UNIVERSITAS INDONESIA

Efficacy of Sternum Guard™ in comparison of Bone Wax in Post Cardiac Surgery Patient: A Single Blind, Single Centre, Randomized Control Trial

STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

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Abstract

Introduction

Median sternotomy is currently the main access site for cardiac surgery. Surgical site infection (SSI) of the sternum is a distressing complication in cardiac surgery after median sternotomy. The incidence of postoperative superficial and deep SSI in cardiac surgery varies from 1.3 to 12.8%. Bone wax is a nonabsorbable substance and it is believed that bone wax may cause inflammation and mechanically inhibit osteoblastic activity, which may eventually lead to increased risk of postoperative sternal dehiscence. Sternum Guard™ is a sternal protection device that covers the sternum after median sternotomy, it has specific mechanical protection that prevents lesions on the sternum. Therefore, we would like to evaluate the efficacy of Sternum Guard™ as opposed to Bone wax in post cardiac surgery patients in reducing the surgical site infection, sternal dehiscence and to assess the satisfaction rate of the surgeons.

Objectives

The aim of the research is to evaluate the efficacy of Sternum Guard™ in post cardiac surgery patient with the application of Sternum Guard™ in comparison with bone wax intraoperatively.

Method

This study will adopt a single blind, single center, randomized control trial design for 3 months.

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Chapter 1

Introduction

1.1 Background

Nowadays, a high volume of cardiac surgery has been performed at National Cardiovascular Centre Harapan Kita, Jakarta, Indonesia. In 2017 there were 1721 cardiac surgery conducted in the adult cardiac surgery division.[1] Of those, 801 were coronary artery bypass graft surgeries, 598 were heart valve repair and replacement surgeries, 93 were vascular surgeries, 116 were congenital cardiac surgeries, 8 surgeries in intracardiac tumour, and 105 other cardiac surgeries.[1]

In cardiac surgeries, the current approach established is through median sternotomy. The sternum consists of a low vascularized tissue and it may be damaged especially when internal thoracic arteries are used for coronary artery bypass grafting. Thus, the postoperative complication related to sternal healing are common. [2-4] The sternotomy wound may be complicated with partial or complete sternal dehiscence and sternal wound infection, osteomyelitis or even mediastinitis. Surgical site infection (SSI) involving the sternum is a distressing complication in cardiac surgery. The incidence of postoperative superficial and deep SSI in cardiac surgery varies from 1.3 to 12.8%. [2]

Subsequent to median sternotomy, bone wax has been applied for decades as a mechanical barrier to maintain the haemostasis on the surface edges of the sternum. Bone wax is a nonabsorbable substance and it is believed that bone wax may cause inflammation as it is produced foreign body reaction and mechanically inhibit osteoblastic activity, which may eventually lead to increased risk of postoperative sternal dehiscence. Apparently, the use of bone wax has no clear recommendation in any guidelines and there are still controversies regarding the efficacy and safety of the application of bone wax. [3-5]

To overcome the problem that may be related to the use of bone wax. Different innovative approaches are evaluated, including, a non-woven material to protect the sternum during operation. Sternum Guard™ is a single use, sterile surgical drape, for sternal protection,

with modified cellulose designed specifically to reduce the risk of surgical site infection. It is a sternal protection device that covers the sternum after median sternotomy and has specific mechanical protection that prevents lesions on the sternum. It is made from a non – woven material. Sternum Guard™ provides haemostatic effect through a natural reaction to compression and blood absorption. Moreover, it decreased the bacterial proliferation by decreasing the pH. The Sternum Guard™ covers the entire incision angle and subcutaneous tissue and it has very low particle release. It is easy to use and maintains a dry surgical site. [6-7]

However, there are still insufficient evidence to support the use of modified cellulose non-woven material in cardiac surgery. Thus, in this study we would like to compare the efficacy of Sternum Guard™ as opposed to Bone wax in post cardiac surgery patients.

1.2 Research Problem Formulation

There is a deficient of evidence to verify the efficacy of Sternum Guard™ in reducing the rates of surgical site infection and sternal dehiscence in post cardiac surgery patients, specifically in Indonesian characteristic subjects. Thus, we would like to conduct this study to provide evidences regarding the use of Sternum Guard™.

1.3 Research Questions

Is Sternum Guard™ more effective than Bone Wax application intraoperatively in reducing surgical site infection and sternal dehiscence for post cardiac surgery patients?

1.4 Hypothesis

We hypothesize that Sternum Guard™ is more effective than Bone Wax in reducing surgical site infection and sternal dehiscence for post cardiac surgery patients.

1.5 Objectives

Overall Objective:

The aim of the research is to compare the efficacy of Sternum Guard™ as opposed to bone wax in post cardiac surgery patient.

Specific Objectives:

1. To compare the surgical site infection and sternal dehiscence rates at the end of hospital stay, day 14 post operation, and day 30 post operation in post cardiac surgery patient with the application of Sternum Guard™ as opposed to bone wax intraoperatively.
2. To compare the haemostasis effect of Sternum Guard™ as opposed to bone wax intraoperatively in cardiac surgery.
3. To compare the satisfaction rate (includes global satisfaction rate, haemostasis and dryness of surgical site, and mechanical protection) of the surgeons who are using the Sternum Guard™ as opposed to bone wax intraoperatively in cardiac surgery.

1.6 Benefit of the Study

1.6.1 Academic Aspect

This study is expected to benefit academically by providing an answer as well as justification on the efficacy of Sternum Guard™ in post cardiac surgery patient in comparison with bone wax intraoperatively.

1.6.2 Clinical Aspect

This study is believed to have impact clinically in reducing surgical site infection and sternal dehiscence in post cardiac surgery patients. By reducing the surgical infection and sternal dehiscence rates it would reduce the morbidities and mortalities rates as well.

1.6.3 Research Aspect

This study could be the foundation of another study in evaluating which aspects that could lead to surgical site infection and sternal dehiscence post cardiac surgery. Additionally, it could identify another effective method to reduce the percentages of surgical site infection and sternal dehiscence in post cardiac surgery patients.

