STUDY PROTOCOL

Does the speed of sternal retraction during coronary artery bypass graft surgery affect postoperative pain outcomes? A randomized controlled trial protocol [version 1; peer review: 2 approved with reservations]

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Abstract

Background: Chronic pain is a serious health issue impacting both the quality of life and productivity of patients. Chronic post-sternotomy pain (CPSP) is characterized by numbness, severe tenderness on palpation, allodynia, as well as constant pain across the anterior chest wall that can persist for months to years after sternotomy. All patients experience early post-operative pain following coronary artery bypass graft (CABG); unfortunately, approximately 30-40% of CABG patients subsequently develop CPSP.

Methods: The current study is a prospective, double-blinded, randomized controlled trial. A sample size of 316 randomly assigned patients (n=158 per group) will provide an 80% power at a 2-sided α of 0.05 to detect a 40% decrease in CPSP incidence at 6 months. Eligible patients scheduled for elective, primary coronary artery bypass graft surgery will be randomly assigned to the CONTROL group, in which sternal retraction is conducted over 30 seconds (as per standard practice); or the SLOW group, in which sternal retraction is achieved over 15 minutes. Surgical and perioperative anesthesia protocols between the two groups are otherwise the same. Our primary outcome is the incidence of CPSP at 6 months. Secondary outcomes are: CPSP incidence at 3 and 12 months, daily sternal incision pain intensity (numeric rating scale (NRS)) at rest and while coughing, and daily analgesic consumption while in hospital and at 7 days postoperatively; pain quality, quality of life, and pain interference

Open Peer Review

Approval Status ? ?

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Any reports and responses or comments on the article can be found at the end of the article.

with daily function at 3, 6, and 12 months post-operatively.

Discussion: Our randomized controlled trial will determine whether retracting the sternum more slowly for exposure of the heart during CABG surgery will decrease the incidence and/or severity of CPSP.

ClinicalTrials.gov registration: NCT02697812 (03/03/2016)

Keywords

Coronary Artery Bypass Surgery; chronic pain

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Abbreviations

Chronic Post-Sternotomy Pain (CPSP)
 Coronary Artery Bypass Graft (CABG)
 Internal Mammary Artery (IMA)
 Activated Clotting Time (ACT)
 Basic History Questionnaire (BHQ)
 Brief Pain Inventory-short form (BPI-SF)
 36-Item Short Form Health Survey (SF-36)
 Short form-McGill pain questionnaire (SF-MPQ)
 Douleur Neuropathique 4 (DN4)
 Numeric Rating Scale (NRS)
 Research Ethics Board (REB)

Introduction

Background and rationale

Coronary artery bypass surgery and chronic post-sternotomy pain. All patients experience pain following coronary artery bypass graft (CABG) surgery both within the early and intermediate postoperative periods. Severe pain may compromise the patients' recovery by affecting breathing, mobility, and sleep. Inadequately controlled postoperative pain has been associated with increased cardiovascular complications, pneumonia, hyper-coagulability, delirium and wound infection¹. Of the patients readmitted following CABG, many report recurrent ischemic cardiac chest pain while others suffer from non-cardiac chest pain. Pain is the fifth most common reason for readmission within 4 weeks of CABG². Severe, inadequately controlled postoperative pain may also be a predisposing factor for developing chronic post-sternotomy pain (CPSP)³. Although CPSP is now becoming recognized as a serious health issue with a major impact on quality of life and productivity, this complication has traditionally been overlooked and/or dismissed as an unavoidable consequence of surgery. CPSP is characterized by numbness, severe tenderness on palpation, allodynia (pain response to normally non-painful stimuli), as well as constant pain across the anterior chest wall⁴, and this pain can persist for up to 16 months⁵. Inter-scapular and shoulder girdle pain may also be present.

Estimates of the incidence of CPSP vary widely depending upon the population, the pain measures used and the time-point under consideration. Although the prevalence of CPSP has been reported as high as 52% 6 months following CABG⁶, most report an incidence of approximately 30–40% between 6 and 16 months postoperatively^{5–7}. Given that almost 500,000 CABG procedures were performed within North America during 2009^{8,9}, this translates to a significant number of patients adversely affected by CPSP. Despite the major impact of chronic post-surgical pain on quality of life, productivity and associated medical expenses, it is still an area of research that receives relatively little attention¹⁰ and the actual process by which acute postsurgical pain transitions into chronic pain receives even less attention¹¹.

