ratio of 1:1:1, and one strata. Then, the randomization schedule was transcribed in opaque envelopes that were numbered sequentially and sealed by a research coordinator not involved in assigning patients to study groups.

Participant recruitment

Patients were recruited pre-operatively when specific eligibility criteria such as age and languages spoken were verified. Then, remaining eligibility criteria (e.g., blood loss, peripheral intravenous lines) were evaluated after patients were admitted to the ICU. After the collection of baseline data, cardiac surgery patients who met all eligibility criteria were assigned the next envelope in the sequence which indicated if they were randomly assigned to either: a) hand massage, b) hand holding or c) rest. Only the interventionist was aware of the group assignment as this was concealed from both participants, ICU clinicians and family members.

Interventions

One interventionist delivered all the hand massages and all except for one hand holding, which was given by a research coordinator. The interventions were standardized across participants. The interventionist was a registered nurse without prior experience in massage therapy. She attended an accredited six-hour workshop given by a professional massage therapist similar to the training offered in the pilot RCT (Boitor et al., 2015).

Although this trial aimed to repeat each intervention three times over the course of 24-hours post-surgery (Boitor, Martorella, et al., 2016), only the results related to the first two administrations will be reported here given that insufficient data was obtained for the third one to be able to run statistical analyses (hand massage, n=5; hand holding, n=5; rest, n=6). The first intervention (hand massage or hand holding) was administered either in the evening of the day of surgery (Postoperative Day, POD 0) or early evening the day after (POD 1), and the second one only the day after (POD 1) when patients were still in the ICU.

Passive control group

The passive control group received the standard ICU care plus a 20-minute rest period during which they were lying in the bed or chair and had no contact with the interventionist. The standard care included the pharmacological and non-pharmacological treatments (e.g., repositioning) performed in the ICU. In the study ICU, a pain management protocol based on regular administration and breakthrough doses of morphine as needed is prescribed to cardiac surgery patients.

Active control group

In addition to standard ICU care, the active control group had the lights dimmed, the door closed, a comfortable positioning ensured, and received hand holding with occasional stroking by the same interventionist. The occasional stroking was added to ensure participant and clinician blinding, given that it was seemingly identical to massage, and to limit drop-out from this group. Patients had their hands held for 5-10 seconds followed by the application of unscented hypoallergenic cream for 30 seconds. Then, the interventionist held each of the patients' hand in her hand for ten minutes with occasional stroking, for a total of 20 minutes.

Experimental group

In addition to standard ICU care, the experimental group received 20-minute hand massage by the interventionist. Before administering the massage, a comfortable positioning of the patient was ensured, the lights dimmed and the door closed. The interventionist held each hand for 5-10 seconds, and applied 5-10 ml of unscented hypoallergenic cream. Massage was performed using moderate pressure, and stroking and kneading for ten minutes (i.e., 5 minutes on the palm and 5 minutes on the back of each hand) as done in the study by Kolcaba et al. (Kolcaba et al., 2006), and was adapted for this study by the massage therapist who offered the interventionist's training (Boitor, Martorella, et al., 2016).

Outcomes and Instrumentation

Pain intensity was the primary outcome and was assessed using the 0 to 10 numeric rating scale (NRS) score. A body map was used to identify the location of pain (Mueller et al., 2000) and an open-ended question was asked to describe the quality of pain. The secondary outcomes, pain unpleasantness and anxiety were assessed in relation to each data collection using the 0-10 NRS. Muscle tension was assessed using an ordinal 0-2 scale (i.e., 0 for no resistance, 1 for resistance and 2 for strong resistance) derived from the Critical-Care Pain Observation Tool, a behavioral pain scale validated for pain assessment in ICU patients post cardiac surgery (Boitor, Fiola, et al., 2016; G  linas, Fillion, Puntillo, Viens, & Fortier, 2006; Keane, 2013; Linde et al., 2013). Vital signs (i.e., blood pressure, heart and respiratory rates) were collected from ICU bedside monitors using means for 1-minute intervals.

The NRS has been shown to have high test-retest reliability (Brunelli et al., 2010), concurrent (Ahlers et al., 2008) and discriminant validity (Brunelli et al., 2010) for the assessment of pain intensity in adults, as well as good convergent and discriminant validation for

the assessment of pain unpleasantness in children and adolescents post-surgery (Page et al., 2012). Although the use of the NRS for the assessment of anxiety was not validated per se, it is part of the Edmonton Symptom Assessment System whose reliability and validity were supported over the years (Nekolaichuk, Watanabe, & Beaumont, 2008). The CPOT from which the muscle tension sub-scale was extracted, has been shown to have moderate to high interrater reliability (Boitor, Fiola, et al., 2016; G  linas et al., 2006; Linde et al., 2013), discriminant (Boitor, Fiola, et al., 2016; G  linas et al., 2006; Keane, 2013; Linde et al., 2013), criterion (Boitor, Fiola, et al., 2016; G  linas et al., 2006) and convergent validation (Boitor, Fiola, et al., 2016) with ICU cardiac surgery patients.

Participants were also asked to complete the Brief Pain Inventory (Cleeland & Ryan, 1994; Larue, Colleau, Brasseur, & Cleeland, 1995) and the Rolland Morris Sleep Questionnaire (Richards, O'Sullivan, & Phillips, 2000) on POD 2 to assess pain interference with recovery activities on POD 1 and sleep in the ICU, and results will be reported elsewhere.

Data collection

Timeline for data collection procedures are presented in Table 1. Patients completed a self-administered data collection sheet that included the 0-10 NRS for the self-report of pain intensity, the 0-10 NRS for pain unpleasantness, the 0-10 NRS for anxiety, a body map to indicate the location of pain, and an open-ended question asking to describe the quality of pain. The interventionist explained the form and responded to questions as needed. The form was completed before, immediately after the intervention (hand massage or hand holding), and 30 minutes later, for a total of three data collection points per intervention. Muscle tension and vital signs were assessed at the same time points. The rest group completed the data collection sheet at similar times. On POD 2, when most patients were discharged from the ICU, they were asked

whether they received hand massage throughout their ICU stay to evaluate the blinding of those assigned to hand holding.

Data analysis

The SPSS software (version 22.0) was used for data analysis. This study uses intention-to-treat analysis by including every participant who has been randomized, regardless of group assignment, study withdrawal, or protocol deviations.

Descriptive statistics were calculated for socio-demographic and medical-surgical data. Group differentiation in socio-demographic and medical-surgical characteristics was investigated using chi-square tests of independence for nominal level variables, and Kruskal-Wallis for interval and ratio level non-normally distributed variables. Frequencies and percentages of the location and descriptors of pain (i.e., sensory dimension of pain) were calculated to describe the pain characteristics of participants.

ANCOVA was used to test post-intervention group differences in symptoms with baseline scores as covariates given their statistically significant difference across groups. Given that no patient had a score of 2 on the 0-2 scale for muscle tension and that results were dichotomous (i.e., 0 or 1), the Pearson Chi-Square test was performed for evaluating differences across groups, and the two-way mixed ANOVA was used to test for group, time and interaction effects for each vital sign (i.e., blood pressure, heart and respiratory rates).

Ethics

Ethical approval was granted by the Research Ethics Committee of the study setting in February 2016. This protocol received independent peer review by McGill University and the Quebec Nursing Intervention Research Network who funded the conduct of this study

(F242710). Informed and written consent was obtained from participants, and potential adverse effects recorded.

RESULTS

The modified CONSORT flow diagram for this trial is displayed in Figure 1. A total of 138 patients were screened, 95 were eligible and approached for participation in this study. Of these, 83 patients consented and completed the preoperative socio-demographic data collection form. Postoperatively, baseline scores could be obtained for only 60 patients who were, then randomized to one of the three groups. Main reasons for postoperative drop-out were not being able to self-report on a 0-10 NRS ($n=8$) due to sedation or postoperative delirium based on a positive Confusion Assessment Method for the ICU (CAM-ICU) (Ely et al., 2001), cancelled or postponed surgery ($n=8$), and being medically unstable ($n=6$). One patient withdrew his consent after surgery. The 23 patients who consented but who were not analysed had a median age of 70 years old (range: 41-82), 15 were males and 8 females. They were not significantly different across socio-demographic characteristics from patients who were randomized (Pearson Chi-Square, $p>0.09$).

The socio-demographic and medical-surgical characteristics of the final study sample ($n=60$) are presented in Table 2. The sample was composed mainly of male patients (76.7%), average age was 65 (range 24-84) years, 81.7% were White/Caucasian and 47.7% had college or university education. The most common areas where patients experienced pain were sternum, left ribs, epigastrium, left shoulder and left upper arm, neck frontal, back right ribs, and between shoulder blades. The most common pain descriptors reported by patients were pressure, pulling, stabbing and stretching. The only statistically significant difference in characteristics between groups was related to the race of participants ($\chi^2=14.19$, $p=0.007$). The massage group was

composed entirely of White/Caucasian patients, whereas the standard care group included most Asian (7/9) and all the Black/African American (2/2) patients of the total sample. Nonetheless, baseline pain and anxiety scores did not significantly vary between patients of different races (Kruskal Wallis Test, $p>0.112$).

Blinding

Of the 19 patients assigned to hand holding, 16 were available on POD 2 to meet the research staff and respond to the question regarding the administration of massage in the ICU. Thirteen (81.3%) reported receiving massage over their hands by the research nurse, and only 3 (18.7%) did not recall being offered massage, suggesting that participant blinding was effective for a high proportion of patients.

Pain intensity

Despite randomization and for the 1st data collection set, baseline pain intensity was significantly different across the three groups ($F_{(2)}=15.04$, $p<0.001$) and was included as a covariate (Table 3). After controlling for baseline scores (mean=4.65), pain intensity immediately after the intervention was significantly lower in the hand massage group (adjusted mean=2.52, SE=0.42) compared to both hand holding (adjusted mean=4.04, SE=0.43) and rest (adjusted mean=4.21, SE=0.41) (ANCOVA, $F_{(2)}=4.85$, $p=0.011$). There were no significant differences between hand holding and rest ($p=0.770$). Pain intensity scores 30 minutes post were collected for only 37 patients mainly because they wanted to be left to sleep or felt tired to complete the self-administered questionnaire again. For these patients and after controlling for baseline scores (mean=5.03), adjusted means were lowest for the hand massage group (3.95, SE=0.72) 30 minutes post compared to hand holding (4.54, SE=0.74) and rest (5.22, SE=0.74), but not statistically different ($F_{(2)}=0.745$, $p=0.482$).

Similar results were observed for the 2nd data collection set (POD 1) (Table 4). With a similar baseline pain intensity (mean=4.29), the adjusted mean for the hand massage group was even lower (1.80, SE=0.55), whereas those assigned to hand holding and rest had similar adjusted means 3.41 and 3.94, respectively (ANCOVA, $F_{(2)}=3.68$, $p=0.034$).

Pain unpleasantness

For the 1st data collection set, pain unpleasantness was also significantly lower in the hand massage group (adjusted mean=2.14, SE=0.64) versus hand holding (adjusted mean=4.10, SE=0.60) and rest (adjusted mean=4.87, SE=0.54) with a mean baseline pain unpleasantness score of 4.85 (ANCOVA, $F_{(2)}=5.31$, $p=0.009$). No significant differences were noted between the hand holding and rest groups.

With a smaller sample size ($n=38$) providing both pre- and post- pain unpleasantness scores at the 2nd data collection set, decrease in pain unpleasantness was not significantly different across groups (ANCOVA, $F_{(2)}=1.59$, $p=0.218$). With a baseline mean of 4.82, the hand massage group had an adjusted mean of 1.78 (SE=0.97) compared to hand holding (adjusted mean=3.71, SE=1.03) and rest (adjusted mean=4.17, SE=1.03).

Anxiety

After controlling for baseline anxiety (mean=3.07) and for the 1st data collection set, the hand massage group reported the greatest reduction in anxiety post-intervention (adjusted mean=0.96, SE=0.41) compared to hand holding (adjusted mean=2.70, SE=0.43) and rest (adjusted mean=2.13, SE=0.41) (ANCOVA, $F=4.58$, $p=0.015$). The hand holding and rest groups were not significantly different.

A tendency for significant differences was observed for the 2nd data collection set (ANCOVA, $F_{(2)}=2.64$, $p=0.084$). With an adjusted mean for baseline anxiety of 2.74, the

massage group reported the lowest scores post-intervention (adjusted mean=0.89, SE=0.54) followed by the rest (adjusted mean=1.90, SE=0.55) and hand holding groups (adjusted mean=2.65, SE=0.54).

Muscle Tension

For the 1st data collection set, muscle tension was not significantly different between groups at baseline (Chi-Square=0.97, $p=0.615$), but a trend for statistical significance has been observed only after the intervention (Chi-Square =5.89, $p=0.053$) (Table 5). A greater proportion of patients from the hand massage group experienced relaxed muscles after the intervention (20/20) compared to hand holding (18/19) and rest (15/19). Muscle tension was similar across groups at all time points for the 2nd data collection set.

Vital Signs

There were no significant differences between groups in terms of blood pressure, heart and respiratory rates at any time point across the two data collection sets. Only, heart and respiratory rates decreased by 2 beats/ breaths per minute on average with the administration of hand massage and hand holding.

Adverse events

No adverse events were documented with the administration of hand massage and hand holding. Overall, patients highlighted the relaxant effect of hand massage and how important that was in the ICU.

DISCUSSION

Despite the recent advances in surgical techniques and postoperative pain management, pain remains one of the most common symptoms cardiac surgery patients experience during their ICU stay. Poorly controlled acute postoperative pain can be deleterious to cardiac surgery

patients during their early recovery, but also over the long term with a heightened risk for developing persistent postoperative pain. The results of this RCT suggest that 20-minute moderate pressure massages over the hands in addition to standard ICU care can concomitantly reduce pain intensity, pain unpleasantness and anxiety by 2 points on average on a 0-10 numeric rating scale in the adult cardiac surgery critically ill patients. Conversely, the use of touch and occasional stroking of the hands (i.e., hand holding) is not sufficient to significantly reduce pain or anxiety in this patient group.

