Peer Review File

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Reviewer A

Comment: Osteomyelitis (OM) was one of the significantly poor complications after a median sternotomy. It may occur relatively longer after surgery, and it takes a long period to treat. The authors presented their 15-years-experience of the treatment of sternal OM after a median sternotomy. The present study enrolled 3,460 patients and was designated to two groups. The study group included 16 patients with the sternal OM that occurred one to eleven months after surgery. The control group was composed of 32 patients with the absence of sternal OM and similar variables using a matching method which could play an essential role in this study. However, it was not clear what the matching method was likely. Therefore, the author might better describe the statistical method for the correction, especially regarding matching. In addition, I believe the author could tell cofounders and propensity scores.

Reply: Thank you for your comments. We carefully selected a control group with exact matching to choose patients negative for sternal OM with demographic variables (i.e., age and sex) similar to those of the patient with sternal OM. Because the number of patients without any signs of wound infections after median sternotomy was rather small, we could only apply 1:2 ratio matching. We added this in the manuscript. Changes were done in line 105

Reviewer B

Dear authors,

I would like to congratulate you for the effort to carry out this study addressing this rare event, but still relevant in the daily life of every surgeon in the cardiothoracic segment.

I present some comments in order to propose improvements:

Comment 1: the reference for the diagnostic criteria for osteomyelitis is from 1992, but the CDC updates them regularly. Is there any difference between the presented version and the current version?

Reply 1: This 1992 data is not the diagnostic criteria for OM, but the terminology of deep sternal wound infection based on involved anatomic layer, which it was type 2D for our sternal OM cases. In this study, these diagnostic criteria was done by today's criteria.

To confirm the diagnosis of DSWI, the group reviewed the database and collected relevant information regarding the patients, including their clinical records, laboratory examination results and also CT findings.We used diagnostic criteria by Centers for Disease Control and Prevention (CDC), DSWI must meet at least one of the following three criteria: 1) organism(s) are identified from mediastinal tissue or fluid by a culture- or nonculture-based microbiologic testing method that is performed for the

purposes of clinical diagnosis or treatment (not for surveillance purpose); 2) evidence of mediastinitis on gross anatomic or histopathologic exam and 3) patient has at least one of the following signs or symptoms: fever (>38.0°C), chest pain, or sternal instability, and at least one of the following: purulent drainage from mediastinal area or mediastinal widening on imaging test. → reference: Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of healthcare-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control. 2008;36(5):309–332. We added this reference in the text. Line 68

Comment 2: were risk factors related to the nutritional status of the patients, such as preoperative albumin and hemoglobin, investigated?
Reply 2: Thank your for nice comments. As reviewer comments, we checked preoperative serum albumin and hemoglobin, however there were no statistical significance in these factors. We have added this in the text. Line 116

Comment 3: Was the postoperative follow-up time in the control group evaluated? As osteomyelitis can take a while to show clinical signs, it may be relevant to inform this data.
Reply 3: Yes, we evaluated postoperative follow up time in the control group as like sternal OM group. 3 patients were follow up loss. The follow up range was between 5 months to 84 months with mean 38 months. We added this in the manuscript. Line 118

Comment 4: as some of the data related to the matching are also historically known risk factors, can the matching performed to choose the control group interfere with the results presented?
Reply 4: We carefully selected a control group with exact matching to choose patients negative for sternal OM with demographic variables (i.e., age and sex) similar to those of the patient with sternal OM. And since age and sex are not historically known risk factor for sternal OM, we believed these factors did not interfere with Because the number of patients without any signs of wound infections after median sternotomy was rather small, we could only apply 1:2 ratio matching. We added this in the manuscript. Line 105

Reviewer C
Thank you for the kind opportunity to review this article.

Firstly, I would like to congratulate the authors on achieving such excellent results in their patient cohort. OM is a devastating complication and such low rates over a sustained period of time has to be congratulated.

I have the following comments:

Comment 1: The overall rate of OM is only 0.47% over a period of 15 years. How

was the number of patients required calculated? With such low incidence rates, it is difficult to draw statistical analysis further.
Reply 1: We analyzed 3410 consecutive patients who underwent cardiothoracic surgery via median sternotomy from January 2005 to December 2019 at our institution. From 3410 patients, 16 patients had sternal OM. And from this data we got 0.47% for sternal OM in our patient cohorts. And we believed there were lot more of DSWI in these 3410 patients, however we only focused and found the incidence and risk factors of sternal OM after the median sternotomy. Most of the papers reported incidence of DSWI after the median sternotomy, but not the sternal OM itself. Text included that this study was to first to present incidence of sternal OM after median sternotomy rather than DSWI. This is in discussion section line 149

Comment 2: How long was the average follow up period for patients? How many patients were lost to Follow up? Would this affect the diagnosis of OM as there would be a percentage of patients who would be undiagnosed? A flow chart would help
Reply 2: Yes, we evaluated postoperative follow up time in the control group as like sternal OM group. 3 patients were follow up loss (control group). The follow up range was between 5 months to 84 months with mean 38 months. We added this in the manuscript. We believe that in our patient groups, follow up period was sufficient enough that undiagnosed sternal OM may have occurred except for 3 patients with follow up loss. Line 118
Three patients were follow up loss.