Chapter 2

Literature Review

2.1 Sternum anatomy

Interestingly, the anatomy and physiology of the chest wall and sternum are completely entangled. The musculoskeletal structure of the chest wall and sternum are served to give protection to the lungs and thoracic viscera. The structure of the skeletal of the thorax consists of 12 pairs of ribs and their cartilages, 12 thoracic vertebrae, the intervertebral discs, and the sternum.[8]

The sternum lies in the anterior midline. It is an elongated and flat bone and has approximately 15 to 20 cm long. It is structured from the cartilaginous precursors that ossify separately to form the components in which divided by three parts: the manubrium, the body, and the xyphoid process.[9-10]

The first part is the manubrium, it is about 5 cm wide in its upper half and around 2.5 to 3 cm wide in its lower half. The upper border of the manubrium is solidified and marked on either side by a notch for articulation with the clavicle. Ventrally, an indentation is present together with the sternal ends of each of the clavicle, it forms the jugular or the suprasternal notch. The widest part is distinct by the bilateral indentations, the costal incisura, in which to accommodate articulation of the first costal cartilage.[9]

The second part is the body of the sternum. It is the longest part and slightly more than twice the length of the manubrium. It is skewed at a steeper angle than the manubrium and its articulation with that bone forms the angle that is called the sternal angle. The lateral side of the body expose segmental incisura for articulation of coastal cartilage 2 to 7. This part ends a about the level of the 10^{th} or 11^{th} of thoracic vertebrae, where it forms a cartilaginous joint with the xyphoid process. [9]

The last part of the sternum called the xyphoid process. It is the shortest and thinnest part of the sternum. Occasionally, this part is bifid or perforated. [9]

The blood supply to the sternum has been studied repeatedly over the past decades especially its association with the notorious complication in sternotomy wound healing. The major source of arterial branches to the sternum is the internal thoracic or mammary artery (ITA or IMA). It originates from the subclavian artery directly or sometimes from a common trunk with another artery of the thyrocervical trunk. Before entering the mediastinum, it crosses the phrenic nerve either dorsally or ventrally. It descends 1–2 cm from the lateral margin of the sternum adjacent to the posterior aspect of the chest wall, partly covered by the transversus thoracic muscle from the third to the sixth costal cartilage.[11]

Blood supply to the sternum originate either directly from the medial aspect of the ITA (non-collateral branches) or from short trunks that also give rise to perforating branches to the intercostal and pectoral muscles and overlying skin or to anterior intercostal rami. Sternal blood supply branches are intersegmental, means that it is located in the intercostal spaces and form arcades at the lateral edge of the sternum. It is also more frequent in cranial than in caudal segments, particularly in the second and third intercostal space.

Based on the blood supply anatomy it is evident that harvesting of the ITA or IMA for coronary bypass surgery will interrupt the sternal circulation to some extent. Therefore, when the ITA or IMA is dissected, any branches should be ligated as close as possible to the main vessel in order to preserve the collateral branches.[12]

2.2 Median sternotomy

Median sternotomy remains the most common incision used for cardiac surgical procedures as it offers straightforward access to all cardiac chambers and to the origins and proximal portions of the great vessels. This incision can also be used to repair aortic arch lesions and descending thoracic aortic lesions.

A straight vertical midline skin incision is generally made in patients undergoing a median sternotomy. This incision commences several centimeters below the suprasternal notch and extends to the tip of the xiphoid. The exact midline over the sternum then is scored with the cautery. A retractor elevates the upper angle of the vertical skin incision, placing the underlying tissues on tension. The soft tissue is separated from the superior

surface of the manubrium, and a right-angled clamp is passed over the denuded manubrium into the space behind, hugging the bone. The clamp is spread to create a space for the tip of the sternal saw. The suprasternal ligament is cut with the cautery.[13]

The blade of an electric or air-driven saw is held snugly against the posterior surface of the manubrium with the cutting edge against the superior manubrial surface. After activating the saw, the surgeon cuts the manubrium and sternum, staying precisely in the midline. The tip of the saw is kept elevated so that the toe of the saw hugs the back of the sternum. During sawing, the anesthesiologist should cease ventilating the patient and exert no pressure on the lungs, so that the soft tissue and pleura will fall away from the sternum. Drifting away from the midline with the saw must be avoided because the sternum will not spread evenly, and its later closure will be more difficult.[13]

Alternatively, the sternum can be divided from the bottom up. The xiphoid process is mobilized or excised, and the tip of the blade is introduced beneath it. In neonates and infants, the xiphoid process may be excised, the costal margin on either side elevated by sharp retractors, and sharp, well-aligned scissors used to cut the sternum in the midline, from below upward.[13]

When the incision is properly made, the pleural spaces are infrequently entered. A thin layer of bone wax is spread over the bone marrow, primarily where the bleeding is active. When the sternum is fragile, as in older patients, it is better to avoid wax altogether. Bleeding points in the cut edge of the anterior and posterior sternal periosteum are cauterized, but excessive cauterization should be avoided. A retractor is inserted and opened just enough to permit dissection. After a few minutes, it is opened further. It should be opened no more than is necessary for the procedure, because excessive retraction, particularly of the upper half of the sternum, may cause rib fractures, dislocation of costochondral junctions, injury to the brachial plexus, and damage to the stellate ganglion.[13]

Dissection continues by incising the fascia that envelops the thymus gland. The right and left lobes of the thymus are separated up to the level of the brachiocephalic vein. In infants

and children, and occasionally in adults, the thymus may be sub-totally resected, leaving only the cervical portion cephalad to the brachiocephalic vein, to avoid expanding hematomas that may cause postoperative bleeding.[13] The pericardium is then opened longitudinally in the midline, from the diaphragm below to the brachiocephalic vein above. Where this incision meets the diaphragm, care must be taken not to incise the parietal peritoneum. If entry is made into the peritoneal cavity, the opening is sutured to avoid sequestration of blood and fluid in it. The pericardium is cut at right angles to the longitudinal incision at its diaphragmatic end, farther on the left than on the right, after pushing back the pleura to avoid entering the pleural spaces. Pericardial stay sutures are then placed.[13]