Over the past decade, several RCTs and a meta-analysis supported the potential of massage to complement pharmacological treatments and reduce symptoms such as pain and anxiety in the postoperative period (Bauer et al., 2010; Boyd et al., 2016b; Braun et al., 2012; Cutshall et al., 2010), yet little was known with regards to its effect on the pain of cardiac surgery critically ill. The pilot RCT conducted with ICU patients post cardiac surgery showed encouraging pain relief effects, yet no significant effects were observed with the administration of a single 15-minute hand massage (Boitor et al., 2015). The present RCT showed not only statistically, but also clinically significant reductions in pain intensity with both one and two 20-minute hand massages given a reported decrease of 2 points on average on a 0-10 numeric rating scale compared to the pain intensity reductions observed with hand holding and rest (Cepeda et al., 2003). Similar results were also observed with cardiac surgery patients receiving 20-minute massages mainly over their backs and as per their preference after discharge from the ICU (Bauer et al., 2010; Braun et al., 2012; Cutshall et al., 2010), suggesting that the duration of massage should be at least 20-minutes to produce significant decreases in pain intensity.

The present RCT was conducted in a single-bed ICU room, which allowed the interventionist to control for the light intensity and noise level, and create a calm and relaxing

environment for the delivery of hand massage without interruptions. This was contrary to the pilot RCT where patients were admitted to an open-bay ICU, thereby subjecting the administration of hand massage to interferences from both the physical and social environments such as high environmental noise and clinician-led conversations at the bedside (Martorella et al., 2014). Creating favorable conditions for the administration of massage such as a calm environment and negotiating with the health care staff an uninterrupted 20-minute period seem to be an essential component in maximizing the effect of massage on the symptoms of cardiac surgery patients, especially in the fast-paced ICU environment.

Massage applied with moderate pressure over both hands and using the techniques described in the study protocol (Boitor, Martorella, et al., 2016) was shown to concomitantly reduce pain intensity, pain unpleasantness and anxiety without any related adverse effects. In the critical care context, where opioid-sparing and analgesia-enhancing treatments are needed to maximize pain relief and decrease opioid-related side effects (Barr et al., 2013), massage appears to be an efficacious and safe complementary non-pharmacological approach in addition to standard care that can address the multidimensionality of pain. Given that its effects expand beyond pain to relieve other symptoms such as anxiety, future research should equally explore its effect on other important aspects of ICU patients' experience including sleep (Hu et al., 2015).

Patients had a decrease in muscle tension and expressed a profound relaxing effect with the administration of massage in addition to the significant decrease in anxiety compared to both hand holding and rest. These results are of great importance in the ICU context where anxiety and agitation occur frequently, and are associated with adverse clinical outcomes including removal of medical devices (Barr et al., 2013; Fraser, Prato, Riker, Berthiaume, & Wilkins, 2000; Tate, Dabbs, Hoffman, Milbrandt, & Happ, 2012). The SCCM guidelines recommend that

efforts to reduce anxiety and agitation, including maintenance of patient comfort and creation of a favorable environment to maintain normal sleep patterns, should be attempted before administering sedatives (Barr et al., 2013). The significant decrease in pain intensity and anxiety related to hand massage calls for the need to further explore its effect on agitation in the ICU. A systematic review and meta-analysis examining the effectiveness of several nonpharmacological interventions for agitation in older adults with dementia concluded that only sensory interventions such as hand massage were efficacious in reducing agitation (Kong, Evans, & Guevara, 2009). A more recent review reported promising results with regards to the efficacy of massage for reducing agitation in patients with dementia, but noted the need for larger rigorously conducted trials (Abraha et al., 2017). To our knowledge, no trial has been conducted to date evaluating the effect of hand massage on agitation in the ICU and could be explored to inform current clinical practice guidelines with regards to the use of this nonpharmacological intervention.

Vital signs were similar across groups for all time points, suggesting that neither massage nor hand holding influence their fluctuations in the early postoperative context when prophylactic cardiac medications are administered. These results concur with the recent studies conducted with cardiac surgery ICU patients, where vital signs did not differ significantly between massage and control groups (Boitor et al., 2015; Lindgren et al., 2013).

Unfortunately, a significant drop-out occurred after patients had their surgery, and not all received at least two sessions of their allocated intervention, partly due to the challenges to obtain their self-report on a 0-10 NRS. Whereas this corresponded to one of the exclusion criteria and thus, negatively affected the feasibility of conducting this study with the critically ill early postop, this does not translate into a limited feasibility of administering hand massage in the

ICU. Several patients were able to indicate being in pain through head shaking or squeezing the hand, and could have been offered to receive the hand massage. With an ongoing bedside presence, patients able to self-report the presence of pain and/or anxiety can be offered hand massage on repeated occasions throughout their ICU stay to maximize their relief of pain and anxiety. Future research is still needed to evaluate the potential benefits of massage in the vulnerable critically ill unable to self-report, and to establish appropriate assessment tools for symptoms that could benefit from this intervention.

Implications

This RCT supports the beneficial effects of hand massage on reducing pain and anxiety in ICU patients post cardiac surgery, and suggests that this safe non-pharmacological intervention can be used to complement pharmacological treatments to improve the management of symptoms. Despite the fast-paced ICU environment and intense monitoring early after cardiac surgery, this RCT showed that in collaboration with the health care staff and family members and in a single-room ICU, it was feasible to ensure a comfortable and quiet environment without interruption for 20 minutes to administer massage over the hands. The positive effects of massage seem to span across multiple symptoms calling forth the need to explore its effectiveness on sleep promotion and management of agitation in the future. The results regarding the effect of hand massage on sleep promotion will be presented elsewhere.

The administration of hand massage using a standardized protocol and following training by a massage therapist were essential for the improvement in pain and anxiety, contrary to the use of touch and occasional stroking, which did not produce significant beneficial effects. Given the expenditure associated with a required training and availability of trained staff, future cost benefit analyses are needed on the use of massage in hospital and other clinical settings.

Limitations

Despite randomization, the hand massage group reported the highest baseline scores for pain and anxiety, and were used as covariates in statistical analyses to control for baseline group differences. Similarly, patients of Asian and Black/African American background were not proportionally distributed across the three groups. The rest group and those responsible for their care could easily recognize the group assignment, although this may have not changed patients' self-reports of symptoms. Only the cardiac surgery ICU patients able to self-report on a 0-10 NRS were included in this study, thereby limiting the generalizability of the findings to other ICU patients including those unable to self-report. The effects of massage on the pain intensity of non-verbal critically ill could be further explored by using alternative pain assessment tools such as the CPOT that have been validated for this specific patient population. Health literacy could also be a factor contributing to being able to participate in the study given that 8.3 % and 41.7 % of participants had primary school and high school education, respectively. This may have contributed to difficulty using a 0-10 NRS. Muscle tension was assessed by the interventionist who was not blinded to group assignment, thereby allowing for potential risk of bias.

Conclusion

This study is one of the first three-arm randomized controlled trials employing a rigorous process, as directed by the CONSORT guidelines, examining the effect of hand massage on the pain and anxiety of cardiac surgery critically ill. Findings suggest that hand massage can concomitantly reduce pain intensity, pain unpleasantness and anxiety by 2 points on average on a 0-10 NRS, and could complement pharmacological treatments for the relief of symptoms in the intensive care unit post cardiac surgery. The administration of at least 20-minute moderate pressure massage sessions over the hands in a calm and uninterrupted environment, using the

techniques described in the protocol (Boitor, Martorella, et al., 2016), appear to be necessary to observe clinically significant reductions in pain intensity, and should be considered in the potential implementation of this intervention in the ICU. Future cost benefit analyses are needed to evaluate the expenditure related to training staff and their availability to deliver this intervention in the critical care context.

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Conflicts of interest

No conflict of interest has been declared by the authors.

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Figure 1. CONSORT Flow Diagram

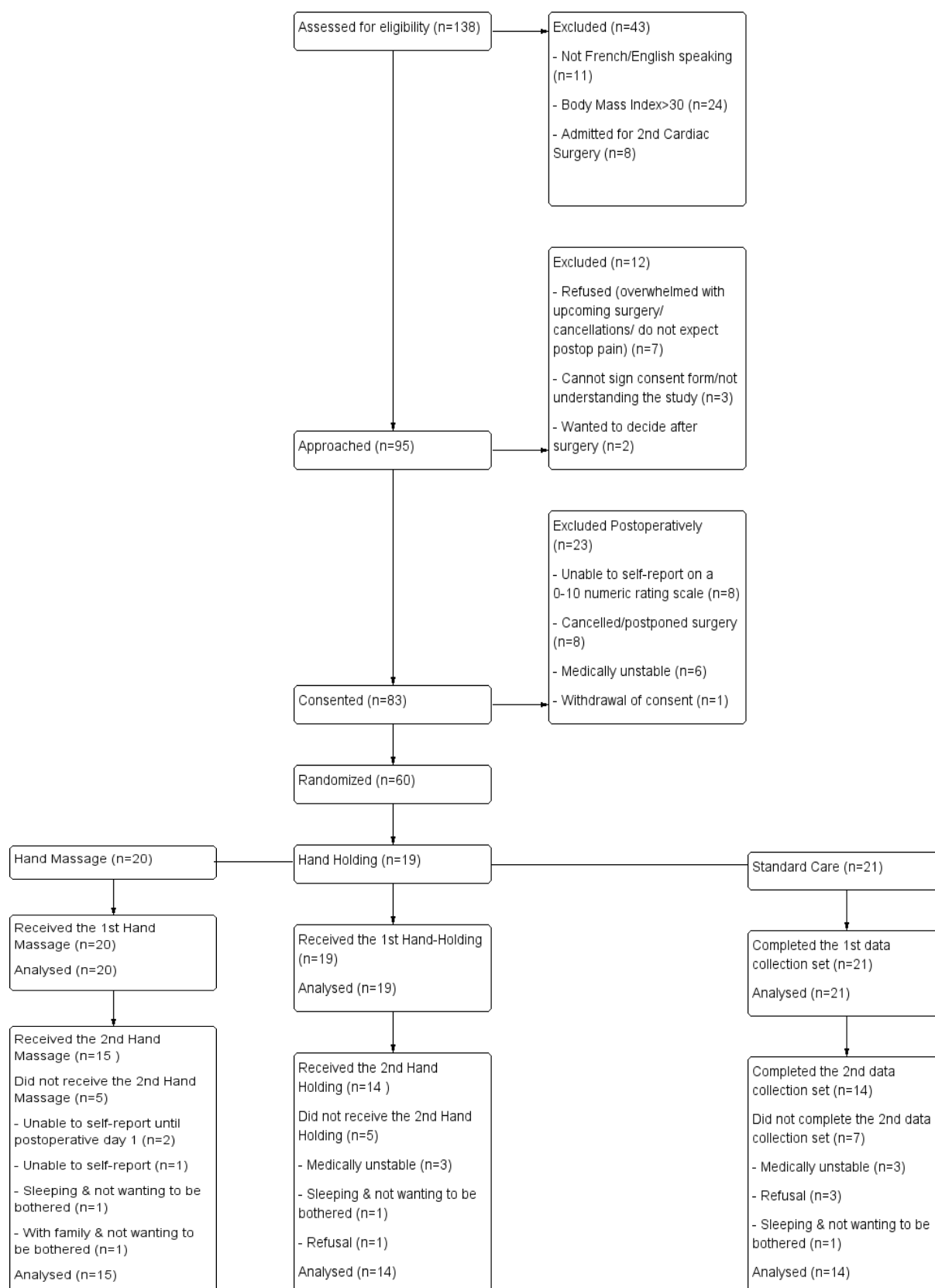


Table 1. Data Collection

| Data/Outcomes | Socio-demographic questionnaire (Pre-op) | Data collection set 1 (POD 0/POD 1) | | | Data collection set 2 (POD 1) | | | Data collection set 3* (POD 1) | | | POD 2 |
|---|--|-------------------------------------|-------|---------------------|-------------------------------|-------|---------------------|--------------------------------|-------|---------------------|-------|
| | | Pre ¹ - | Post- | 30 mins later | Pre- | Post- | 30 mins later | Pre- | Post- | 30 mins later | |
| Gender, age, race, education, chronic pain, prior use of massage and/or alternative therapies | X | | | | | | | | | | |
| Pain intensity | | | X | | | X | | | X | | |
| Pain unpleasantness | | | X | | | X | | | X | | |
| Anxiety | | | X | | | X | | | X | | |
| Muscle tension | | | X | | | X | | | X | | |
| Vital signs | | | X | | | X | | | X | | |
| Question regarding massage administration in the ICU | | | | | | | | | | | X |

*not included in this report due to insufficient data for statistical analyses.

¹ randomization was done after baseline data collection.