The etiology of CPSP is complex and not well understood. As mentioned previously, the development of CPSP is positively correlated with severe and inadequately controlled acute post-operative pain. However, the fact that not all who experience severe post-operative pain go on to develop CPSP, suggests that other factors such as the genetic variation in the underlying pain mechanisms and/or prior experiences may alter one's response to painful stimuli both in the short and long term. It has also been suggested that techniques associated with internal mammary artery (IMA) harvesting increase the likelihood of CPSP^{12,13} but even patients who do not undergo IMA harvesting may report an equally high incidence of CPSP¹⁴. The high incidence of CPSP associated with cardiac surgery can likely be attributed largely to the extensive nerve and tissue damage¹⁵ from the shear forces applied during rapid sternal retraction. Shear forces are not only applied in the lateral-dorsal-ventral directions but also on the rostral-caudal plane.

To our knowledge, no clinical investigations have examined the sternal retraction maneuver as a causal determinant in the severity of postoperative pain or the subsequent development of CPSP. However, Bolotin *et al.* (2007)¹⁶ did use anesthetized sheep to demonstrate that controlled retraction forces (and hence increased time) to sternal retraction, resulted in significantly lower maximal and average applied forces. In addition, using controlled force to allow equivalent exposure resulted in significantly reduced alterations in blood pressure and heart rate thought to be indicative of reduced pain and/or stress compared to standard sternal retraction forces. A similar study with lateral open thoracotomies in sheep with standard versus slower retraction, observed significant reductions in applied forces and this was associated with reduced animal stress and tissue damage¹⁷. Several other investigations have explored the use of mini-sternotomies for aortic valve surgery^{18–20} with mixed results on pain, length of hospital stay, blood loss and/or pulmonary function. The one study which compared mini vs. standard sternotomy for CABG examined only postoperative pulmonary function and observed no difference²¹.

Acute post-sternotomy pain occurs as a result of tissue and nerve damage (intercostal nerves and thoracic nerves (T2–T6) which innervate the sternum and/or ribs) which provokes direct nociceptive input. However, with the physical trauma, numerous inflammatory mediators (i.e., bradykinin, substance P, histamine, 5-Hydroxytryptamine, adenosine triphosphate, nitric oxide, prostanoids and leukotrienes) are released and these induce pain and inflammation at more remote sites²². Furthermore, these inflammatory mediators induce sensitization of both peripheral and central neural pathways. It is the sensitization of central pain-signalling neurons from intense and prolonged nociceptive activity which is thought to result in the transition from acute to chronic pain^{22–24}. The prolonged sensory input provokes abnormal responses to low-threshold mechanoreceptor activity (allodynia and hyperalgesia) and central nervous system remodelling that contributes to this persistent pain state.

Objectives

The overall objective of the current investigation is to determine whether increasing the time to achieve sternal retraction to 15 minutes (from the standard ~30 seconds), will result in reduced acute and chronic post-sternotomy pain and an improved quality of life. We hypothesize that increasing the time to sternal retraction will result in reduced required force, less physical trauma, less inflammation, and less nerve damage. Specifically, we expect SLOW steady sternal retraction (occurring over 15 minutes) to: 1) reduce the incidence of CPSP by 40% and 2) significantly improve quality of life 6 months postoperatively.

Methods

Trial design and setting

This is a prospective, double-blind, randomized controlled superiority trial. It will take place at Kingston General Hospital site, Kingston Health Sciences Centre, Ontario, Canada which is a medium size (~470 beds), academic, tertiary care centre.

Eligibility criteria

Inclusion criteria

- Elective primary coronary artery bypass surgery
- Understanding and provision of written informed consent
- Age > 18 years

Exclusion criteria

- Any combined or redo cardiac procedure
- Current alcohol or substance abuse
- Pre-existing chronic pain requiring chronic analgesic use
- Rest pain in proposed surgical area at baseline, preoperatively
- Chronic Steroid use
- Inability to perform post-operative assessments
- Planned bilateral internal thoracic artery harvest for bypass conduits
- Rheumatoid arthritis
- Prior radiation to the chest

Coronary artery bypass surgeries for participants in the study will be conducted by cardiac surgeon Dr. Dimitri Petsikas (MD, FRCS(C)) and colleagues at Kingston Health Sciences Centre.