2.3 Complications following median sternotomy

Sternal wound complications following median sternotomy remain a challenge in cardiac surgery with a severe burden for the patient and high costs for health care providers.[14-16] According to previous studies, superficial problems occurred in 1.1–6.7% whereas the incidence of deep sternal wound complications ranged from 0.1 to 3.7%.[17-19]

A change in the spectrum of cardiac surgery has been observed in recent years. Patients are older, suffer more frequently from diabetes mellitus and have a higher average body mass index (BMI). There is a decreasing number of surgical bypass grafts[20,21] accompanied by a trend towards more valve operations and complex procedures. In addition, the frequency of emergency procedures is rising.[22]

2.4 Surgical site infection

Over 234 million surgeries are performed around the world every year[23], yet despite the remarkable advances in surgical technologies and anaesthetic techniques, surgical site infections (SSIs) remain a major cause of patient morbidity and mortality.[24] SSIs are potential complications associated with any surgical procedure; however, they are the most preventable hospital acquired infection (HAI). It is estimated that SSI will occur in up to 9.5% of inpatient surgical procedures. SSI is defined as any infection occurring within 30 days after surgery or within 12 months of surgical implantation of a prosthesis or foreign body.[23]

Millions of surgical procedures are conducted around the world each year. Most procedures result in surgical wounds that heal by primary intention, where wound edges are re-approximated using sutures, staples, clips or glue. Some surgical wounds are left open to heal (where closure is not appropriate because of infection, physical impossibility of approximating wound edges or because of the need to allow drainage) and some wounds break down following closure; these open wounds heal from the 'bottom-up' (known as 'healing by secondary intention').[23]

Surgical wounds are at risk from microbial contamination and thus possible infection. Contamination may originate from the patient, for example when microbes on the skin enter a wound, or from the surrounding environment, for example from operating staff, the theatre, or wider hospital and home environments. SSI was identified as the leading cause of hospital-acquired infection in a systematic review of studies in low-and middle-income countries.[25]

SSI is a serious global issue that can lead to significant morbidity, need for re-intervention and treatment (including antibiotic use), delayed wound healing, and in very serious infections, the possibility of death.[26,27] SSIs also increase consumption of healthcare resources. Recent figures from the UK suggest that SSIs lead to a median increased hospital stay of 10 days (95% confidence interval (CI) 7 to 13 days) with an associated median additional cost attributed to SSI of GBP 5239 (95% CI GBP 4622 to 6719). The UK National Institute for Health and Care Excellence (NICE) identified that an SSI increased the costs of surgery by two to five times.[28] In the USA, Lissovoy et al[29] estimated that the extended length of stay and increased treatment costs associated with SSIs over a one-year period led to approximately 1 million additional inpatient-days, costing an additional USD 1.6 billion.

Definition of SSI

Although there is no single agreed diagnostic tool or protocol to confirm the presence of an SSI, Bruce et al [30] identified 41 different definitions for SSI and 13 grading scales, the Centers for Disease Control and Prevention (CDC) definition is commonly used.[31]

A **superficial SSI** is defined as: an infection occurring within 30 days after the operation and only involving the skin and subcutaneous tissue of the incision that is associated with at least one of the following:

- Purulent drainage, with or without laboratory confirmation, from the surgical site;
- Organisms isolated from an aseptically-obtained culture of fluid or tissue from the surgical site;
- At least one of the following signs or symptoms of infection: pain or tenderness, localised swelling, redness or heat, *and* superficial incision is deliberately opened by the surgeon and is culture-positive or not cultured. A culture-negative finding does not meet this criterion;
- Diagnosis of SSI by the surgeon or attending physician.

A **deep incisional SSI** is defined as: infection that occurs within 30 days after the operative procedure if no implant is left in place, or within one year if an implant is left in place, and the infection appears to be related to the operative procedure *and* involves deep soft tissues (e.g. fibrous connective tissues and muscle layers) of the incision associated with one of the following:

- purulent drainage from the deep incision, but not from the organ/space component of the surgical site;
- a deep incision spontaneously dehisces (opens up) or is deliberately opened by the surgeon and is culture-positive or not cultured when the patient has at least one of the following symptoms: fever or localised pain or tenderness;
- an abscess, or other evidence of infection involving the deep incision is found on direct examination, during re-operation, or by histopathologic or radiologic examination;
- diagnosis of a deep incisional SSI by a surgeon or attending physician.

Interventions

Many interventions are used with the aim of reducing the risk of SSI in people undergoing surgery. These interventions can be delivered at three stages: preoperatively, intraoperatively and postoperatively[32]

- Preoperative phase: the time period between the decision for the need for surgery and when everything is ready for the operation to start, that is, the patient is on the operating table.
- Intraoperative phase: the time period from when the patient is on the operating table to when the operation has finished and the wound is closed (if relevant). Any activity taking place after induction of anaesthesia to be in this phase because this starts in the operating theatre itself.
- Postoperative phase: as the time period from the end of the intraoperative phase to resolution of surgical procedure. Whilst dressings, wound drains and negative pressure wound therapy are often placed over wounds at the end of surgery, their use is predominantly outside of theatre, so they are considered in the postoperative phase.