POD: Post-Operative Day

Table 2. Socio-demographic and Medical-Surgical Characteristics for each Group (N=60)

| | Massage | Hand-Holding | Rest | Overall | Statistical comparison between groups |
|--------------------------|------------|--------------|-----------|-----------|---------------------------------------|
| | n (%) | n (%) | n (%) | n (%) | |
| Gender | | | | | |
| Male | 14 (70.0) | 16 (84.2) | 16 (76.2) | 46 (76.7) | $\chi^2=1.10$, p=0.576 |
| Female | 6 (30.0) | 3 (15.8) | 5 (23.8) | 14 (23.3) | |
| Age (years) | | | | | Kruskal Wallis=1.04, p=0.593 |
| Median | 64 | 68 | 63 | 65 | |
| Range | 36-78 | 24-79 | 44-84 | 24-84 | |
| 18-29 | - | 1 | - | 1 | |
| 30-55 | 2 | 1 | 7 | 10 | |
| 56-64 | 9 | 5 | 4 | 18 | |
| 65-79 | 9 | 12 | 8 | 29 | |
| 80+ | - | - | 2 | 2 | |
| Race | | | | | |
| White/Caucasian | 20 (100.0) | 17 (89.5) | 12 (57.2) | 49 (81.7) | $\chi^2=14.19$, p=0.007 |
| Asian | 0 (0.0) | 2 (10.5) | 7 (33.3) | 9 (15.0) | |
| Black/African American | 0 (0.0) | 0 (0.0) | 2 (9.5) | 2 (3.3) | |
| First Language | | | | | |
| French | 11 (55.0) | 11 (57.9) | 7 (33.3) | 29 (48.3) | $\chi^2=7.74$, p=0.654 |
| English | 6 (30.0) | 5 (26.3) | 9 (42.9) | 20 (33.3) | |
| Bilingual | 2 (10.0) | 1 (5.3) | 1 (4.8) | 4 (6.7) | |
| Other | 1 (5.0) | 2 (10.5) | 4 (19.0) | 7 (11.7) | |
| Education | | | | | |
| Primary | 0 (0.0) | 3 (15.8) | 2 (9.5) | 5 (8.3) | $\chi^2=4.21$, p=0.648 |
| Secondary | 9 (45.0) | 9 (47.4) | 7 (33.3) | 25 (41.7) | |
| College | 3 (15.0) | 2 (10.5) | 4 (19.1) | 9 (15.0) | |
| University | 7 (35.0) | 5 (26.3) | 7 (33.3) | 19 (31.7) | |
| NR | 1 (5.0) | - | 1 (4.8) | 2 (3.3) | |
| Non-anginal chronic pain | | | | | |

| | | | | | |
|---|-----------|-----------|------------|--------------|------------------------|
| No | 12 (60.0) | 12 (63.2) | 14 (66.7) | 38 (63.3) | $\chi^2=0.19, p=0.906$ |
| Yes | 8 (40.0) | 7 (36.8) | 7 (33.3) | 22 (36.7) | |
| Use of Treatments | 5 | 4 | 5 | 14/22 (63.6) | |
| Prior use of massage therapy | | | | | |
| Yes | 9 (45.0) | 6 (31.6) | 8 (38.1) | 23 (38.3) | $\chi^2=0.74, p=0.690$ |
| No | 11 (55.0) | 13 (68.4) | 13 (61.9) | 37 (61.7) | |
| Prior use of other alternative therapies than massage | | | | | |
| Yes ¹ | 3 (15.0) | 1 (5.3) | 0 (0.0) | 4 (6.7) | $\chi^2=3.79, p=0.150$ |
| No | 17 (85.0) | 18 (94.7) | 21 (100.0) | 56 (93.3) | |
| Surgery | | | | | |
| CABG | 16 (80.0) | 16 (84.2) | 14 (66.7) | 46 (76.7) | $\chi^2=6.61, p=0.358$ |
| VR | 4 (20.0) | 2 (10.5) | 6 (28.6) | 12 (20.0) | |
| CABG & VR | 0 (0.0) | 1 (5.3) | 1 (4.8) | 2 (3.3) | |
| Surgical technique | | | | | |
| Via sternotomy | 18 (90.0) | 16 (84.2) | 14 (66.7) | 48 (80.0) | $\chi^2=3.79, p=0.150$ |
| Robotic | 2 (10.0) | 3 (15.8) | 7 (33.3) | 12 (20.0) | |
| Opioid use POD0 ² (mg Morphine) | | | | | |
| Median | 12.25 | 15.0 | 10.0 | 12.5 | $\chi^2=4.67, p=0.097$ |
| Range | 4.5-20.0 | 0-30.0 | 3.0-23.0 | 0-30.0 | |
| Opioid use POD1 (mg Morphine) | | | | | |
| Median | 23.25 | 25.0 | 24.0 | 24.0 | $\chi^2=0.75, p=0.686$ |
| Range | 0-32.5 | 10.0-40.5 | 4.0-40.0 | 0-40.5 | |

CABG: Coronary Artery Bypass Graft; NR: not reported; POD: Postoperative Day; SD: Standard Deviation; VR: Valve Replacement;

¹Responses included music therapy, chiropractic and light therapy.

²Length of stay was variable depending on the time they were admitted in the ICU from the operating room.

Table 3. Means (SDs) and medians (min-max) of symptoms before, immediately after and 30 minutes later for the 1st data collection set (POD 0/1)

| | Hand Massage | Hand Holding | Rest | Level of significance (p) |
|--|--------------------------------------|------------------------------------|------------------------------------|---------------------------|
| Pain Intensity | | | | |
| Before Mean(SD) Md (min-max) | N=20 5.38 (2.76) 5.25 (0-10) | N=19 3.92 (2.65) 4.00 (0-8) | N=21 4.62 (2.43) 5.00 (0-9) | P<0.001 |
| After Mean(SD) Md (min-max) | N=20 2.98 (2.17) 2.00 (0-7.5) | N=19 3.58 (2.67) 4.00 (0-8) | N=21 4.19 (2.54) 4.50 (0-10) | *P=0.011 |
| 30 mins post Mean(SD) Md (min-max) | N= 13 4.46 (3.04) 4.00 (0-7.5) | N=12 4.29 (2.94) 4.50 (0-10) | N=12 4.92 (3.09) 4.50 (0-10) | P=0.872 |
| Pain Unpleasantness | | | | |
| Before Mean(SD) Md (min-max) | N=14 6.04 (3.48) 7.00 (0-10) | N=13 4.15 (3.11) 3.00 (0-10) | N=18 4.58 (2.77) 4.50 (0-10) | P<0.001 |
| After Mean(SD) Md (min-max) | N=13 3.15 (2.61) 3.00 (0-9) | N=13 3.38 (3.34) 3.00 (0-8) | N=16 4.56 (2.98) 4.00 (0-10) | *P=0.009 |
| 30 mins post Mean(SD) Md (min-max) | N=8 3.69 (3.37) 2.50 (0-9.5) | N=8 4.69 (3.22) 4.25 (0-10) | N=10 4.25 (3.21) 3.50 (0-10) | P=0.750 |
| Anxiety | | | | |
| Before Mean(SD) Md (min-max) | N=20 3.05 (2.65) 3.00 (0-10) | N=19 4.03 (3.89) 4.00 (0-10) | N=21 2.82 (3.11) 2.00 (0-10) | P<0.001 |
| After Mean(SD) Md (min-max) | N=20 .95 (1.67) .00 (0-6) | N=18 3.17 (3.67) .50 (0-9) | N=20 1.73 (2.45) .50 (0-8) | *P=0.015 |
| 30 mins post Mean(SD) Md (min-max) | N=13 1.54 (2.11) .00 (0-6) | N=10 2.80 (3.61) .50 (0-9) | N=11 1.41 (1.86) .00 (0-5) | P=0.758 |

Md=Median; POD=PostOperative Day; *ANCOVA (adjusted for baseline scores)

Table 4. Means (SDs) and medians (min-max) of symptoms before, immediately after and 30 minutes later for the 2nd data collection set (POD 1)

| | Hand Massage | Hand Holding | Rest | Level of significance (p) |
|--|------------------------------------|-----------------------------------|-------------------------------------|---------------------------|
| Pain Intensity | | | | |
| Before Mean(SD) Md (min-max) | N=15 5.63 (2.33) 5.00 (2-10) | N=15 4.07 (2.22) 4.00 (1-8) | N=15 3.23 (2.37) 3.50 (0-8) | P<0.001 |
| After Mean(SD) Md (min-max) | N=15 2.67 (2.10) 2.00 (0-7) | N=14 3.18 (2.66) 3.00 (0-8) | N=14 3.25 (2.72) 3.00 (0-10) | *P=0.034 |
| 30 mins post Mean(SD) Md (min-max) | N=8 4.13 (2.31) 4.25 (0-7) | N=7 3.57 (2.21) 4.00 (0-6) | N=12 3.25 (2.42) 3.00 (0-9) | P=0.525 |
| Pain Unpleasantness | | | | |
| Before Mean(SD) Md (min-max) | N=15 5.97 (2.81) 5.00 (0-10) | N=14 4.54 (2.75) 4.50 (0-9) | N=12 4.17 (3.61) 3.50 (0-10) | P=0.001 |
| After Mean(SD) Md (min-max) | N=14 2.50 (5.20) 1.00 (0-20) | N=12 3.33 (3.14) 3.50 (0-8) | N=12 3.71 (3.62) 2.75 (0-10) | *P=0.218 |
| 30 mins post Mean(SD) Md (min-max) | N=8 4.38 (3.47) 3.25 (0-10) | N=7 3.74 (3.11) 4.50 (0-8) | N=11 3.46 (3.88) 1.00 (0-10) | P=0.695 |
| Anxiety | | | | |
| Before Mean(SD) Md (min-max) | N=15 3.70 (2.64) 4.50 (0-7) | N=15 2.90 (2.90) 2.00 (0-9) | N=15 1.73 (2.00) 1.00 (0-5.5) | P<0.001 |
| After Mean(SD) Md (min-max) | N=15 1.43 (2.11) .00 (0-7) | N=14 2.57 (3.16) 1.00 (0-9) | N=14 1.39 (1.96) .50 (0-5) | *p=0.084 |
| 30 mins post Mean(SD) Md (min-max) | N=8 2.50 (2.93) 1.50 (0-8) | N=7 1.43 (1.51) 1.00 (0-3) | N=12 1.46 (2.13) .00 (0-5) | P=0.663 |

Md=Median; POD=PostOperative Day; *ANCOVA (adjusted for baseline scores)

Table 5. Frequency of presence/absence of muscle tension before, immediately after and 30 minutes later for the 1st (POD 0/1) and 2nd data collection sets (POD 1)

| | Hand Massage | Hand Holding | Rest | Level of significance (p)* |
|---|--------------|--------------|------|----------------------------|
| 1st data collection set | | | | |
| Before | N=20 | N=19 | N=19 | P=0.615 |
| Absent (0) | 13 | 14 | 15 | |
| Present (1) | 7 | 5 | 4 | |
| After | N=20 | N=19 | N=19 | P=0.053 |
| Absent (0) | 20 | 18 | 15 | |
| Present (1) | 0 | 1 | 4 | |
| 30 mins post | N= 13 | N=11 | N=10 | P=0.222 |
| Absent (0) | 10 | 10 | 10 | |
| Present (1) | 3 | 1 | 0 | |
| 2nd data collection set | | | | |
| Before | N=15 | N=15 | N=14 | P=0.451 |
| Absent (0) | 10 | 12 | 12 | |
| Present (1) | 5 | 3 | 2 | |
| After | N=15 | N=14 | N=13 | P=0.108 |
| Absent (0) | 15 | 13 | 10 | |
| Present (1) | 0 | 1 | 3 | |
| 30 mins post | N=8 | N=7 | N=12 | P=0.531 |
| Absent (0) | 7 | 7 | 10 | |
| Present (1) | 1 | 0 | 2 | |

POD=PostOperative Day; Absent=0 on the 0-2 ordinal muscle tension scale; Present=1 on the 0-2 ordinal muscle tension scale; * Pearson Chi-Square

Manuscript 4**TITLE PAGE**

Title: Does hand massage have sustained effects on pain intensity and pain-related interference in the cardiac surgery critically ill? - A randomized controlled trial

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Reference: Boitor, M., Martorella, G., Maheu, C., Laizner, A. M. & Gélinas, C. (under review). Does hand massage have sustained effects on pain intensity and pain-related interference in the cardiac surgery critically ill? - A randomized controlled trial. Pain Management Nursing.

Abstract

Background

Despite the promising short-term pain relief effect of massage, little is known with regards to its sustained effects on pain intensity and pain-related interference with functioning.

Aim

To evaluate the sustained effect of hand massage on the pain intensity and pain-related interference with functioning of the cardiac surgery patients.

Design

A randomized controlled trial.

Setting

A medical-surgical intensive care unit in Canada.

Participants

Adult patients undergoing cardiac surgery and at low risk for postoperative complications were eligible.

Methods

In the intensive care unit, patients were randomly assigned to either 20-minute hand massage, hand holding or rest. Pain intensity and pain-related interference with functioning were assessed on the second postoperative day.

Results

A total of 60 patients were randomized and 46 completed data collection on the second postoperative day. Although no significant differences were observed across groups, the hand massage group reported a maximum pain intensity (median=5.75, range: 2-10) that was lower than the hand holding (median=6.50, range: 1-10) and rest groups (median=6.25, range: 0-10). The hand massage group was more likely to reach 0 pain intensity throughout a 24-hour period (median=0, range: 0-7) compared to the hand holding (median=2, range: 0-5) and rest groups (median=1.75, range: 0-4.5). A trend for statistical significance was noted for dichotomized ratings on pain interference with sleep ($p=0.050$).

Conclusion

Hand massage could help patients experience longer periods of time without pain and lower levels of maximum pain intensity. When coupled with recovery activities, hand massage could reduce pain-related interference with functioning.

Keywords: massage, pain, interference, sleep, critical care, cardiac surgery

BACKGROUND

Cardiac surgery is one of the most frequently performed surgical procedures worldwide that requires the routine admission to the intensive care unit (ICU). Acute postoperative pain is a common consequence of undergoing cardiac surgery (Choiniere et al., 2014; Denault et al., 2014; Gélinas, 2007b; Watt-Watson et al., 2004), and when poorly relieved, can interfere with functioning, sleep and recovery. Many pre-, intra-, and postoperative interventions and management approaches have evolved for relieving postoperative pain, yet more than half of patients undergoing surgery reported that pain continues to be undermanaged (Gan, Habib, Miller, White, & Apfelbaum, 2014).

Both clinical practice guidelines from the Society of Critical Care Medicine (SCCM) for the management of pain in the ICU (Barr et al., 2013) and guidelines on the management of postoperative pain from the American Pain Society (Chou et al., 2016) support the use of multimodal regimens including the use of a variety of analgesic medications combined with non-pharmacologic interventions. Despite the growing popularity and clinical use of non-pharmacological interventions in the management of acute pain, research gaps persist with regards to the strength of evidence for their effectiveness in decreasing pain (Gordon et al., 2016). Massage is one non-pharmacological intervention that has shown promise to reduce pain and anxiety in surgical pain populations including cardiac surgery (Boitor et al., 2017; Boyd et al., 2016b). Although these beneficial effects of massage are highly valued post cardiac surgery, it is equally important to evaluate if massage can have a positive impact on other clinically relevant outcomes in the ICU such as pain-related functional deficits and sleep.