Ethical approval

The Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board approved this study (ANAE-233-13, May 21, 2013). Written, informed consent for participation will be obtained from all participants²⁵.

Interventions

Explanation for the choice of comparators

To our knowledge, no clinical investigations have examined the sternal retraction maneuver as a causal determinant in the severity of postoperative pain or the subsequent development of CPSP. However, Bolotin *et al.* (2007)¹⁶ did use anesthetized sheep to demonstrate that controlled retraction forces (and hence increased time) to sternal retraction, resulted in significantly lower maximal and average applied forces. In addition, using controlled force to allow equivalent exposure resulted in significantly reduced alterations in blood pressure and heart rate thought to be indicative of reduced pain and/or stress compared to standard sternal retraction forces. A similar study with lateral open thoracotomies in sheep with standard versus slower retraction, observed significant reductions in applied forces and this was associated with reduced animal stress and tissue damage¹⁷. Several other investigations have explored the use of mini-sternotomies for aortic valve surgery^{18–20} with mixed results on pain, length of hospital stay, blood loss and/or pulmonary function. The one study which compared mini vs. standard sternotomy for CABG examined only postoperative pulmonary function and observed no difference²¹.

Thus, the overall objective of the current investigation is to determine whether increasing the time to achieve sternal retraction to 15 minutes (from the standard ~30 seconds), will result in reduced acute and chronic post-sternotomy pain and an improved quality of life.

Intervention

Anesthesia. Patients will receive general anesthesia with endotracheal intubation, using moderate dose opioid (fentanyl 10–20 mcg/kg or sufentanil 1–2 mcg/kg), inhalational anesthesia (isoflurane or sevoflurane up to 1.5 MAC), propofol, midazolam and succinylcholine and/or rocuronium. Monitoring will include standard Canadian Anesthesia Society (CAS) monitors, an invasive arterial line, a central venous line and a Foley catheter. In preparation for cardiopulmonary bypass, all patients will receive intravenous unfractionated heparin to achieve an activated clotting time (ACT) > 480 seconds. The ACT will be maintained at this level with additional heparin as necessary. Following separation from cardiopulmonary bypass, the heparin effects will be reversed with protamine administration to achieve an ACT within 10% of baseline. On admission to the intensive care unit, patients will remain sedated using a propofol infusion 25–75 mcg/kg/min until extubation; and patients will receive protamine 50 mg/hr for 3 consecutive hours.

Surgery. Participants will then receive one of two surgical conditions:

Standard “normal speed” sternal retraction (approximately 30 seconds)

- Median sternotomy carried out, and sternal hemostasis obtained

- Sternum retracted to a width which will allow adequate exposure to allow performance of the coronary bypass procedure at the individual surgeon's discretion
- Maximum distance between sternal edges at full retraction will be measured with distance calipers
- The sternal retractor will then be removed and the left or right internal thoracic artery will be harvested as a bypass conduit
- Sternal retractor will be re-inserted and sternum retracted to the previously determined MAXIMAL STERNAL RETRACTION distance. The coronary bypass procedure will then proceed at the surgeon's discretion, (i.e. number and type of bypass grafts)

Slow sternal retraction (approximately 15 minutes)

- Median sternotomy carried out and sternal hemostasis obtained
- Sternum retracted to a width allowing adequate exposure to perform the coronary bypass procedure over 15 minutes
- Maximum distance between sternal edges at full retraction will be measured with distance calipers
- The sternal retractor will then be removed and the left or right internal thoracic artery will be harvested as a bypass conduit
- Sternal retractor will be re-inserted and sternum retracted to the previously determined MAXIMAL STERNAL RETRACTION distance. The coronary bypass procedure will then proceed at the surgeon's discretion, (i.e. number and type of bypass grafts)

All cases will be performed via median sternotomy with cardiopulmonary bypass support, using standard aortic and single two-stage right atrial venous cannulation. Intermittent antegrade blood cardioplegia will be utilized. All bypasses will be performed under a single cross-clamp. All patients will have a single 32 French anterior mediastinal drain. A 28 French chest tube will be placed in either or both of the pleural spaces should they be opened at any point during the surgery. All chest drains will be placed to suction at $-20 \text{ cmH}_2\text{O}$.

Criteria for discontinuing or modifying allocated interventions.

At any time, either prior to anaesthetic induction or afterward, should the patient become electrocardiographically or hemodynamically unstable, he/she will be withdrawn from the intervention and the operation will proceed as per standard of care for optimal patient safety. Participants will be withdrawn from the study if there is a change in planned surgical procedure.