2.5 Risk factors for sternal wound infections

The risk factors for sternal wound infection is multifactorial. Any factors that contributes to poor wound or bone healing (e.g. malnutrition, osteopenia) or increases the risk for surgical site infection (e.g. diabetes mellitus, immunosuppression) may influence the manifestation of sternal wound infection, especially if two or more factors are present. [33-40] There are several retrospective and prospective studies that have identified other factors relating to sternal wound infection. It is included obesity, diabetes mellitus, hypertension, chronic obstructive lung disease (COPD), smoking, steroid therapy, immunosuppression, advanced age, congestive heart failures, and respiratory failures. [41-42]

There are also technical factors that play a role in the risk of sternal wound infection or even sternal dehiscence. It may include prolonged operative time, the need for chest compression, postoperative bleeding, intraoperative complication, transfusion, reoperation, asymmetric sternotomy incision that is difficult to realign, bone ischemia due to excessive use of electrocautery or possibly internal thoracic artery harvesting

(especially if bilateral), or even the excessive use of bone wax around the sternal edges intraoperatively. [42-45]

Bone Wax

Bone wax was first introduced in medicine in 1886. It is a sterile stick and is used as a topical haemostatic material composed of a softening agent such as Vaseline and beeswax. When it is applied on the surface of the bones, it remains indeterminately and may cause various adverse effects. [46-48]

At first the primary reason for using bone wax is to maintain haemostasis. However, it has no biological or chemical hemostatic effect. One study stated that the hemostatic effect of bone wax is associated with the physical blocking of the holes in the bone and stopping the blood flow from damaged vessels into the bone. However, the literature data do not support a reduction of blood or blood product consumption as a result of a presumably decreased perioperative blood loss when using bone wax. [46]

Additionally, bone wax is known to inhibit bone healing and osteogenesis. It inhibits the osteoblastic activity, prevent bone healing and may lead to creation of a pseudo-arthrosis. A sternal wound is different than other bone wound, it is associated with the exertion of dynamics of a chest wall mobility especially in the work of breathing. Thus, the osteogenesis and the wound healing is very important. It is reported that chronic inflammatory reactions with the presence of residual bone wax exist up to 10 years after the operation. [48-54]

Bone wax is not an absorbable or metabolized material. It may induce a foreign body reaction which characterized by giant cells, plasma cells, fibrous tissue, and a lack of bone formation, that may trigger an allergic reaction or granuloma formation. [47-48, 52-54] In anatomic-pathology study of 18 cadavers by Sudmann et al, it was reported that bone wax induces chronic inflammation and granuloma formation in the sternum postoperatively.[55]

Moreover, bone wax has shown to be related with pulmonary embolic events. In an experimental study, in which, there were radioactively labelled bone wax applied at the sternal wound. It was found that bone wax accumulated in significant quantities in the

lung. This shows that bone wax may embolize and may give rise to secondary pulmonary complications.[54]

2.6 Deep sternal wound infection

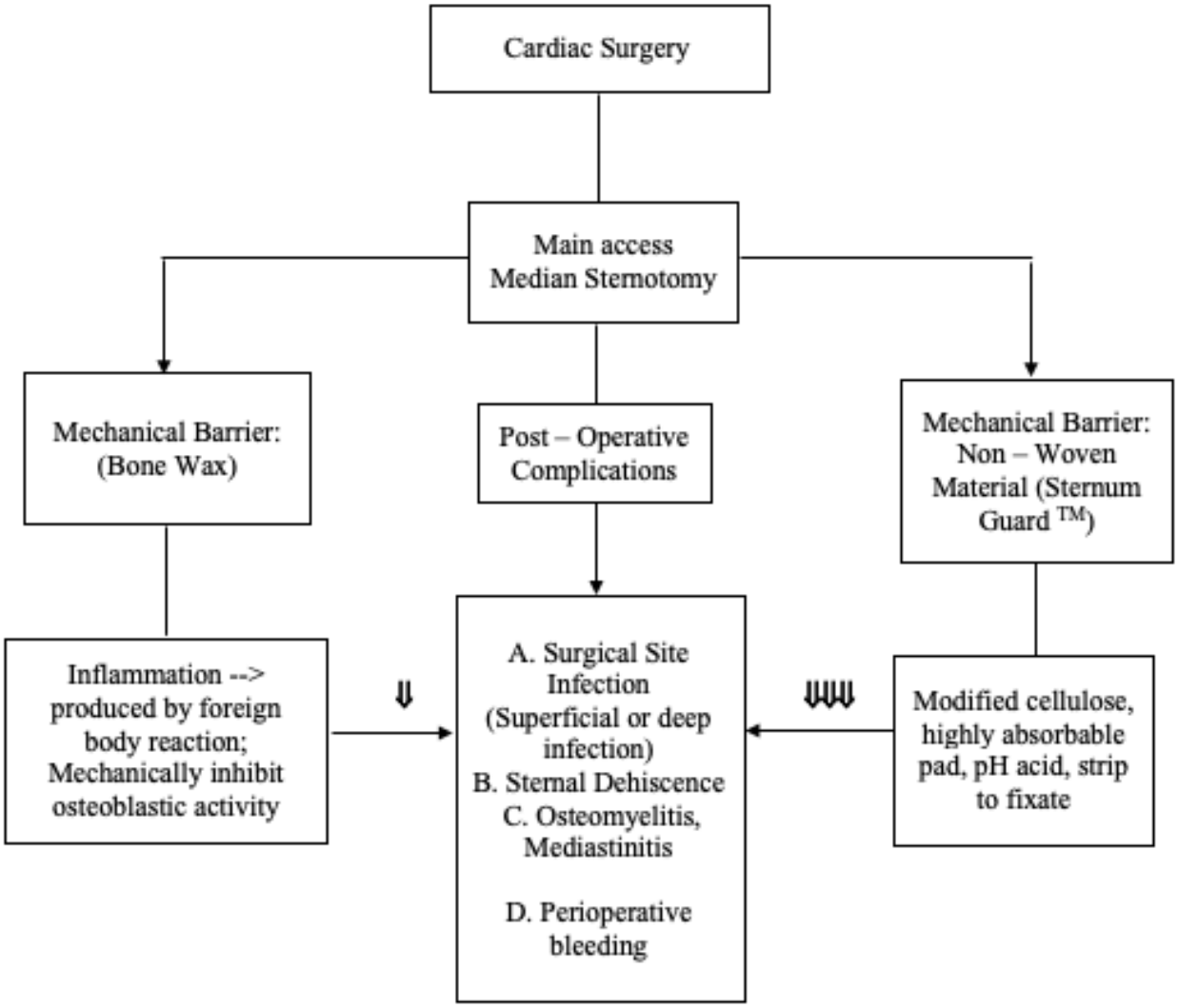
Deep sternal wound infection (DSWI) is a serious postoperative complication of cardiac surgery. According to the literature, the incidence of DSWI after cardiac surgery has been variously reported as between 0.8 and 5.0%.[55-59] This postoperative complication is a serious one, being responsible for a mortality rate varies between 19% and 29% in different series of adult cardiac surgical patients. [55-59] Based on JACVSD registered data from 2004 to 2009, the overall incidence of DSWI after cardiac surgery was 1.8%, as for each operative procedure, the incidence of postoperative DSWI was 1.8% in isolated CABG group, 1.3% in valve group, 2.8% in valve with CABG group, 1.9% in thoracic aorta group and 3.4% in thoracic aorta with CABG group. When operative procedure concomitant with CABG was done, the incidence of postoperative DSWI showed 1.5% of elevation compared with isolated original valve and thoracic aortic procedure. Internal thoracic artery use, prolonged operative time and longer cardiopulmonary bypass time are possible mechanisms to explain these increased rates of DSWI.