Comment 3: What was the overall morbidity associated with OM?
Reply 3: We included in the text. Line 127

	Sternal OM group	Control group
Bleeding control	3	1
VA ECMO or IABP	2	2
ARDS	0	1
CVA	0	1
ICU stay > 10 days	1	2
Preoperative CPR	1	1

Comment 4: What was the mortality rate in your series?
Reply 4: Mortality rate was 5/32 (16%) from the control group, however no case of mortality was found on the sternal OM group. We included this in the text. Line 128

Comment 5: What percentage of patients required prolonged ICU stay?
Reply 5: In our study group, patients with prolonged ICU stay (more than 10 days) were 3 patients. 17, 18 and 51 days respectively. 2 of 32 patients (6.3%) of control group had prolonged ICU stay and one of 16 patients (63%) of sternal OM group had prolonged ICU stay (51 days) and this patient is still follow up on our hospitial without any signs of wound problem (19.9 months). We included this in the text. Line 120

Comment 6: reoperation/flap coverage etc?
Reply 6: In the sternal OM group, reoperation for postoperative wound rate was 10/16 (63%) and only one patient had omental flap coverage, whereas 9 patients received surgical debridement. We included this in the text. Line 123

Comment 7: Postop CABG OM occurred in 7/16 Patients:
what was the surgical technique used for CABG? grafts used included SVG ? BIMA? RA? please clarify
Reply 7: We used bypass graftof left internal thoracic artery, right internal thoracic artery and great saphenous vein. For LAD we used LITA and for OM, PDA and PL branches, we usued as by surgeons' preference for right internal thoracic artery and great saphenous vein. We added this in the text. Line 82

Operation type	Sternal OM	Control group
CABG	7	19

	Study group	Control group
Conventional CABG	3	0
On-pump beating heart CABG	4	5
OPCAB	.0	14

Comment 8: The paper states there was only 3 surgeons who performed surgery over 15 years. Please clarify. Was the surgical technique standardized over 15 years?
Reply 8: All the surgical procedure were performed as standardized technique at the time and cardiac or aortic surgeries were performed 45 cases and 3 cases of thoracic surgery were performed. We included this in the text. Line 85

Comment 9: How was the control group selected? randomly? was propensity matching used for risk factor control? please clarify
Reply 9: We carefully selected a control group with exact matching to choose patients negative for sternal OM with demographic variables (i.e., age and sex) similar to those of the patient with sternal OM. Because the number of patients without any signs of wound infections after median sternotomy was rather small, we could only apply 1:2 ratio matching. We added this in the manuscript. Line 105

Comment 10: The conclusion of the article as it stands, fails to add significant educational value. If there is discrepancy between known risk factors for OM and your database, how do you explain this?
Reply 10: The sentinel event for the pathogenesis of sternal OM after median sternotomy remains a matter of debate. The proposed causes include the direct spread of pathogens associated with a local infection versus hematogenous dissemination. Regardless of the inciting event, pathogens invade the metaphyseal arterioles and

cause microabscesses, which eventually coalesce into larger macroabscesses, resulting in pressure erosion on the surrounding bone, which leads to OM. The abovementioned known risk factors associated with DSWIs may be associated with delayed wound healing and these factors might have resulted from the direct spread of a wound infection. Since sternal OM can occur due to the direct spread of local infection or by the hematogenous dissemination of pathogens, the hematogenous dissemination of infection may act through a different mechanism than the direct spread of local infection and these DSWI risk factors may not be involved in the context of sternal OM. We included this in the text and we believe since our numbers of sternal OM was too small, there was a limit to demonstrating statistical significance. We applied this in the limitation section. Line 180

Comment 11: Was any particular surgical technique used to decrease the risk of OM? The discussion should focus on postulations on why the incidence is low compared to previous publications.

Reply 11: Thank you for nice comments. Since we only applied sternal OM after the median sternotomy, which is the rarest form of wound complication. All the other reports were emphasized on DSWI, our sternal OM patients were part of the DSWI, and we believe this report was first to address the actual incidence of sternal OM itself, we believe this incidence is not low compared to other reports. We did not collected all the DSWI cases, we believe our data had met the other papers' incidence on DSWI after median sternotomy.

We wrote this in the discussion section. Line 161; Since sternal OM is a subgroup of DSWIs and is the rarest form of DSWIs (2,3), the exact incidence and risk factors have not been studied yet. There are many reports of the incidence of DSWIs after cardiac surgery. According to the literature, the incidence of DSWIs after cardiac surgery has been reported to be between 0.2 and 8.0% (4,5). However, a recent study by Robinson et al. (15) reported a 1.2% incidence of DSWIs and Pan et al. (16) reported that the incidence of DSWI was 1.33% after cardiac surgery. Improvements in aseptic techniques and prophylactic antibiotic use may have contributed to the reduction in the incidence of DSWIs after cardiac surgery (16). Some studies have reported that antibiotic prophylaxis was beneficial for reducing the incidence of DSWIs after surgery (17-20). In this study, the incidence of sternal OM was 0.47% and we believe that this study was the first to report the incidence of sternal OM alone after median sternotomy in a single institution. However, considering that there some patients were lost to follow and not readmitted to the institution and that sternal OM may present even years following median sternotomy, the occurrence of DSWIs may have been underestimated.

Thank you for your nice comments.