Strategies to improve adherence to interventions

Study staff, who otherwise have no involvement in the study in terms of patient enrolment or assessment, will be in the operating room (OR) to facilitate protocol compliance with the intervention and measure the time to achieve sternal retraction.

Provisions for post-trial care

Postoperative care for study participants is standard of care. Additionally, as stated in the informed consent form, if participants become ill or injured as a direct result of participating in this study, necessary medical treatment will be available to them at no cost to them²⁵.

Outcomes

The primary outcome measure will be the incidence of chronic post-sternotomy chest pain at 6 months following CABG with median sternotomy. However, we will also measure the incidence of CPSP at 3 and 12 months to determine the trajectory.

Secondary outcomes (in addition to CPSP at 3 and 12 months) will include: Pain intensity (NRS scale) of sternal incision pain at rest and while coughing daily while in hospital until discharge and then at 1 week postoperatively (via telephone call). Analgesic consumption (morphine equivalents) daily while in hospital until discharge, and then at 1 week post-operatively and 3, 6, and 12 months post-operatively. Intra-operative data will include time from initiation to full retraction, latency from full retraction to sternal closure, width of sternal opening at full retraction. Pain quality (McGill Pain Questionnaire short form (MPQ-SF)), quality of life (SF-36 questionnaire), and pain interference with daily function (Brief Pain Inventory (BPI)) at 3, 6 and 12 months post-operatively. All assessments following discharge from the hospital will be via telephone calls from a research nurse blinded to randomization assignment. In-hospital assessments will also be done by a research nurse blinded to group assignment (Table 1). All data collection forms can be found as extended data²⁵.

Sample size

We consider a 40% reduction in the incidence of CPSP at 6 months to be clinically significant. Since the prevalence of CPSP varies between 14–52% using current surgical methods and pain control strategies, and based on the work of Van Gulik *et al.* (2011)⁷ which observed a 35% incidence of CPSP at 12 months, we expect to see an incidence of 40% CPSP at 6 months, and expect to observe a 40% reduction (i.e., from 40% to 24%) with SLOW sternal retraction. Under these assumptions, we will require 132 patients per group to achieve 80% power at a two-sided $\alpha=0.05$. We will conservatively increase our sample size to 158 per group to allow for up to 20% loss to follow-up (N=316) given the long duration of the follow-up period (i.e. 6 for the primary outcome and 12 months for secondary outcomes). A total of 10 additional patients will also be randomized to account for participants who may not receive the intervention (i.e., protocol non-compliance) or may be lost post-randomization due to surgical complications.

Recruitment

Patients will be approached in the Pre-Anesthesia clinic by the research nurse prior to their surgery date. Eligible patients will be informed about the study and their eligibility to participate assessed. Informed consent will be obtained for all eligible and interested participants. If potential participants require

Table 1. Example template of recommended content for the schedule of enrolment, interventions, and assessments*.

TIMEPOINT	STUDY PERIOD						
	Enrolment	Allocation	Post-allocation				
	<i>Pre-operative</i>	0	<i>POD0-d/c*</i>	<i>7 days</i>	<i>3 months</i>	<i>6 months</i>	<i>12 months</i>
ENROLMENT:							
Eligibility screen	X						
Informed consent	X						
Allocation		X					
INTERVENTIONS:							
<i>FAST group</i>		X					
<i>SLOW Group</i>		X					
ASSESSMENTS:							
<i>Patient Demographics</i>	X						
<i>Intraoperative Data</i>		X					
<i>Pain Scores (NRS), analgesic consumption</i>			X	X	X	X	X
<i>CPSP Screen</i>					X	X	X
<i>SF36</i>					X	X	X
<i>BPI-SF**</i>					X	X	X
<i>SF-MPQ**</i>					X	X	X
<i>DN4**</i>					X	X	X

*Postoperative day 0 until patient discharge (d/c) from hospital

**Completed if CPSP screen positive.

BPI-SF-Brief pain inventory-short form; CPSP-Chronic post-sternotomy pain; D/C-discharge; DN4-Douleur Neuropathique 4; SF-MPQ-Short form McGill pain questionnaire; NRS-Numeric rating scale; POD0-Postoperative Day 0; SF36-36 item short form survey

more time to make a decision or would prefer to talk to others before making a decision, they can also take the forms home and if they do decide to participate, written informed consent will be obtained by research personnel on the day of surgery.