2.7 Sternal dehiscence

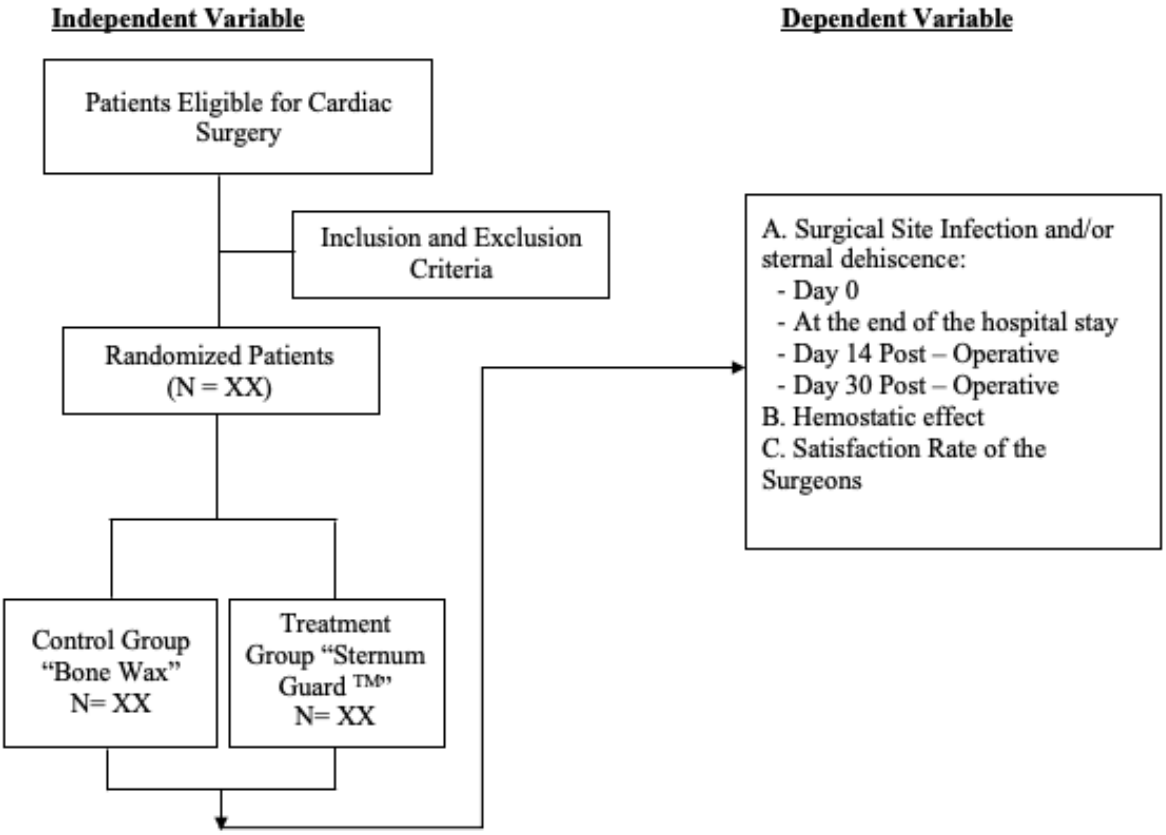
Sternal Dehiscence is a serious complication of cardiac surgery which is often a predecessor to mediastinitis, in fact it is often accompanied with mediastinitis. The incidence of sternal dehiscence after median sternotomy is varied between 0.5% to 8.4%. [60-63] Sternal dehiscence is defined as the separation of the edges of the sternum from one to another and can occur in the absence of soft tissue dehiscence. This condition can be caused by wire fracture, loosening, or “puling through” the sternal edges. [64]

Patients may complain of a painful chest motion and “clicking”. The diagnosis is made upon physical examination by placing each hand on either side of the sternum and having the patient cough, which will cause a click or “rocking” of the sternum[64]. Sternal dehiscence is a surgical emergency as the complication may include an increased risk of ventricular rupture due to sharp wires or bone fragments rubbing against the heart. When sternal dehiscence occurs in the early postoperative period, the patient is taken to the operating room for exploration.[64-65]

Theoretical Framework



Conceptual Framework



Chapter 3

Methods

3.1 Design

This study will adopt a single blind randomized control trial design for 3 months.

3.2 Time and location

This study will be conducted for 3 months, starting from December 2019 – February 2020. It will be held at the National Cardiovascular Centre Harapan Kita, Jakarta, Indonesia.

3.3 Sample and population

The participant in this study will be recruited from the adult cardiac surgery division at the National Cardiovascular Centre Harapan Kita, Jakarta, Indonesia. All participants will be selected randomly and are eligible for cardiac surgery. Participants then will undergo an eligibility assessment based on the inclusion and exclusion criteria. Afterwards, the participants that are qualified for this study will be divided into two groups (control vs treatment group) randomly.