Most randomized controlled trials focus on the immediate post-administration effect of massage on pain intensity, but fail to consider its sustained effect, and if the decreases in pain

intensity due to massage translate in less interference with functioning in the early recovery phase. The National Institute of Health Patient-Reported Outcomes Measurement Information System defines pain interference as a measure of the extent to which pain hinders engagement with physical, cognitive, emotional and recreational activities, sleep and enjoyment in life (Amtmann et al., 2010). Improvements in pain intensity and ability to engage in activities such as walking are predominant indicators used to evaluate the recovery progress in postoperative patients (Gornall et al., 2013; Myles, Weitkamp, Jones, Melick, & Hensen, 2000), and should be measured in an effort to restore the physical and psychosocial health of patients in pain.

Sleep is a basic human need that is frequently fragmented and disrupted in the ICU. Critically ill patients are susceptible to have very little deep or restorative sleep during the ICU stay (Frieze, 2008; Kamdar, Needham, & Collop, 2012), and to continue to experience sleep disturbances even 6 to 12 months after discharge (Franck, Tourtier, Libert, Grasser, & Auroy, 2011). Despite the fact that opioids can promote sleep by relieving pain, they are also known to cause disturbed sleep in the ICU because they interact with the natural sleep pathway (Saper, Scammell, & Lu, 2005), and may decrease deep sleep and increase nocturnal wake time (Dimsdale, Norman, De Jardin, & Wallace, 2007).

The SCCM also advocates for the use of non-pharmacological interventions for sleep promotion in the ICU (Barr et al., 2013) as a promising alternative to the pharmacological approach as they may contribute to disturbed sleep, drug tolerance, withdrawal and delirium (Pulak & Jensen, 2016). One randomized controlled trial (RCT) including critically ill men with cardiovascular illness compared a six-minute back massage versus relaxation intervention plus relaxing music (combined muscle relaxation, mental imagery, and audiotape) and versus usual care (Richards, 1998). Participants in the back-massage group (mean=319.82 minutes of sleep,

SD=48.45) slept more than one hour longer than those in the usual care group (mean=257.33 minutes of sleep, SD=108.22; p value not reported). In another RCT, cardiac surgery patients receiving massage after ICU discharge reported an increased sleep effectiveness compared to control (p=0.019) (Nerbass et al., 2010), thereby supporting the potential benefit of massage in this surgical patient population. To date, the effect of massage on sleep in the ICU is largely unexamined (Hu et al., 2015), and more research is awaited to verify its potential to improve the much needed quantity and quality of sleep in the critically ill post-cardiac surgery.

Aim

This research study aimed to compare the sustained effect of standard care plus three 20-minute hand massage interventions by a trained nurse within 24 hours post cardiac surgery versus hand holding plus standard care, and standard care with rest on the pain intensity and pain-related interference with functioning of the adult critically ill. A secondary objective was added while conducting the RCT, which aimed to describe patients' perceptions of sleep quality in the ICU on the second postoperative day.

METHODS

Design and trial registration

This experimental study used a randomized, controlled, single center trial design with three parallel groups. The study follows the modified CONSORT guidelines for RCTs of non-pharmacological treatments (Boutron et al., 2008). This RCT is registered with ClinicalTrials.gov (NCT02679534), and the protocol is published in JMIR (Boitor, Martorella, et al., 2016). Results of the immediate effects of massage on pain intensity, pain unpleasantness, anxiety, muscle tension and vital signs are published elsewhere (Manuscript 3).

Setting

This research study was conducted in a medical-surgical ICU in a university-affiliated hospital in Montreal, Canada. In an attempt to standardize the routine care, pain management practices and physical context of the ICU across all participants, a single setting was used. The study ICU uses a pain management protocol based on regular opioids and acetaminophen for cardiac surgery patients, and has only single-patient rooms allowing to control for environmental light and noise.

Participants

Patients were considered eligible for inclusion in this RCT if they were admitted in the ICU after undergoing their first elective cardiac surgery, 18 years and older, French or English speaking, able to self-report, at low risk for postoperative complications and without contraindications to having their hands massaged (Boitor, Martorella, et al., 2016).

Sample size and randomization

The power analysis for this RCT was based on pain intensity reduction of 1.5 points on a 0-10 scale (SD=2.0) with a two-sided significance level of .05, power of .80 and a 10% drop out rate, resulting in a required total sample size of 79 patients. A data analyst generated a permuted-block randomisation using the SAS software based on block sizes of three, one strata and 1:1:1 allocation ratio. The randomization schedule was transcribed in sequentially numbered opaque sealed envelopes by a research coordinator not involved in assignment allocation.

Procedures

Patients were first screened pre-operatively to verify the language spoken, if admitted for first cardiac surgery, and the risk factors for postoperative complications (e.g., ejection fraction<35%). Once admitted to the ICU post-surgery, patients were screened for ability to self-

report and eligibility for safe massage administration (e.g., peripheral intravenous lines, hypersensitivity to touch). Eligible patients were asked to self-report their pain intensity, pain unpleasantness and anxiety (Manuscript 3), and then, were assigned the next envelope in the sequence to allocate to either the hand massage, hand holding or standard care groups. Group assignment was concealed from participants, family members, and ICU clinicians.

Interventions

One interventionist delivered all hand massages and hand holdings except for one, which was given by a research coordinator. The interventions were standardized across participants. The interventionist was a registered nurse trained in massage therapy through an accredited workshop of six hours as done in the pilot RCT (Boitor et al., 2015). The training was provided by a professional therapist and consisted of practical exercises and verification of competency in administering hand massage as per protocol.

This RCT aimed to repeat each intervention (i.e., hand massage or hand holding) three times within 24 hours post-op and while patients were still in the ICU. The first intervention was administered in the evening of the day of surgery (Postoperative Day, POD 0) or early evening the day after (POD 1), and the second and third ones in the evening of POD 1.

Passive control group

The passive control group received the standard care provided in the ICU and a 20-minute rest period. There was no contact with the interventionist throughout the 20 minutes. Patients received the routine pain management protocol for ICU patients post cardiac surgery including the non-pharmacological interventions (e.g., repositioning) used to promote comfort.

Active control group

In addition to the standard ICU care, patients assigned to this group received 20-minute hand holding with occasional stroking. After the door was closed, the lights dimmed and the patient was comfortably positioned, the interventionist held their hands for 5-10 seconds, applied unscented hypoallergenic cream to both hands and held each of the patient's hand for ten minutes. Occasional stroking was added to ensure patient, family and clinician blinding given that it was seemingly identical to massage, and to limit drop-out from this group.

Experimental group

The experimental group received 20-minute hand massage by the interventionist in addition to the standard ICU care. The same environmental adjustments were done as for the active control group, the interventionist held each hand for 5-10 seconds, applied unscented hypoallergenic cream and massaged both hands using moderate pressure, stroking and kneading techniques for a total of 20 minutes. The massage protocol is inspired by the procedure by Kolcaba et al. (Kolcaba et al., 2006), and was developed with the support of the professional massage therapist who provided the training. The detailed massage protocol can be consulted in the published protocol of this RCT (Boitor, Martorella, et al., 2016).

Outcomes

This manuscript presents the results related to the sustained effects of massage on pain intensity and pain-related interference with functioning as well as descriptive data on sleep. An adapted version of the Brief Pain Inventory (BPI) was used to assess the sustained effects of massage on pain intensity on POD 2 as well as the interference of the pain on patient's functioning (Cleeland & Ryan, 1994; Larue et al., 1995). The four pain intensity items are rated individually on a 0-10 numeric rating scale (0 for "no pain" and 10 for "pain as bad as you can

imagine”) for pain at the time of interview (pain now) and the worst, least and average pain during the last 24 hours.

The pain interference items comprise seven 0-10 numeric rating scales with the anchors 0 for “no interference” and 10 for “interferes completely”. The seven items of pain interference included in the actual BPI evaluate the impact of pain on general activity, mood, walking/mobilisation, work, relationships, sleep and enjoyment of life. The version used in this study does not include the item “work” as it is not considered relevant in the early postoperative context, but comprises items that could generate moderate-severe pain interference in cardiac surgery patients such as coughing, deep breathing, appetite and concentration (Choiniere et al., 2014; Martorella, Cote, Racine, & Choiniere, 2012; Watt-Watson et al., 2004).

The original BPI has demonstrated internal consistency for this patient population with Cronbach’s alpha coefficients between 0.84-0.89 for the severity scale, and 0.91-0.94 for the interference scale. Scores on both scales declined significantly from baseline to the six months postop follow-up, thus testifying to the responsiveness of the BPI for detecting changes over time (Gjeilo, Stenseth, Wahba, Lydersen, & Klepstad, 2007).

The Richards-Campbell Sleep Questionnaire (RCSQ) was used to evaluate patients’ perception of their sleep quality while in the ICU. The questionnaire was developed as a five-item scale for patients to report on the sleep in the critical care environment (Richards, O’Sullivan, et al., 2000), more specifically on the depth, latency, awakenings, amount of time awake and overall quality of sleep. Each item is scored on a 0-100 mm visual analog scale, and the full questionnaire takes approximately two minutes to complete. Items of the RCSQ correlated with polysomnography on sleep onset, sleep depth, awakenings and total sleep time (Richards, O’Sullivan, et al., 2000). The RCSQ has been validated with ICU patients and was

shown to have good internal consistency, convergent validation with polysomnography (Richards, O'Sullivan, et al., 2000), and good inter-rater correlation between patients and nurses (Frisk & Nordstrom, 2003).

Data collection

Socio-demographic and medical-surgical data were collected using standardized data collection sheets. On POD 2, research assistants and the interventionist, met 22 and 24 participants, respectively, for a brief interview using the BPI. On the same occasion, a subgroup of patients was invited to mark an X along each of the five scales of the RCSQ.

The interventionist collected field notes that covered comments made by patients related to the intervention administered (i.e., hand massage, hand holding) and observations such as falling asleep during and/or after the intervention.

Data analysis

The data was entered in the SPSS software (version 22.0), which was used for statistical analysis. This study uses intention-to-treat analysis by including every participant who has been randomized.

Descriptive statistics were calculated for socio-demographic and medical-surgical data to describe the study sample. Group differentiation on these variables was investigated using chi-square tests of independence for nominal level variables, and Kruskal-Wallis for interval and ratio level non-normally distributed variables. The Kruskal-Wallis test was used to evaluate group differences in scoring of the BPI items. A dichotomized score was calculated for each BPI item of the pain intensity and pain interference scales where ratings below 4/10 (i.e., mild) (Barr et al., 2013) were assigned a score of 0 and ratings of moderate to severe (i.e., 4/10 and above)

were assigned a score of 1. Pearson Chi-Square test was used for the analysis of the dichotomized BPI items.

Descriptive statistics were calculated for each item of the RCSQ and the total score to provide preliminary data on the quality of sleep of cardiac surgery critically ill.

Ethics

The Research Ethics Committee of the study setting approved the conduct of this study in February 2016. Throughout the study, sleep resurfaced as an important aspect of the ICU experience of the cardiac surgery critically ill who fell asleep during and after the hand massage administration, and who reported that hand massage promoted sleep. Consequently, an amendment of the protocol was done in June 2016 to include the RCSQ. Informed and written consent was obtained from participants. This protocol has been independently peer reviewed by the McGill University and Quebec Nursing Intervention Research Network who funded the conduct of this study (F242710).

RESULTS

A total of 138 patients were screened, 95 met the eligibility criteria and 83 consented for participation in the study (see Figure 1 for the modified CONSORT flow diagram). Of these, only 60 were randomized as eight were not able to self-report on a 0-10 NRS, eight had cancelled/postponed surgery, six were medically unstable and one withdrew consent after surgery. Among those who consented to participate in this trial, there were no significant differences in socio-demographic characteristics between those randomized and those lost postoperatively (Pearson Chi-Square, $p>0.09$).

On POD 2, 46 patients (18 hand massage, 16 hand holding, 12 rest) were available and willing to complete the BPI. Main reasons for drop-out ($n = 14$) were being discharged home or

to another hospital (n=4), finding it challenging to report pain interference on a 0-10 scale (n=3), experiencing confusion (n=2), not available for interview (n=2), medically unstable (n=1), underwent 2nd surgical procedure on POD2 (n=1) and refusal (n=1). The 46 patients completing data collection on POD 2 had a mean age of 64 years and the majority were male (n=35, 76.1%) (Table 1). They were not significantly different across groups in terms of sociodemographic and medical characteristics except for the surgical technique employed for the cardiac surgery (Pearson Chi-Square=7.06, p=0.029). All 18 patients from the massage group who completed the BPI had surgery via sternotomy, whereas those undergoing robotic surgery were distributed across the hand holding (n=2) and rest groups (n=4).

The RCSQ was completed by only 25 patients (hand massage, n=10; hand holding, n=9; rest, n=6) given that it was added to the BPI questionnaire 3 months after the beginning of recruitment and data collection.

Sustained effects on pain

The pain intensity index of the BPI provided insight into the sustained effects of hand massage and hand holding on pain. Although no significant differences were observed across groups, the hand massage group reported a maximum pain intensity (median=5.75, range: 2-10) that was lower than what was reported by the hand holding (median=6.50, range: 1-10) and rest groups (median=6.25, range: 0-10) (Table 2). Those receiving hand massage were also more likely to reach 0 pain intensity over the course of 24 hours (median=0, range: 0-7) compared to those assigned to hand holding (median=2, range: 0-5) and rest (median=1.75, range: 0-4.5). The average pain over 24 hours was moderate and similar across the three groups (Kruskal-Wallis Test=0.03, p=0.984). When dichotomized, ratings on pain intensity BPI items were similar across groups (Pearson Chi-Square, p>0.10).

Pain-related interference

Regardless of group assignment, patients reported small to moderate interference of pain with early recovery activities (Table 2). Pain interfered most with coughing (medians between 2 and 5) and taking deep breaths (medians 3 and 5), and least with humour, appetite, relations with others, concentration and enjoyment with life (median=0). Overall, no statistically significant differences were observed in pain-related interference across groups (Kruskal Wallis Test, $p>0.224$).