Assignment of interventions: allocation

A computer-generated randomization table will be prepared by the institutional biostatistician and patients randomly assigned in equal proportions to the standard or slow sternal retraction groups. Randomization will be unstratified in permuted blocks of randomly selected sizes of 4 or 8.

The institutional biostatistician will send the computer-generated randomization table directly to the departmental research secretary who has no involvement in the study other than preparation of the study envelopes. Sequentially numbered, sealed, opaque envelopes will be used to conceal the sequence allocation until the intervention is assigned in the operating room while the patient is under general anesthetic.

A study nurse will enrol patients and assign them to the intervention based upon the consecutively numbered (and concealed) randomization assignment.

Assignment of interventions: blinding

This is a double-blinded clinical trial (Participant, Outcomes Assessor). All OR staff, including surgeon(s) and anesthesiologist(s), will be unblinded during the surgery. Research staff who have no involvement in patient assessments will also be unblinded and in the OR to facilitate protocol compliance with the intervention and to measure the time to achieve sternal retraction.

Data collection and management

Dedicated, blinded research nurses will collect and compile the data. All assessment tools (described below) will be administered to the participant over the telephone at specified time-points (see Table 1). Kingston Health Sciences Centre biostatisticians will complete the majority of the data analysis.

A research assistant will assist with the data cleaning and verification.

Scoring & description assessment tools

The Brief Pain Inventory-short form (BPI-SF) is a validated and reliable tool for measuring pain intensity and interference with daily activities. Scoring 1–10, where 1–4 = mild pain, 5–6 = moderate pain and 7–10 = severe pain. Developed by the Pain Research Group of the WHO Collaborating Centre for Symptom Evaluation in Cancer Care²⁶.

The 36-Item Short Form Health Survey (SF-36) is a validated and well-established tool which measures overall mental & physical health as a measure of Quality of life. Scores range from 0–100 where 0 is the lowest quality of life and 100 is the highest²⁷.

The Short form-McGill pain questionnaire (SF-MPQ) will be used to evaluate the intensity & properties of the pain experience. The main component of the SF-MPQ consists of 15 descriptors (11 sensory; 4 affective) which are rated on an intensity scale as 0 = none, 1 = mild, 2 = moderate or 3 = severe. Three pain scores are derived from the sum of the intensity rank values of the words chosen for sensory, affective and total descriptors. The SF-MPQ also includes the Present Pain Intensity (PPI) index of the standard MPQ and a visual analogue scale (VAS)²⁸.

The Douleur Neuropathique 4 (DN4) is a validated clinician-administered tool used to screen for patients experiencing neuropathic pain. The DN4 consists of 10 items split between 4 questions, where yes = 1, and no = 0. A score of 4 or greater indicates a patient likely experiencing neuropathic pain, with a sensitivity of 83% and a specificity of 90%²⁹.

The Numeric Rating Scale (NRS) for pain is commonly used and validated tool used to measure pain intensity in adults. The NRS for pain uses an 11-point numeric scale (0–10) to represent a patient's pain, where 0 represents one pain extreme (e.g., "no pain") and 10 representing the other pain extreme (e.g., "worst pain imaginable")³⁰.

Plans to promote participant retention and complete follow-up

At the time of enrolment and randomization, participant contact information will be confirmed to ensure successful follow up. Permission to contact alternate contacts, family members, and/or the patients family physician will also be sought at the time of enrolment, to promote follow up if we are unable to contact the patient.

Data management

Data will be entered, verified, and stored in a password protected Excel spreadsheet. The study data will be identified only by a study ID number which will be linked to the patient's

identity only on a master (password-protected) spreadsheet stored separately from the data on a secure server. The de-identified data will be exported to SPSS for analysis purposes.

Confidentiality

A unique study ID number will be assigned to each participant. This study ID will be used on all data collection forms and will be linked with the true identity only on a master sheet which will be kept separate from the data in a locked cabinet. Data will be entered into electronic data spreadsheets and stored securely as described above. Only information directly surrounding the surgical procedure and/or relevant to this investigation will be collected. This will either come directly from the patient or from the medical record. Health information will only be used by the study investigators and will not be linked to any other sources. As stated above the information will be identified only by a study ID number. This data may be used for presentation or publication, but no identifiable information will be used. Only principal investigators or their delegates at KHSC will have access to this information. Delegates will include the research nurses who will collect and compile the data, the KHSC biostatisticians who will complete the majority of the data analysis, a research assistant who will assist with the data cleaning and verification. Data will be stored securely for 25 years as required, following which it will permanently destroyed.

Statistical methods

Data will be imported into IBM SPSS (version 26 for Windows, Armonk, New York, 2018) for statistical analysis. Data will initially be described using frequencies and percentages, means and standard deviations or medians and quartiles as appropriate, to examine the data and identify any inappropriate values. The normality of the continuous data will be assessed using the Shapiro-Wilk test. The two groups will then be compared using the Pearson chi-square test (or Fisher's Exact test in the event of small cells) for the primary outcome of the incidence of CPSP at 6 months, as well as at 3 and 12 months. Secondary outcomes will be similarly assessed using Chi-square tests for categorical outcomes, and independent samples t-tests (or the Mann-Whitney U) for continuous outcomes. Multivariable logistic regression analyses will be conducted to determine which factors are associated with the development of CPSP. Variables entered into the model will include those with a p-value of <0.15 in bivariate analyses, as well as the assigned group. Statistical comparisons of the secondary outcomes will be considered exploratory and will not be used to assert the efficacy of the treatment in the absence of a statistically significant benefit in the primary outcome. A p-value of <0.05 will be considered as criteria for statistical significance, and no adjustment will be made for multiple comparisons.

Intent to treat analyses will not be conducted. Only data for those participants who completed the trial will be included in the analysis, with no corrections made for missing values.

Oversight and monitoring

Composition of the coordinating centre and trial steering committee

Dr. Tarit Saha is the Principal Investigator (MD, FRCPC) and cardiac anesthesiologist at Queen's University & affiliated teaching hospitals. Dr. Saha is a new investigator despite the fact that he has been an attending cardiac anesthesiologist at Kingston area hospitals since 2004.

Dr. Dimitri Petsikas is the Co-Principal Investigator (MD, FRCSC) and a cardiac surgeon at Queen's University and affiliated teaching hospitals.

Composition of the data monitoring committee, its role and reporting structure

Our Data Safety Monitoring Committee is composed of Dr. Ken Reid, Thoracic Surgeon, and Dr. Catherine McLellan, Cardiologist. None of them have any direct contact with the study. This committee will review adverse outcomes in a blinded fashion half of the way through enrolment.

Adverse event reporting and harms

All serious adverse events (SAEs) will be reported to Principal Investigator immediately and the Research Ethics Board (REB) will be notified. Adverse events also be reported as per institutional policy and will be followed to resolution or stabilization.

A trial audit by our DSMB members will be conducted mid-trial to investigate relevant SAEs in both groups to determine if it is safe to continue.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees)

Any protocol modifications or deviations will be reported to all investigators and will be approved by the REB. The trial Registry will be updated accordingly.

Dissemination plans

The results of our trial will be disseminated through national and/or international conferences, publications, as well as through discussions with cardiac surgeons at other centers.

Trial status

The current investigation is near completion, having randomized and collected primary endpoint data on all patients enrolled. Data collection of remaining secondary endpoints will be completed in early 2021. This is protocol version 1.2.

Data availability

Underlying data

No data are associated with this article.

Extended data

Queen's University Dataverse: Does the Speed of Sternal Retraction during Coronary Artery Bypass Graft Surgery affect Postoperative Pain Outcomes? A Randomized Controlled Trial Protocol <https://doi.org/10.5683/SP2/LQC1JH²⁵>

This project contains the following extended data:

- Consent form
- Post operative data collection form
- Follow up questionnaire (SF-36)
- Follow up questionnaire (BPI, DN4, MPQ-SF)

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](#) (CC-BY 4.0).

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References

1. Liu SS, Wu CL: **Effect of postoperative analgesia on major postoperative complications: a systematic update of the evidence.** *Anesth Analg.* 2007; **104**(3): 689–702.
[PubMed Abstract](#) | [Publisher Full Text](#)
2. Li Z, Armstrong EJ, Parker JP, et al.: **Hospital variation in readmission after coronary artery bypass surgery in California.** *Circ Cardiovasc Qual Outcomes.* 2012; **5**(5): 729–37.
[PubMed Abstract](#) | [Publisher Full Text](#)
3. Jensen TS, Turner JA, Wiesenfeld-Hallin Z, et al.: **Proceedings of the 8th World Congress on Pain.** Progress in Pain Res Manag Seattle IASP Press, 1997; **8**: 231–240.
[Reference Source](#)
4. Rowe MA, King KB: **Long-term chest wall discomfort in women after coronary artery bypass grafting.** *Heart Lung.* 1998; **27**(3): 184–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
5. Steegers MAH, van de Luijckgaarden A, Noyez L, et al.: **The role of angina pectoris in chronic pain after coronary artery bypass graft surgery.** *J Pain.* 2007; **8**(8): 667–73.
[PubMed Abstract](#) | [Publisher Full Text](#)
6. Cantero C, Carolina G, Matute P, et al.: **Eur J Anaesthes conference proceedings EUROANAESTHESIA.** 2011; **28**: 193–194.
7. van Gulik L, Janssen LI, Ahlers SJGM, et al.: **Risk factors for chronic thoracic pain after cardiac surgery via sternotomy.** *Eur J Cardiothorac Surg.* 2011; **40**(6): 1309–13.
[PubMed Abstract](#) | [Publisher Full Text](#)
8. Centers for disease control: **US National Hospital discharge survey.** 2009.
[Reference Source](#)
9. Canadian Institutes for Health Information: **Health indicators interactive tool.** (Information from the discharge abstracts database Jan 1-Dec 31, 2009). Accessed Nov 25, 2012.
[Reference Source](#)
10. Kissin I, Gelman S: **Chronic postsurgical pain: still a neglected topic?** *J Pain*

Res. 2012; **5**: 473–89.

[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

11. Katz J, Seltzer Z: **Transition from acute to chronic postsurgical pain: risk factors and protective factors.** *Expert Rev Neurother.* 2009; **9**(5): 723–44.
[PubMed Abstract](#) | [Publisher Full Text](#)
12. Mailis A, Chan J, Basinski A, *et al.*: **Chest wall pain after aortocoronary bypass surgery using internal mammary artery graft: a new pain syndrome?** *Heart Lung.* 1989; **18**(6): 553–8.
[PubMed Abstract](#)
13. King KM, Parry M, Southern D, *et al.*: **Women's Recovery from Sternotomy-Extension (WREST-E) study: examining long-term pain and discomfort following sternotomy and their predictors.** *Heart.* 2008; **94**(4): 493–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
14. Kalso E, Mennander S, Tasmuth T, *et al.*: **Chronic post-sternotomy pain.** *Acta Anaesthesiol Scand.* 2001; **45**(8): 935–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
15. Lamacraft G: **The link between acute postoperative pain and chronic pain syndromes.** *Southern African Journal of Anaesthesia and Analgesia.* 2012; **18**(1): 45–50.
[Publisher Full Text](#)
16. Bolotin G, Buckner GD, Campbell NB, *et al.*: **Tissue-Disruptive Forces during Median Sternotomy.** *Heart Surg Forum.* 2007; **10**(6): E487–92.
[PubMed Abstract](#) | [Publisher Full Text](#)
17. Bolotin G, Buckner GD, Jardine NJ, *et al.*: **A novel instrumented retractor to monitor tissue-disruptive forces during lateral thoracotomy.** *J Thorac Cardiovasc Surg.* 2007; **133**(4): 949–54.
[PubMed Abstract](#) | [Publisher Full Text](#)
18. Moustafa MA, Abdelsamad AA, Zakaria G, *et al.*: **Minimal vs median sternotomy for aortic valve replacement.** *Asian Cardiovasc Thorac Ann.* 2007; **15**(6): 472–5.
[PubMed Abstract](#) | [Publisher Full Text](#)
19. Candaele S, Herijgers P, Demeyere R, *et al.*: **Chest pain after partial upper versus complete sternotomy for aortic valve surgery.** *Acta Cardiol.* 2003; **58**(1): 17–21.
[PubMed Abstract](#) | [Publisher Full Text](#)
20. Aris A, Cámara ML, Montiel J, *et al.*: **Ministernotomy versus median sternotomy for aortic valve replacement: a prospective, randomized study.** *Ann Thorac Surg.* 1999; **67**(6): 1583–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
21. Bauer M, Pasic M, Ewert R, *et al.*: **Ministernotomy versus complete sternotomy for coronary bypass operations: no difference in postoperative pulmonary function.** *J Thorac Cardiovasc Surg.* 2001; **121**(4): 702–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
22. Mazzeffi M, Khelemsky Y: **Poststernotomy pain: a clinical review.** *J Cardiothorac Vasc Anesth.* 2011; **25**(6): 1163–78.
[PubMed Abstract](#) | [Publisher Full Text](#)
23. Casey KL: **Concepts of pain mechanisms: the contribution of functional imaging of the human brain.** *Prog Brain Res.* 2000; **129**: 277–87.
[PubMed Abstract](#) | [Publisher Full Text](#)
24. Julius D, Basbaum AI: **Molecular mechanisms of nociception.** *Nature.* 2001; **413**(6852): 203–10.
[PubMed Abstract](#) | [Publisher Full Text](#)
25. Petsikas D, Stewart C, Phelan R, *et al.*: **Does the Speed of Sternal Retraction during Coronary Artery Bypass Graft Surgery affect Postoperative Pain Outcomes? A Randomized Controlled Trial Protocol.** *Scholars Portal Dataverse, V1.* 2021.
<http://www.doi.org/10.5683/SP2/LQC1JH>
26. Cleeland CS, Ryan KM: **Pain assessment: global use of the Brief Pain Inventory.** *Ann Acad Med Singap.* 1994; **23**(2): 129–38.
[PubMed Abstract](#)
27. Ware JE Jr, Sherbourne CD: **The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection.** *Med Care.* 1992; **30**(6): 473–83.
[PubMed Abstract](#) | [Publisher Full Text](#)
28. Melzack R: **The short-form McGill Pain Questionnaire.** *Pain.* 1987; **30**(2): 191–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
29. Bouhassira D, Attal N, Alchaar H, *et al.*: **Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4).** *Pain.* 2005; **114**(1–2): 29–36.
[PubMed Abstract](#) | [Publisher Full Text](#)
30. Downie WW, Leatham PA, Rhind VM, *et al.*: **Studies with pain rating scales.** *Ann Rheum Dis.* 1978; **37**(4): 378–81.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

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Ferhat Borulu

Department of Cardiovascular Surgery, Atatürk University Faculty of Medicine, Erzurum, Turkey

First of all, I would like to congratulate the authors for this study, which considers it to be beneficial for postoperative sternotomy pain, which is neglected by most cardiac surgeons.

I'm quite curious about the authors' approach to some issues:

1. Is it considered to establish a relationship between pain and the drains used? Because especially thoracic drains have a highly increasing aspect for postoperative pain. Is there a plan for the effect of drains on the need for pain relief?
2. Information should be given about the retractors to be used in the preparation of the internal thoracic artery. The types of retractors used for this procedure may also contribute to sternum pain.
3. All the details of the study are presented very well. However, it will be very difficult to involve so many patients in working with phones for quite a long time. How will the motivation of the patient and the work team be provided in this regard? It seems to be quite difficult to follow up, especially with the phone.

Since I do not have enough knowledge about statistics, there is no statistical part in my analysis.

I would like to wish success to the working team in advance.

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?

Partly

Are the datasets clearly presented in a useable and accessible format?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Cardiovascular surgery, vascular surgery

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 11 June 2021

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Amr A Arafat

Department of Cardiothoracic Surgery, Tanta University, Tanta, Egypt

The authors submitted a proposal for a randomized clinical trial comparing the effect of the speed of sternal retraction on postoperative pain after coronary artery bypass grafting. The topic is interesting and was not thoroughly evaluated before. Here are my comments and questions related to this proposal:

Title:

- The title is suitable and clearly defines the research topic.

Abstract:

- Please state the objective of your research at the end of the background.
- In the method section, please explain what do you mean by a double-blind study in the abstract?
- The introduction and objectives clearly stated the research gap and question.

Design:

- Suitable to answer the research question.
- Inclusion and exclusion criteria were clearly defined, but please give examples of conditions leading to the inability to perform postoperative assessments.
- The authors did not clarify if the slow method will be used every time the sternal retractor needs to be reinserted. Will you exclude patients who required sternal opening more than the pre-defined diameter?

- Sample size calculation is adequate.

Statistical analysis:

- Longitudinal analysis for repeated measures is required.
- Method sections were clearly described and presented.

References are old. Please cite recent references or state whether there are no recent publications on this topic.

Lastly, I'd like to congratulate the authors on this well-written proposal.

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?

Partly

Are the datasets clearly presented in a useable and accessible format?

Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Cardiothoracic Surgery

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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