3.4 Inclusion and exclusion criteria

Inclusion Criteria:

1. Patients ages > 18 years old
2. Patients who are scheduled electively for cardiac surgery
3. Cardiac surgery with the usage of cardiopulmonary bypass machine
4. Patients who are agreed to participate in this study

Exclusion Criteria:

1. Patients who are scheduled for surgery in emergency or urgent manner
2. Patients with the history of uncontrolled hypertension and uncontrolled diabetes mellitus.
3. Patients with the history of past cardiac surgery

Drop – out Criteria:

1. Patients who are pronounced death on operation table
2. Patients who are pronounced death within hospitalization
3. Patients who are lost to follow up (Day 30 post-operative)
4. Patients who are not committed for the whole stage of the research

3.5 Randomization and blinding procedure, and assessment schedule

Participants which are included in this study will be randomized into two groups: A. Control Group (Bone Wax) and B. Treatment Group (Sternum Guard™). The randomization process will be conducted by a *block randomisation technique*. This study is conducted in a single blind manner. The surgeons will not be blinded by the intervention, as it is impossible for the surgeons to not acknowledge the intervention. The participants on both groups will be blinded for the intervention given. The project leader will also be blinded when gathering and assessing the data from the study. Both of the groups then will be assessed for outcomes intraoperatively, at the end of the hospital stay, day 14 post – operative, and day 30 post - operative. The surgeons' point of view on both interventions will be evaluated after the surgery.

3.6 Data extraction

Every participant included in this study will be scheduled for any cardiac surgery electively. Every participant will undergo the surgery with cardiopulmonary bypass. All of the surgery will be conducted in a similar manner, however, if there is any complication intraoperatively, every action will be taken according to the situation and will be recorded. Before incision the Sternum Guard™ and sterile drapes for the bone wax group will be weighed. After median sternotomy, the surgeons will be given Bone Wax or Sternum Guard™ to be applied to the sternum. The decisions will be made based on the block randomisation technique and will be informed beforehand to the nurse scrub and the surgeon. In the Bone Wax group, cauterization will be used according to the sternum's condition and surgeon's decision before applying the sterile draping and after removing it if needed. In the Sternum Guard™ group, cauterization will also be applied before inserting it to the sternum and after removing the Sternum Guard™ if needed.

Subsequent to median sternotomy, sternal bleeding will be assessed. In the Sternum Guard™ group, immediately before cauterization and in Bone Wax group right before applying the bone wax.

Once the surgery is done, the Sternum Guard™ and the sterile drapes will be weighed again. Sternal trauma will be evaluated at the end of surgery (visible trauma or no visible trauma). In the Sternum Guard™ group, within 5 minutes of Sternum Guard and sternal retractors removal and on the Bone Wax group within 5 minutes of removal of the sterile drapes and sternal retractors. Another sternal bleeding assessment will be done on both groups. in the Sternum Guard™ group it will be assessed immediately after removing the Sternum Guard, before the cauterization, while on the Bone Wax group, before applying any bone wax and cauterization. The sternotomy wound will be evaluated and documented at Day 0, at the end of hospital stay, Day 14 post - operative, and Day 30 post-operative. After the surgery, the surgeons will be given questionnaire regarding the use of Sternum Guard™ as opposed to Bone Wax.

3.7 Sample size estimation

The sample size in this study is estimated by using the formula for hypothesis tests for two population proportions (two-sided test)

$$n = \frac{\left\{Z_{1-\alpha/2}\sqrt{2\bar{P}(1-\bar{P})} + Z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}\right\}^2}{(P_1-P_2)^2}$$

details:

α : 5

1-β : 90

P_1 : 0.15

P_2 : 0.05

n : 376

From the equation above, it is estimated for the sample size of the study to be 376 samples, with estimated drop out proportion of 10%, it is deduced the sample size of 414 samples.

3.8 Variable identification

Independent variable in this study included the patient that are eligible for cardiac surgery. Dependent variable in this study are the assessment of surgical site infection and sternal dehiscence, haemostasis effect in Sternum Guard™ and Bone Wax group, and satisfaction rates of the surgeons.

3.9 Data analysis

All collected data will be verified and will be statistically analyzed using SPSS and the result from the data analysis was considered statistically significant with a p-value of < 0.05. For descriptive analysis, we will perform the analysis independently for numerical and categorical data. All numerical data will be analyzed using Coefficient of Variance and confirmed by Kolmogorov-Smirnov normality test. Normally distributed data will be analyzed using mean and standard deviation, meanwhile the abnormally distributed data will be analyzed using median, minimum value and maximum value. Categorical data analysis will be presented by percentage and frequencies table.

For inferential data analysis, we will perform the comparison tests and mean comparison test. The proportion comparison tests are applied for comparing categorical independence variable between Sternum Guard™ and bone wax group, such as Chi-square test and Fisher's Exact test as an alternative for chi-squared test. Mean comparison tests are utilized for comparing numerical independence variable between Sternum Guard™ and bone wax group, such as Independent T-Test and Mann-Whitney test for the non-parametric test.

3.10 Clinical outcome indicators and assessments

1. Surgical site infection: assessment of the surgical site infection includes the types of infection (deep and superficial), sternal dehiscence, and percentage of the surgical site infection and sternal dehiscence. The participants will be assessed at day 0, at the end of the hospital stay, day 14 post - operative, and day 30 – post operative. All of the sternotomy wound will be documented digitally at day 0, at the end of the hospital stay, day 14 post – operative, and day 30 post-operative.

2. Haemostasis effect: It will assess the quantity of blood lost from the sternal edges in Sternum Guard™ and Bone Wax group. The Sternum Guard™ and sterile drapes will be weighed before and after surgery to estimate the blood lost.