A trend for statistical significance was noted for dichotomized ratings on pain interference with sleep (Pearson Chi-Square=5.98, $p=0.050$). A higher proportion of patients in the hand massage group ($n=12$, 71%) reported none or mild (i.e., <4) pain interference with walking compared to hand holding ($n=6$, 40%) and rest ($n=8$, 67%) (Pearson Chi-Square=3.47, $p=0.176$). Pain interfered little with sleep for most patients in the hand massage ($n=14$, 82%) and rest groups ($n=10$, 90%) compared to those receiving hand holding ($n=6$, 50%).

Sleep quality

Patients in the hand massage group reported that the massage was relaxing and conducive to falling asleep. All patients fell asleep during and continued to sleep after the hand massage administration, except for two occasions when they were sitting in chair.

Overall, patients in all groups reported predominantly light sleep (medians 68.75-91.88) and being awake roughly 50% of the night time (medians 47.50-71.88) (Table 3). The quality of sleep was also reported to be rather poor (medians 50-88.75). The rest group experienced the greatest challenges falling asleep (median=87.50).

DISCUSSION

This RCT is one of the first three-arm RCTs evaluating the sustained effect of hand massage administration in the ICU on the pain and pain-related interference with activities, and to provide preliminary results on the sleep quality of cardiac surgery patients. Preliminary results suggest that hand massage may help cardiac surgery patients to experience pain-free periods and to have a lower maximum pain intensity over 24 hours, but more research is needed to test this hypothesis. Trends for statistical significance were observed with regards to the interference of pain with sleep. This study also indicates that cardiac surgery patients in the ICU experience nocturnal sleep that is generally light, short and poor in quality.

Cardiac surgery patients continue to experience, on average, moderate pain intensity throughout the 1st and 2nd postoperative days regardless of their group assignment. Although massage has been shown to have significant short-term pain relief effects with the cardiac surgery (Boitor et al., 2017) and other surgical patient populations (Boyd et al., 2016b), its sustained effects have been rarely examined. There were no statistically significant differences in least and most intense pain intensity between groups, yet the calculated medians suggest that hand massage could help patients attain 0 pain levels and lower the maximum pain intensity reached. The lack of statistical significance could be due to the smaller sample size of patients who were available and able to complete the BPI on POD2, although other explanations are equally plausible. In a previous RCT with 40 cardiac surgery ICU patients, the administration of hand massage did not have sustained pain relief effects when compared to hand holding ($p=0.10$), and the average pain was moderate for both groups (Boitor et al., 2015). Future massage trials are needed to verify if the pain relief effects can be sustained over time.

One of the negative consequences of unrelieved postoperative pain is its potential to interfere with recovery activities including taking deep breaths, coughing, walking and sleep as observed in this RCT and other studies with postoperative patients (Leegaard, Rustoen, & Fagermoen, 2010; Miller, Roth, Roehrs, & Yaremchuk, 2015; Wu et al., 2005). The effects of hand massage did not appear to significantly benefit patients in terms of pain-related interference, but a higher proportion of patients in the hand massage group reported little or no interference with walking compared to those in the rest and hand holding groups. The administration of hand massage was not coupled with any of the recovery activities, which may explain the non-significant effect on pain-related interference. Hand massage could facilitate engaging in recovery activities such as walking, if they are initiated immediately after the delivery of hand massage given its clinically significant short-term reductions in pain and anxiety (Manuscript 3).

The descriptive self-reports of nocturnal sleep quality are preliminary data that concur with previous descriptive research studies on the poor quality of sleep in the ICU (Nicolas et al., 2008; Zhang et al., 2013), and highlight the need to improve this important aspect of the experience of cardiac surgery patients in the ICU. Although the data collected is insufficient to examine the effectiveness of hand massage in promoting sleep in the ICU, the field notes and anecdotal reports of patients seem to indicate that hand massage could potentially promote sleep during and after its administration. Hand massage has been shown to decrease pain intensity and unpleasantness, to lower anxiety and promote muscle relaxation in the ICU (Manuscript 3), all of which could promote comfort, and create a state of decreased arousal that is conducive to sleep. Indeed, critically ill patients identify pain to be a significant factor that contributes to worsened sleep (Nicolas et al., 2008; Zhang et al., 2013). Anxiety has also been shown to produce

significant sleep disturbance by taking longer to fall asleep and having a greater percentage of light sleep (Fuller, Waters, Binks, & Anderson, 1997; Gould, Beaudreau, O'Hara, & Edelstein, 2016). In fact, the relationship between sleep disturbance and affective symptoms such as anxiety and depression appears to be bi-directional. Poor sleep increases daytime anxiety, which then, triggers greater sleep difficulties the next night (Kalmbach, Arnedt, Swanson, Rapier, & Ciesla, 2017). Therefore, the assessment and treatment of anxiety has been called into being the focus of sleep research and be used as a means to address sleep problems (Spoormaker & van den Bout, 2005).

Depending on the time of administration, hand massage could promote sleep during day- or night-time. Given that RCSQ provides data on the patient's perception of nocturnal sleep, future RCTs aiming to test the effectiveness of massage on sleep quality in the ICU should also seek to use assessment tools that evaluate sleep throughout the day. In the ICU, approximately 50% of sleep occurs during daytime (Freedman, Kotzer, & Schwab, 1999; Tembo, Parker, & Higgins, 2013), which underscores the importance of equally promoting daytime sleep.

Limitations

This RCT should be interpreted in the context of some limitations. Not all patients who were randomized were available or able to participate in the BPI interview, thereby weakening the power of this study. The RCSQ was only added later throughout the data collection phase, which did not allow for sufficient data to be collected and to test the effectiveness of hand massage on sleep quality in the ICU. The BPI interview is based on patient's recall of interference in the preceding 24 hours and allows for the possibility of recall bias. The amount of analgesia administered on POD 2 was not documented and could have varied across groups.

Although patient self-report is recommended for sleep assessment in the ICU (Jacobi et al., 2002), critical care patients who are prone to experience circadian rhythm abnormalities and who receive sedative drug regimens may have a poor recall of their own sleep quality and quantity (Bourne, Minelli, Mills, & Kandler, 2007). The RCSQ allows patients to report on the depth, latency, awakenings, amount of time awake and overall quality of sleep, but is limited to critically ill able to complete the questionnaire and those without active cognitive dysfunction. Polysomnography could be used in future massage trials as it provides a more comprehensive evaluation of sleep including its duration, continuity and physiology, and was shown to be feasible for unattended use in the ICU (Knauert et al., 2014), however, it requires training for use and interpretation.

Implications for nursing education, practice and research

Nurses are vital agents in assisting patients with postoperative activities including recovery exercises such as taking deep breaths and walking. The present RCT does not present statistically significant effects of hand massage on pain-related interference with activities, but suggests that coupling hand massage with recovery activities could assist patients in performing them.

Descriptive data of this study suggest that sleep is inadequate for the cardiac surgery critically ill despite being admitted in single-patient rooms, which allow for noise and light reduction by having the doors closed and lights turned off, respectively. Hand massage could create conditions that are conducive to sleep, as observed in this RCT, and through its pain relieving, anxiolytic and muscle relaxant effects (Manuscript 3). Future research is still needed to test the effectiveness of this intervention on the diurnal and nocturnal sleep in the ICU.

CONCLUSION

In the context of a multimodal pain management approach, this RCT provides promising results on the preliminary sustained effectiveness of hand massage on pain intensity and pain-related interference with activities, as well as descriptive data on the quality of sleep in the ICU. In regard to pain intensity, patients could experience longer periods of time without pain and lower levels of maximum pain intensity, which would promote recovery. While the coupling of hand massage with recovery activities could maximize the benefits of massage in assisting patients to initiate them, future research is needed to unravel the sustained effects of this intervention on postoperative activities on the long term. Preliminary observations come in support of the potential of this intervention to promote sleep, yet future RCTs are currently awaited to test this hypothesis.

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Figure 1. Adapted CONSORT Flow Diagram

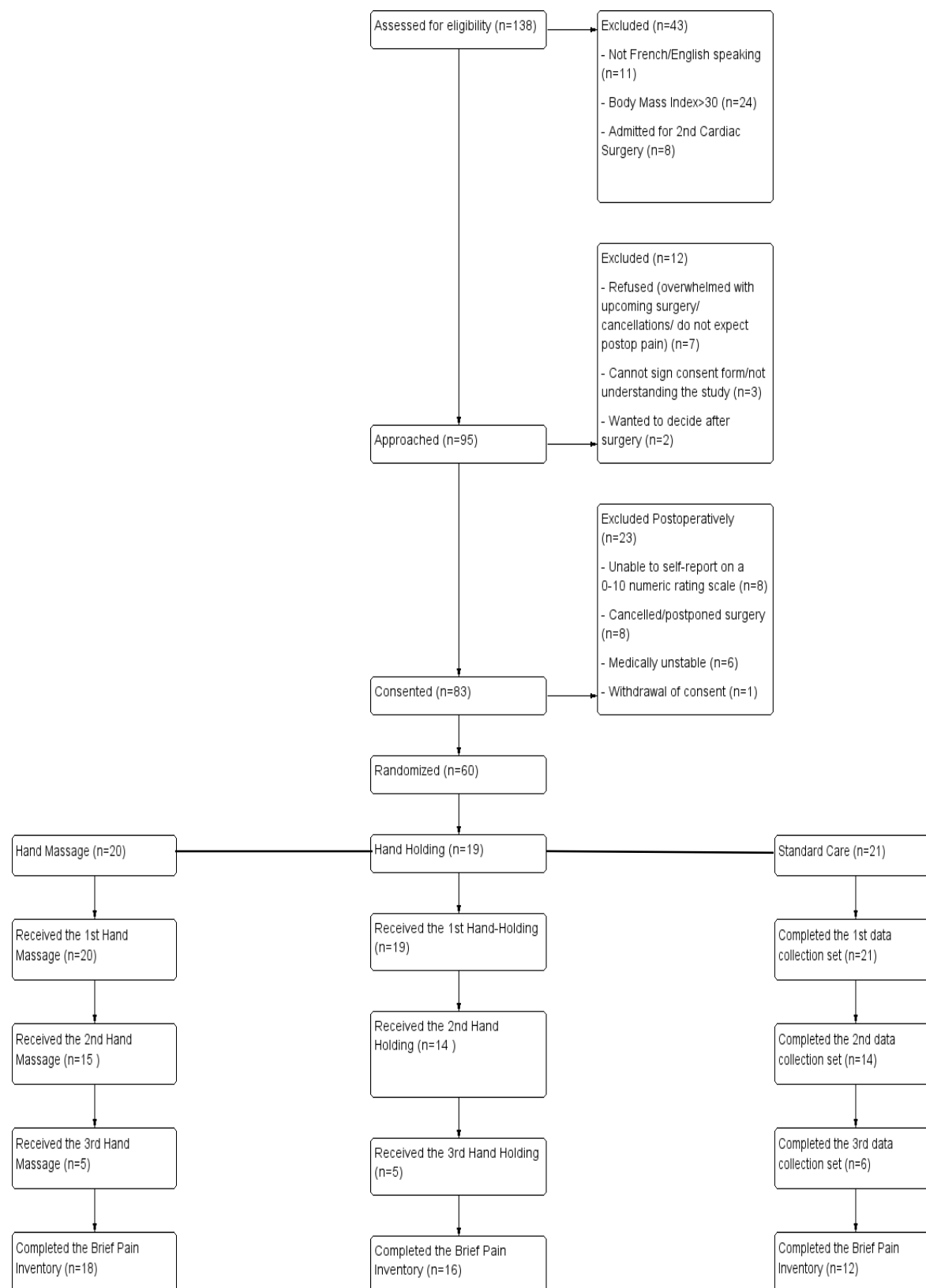


Table 1. Socio-demographic and Medical-Surgical Characteristics for each Group (N=46)

| | Massage | Hand-Holding | Standard Care | Overall | Statistical comparison between groups |
|----------------------------------|---------|--------------|---------------|---------|---------------------------------------|
| | N=18 | N=16 | N=12 | N=46 | |
| Gender (n) | | | | | |
| Male | 12 | 13 | 10 | 35 | $\chi^2=1.46, p=0.482$ |
| Female | 6 | 3 | 2 | 11 | |
| Age (years) | | | | | Kruskal Wallis=1.88, p=0.391 |
| Median | 64 | 68 | 62 | 65 | |
| Range | 36-78 | 51-79 | 44-84 | 36-84 | |
| Race (n) | | | | | |
| White/Caucasian | 18 | 14 | 8 | 40 | $\chi^2=7.95, p=0.093$ |
| Asian | 0 | 2 | 3 | 5 | |
| Black/African American | 0 | 0 | 1 | 1 | |
| First Language (n) | | | | | |
| French | 10 | 9 | 5 | 24 | $\chi^2=5.98, p=0.650$ |
| English | 6 | 4 | 6 | 16 | |
| Bilingual | 1 | 1 | 0 | 2 | |
| Other | 1 | 2 | 1 | 4 | |
| Education (n) | | | | | |
| Primary | 0 | 2 | 1 | 3 | $\chi^2=2.31, p=0.890$ |
| Secondary | 9 | 7 | 6 | 22 | |
| College | 2 | 2 | 1 | 5 | |
| University | 6 | 5 | 4 | 15 | |
| NR | 1 | - | - | 1 | |
| Non-anginal chronic pain (n) | | | | | |
| No | 10 | 11 | 9 | 30 | $\chi^2=1.34, p=0.513$ |
| Yes | 8 | 5 | 3 | 16 | |
| Use of Treatments | 5 | 4 | 2 | 11 | |
| Prior use of massage therapy (n) | | | | | |

| | | | | | |
|---|--------|---------|-------|--------|------------------------------|
| Yes | 8 | 6 | 4 | 18 | $\chi^2=0.40, p=0.818$ |
| No | 10 | 10 | 8 | 28 | |
| Prior use of other alternative therapies than massage (n) | | | | | |
| Yes ¹ | 3 | 1 | 0 | 4 | $\chi^2=2.70, p=0.259$ |
| No | 15 | 15 | 12 | 42 | |
| Surgery (n) | | | | | |
| CABG | 14 | 14 | 9 | 37 | $\chi^2=3.82, p=0.431$ |
| VR | 4 | 1 | 3 | 8 | |
| CABG & VR | 0 | 1 | 0 | 1 | |
| Surgical technique (n) | | | | | |
| Via sternotomy | 18 | 14 | 8 | 40 | $\chi^2=7.06, p=0.029$ |
| Robotic | 0 | 2 | 4 | 6 | |
| Opioid use POD0 ² (mg Morphine) | | | | | Kruskal Wallis=1.39, p=0.498 |
| Median | 13.75 | 16.75 | 12.25 | 15.00 | |
| Range | 4.5-20 | 0-30 | 5-23 | 0-30 | |
| Opioid use POD1 (mg Morphine) | | | | | Kruskal Wallis=0.78, p=0.677 |
| Median | 24.5 | 26.25 | 23 | 25.00 | |
| Range | 0-32.5 | 10-40.5 | 6-40 | 0-40.5 | |

CABG: Coronary Artery Bypass Graft; NR: not reported; POD: Postoperative Day; SD: Standard Deviation; VR: Valve Replacement;

¹Responses included music therapy, chiropractic and light therapy.

²Length of stay was variable depending on the time they were admitted in the ICU from the operating room.

Table 2. Medians (min-max) of scores obtained with the Brief Pain Inventory on the second postoperative day

| Brief Pain Inventory Item | Hand Massage (n=18) | Hand Holding (n=16) | Standard Care (n=12) | Level of significance (p) Kruskal-Wallis Test |
|---------------------------|---------------------|---------------------|----------------------|---|
| Most intense pain | 5.75 (2-10) | 6.50 (1-10) | 6.25 (0-10) | P=0.987 |
| Least intense pain | .00 (0-7) | 2.00 (0-5) | 1.75 (0-4.5) | P=0.435 |
| General pain | 4.00 (0-9) | 4.50 (1-7) | 4.00 (0-7) | P=0.984 |
| Pain now | 2.00 (0-9) | 3.00 (0-7) | 2.50 (0-5) | P=0.717 |
| General activity | 3.50 (0-9) | 4.00 (0-9) | .00 (0-9) | P=0.403 |
| Humour | .00 (0-9) | .00 (0-8) | .00 (0-10) | P=0.957 |
| Walk | 2.00 (0-8) | 5.00 (0-8) | 1.25 (0-10) | P=0.588 |
| Cough | 5.00 (0-10) | 2.00 (0-7) | 4.50 (0-9) | P=0.224 |
| Deep breaths | 3.00 (0-10) | 5.00 (0-7) | 3.00 (0-7) | P=0.388 |
| Relations with others | .00 (0-5) | .00 (0-9) | .00 (0-5) | P=0.628 |
| Sleep | .00 (0-9) | 2.50 (0-8) | .00 (0-8) | P=0.267 |
| Appetite | 1.00 (0-8) | .00 (0-8) | .00 (0-10) | P=0.857 |
| Concentration | .00 (0-7) | .00 (0-9) | .00 (0-10) | P=0.755 |
| Enjoyment with life | .00 (0-9) | .00 (0-10) | .00 (0-10) | P=0.583 |

Table 3. Medians (min-max) of scores obtained with the Richards Campbell Sleep Questionnaire on the second postoperative day

| Richards Campbell Sleep Questionnaire Item | Hand Massage (n=10) | Hand Holding (n=9) | Standard Care (n=6) |
|--|---------------------|--------------------|---------------------|
| Sleep depth | 90.00 (1.25-95.00) | 68.75 (3.75-90.00) | 91.88 (5.00-100.0) |
| Falling asleep | 43.13 (2.50-90.00) | 16.25 (0.00-85.00) | 87.50 (8.75-100.0) |
| Awake | 71.88 (15.00-92.50) | 47.50 (0.00-100.0) | 51.25 (18.75-100.0) |
| Falling back asleep | 60.00 (3.75-91.25) | 22.50 (2.50-100.0) | 43.75 (25.00-100.0) |
| Quality of sleep | 88.75 (2.50-97.50) | 50.00 (0.00-78.75) | 83.75 (0.00-98.75) |
| Total | 65.13 (12.75-88.50) | 50.00 (7.25-56.75) | 58.25 (47.00-86.00) |

Additional Descriptive Data

Results Related to the Third Hand Massage and Hand Holding Administration

In the context of this RCT, only a few patients received a third hand massage (n=5) or hand holding (n=5), and six patients assigned to the rest group completed the third data collection set. This increased loss of patients for the third intervention administration was mainly due to delays in the delivery of the first intervention followed by discharges from the ICU and deteriorating medical condition. This RCT aimed to deliver three 20-minute hand massages within 24 hours post-cardiac surgery, but given the delays in patients' ability to self-report their symptoms, achieving this objective was challenging for most cardiac surgery critically ill. Overall, at the time of the third data collection set, patients experienced low to moderate pain intensity, pain unpleasantness and anxiety (Table 1). Two patients (40%) with muscle tension prior to receiving hand massage had relaxed muscles post. Slight fluctuations in vital signs were observed during the third data collection set across groups (Table 2).

Table 1. Medians (min-max) of symptoms and muscle tension before, immediately after and 30 minutes later for the 3rd data collection set (POD 1)

| | Hand Massage | Hand Holding | Rest |
|---|--------------------|------------------|------------------|
| Pain Intensity | | | |
| Before Md (min-max) | N=6 3.5 (2-7) | N=5 3.0 (0-5) | N=8 3.0 (0-8) |
| After Md (min-max) | N=5 2.5 (2-5.5) | N=5 1 (0-2) | N=6 2.5 (0-4) |
| 30 mins post Md (min-max) | N=4 4.25 (2-10) | N=4 0 (0-2) | N=5 1 (0-4.5) |
| Pain Unpleasantness | | | |
| Before Md (min-max) | N=4 4.5 (4-7) | N=5 3 (0-8) | N=7 3 (0-8) |
| After Md (min-max) | N=4 3.5 (0-7) | N=5 1 (0-4) | N=6 0.5 (0-4) |
| 30 mins post Md (min-max) | N=4 6 (0-10) | N=4 1.5 (0-2) | N=5 - |
| Anxiety | | | |
| Before Md (min-max) | N=5 2 (0-10) | N=5 0 (0-2) | N=8 0 (0-8) |
| After Md (min-max) | N=5 1 (0-9) | N=5 0 (0-3) | N=6 0 (0-2.5) |
| 30 mins post Md (min-max) | N=4 5.25 (0-10) | N=4 0.5 (0-2) | N=5 0 (0-1) |
| Muscle Tension | | | |
| Before No resistance Resistance | N=3 N=2 | N=5 N=0 | N=5 N=1 |
| After No resistance Resistance | N=5 N=0 | N=5 N=0 | N=4 N=1 |
| 30 mins post No resistance Resistance | N=3 N=1 | N=3 N=0 | N=3 N=1 |

Md=Median; POD=Post Operative Day;

Table 2. Medians (min-max) of vital signs before, immediately after and 30 minutes later for the 3rd data collection set (POD 1)

| | Hand Massage | Hand Holding | Rest |
|---------------------------------|------------------------------|-------------------------------|-------------------------------|
| Systolic Blood Pressure | | | |
| Before Md (min-max) | N=3 112.00 (99.00-130.00) | N=4 123.50 (104.00-129.00) | N=7 132.00 (107.00-155.00) |
| After Md (min-max) | N=4 99.00 (84.00-132.00) | N=3 125.00 (119.00-129.00) | N=6 122.00 (107.00-135.00) |
| 30 mins post Md (min-max) | N=3 111.00 (92.00-123.00) | N=2 124.00 (120.00-128.00) | N=6 114.50 (101.00-163.00) |
| Diastolic Blood Pressure | | | |
| Before Md (min-max) | N=3 55.00 (53.00-65.00) | N=4 66.00 (61.00-80.00) | N=7 56.00 (48.00-78.00) |
| After Md (min-max) | N=4 61.00 (57.00-64.00) | N=3 68.00 (57.00-74.00) | N=6 55.00 (42.00-76.00) |
| 30 mins post Md (min-max) | N=3 63.00 (50.00-64.00) | N=2 63.50 (59.00-68.00) | N=6 58.50 (47.00-79.00) |
| Heart Rate | | | |
| Before Md (min-max) | N=5 92.00 (64.00-98.00) | N=4 77.50 (68.00-82.00) | N=7 78.00 (70.00-94.00) |
| After Md (min-max) | N=5 86.00 (59.00-95.00) | N=4 77.00 (66.00-85.00) | N=6 76.50 (69.00-91.00) |
| 30 mins post Md (min-max) | N=5 71.00 (62.00-96.00) | N=4 77.00 (66.0-85.00) | N=6 78.50 (71.00-95.00) |
| Respiratory Rate | | | |
| Before Md (min-max) | N=5 21.00 (19.00-28.00) | N=4 18.50 (9.00-27.00) | N=7 19.00 (17.00-31.00) |
| After Md (min-max) | N=5 19.00 (14.00-22.00) | N=4 22.00 (17.00-29.00) | N=6 18.50 (13.00-23.00) |
| 30 mins post Md (min-max) | N=5 18.00 (17.00-24.00) | N=4 19.00 (12.00-28.00) | N=6 18.50 (11.00-25.00) |

Md=Median; POD=Post Operative Day;

Fidelity of Hand Massage Administrations

Intervention fidelity is contingent on two main components, namely competence in delivering the intervention and adherence to the treatment protocol (Stein, Sargent, & Rafaels, 2007). In this RCT, several strategies were used to improve the fidelity of hand massage administrations. First, the interventionist's competence was enhanced by undergoing formal training on hand massage administration including practical exercises and assessment of competency. Moreover, the interventionist followed a detailed protocol for hand massage, which was prepared by an experienced massage therapist.

Second, adherence to the protocol was evaluated using video recordings of hand massage administrations, and field notes that described all occurring interferences with the administration of hand massage in the selected mode (i.e., as per the techniques described in the protocol) and dose (i.e., 20 minutes). Overall, there were eight instances in which participants did not want the camera in the room during the hand massage administration due to heightened anxiety or not being at ease with the use of a camera. Of the 35 hand massage administrations (i.e., 20 of 1st administrations, 15 of 2nd administrations and 5 of 3rd administrations), there were eleven during which interferences occurred. The most common interference with delivering hand massage as per protocol was the limited range of motion of the hand in which the arterial line was positional and less surface area on the back of the hand due to the use of tape (n=6) followed by having the bedside monitor or intravenous pump beeping (n=3), clinician quietly administering an injection via butterfly (n=1) and the patient coughing (n=1).

Chapter 6. Significance and Conclusion

Main Outcomes

The results of this RCT suggest that 20-minute moderate pressure massages over the hands in addition to standard ICU care can concomitantly reduce pain intensity, pain unpleasantness and anxiety by 2 points on average on a 0-10 numeric rating scale in the adult cardiac surgery critically ill patients. Conversely, there were no significant reductions in any of these symptoms with the use of hand holding and rest, suggesting that hand holding and occasional stroking are not sufficient to produce clinically significant reductions in these outcome variables. These results are promising as they constitute both statistically and clinically significant reductions not only in pain intensity, but also in other dimensions of pain (i.e., pain unpleasantness) and other symptoms related to the stress response such as anxiety.

This RCT aimed to test the effectiveness of hand massage on the pain intensity, pain unpleasantness, anxiety, muscle tension, vital signs and pain-related interference with functioning of the cardiac surgery critically ill. After launching recruitment and data collection, sleep resurfaced as an important outcome for patients in the early postoperative phase. Based on preliminary observations and patients' reports of the potential beneficial effect of hand massage on sleep in the ICU, sleep quality was included as an outcome variable after ethics approval of the amended protocol.

This RCT showed that patients awaiting cardiac surgery demonstrate interest in complementing standard ICU pharmacological analgesia with non-pharmacological interventions such as hand massage, given that only seven (7%) of the 95 patients who were approached refused to take part in this study. Unfortunately, only 60 patients were randomized as several (n=23) were lost postoperatively: hand massage (n=20), hand holding (n=19) and rest (n=21).

The use of hand holding with occasional stroking appeared to be successful at masking patients with regards to their group assignment as the majority reported receiving hand massage by the research nurse while in the ICU.

In addition to the beneficial effects of hand massage on pain and anxiety, improvements were also observed in terms of muscle tension such that a greater proportion of patients from the hand massage group experienced relaxed muscles after the intervention (20/20) compared to hand holding (18/19) and rest (15/19) (Chi-Square =5.89, $p=0.053$). Small fluctuations in vital signs were observed with the administration of hand massage and hand holding, but also in the rest group. The systolic blood pressure as well as the heart and respiratory rates decreased by less than two units across all groups, thereby making the group differences not statistically significant.

On POD 2, 46 patients (18 hand massage, 16 hand holding, 12 rest) were available and willing to participate in the brief interview about their pain intensity and pain-related interference with functioning. Sleep quality was evaluated by only 25 patients (hand massage, $n=10$; hand holding, $n=9$; rest, $n=6$) given that the RCSQ was added three months after the beginning of recruitment and data collection. The hand massage group reported a maximum pain intensity (median=5.75, range: 2-10) that was lower than what was reported by the hand holding (median=6.50, range: 1-10) and rest groups (median=6.25, range: 0-10), although not statistically significant. Those receiving hand massage were also more likely to reach a median of 0 pain intensity over the course of 24 hours (median=0, range: 0-7) compared to those assigned to hand holding (median=2, range: 0-5) and rest (median=1.75, range: 0-4.5). A trend for statistically significant group differences was observed only for pain interference with sleep such that a higher proportion of patients in the hand massage group reported none or mild (i.e., <4) pain

interference with sleep compared to hand holding and rest. Overall, patients in all groups reported predominantly light sleep (medians 68.75-91.88), being awake roughly 50% of the night time (medians 47.50-71.88) and having poor quality sleep (medians 50-88.75). The hand massage group reported that massage was relaxing and conducive to sleep, and all of them fell asleep during except for two occasions when they were sitting in chair.

No adverse events were documented with the administration of hand massage and hand holding. Overall, patients highlighted the relaxant effect of hand massage and how important that was in the ICU context.

Limitations

Despite randomization, the hand massage group reported the highest baseline scores for pain intensity, pain unpleasantness and anxiety. These scores were used as covariates in statistical analyses to control for baseline group differences. Similarly, patients of Asian and Black/African American background were not proportionally distributed across the three groups. The rest group and those responsible for their care could easily recognize the group assignment, although this may have not changed patients' self-reports of symptoms. Muscle tension was assessed by the interventionist who was not blinded to group assignment, thereby allowing for potential risk of bias.

Not all patients who were randomized were available or able to participate in the interview conducted on POD 2 regarding pain-related interference with functioning. The RCSQ was only added later throughout the data collection phase, which did not allow for sufficient data to be collected and to test the effectiveness of hand massage on sleep quality in the ICU. The BPI interview and the RCSQ are based on patient's recall and allows for the possibility of recall bias. Furthermore, the RCSQ is limited to ICU patients who are able to complete the questionnaire

and those without active cognitive dysfunction, and polysomnography could be used in future massage trials as it provides a more comprehensive evaluation of sleep including its duration, continuity and physiology.

Intervention fidelity was evaluated by recording the frequency and type of interferences with the delivery of the hand massage in the selected mode and dose, yet no specific tool was used to assess strict adherence to the massage protocol given that, to date, there are no validated tools to assess the fidelity of non-pharmacological interventions. Nonetheless, hand massage was administered by the same person throughout the RCT, thereby enhancing the consistency of hand massage administration across patients.

Contribution and Future Directions

This RCT brings several contributions to practice, research and policy.

1. Practice

The use of hand massage can reduce the pain intensity, pain unpleasantness and anxiety of cardiac surgery patients during their ICU stay. These benefits are contingent on ensuring a calm environment, offering hand massage for at least 20 minutes without interruptions and eliciting patients' preferences regarding the timing of its delivery. Clinicians or family members who wish to try this non-pharmacological intervention should follow a short training by a massage therapist, and adhere to the protocol for hand massage administration.

2. Research

Considering the cumulating evidence on the effectiveness of massage in relieving the pain of the cardiac surgery patients, including during their ICU stay, the next step would be to conduct a pragmatic RCT in which hand massage is given by ICU nurses. In the context of a pragmatic RCT, some ICU nurses would be trained on hand massage administration followed by

its delivery in their practice. This RCT could be complemented with a qualitative evaluation of the feasibility of administering massage by the ICU staff nurses including their perception of the facilitators and barriers to its implementation in clinical practice. Similarly, a cost effectiveness analysis could accompany the pragmatic RCT by comparing the cost of training nurses and of the time dedicated to administering massage versus other nursing activities, to the benefits drawn from this intervention (e.g., improved symptom management, sleep, length of ICU stay).

This RCT showed that hand massage can have beneficial effects on multiple symptoms and aspects of the ICU experience, all of which are important for recovery and patient well-being. Preliminary observations suggest that hand massage could enhance sleep in the ICU, yet future RCTs are still awaited to provide evidence for the use of this non-pharmacological intervention for sleep promotion in the ICU. Furthermore, there is a need to develop a tool to evaluate the fidelity of massage administration.

3. Policy

This RCT provides evidence for the benefits of massage in complementing pharmacological treatments for symptom control in the ICU. In conjunction with future massage RCTs in the ICU, this study will help formulate clinical practice guidelines for the use of massage in the critical care context including the minimum effective dose, target body areas, and protocol for massage administration.

Conclusions

ICU patients post cardiac surgery are highly susceptible to experience a multitude of distressing symptoms. Pain is one of those symptoms that are warranted special consideration in attempting multiple approaches for its relief such as pharmacological and non-pharmacological interventions. This RCT provided support for the potential of hand massage in assisting with the

management of symptoms early post cardiac surgery and in the critical care context. The use of touch with occasional stroking of the hands does not seem to be sufficient to produce beneficial effects in terms of symptom management, but could have positive effects on other variables, which were not studied in this RCT. The clinically significant reductions in pain intensity, pain unpleasantness and anxiety that were observed with the administration of hand massage are contingent on following the standardized protocol for the 20-minute hand massage as well as ensuring a calm and quiet environment without interruptions, and seeking patients' preference with regards to the appropriate timing for its delivery. More research is needed to evaluate the sustained effect of hand massage on pain intensity and to explore avenues to sustain its beneficial effects. Whereas this RCT did not initially aim to test the effect of hand massage on the sleep of the cardiac surgery critically ill, preliminary observations and patient reports suggest that hand massage may promote sleep in the ICU through its relaxant, pain relieving and anxiolytic effect. Future RCTs are needed to test this hypothesis and provide evidence on the use of hand massage for sleep promotion in the ICU.

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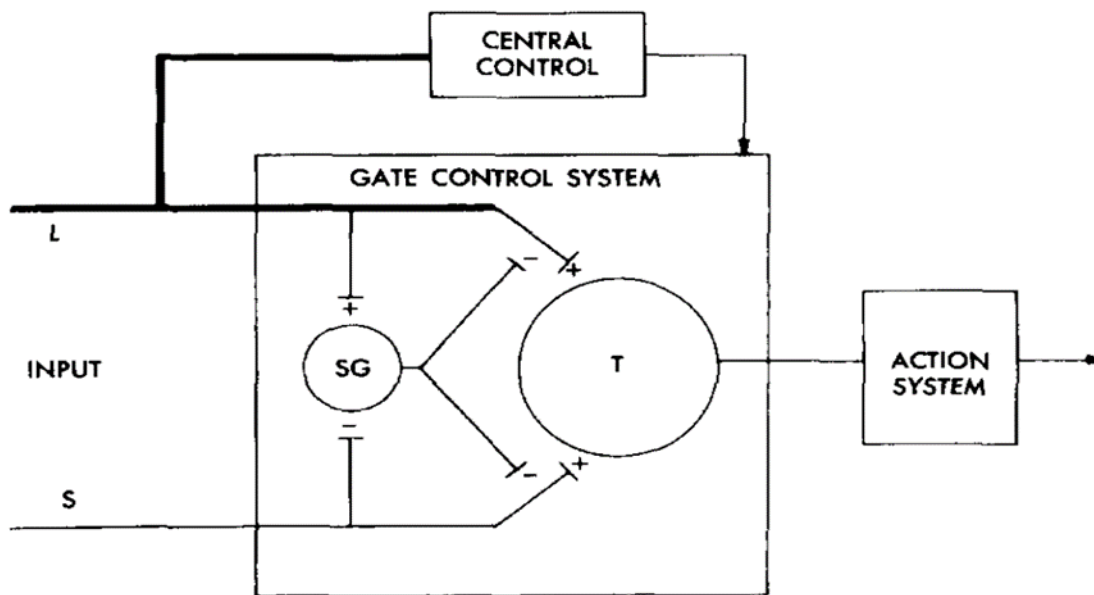
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Appendix A
Diagram of the Gate Control Theory of Pain Mechanisms



Legend:

L: large diameter fibers

S: small diameter fibers

SG: substantia gelatinosa

T: first central transmission cells

Melzack, R. & Wall, P. D. (1965). "Pain mechanisms: a new theory," Science, vol. 150, no. 699, pp. 971-979, Nov.1965.

Appendix B1
Socio-Demographic and Medical-Surgical Data Collection Form

Participant Code: _____

Admission to the ICU:

Date: _____ Time: _____

Admission to the step-down unit:

Date: _____ Time: _____

Age: _____

Gender: M ☐ F ☐

Ethnic origin:

Caucasian ☐

African ☐

Asian ☐

Hispanic ☐

Aboriginal ☐

Métis ☐

Other ☐

Language spoken:

French ☐

English ☐

Other ☐

Highest level of education completed:

Primary ☐

Secondary ☐

College diploma (CEGEP) ☐

University ☐

Appendix B2
Socio-Demographic and Medical-Surgical Data Collection Form

Participant Code: _____

Nonanginal chronic pain (for more than 3 months):

Yes ☐

No ☐

If yes, treatments used: a) pharmacological: _____

b) non-pharmacological: _____

Use of alternative therapies:

Yes ☐ Type of alternative therapy: _____

No ☐

Use of massage therapy before surgery:

Yes ☐

No ☐

Use of massage therapy since enrollment in the study:

Yes ☐

No ☐

Cardiac surgery:

CABG ☐

Valve replacement ☐

Other: _____

Analgesia administration:

POD 0:

| Medication | Dose/ Rate | Time | Route |
|------------|------------|------|-------|
| | | | |

Appendix B3
Socio-Demographic and Medical-Surgical Data Collection Form

Participant Code: _____

POD 1:

| Medication | Dose/ Rate | Time | Route |
|------------|------------|------|-------|
| | | | |

POD 2:

| Medication | Dose/ Rate | Time | Route |
|------------|------------|------|-------|
| | | | |

Appendix C1a
The Patient Data Collection Form (English Version)
Pain Intensity, Pain Unpleasantness, and Anxiety

Participant code: _____

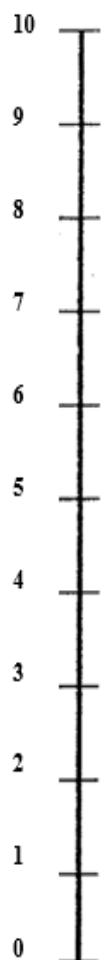
Timing of assessment:

T1 T2 T3

B1 B2 B3

**How much pain do you feel
right now?**

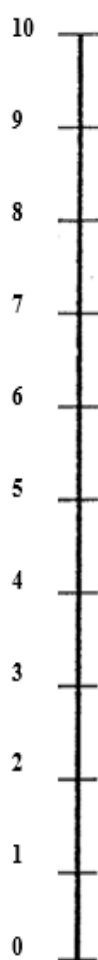
Worst possible pain



No pain

**How unpleasant is the pain
right now?**

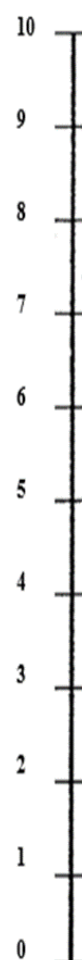
**Most unpleasant feeling
possible**



Not at all unpleasant

**How anxious/nervous do you
feel right now?**

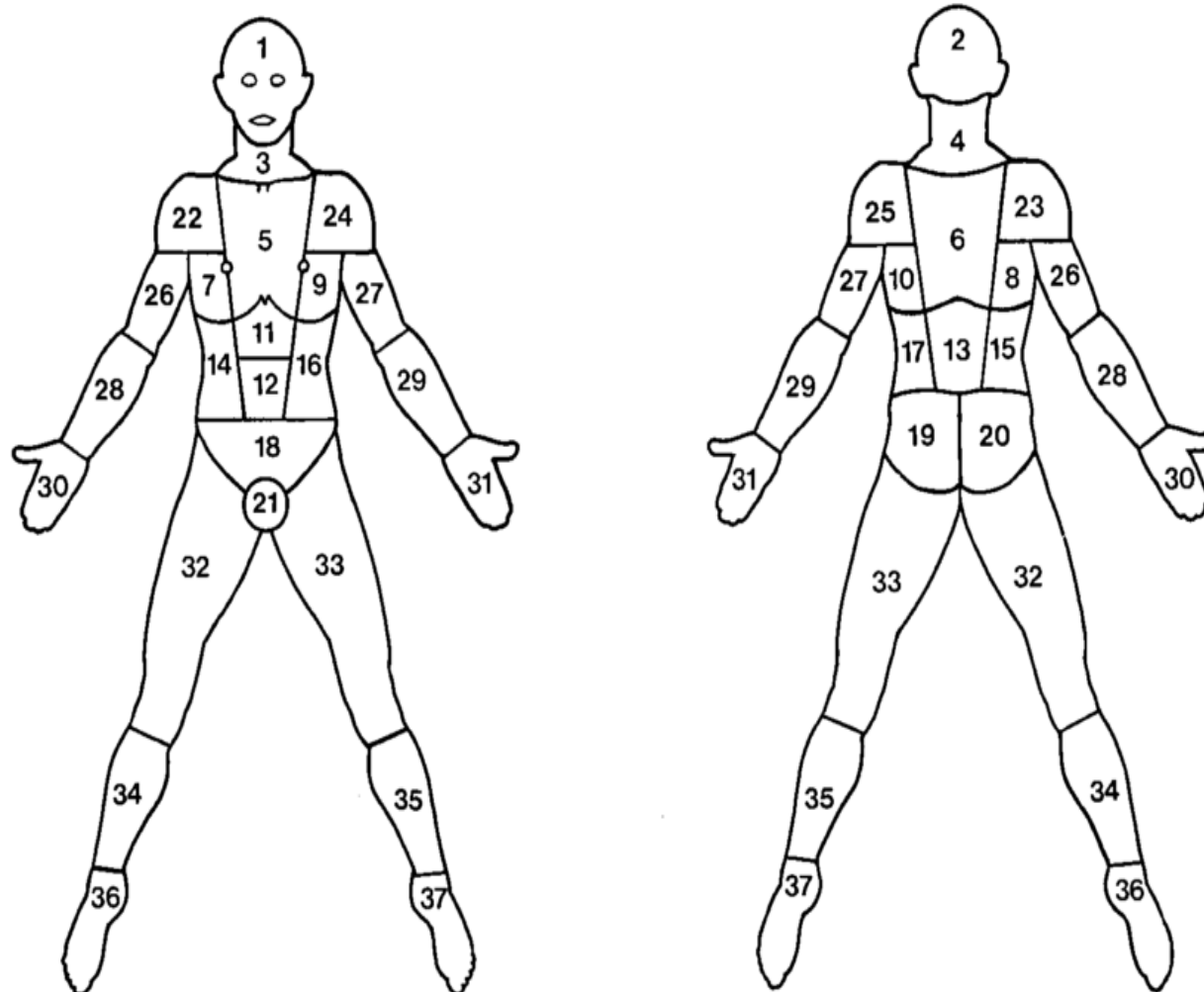
Worst possible anxiety



No anxiety

Appendix C1b
The Patient Data Collection Form (English Version)
Pain Location and Pain Quality

If you experience pain, please indicate the body area that is painful by circling the corresponding number:



(Muller et al., 2000)

If you experience pain, please describe in your own words what your pain feels like:

Appendix C2a
The Patient Data Collection Form (French Version)
Pain Intensity, Pain Unpleasantness, and Anxiety

Participant code: _____

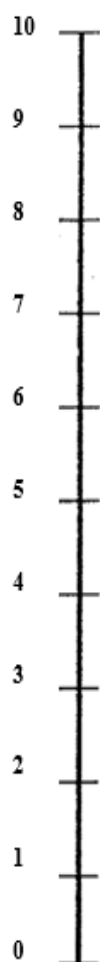
Timing of assessment:

T1 T2 T3

B1 B2 B3

**À quel point vous
ressentez de la douleur
en ce moment?**

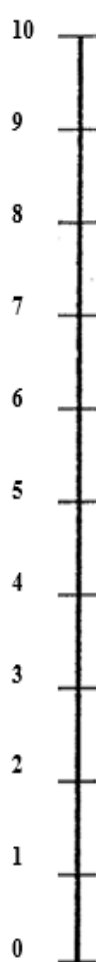
**La pire douleur
possible**



**Pas de
douleur**

**À quel point votre
douleur est
désagréable en ce
moment?**

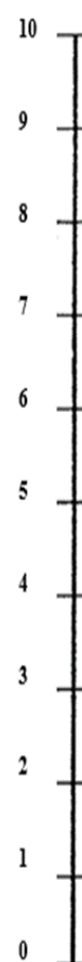
**La douleur la plus
désagréable possible**



Pas du tout désagréable

**À quel point vous
ressentez de
l'anxiété/nervosité en
ce moment?**

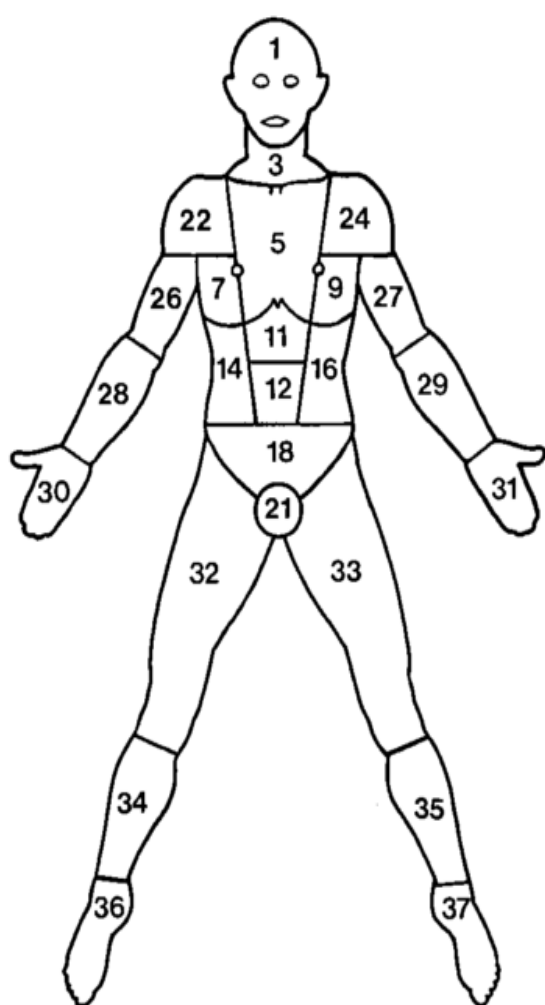
La pire anxiété possible



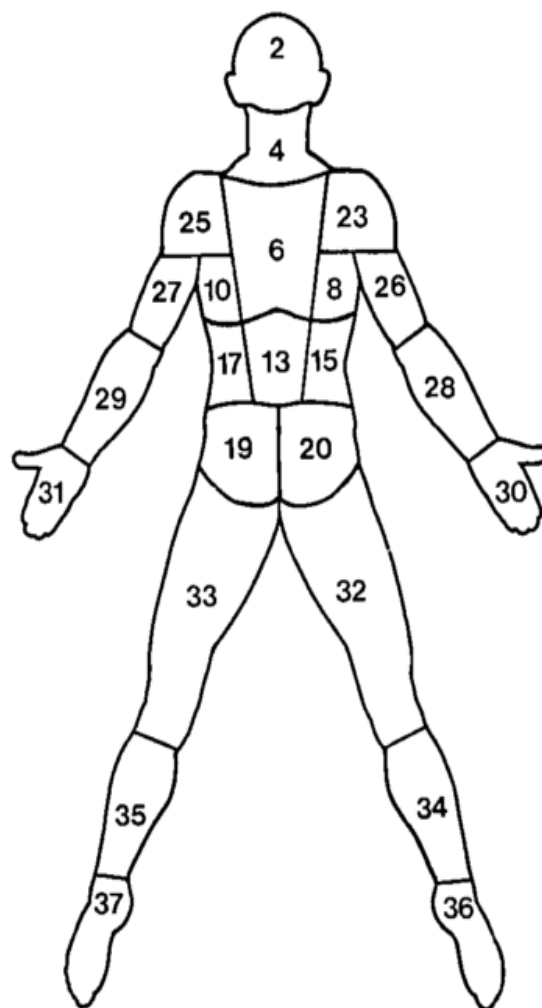
**Pas
d'anxiété**

Appendix C2b
The Patient Data Collection Form (French Version)
Pain Location and Pain Quality

Si vous ressentez de la douleur, veuillez SVP encercler le(s) numéro(s) qui correspond/ent le mieux à l'endroit de votre douleur:



(Muller et al., 2000)



Si vous ressentez de la douleur, veuillez SVP décrire en vos propres mots à quoi ressemble votre douleur:

Appendix D
Muscle Tension Scale

| | | | |
|--|---------------------|---|---|
| Muscle Tension Evaluation by passive flexion and extension of upper limbs when patient is at rest. | Relaxed | 0 | No resistance to passive movements |
| | Tense, rigid | 1 | Resistance to passive movements |
| | Very tense or rigid | 2 | Strong resistance to passive movements or incapacity to complete them |

Extracted from the Critical-Care Pain Observation Tool (CPOT) (Gelinas et al., 2006).

The Adapted Brief Pain Inventory (BPI) administered by interview

1. At its worst in the last 24 hours: _/10
2. At its least in the last 24 hours: _/10
3. On average in the last 24 hours: _/10
4. Right now: _/10

| | | |
|------------------------------|-----|----|
| General activity | /10 | NA |
| Mood | /10 | NA |
| Walking/mobilization ability | /10 | NA |
| Coughing | /10 | NA |
| Deep breathing | /10 | NA |
| Relations with others | /10 | NA |
| Sleep | /10 | NA |
| Appetite | /10 | NA |
| Concentration | /10 | NA |
| Enjoyment with life | /10 | NA |

Use of massage therapy since surgery:

No ☐[illegible]

Appendix E1b
The Richards-Campbell Sleep Questionnaire

Each of these questions is answered by placing an "X" on the answer line. Place your "X" anywhere on the line that you feel best describes your sleep when you were in the ICU.

1. My sleep in the ICU was:

Deep sleep _____ Light sleep
0 100

2. In the ICU, when I got to sleep, I:

Fell asleep almost _____ Just never could fall
immediately _____ asleep
0 100

3. In the ICU, I was:

Awake very little _____ Awake all night long
0 100

4. In the ICU, when I woke up or was awakened, I:

Got back to sleep _____ Couldn't
immediately _____ get back to sleep
0 100

5. I would describe my sleep in the ICU as:

Good night's sleep _____ Bad night's sleep
0 100

Appendix E2a
The Adapted Brief Pain Inventory (BPI) administered by interview

Sur une échelle de 0 à 10, 0 étant *pas de douleur* et 10 étant *la douleur la plus horrible que vous puissiez imaginer*, SVP évaluez votre douleur:

1. La plus intense que vous ayez ressenti pendant le dernières 24 heures: _ /10
2. La plus faible que vous ayez ressenti pendant le dernières 24 heures: _ /10
3. La douleur en général que vous ayez ressenti pendant le dernières 24 heures: _ /10
4. La douleur en ce moment: _ /10

Sur une échelle de 0 à 10, 0 étant *ne gêne pas* et 10 étant *gêne complètement*, SVP décrivez comment, pendant les dernières 24 heures, la douleur a gêné votre:

| | | |
|---------------------------|-----|----|
| Activité générale | /10 | NA |
| Humeur | /10 | NA |
| Capacité à marcher | /10 | NA |
| Tousser | /10 | NA |
| Respirations profondes | /10 | NA |
| Relations avec les autres | /10 | NA |
| Sommeil | /10 | NA |
| Appétit | /10 | NA |
| Concentration | /10 | NA |
| Goût de vivre | /10 | NA |

NA: Not Applicable

Avez vous reçu des massages depuis votre chirurgie:

Oui ☐ Sur quelle partie du corps? _____ Les mains? Oui ☐ Non ☐

Non ☐

POD 2: Analgesia administration

| Medication | Dose/ Rate | Time | Route |
|------------|------------|------|-------|
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |

Appendix E2b

The Richards-Campbell Sleep Questionnaire

Pour chacune de ces questions, placer un « x » sur la ligne de réponse au niveau qui décrit le mieux votre sommeil lors de votre séjour à l'USI.

1. Mon sommeil lors de mon séjour à l'USI était :

Sommeil profond Sommeil léger

0 100

2. Lors de mon séjour à l'USI, je décrirais la façon de m'endormir :

Endormi(e) Jamais endormi(e)
immédiatement

0 100

3. Lors de mon séjour à l'USI, j'étais :

Très peu éveillé(e) 0 100 Éveillé(e) toute la nuit

4. Lors de mon séjour à l'USI, quand je me suis réveillé(e) ou lorsque j'étais éveillé(e), je me suis :

Recouché(e) immédiatement N'ai pas pu me recoucher

0 100

5. Je décrirais mon sommeil à l'USI comme de :

Bonnes nuits de sommeil 0 100 Mauvaises nuits de sommeil

Appendix F1

Means (SDs) of vital signs before, immediately after and 30 minutes later for the 1st data collection

| Vital signs | Massage (n=20) | Hand Holding (n=19) | Rest (n=21) | Leve of significance (p) |
|--------------------------|----------------|---------------------|----------------|--|
| Systolic Blood Pressure | | | | |
| Before | 114.38 (18.67) | 118.56 (22.52) | 123.90 (16.40) | Group (p=0.652) Time (p=0.315) Interaction (p=0.109) |
| After | 113.15 (16.48) | 116.00 (23.04) | 120.90 (18.77) | |
| 30 mins post | 116.45 (19.25) | 119.72 (19.51) | 116.10 (16.89) | |
| Diastolic Blood Pressure | | | | |
| Before | 60.19 (9.56) | 59.78 (12.68) | 62.71 (10.75) | Group (p=0.868) Time (p=0.741) Interaction (p=0.154) |
| After | 60.50 (13.09) | 60.11 (17.43) | 59.20 (12.29) | |
| 30 mins post | 62.15 (12.04) | 59.61 (12.52) | 57.85 (9.55) | |
| Heart Rate | | | | |
| Before | 83.62 (16.95) | 85.50 (13.14) | 82.76 (10.88) | Group (0.884) Time (p=0.050) Interaction (p=0.749) |
| After | 82.00 (16.28) | 83.39 (13.35) | 82.29 (11.82) | |
| 30 mins post | 84.10 (17.36) | 83.50 (13.47) | 81.55 (11.92) | |
| Respiratory Rate | | | | |
| Before | 18.20 (3.69) | 18.61 (3.55) | 21.14 (4.73) | Group (p=0.265) Time (p=0.002) Interaction (p=0.526) |
| After | 15.86 (3.93) | 16.28 (5.11) | 18.00 (4.95) | |
| 30 mins post | 17.80 (4.02) | 18.65 (5.63) | 18.55 (3.63) | |

Appendix F2

Means (SDs) of vital signs before, immediately after and 30 minutes later for the 2nd data collection

| Vital signs | Massage | Hand Holding | Rest | Leve of significance (p) |
|--------------------------|----------------|----------------|----------------|--|
| Systolic Blood Pressure | | | | |
| Before | 114.71 (17.16) | 124.00 (17.41) | 123.64 (16.91) | Group (p=0.477) Time (p=0.207) Interaction (p=0.889) |
| After | 112.72 (16.84) | 117.84 (20.35) | 122.33 (16.23) | |
| 30 mins post | 111.18 (15.06) | 118.17 (16.15) | 122.62 (19.44) | |
| Diastolic Blood Pressure | | | | |
| Before | 61.00 (9.12) | 62.29 (12.18) | 65.86 (14.22) | Group (p=0.241) Time (p=0.028) Interaction (p=0.463) |
| After | 57.55 (6.90) | 56.93 (9.88) | 59.67 (9.06) | |
| 30 mins post | 60.09 (11.58) | 56.33 (6.31) | 60.00 (8.37) | |
| Heart Rate | | | | |
| Before | 80.47 (12.06) | 82.80 (10.84) | 78.29 (11.00) | Group (p=0.503) Time (p=0.028) Interaction (p=0.917) |
| After | 79.27 (12.24) | 81.07 (10.83) | 76.71 (11.55) | |
| 30 mins post | 80.00 (13.78) | 82.79 (9.66) | 78.71 (11.24) | |
| Respiratory Rate | | | | |
| Before | 19.07 (4.54) | 20.13 (4.61) | 19.50 (7.53) | Group (p=0.139) Time (p=0.102) Interaction (p=0.180) |
| After | 17.02 (3.09) | 19.87 (4.85) | 19.23 (4.34) | |
| 30 mins post | 14.62 (4.43) | 18.57 (4.68) | 20.31 (4.89) | |