3. Satisfaction Rate: The satisfaction rate will be evaluated using a questionnaire distributed to the surgeons. The questionnaire will contain overall satisfaction, ease of placement, maintenance of a dry field throughout the surgery, ease of removal; each of this question will have four different response which are satisfied, fairly satisfied, fairly dissatisfied, dissatisfied. Additionally, the surgeons will be asked about the experience in using Sternum Guard™ as compared to Bone Wax and it will contain 3 different response: worse, similar, better.

3.11 Operational definition

A. Control Group with Bone Wax:

Group of patients who undergo cardiac surgery with the use of cardiopulmonary bypass and use Bone Wax to protect the sternum after median sternotomy.

B. Treatment Group with Sternum Guard™:

Group of patients who undergo cardiac surgery with the use of cardiopulmonary bypass and use Sternum Guard™ to protect the sternum after median sternotomy.

Table 1 - Table of Operational Definition

	Variable	**Definition**	**Type of Data**	**Code**
1	Age	The age of participant when undergo the cardiac surgery, it defines with calculated birth year taken from the medical record	Numerik	
2	Gender	Gender which is included in this study are based one the	Categorical	1 = Male 2 = Female

		data recorded in the medical record.		
3	Comorbid	Data extracted from anamnesis and the medical record, with blood pressure ≥140/90 mmHg and diabetes mellitus (Fasting Blood Glucose >126 mg/dL or 2 hr post prandial blood glucose or one time blood glucose >200 mg/dL)	Categorical	1 = Yes 2 = No
6	Cardiac Surgery	Any cardiac surgery that are conducted in adult cardiac surgery division which are using cardiopulmonary bypass	Categorical	1 = CABG 2 = Valve 3 = CABG + Valve 4 = Vascular
7	Surgical Site Infection	Surgical site infection is divided by 2 categories (Superficial: infection occurs just in the area where the incision is made; Deep: occurs beneath the incision area in muscle and the tissues surrounding the muscle). It is evaluated at day 0, at the end of hospital stay, day 14 post – operative and day 30 post-operative	Categorical	1 = Deep 2 = Superficial
8	Sternal Dehiscence	Occurs when there is an evidence of sternum separation. Often	Categorical	1 = Yes 2 = No

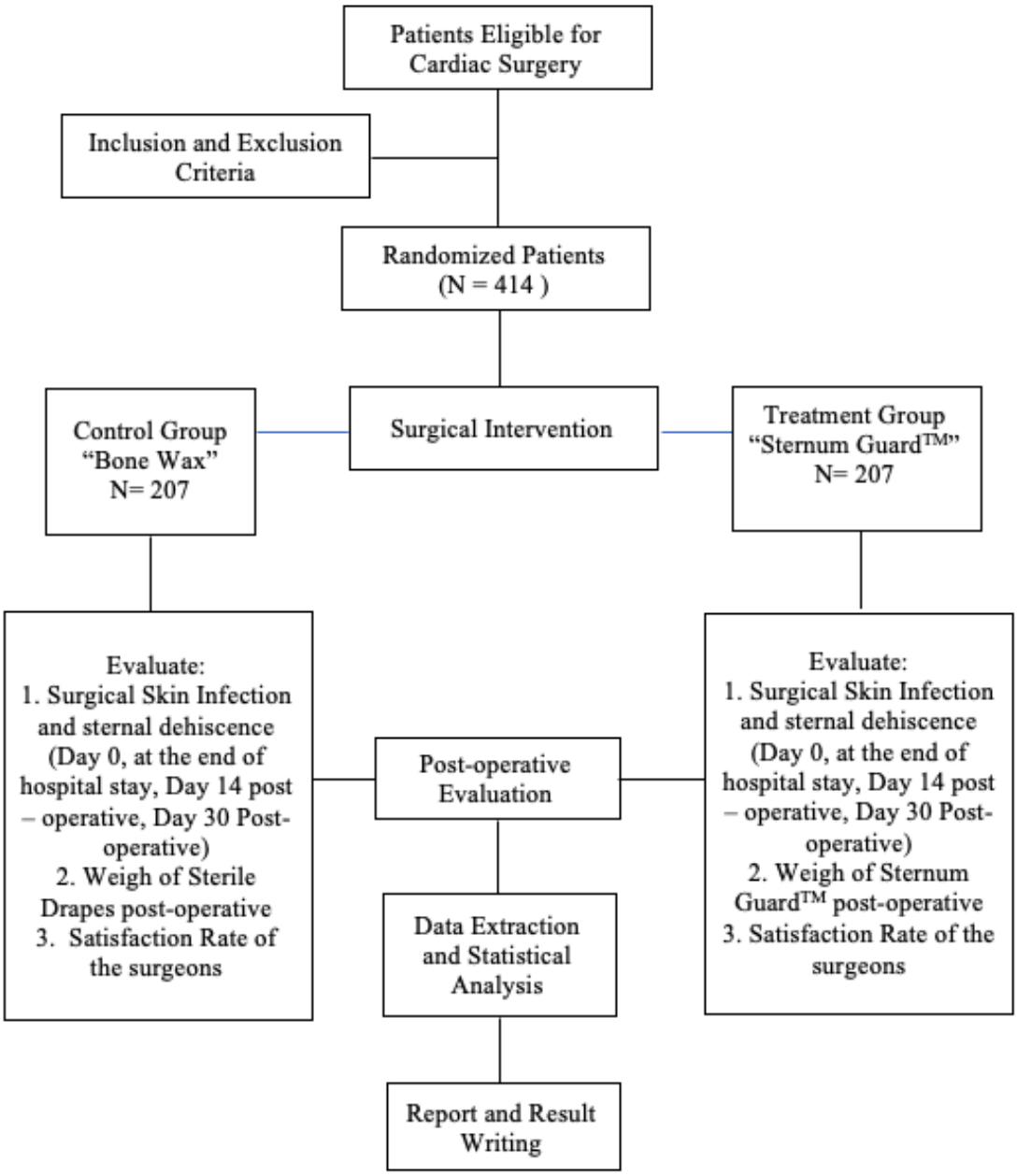
		accompanies with mediastinitis.		
9	Haemostasis Effect	The data obtained by quantity of blood lost from the sternal edges in Sternum Guard™ and Bone Wax group. The Sternum Guard™ and sterile drapes will be weighed digitally before and after surgery to estimate the blood lost.	Numeric	
10	Satisfaction Rate	The result obtained by the questionnaire in both groups. Overall satisfaction rate Maintenance of a dry surgical field during intervention (both groups) Haemostatic effect Ease of insertion (Sternum Guard™ group) Ease of removal (Sternum Guard™ group)	Categorical	1 = Satisfied 2 = fairly satisfied 3 = fairly dissatisfied 4 = dissatisfied
12	Experience satisfaction rate	The result obtained by the questionnaire for the Sternum Guard™ group.	Categorical	1 = worse 2 = similar 3 = better

13	Uncontrolled Diabetes Mellitus	A fasting plasma glucose (FPG) level of 126 mg/dL or higher, *or* a random plasma glucose of 200 mg/dL or higher, *or* hemoglobin A1c (HbA1c) level of 6.5% or higher.	Categorical	1 = yes 2 = no
14	Uncontrolled Hypertension	An average Systolic Blood Pressure of ≥140 mmHg or an average Diastolic Blood Pressure of ≥90 mmHg, among those with hypertension	Categorical	1 = yes 2 = no

3. 12 Ethics

This study will be reviewed by the committee ethics in the National Cardiovascular Centre Harapan Kita.

3. 13 Research flow



3.14 Dummy table

Participant Characteristic

Table 2 - Dummy Table 1

	Sternum Guard ™		Bone Wax	
	N	%	N	%
Age **				
Male *				
CABG *				
CABG + VALVE*				
VALVE *				
VASCULAR *				
Hypertension *				
Diabetes Mellitus *				
CPB time < 60 minutes *				
CPB time > 60 minutes *				

***) n(%)**
****) mean + SD**

Outcomes

Table 3 - Dummy Table 2

	Sternum Guard ™		Bone Wax	
Primary Outcomes	N	%	N	%
Surgical Site Infection:				
Superficial *				
Deep *				
Sternal Dehiscence:				
Yes *				
No *				
Haemostasis Effect (gr)**				
Satisfaction Rates **				
Satisfied				
Fairly satisfied				
Fairly dissatisfied				
Dissatisfied				

***) n(%)**
****) mean + SD**

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Appendix

Table 4 - Time Schedule

	Activity	Months (2019-2020)								
		7	8	9	10	11	12	01	02	03
1	Literature Writing									
2	Ethical Approval									
3	Data extraction									
4	Statistical Analysis									
5	Result									

Cost Details:

Table 5 – Resources fee

	Resources	Persons	Fee/hours	Hours/week	Total hours	Total Amount
1.	Researcher	1	Rp. 170.000*	30 hours	360 hours	Rp. 61.200.000
2.	Assistant	2	Rp. 100.000*	30 hours	360 hours	Rp. 36.000.000
		Total Amount				Rp. 97.200.000

Remarks: * (estimated fee)

Table 6 - Materials Cost

No	Materials	Pieces	Price Per piece	Total Amount
1.	Sternum Guard™	207	Rp. 1,280,000	Rp. 264.960.000 **(FREE FROM VYGON)**
2.	Scale	4	Rp. 100,000	Rp. 400,000
	Total Amount			Rp. 400.000

Table 7 - Operational Cost

No	Details	Pieces	Price per Piece	Total Amount
1.	Stationery	10	Rp. 50,000	Rp. 500,000
2.	Copies of Files	500	Rp. 500	Rp. 250,000
3.	Miscellaneous (file holder, binder, printer ink jet, etc)	200	Varies (Rp. 10.000 – Rp. 400.000)	Rp. 2,500,000
	Total Amount			Rp. 3.250,000

Table 8 - Total Amount

Total Amount (Rp)	Rp. 100.850.000
Statement	One hundred million and eight hundred and fifty thousand rupiah

Questionnaire for the Surgeons

Efficacy of Sternum Guard™ in comparison of Bone Wax in Post Cardiac Surgery Patient: A Single Blind, Single Centre, Randomized Control Trial

Research Principles: dr. Konda Kinanti Muroso, B.MedSc. ; Dr. dr. Dudy A Hanafy, Sp. BTKV (K) MARS.

Please tick (√) the box accordingly; Please leave your comment(s)

Section 1 (Sternum Guard)	**Surgeon's Satisfaction with Sternum Guard**				
	Satisfied	**Fairly Satisfied**	**Fairly Dissatisfied**	**Dissatisfied**	**Comments**
Overall Satisfaction					
Ease of placement					
Maintenance of a dry field throughout the surgery					
Haemostasis effect					
Ease of removal					
Section 2	**Surgeon's Experience in using Sternum Guard as opposed to Bone Wax**				
	Worse	**Similar**	**Better**		**Comments**
Experience of the surgeon in using Sternum Guard as compared to Bone Wax					

Comment(s):
1.

Time and Date: Group:
Investigator: Patient's initial:

Questionnaire for the Surgeons

Efficacy of Sternum Guard™ in comparison of Bone Wax in Post Cardiac Surgery Patient: A Single Blind, Single Centre, Randomized Control Trial

Research Principles: dr. Konda Kinanti Muroso, B.MedSc. ; Dr. dr. Dudy A Hanafy, Sp. BTKV (K) MARS.

Section 1 (Bone Wax)	**Surgeon's Satisfaction with Bone Wax**				
	Satisfied	**Fairly Satisfied**	**Fairly Dissatisfied**	**Dissatisfied**	**Comments**
Overall Satisfaction					
Ease of placement					
Maintenance of a dry field throughout the surgery					
Haemostasis effect					
Ease of removal (if any)					

Comment (s):
1.

Time and Date: Group:
Investigator: Patient's initial: