Review article

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Post-sternotomy mediastinitis: What the intensivist needs to know

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Abstract

Deep sternal wound infection (DSWI) is a dreaded complication after cardiac surgery, which dramatically increases health costs, in addition to high morbidity and mortality. The diagnosis and treatment of post-sternotomy mediastinitis (PSM) is a professional challenge. The aim of this current narrative mini review, we will consider epidemiology, implicit risk factors, the basis of diagnosis, preoperative, intraoperative, and postoperative prevention, and antimicrobial procedures, as well as the management of an optimal antimicrobial policy including an antimicrobial switch therapy.

Antibiotic cost represents a significant part of hospital budgets all over the world and more when the cost falls directly on the patient in those health systems that do not cover assistance and treatment. The management of switch therapy is not yet well known in patients with mediastinitis and it is common to find some objection in its use due to the change from long-acting intravenous antimicrobial antibiotics to oral regimen in this type of patients, most of them with high hospitalization rates.

Key words: Mediastinitis, infectious diseases, switch therapy, microbiology, critical care, antimicrobial stewardship.

Introduction

Mediastinitis is a life-threatening condition that carries an extremely high mortality if recognized late or treated improperly. Mediastinitis after cardiac surgery is rare (0.25%-2.9%), (1) but can reach a high morbidity and mortality (1.1-19% in the hospital). (2) Patients stay twice as many hospital days as others and reach three times the cost of care. Changes in cardiac surgical patient population and contributing pathogens, amongst others, have ensured that the incidence of post-sternotomy mediastinitis (PSM), despite many advances in prevention, remains significant. (3) There are many factors that contribute to increase risk of infection, including overall acuity, age, delayed sternal closure, steroid use, and length-of-stay in ICU. (4,5)

The usual treatment is based on surgical and medical support based on the use of antimicrobials. There is little experience in the use of a switch therapy from intravenous to oral route antimicrobials therapy and perhaps should be considered as an antimicrobial stewardship in the future. Due to complex situation of the PSM, the management of such complications requires the involvement of a multidisciplinary team of cardiothoracic surgeons, intensivists, infectious disease specialists, and clinical microbiologists when they are available.

Epidemiology and risk factors

The specific knowledge of each patient is crucial in this type of pathology. Initially we must know those risk factors that can change in the patient's evolution after cardiac surgery because although the incidence is substantially low, the PSM has been reported increases 1-year mortality of 10.7% (compared with 2.5% in patient without PSM). (6) The ICU length of stay (LOS) is increased also longer mean hospital stay of 33 days versus 7-9 days. (7)

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The patient characteristic with sternal wound complications is an older male, current smoker, obese with diabetes mellitus with a very severe coronary disease with left ventricular ejection fraction (LVEF) below 40%. Operative risk factors include an intraaortic balloon pump (IABP) for management of the chest pain or from the hemodynamic point of view and going to an emergent coronary artery by-pass grafting (CABG) with valve or aortic surgery. Also, long operation time, and the use of bilateral internal thoracic artery graft (BITA) are surgery-associated risk factors, but this effect is reduced when both internal thoracic arteries (ITA) are taken down in a skeletonized fashion, even in diabetics. (2) Other patients have pulmonary complications (thoracic malignancy, chronic obstructive pulmonary disease [COPD] and the use of corticoids therapy for acute exacerbations). A recent case control study showed chronic infections or bacterial infection longer than 4 weeks or on antibiotics at surgery as another risk factor for PSM. (8)

Poor nutritional status results in a higher post-op infection. Chermesh, et al (9) identified up to 20% of their studied population of over 400 patients had at least moderate risk for malnutrition.

Pre-operative optimization of nutritional status in patients undergoing cardiac surgery is therefore paramount. The American Association for Thoracic Surgery (AATS) expert consensus review recommends that surgery should be postponed for patients with pre-operative hypoalbuminemia to receive nutritional nutrition for 7-10 days if the procedure can be safely delayed. (2,10)

Classification and diagnosis

Based on the time to presentation after surgery, this classification reported by El Oakley and Wright in 1966 (11) classified deep sternal wound infection (DSWI) into five classes (**Table 1**).

This classification of El Oakley and Wright is world widely used for cardiothoracic centers, although we can find other classifications based on anatomical site proposed by Jones in 1997 (12) in six types depending on the depth surgical wound and the presence of septicemia. Greig in 2007 (13) proposed other classification considering the regional location of the wound in three types (upper half of sternum, lower half of sternum, and the whole sternum). In 2015 a new classification of post-sternotomy dehiscence was proposed by Anger J, et al. (14) This classification considers the depth and location of the surgical wound in four types, which defines upper or lower region for the inclusion of the lower margin of the pectoralis major muscle.

The diagnosis of DSWI is often difficult to be made. It is based on the combination between clinical symptoms and signs, and laboratory and radiological findings. (7) According to the Centers for Disease Control and Prevention (CDC), (15) DSWI must meet at least one of the following three criteria: 1) Organism is identified, 2) evidence de mediastinitis on gross anatomic or histopathologic exam and 3) at least one of the following signs or symptoms (fever > 38º Celsius), chest pain or sternal instability and at least one of the following: purulent drainage from mediastinal area or mediastinal widening on imaging test (7,15). Fever may be absent in elderly patients. Other symptoms include wound dehiscence and surrounding cellulitis. (7) Systemic inflammatory response syndrome (SIRS) and hemodynamic changes as tachycardia, hypotension, oliguria, can dramatically to be the first signs of a septic shock state.

Microbiology

Cultures from tissue samples obtained during surgical debridement are positive in 62% of patients, and among them, most (94%) were monomicrobial. (16)

Gram-positive and gram-negative microorganisms both contribute to the pathogenesis of DSWI. Staphylococci, either Staphylococci aureus (S. aureus) or coagulase-negative Staphylococcus (CoNS), represent the most common organism of DSWI, accounting for 60-80% of cases. (17) The other group of pathogens in DSWI are aerobic gram-negative rods in 10%. The most common gram-negative microorganisms involved are Klebsiella and Enterobacter species. (17)

Although the numbers and percentages are different in various studies, the findings that CoNS and S. aureus are the most common pathogens are consistent throughout the years. (7,16,18) Non-fermenters such as Pseudomonas aeruginosa and yeasts are found less common in DSWI, but their frequency increases with the number of surgical revisions.

In a report from a clinical retrospective review over the last 21 years by Barber Ansón M, et al, (19) once the deep sternal wound infection is suspected, 54.5% of diagnosis was established by three criteria: infection in sternotomy or mediastinum during the cleaning surgery, isolation of some microorganism (in tissue/mediastinal or sternal luteum) or leakage of purulent content from one of the two locations, and chest pain, sternal instability or fever. In the remaining patients

(45.5%) the diagnosis was based on two criteria. Microbiological identification was obtained in 95.45%. The isolated germs were gram-positive in 59.1% (S. aureus being the most usual), gram-negative in 9.1%, and fungi in 4.5%. The diagnosis was polymicrobial in 22.7%, including 9.1% with the presence of fungi. The treatment in 12 patients (54.6%) consisted of prolonged antibiotic therapy and radical debridement together with drain washer. Twenty-seven point three percent were treated exclusively with antibiotic therapy. **Figure 1** corresponds to immediate debridement and reconstruction with a pectoralis major muscle flap for post-sternotomy mediastinitis. (20)

Surgical management

Due a unsatisfactory treatment results and advanced in surgical techniques, alternative surgical concepts were evaluated including surgical revision with debridement, open dressing, and secondary closure, with or without reconstruction with vascularized soft tissue flaps such as greater omentum or pectoral muscles. (7, 21) Aside from flap coverage, another option for sternal wound closure is negative pressure wound therapy (NPWT; also known as vacuum-assisted closure [VAC]). Prompted by its increasing use, several studies have found the clinical effect of VAC to be comparable to traditional closed drainage or open packing, with improvement in sternal wound healing, reinfection rates, length of ICU stay, and possibly mortality. (7,22,23)

Antimicrobial prophylaxis, prevention, and treatment of sternal wounds in cardiac surgery

The AATS recently has reported an expert consensus review for the management of the DSWI. Perioperative, intraoperative, and postoperative strategies are recommended derived from evidence-based recommendations (**Table 2**). (10)

Preoperative

1. Screening for nasal carriers of Staphylococcus (Class I, Level A). It is mandatory because most of the surgical wound infections arise from the patient´s own nasal flora.
2. Nasal disinfectants (Class I, Level A). Routine mupirocin should not be used for all cardiac procedures in the absence of polymerase chain reaction (PCR) testing or nasal cultures positive for Staphylococcus colonization. Hence, mupirocin therapy should only be used for those patients with positive result on nasal culture, or PCR assay or in those patients whose culture are not available.
3. Preoperative bathing (Class IIb, Level B).
4. Hypoalbuminemia and poor nutritional state (Class I, Level B).
5. Remote infections (Class I, Level C). Whenever possible in non-emergent cases.
6. Preoperative glycemic control (Class I, Level B). Optimizing glycemic control is recommended in patients with increased HbA1c levels (>7.5) and serum glucose levels >200 mg/dl before any cardiac surgery procedure. If emergent surgery in whom serum glucose levels are persistently >180 mg/dl, intravenous insulin infusions are the most effective method to rapidly achieve glycemic control.
7. Smoking cessation (Class I, Level B).
8. Preoperative antibiotics (Class I, Level A). All patients received standardized preoperative intravenous antibiotics (first generation cephalosporin) within 1 hour of operation and for the next 48 hours (redosing is indicated in procedures >4 hours). Vancomycin (Class I, Level B) is reserved in patients with a history of type allergic reaction to β-lactam agents or in cases of methicillin resistant staphylococcus aureus (MRSA).

Intraoperative prevention

1. Antibiotics (Class I, Level A). A cephalosporin should be administered within 60 minutes of a cardiac surgical procedure and redosed for those procedures lasting >4 hours. Cephazolin or cefuroxime are routinely administered for 48 hours.
2. Glycemic control (Class I, Level A).
3. Topical antibiotics (Class I, Level B). Lazar (24) and colleagues in a retrospective, nonrandomized, single-center study involving over 3000 patients who underwent cardiac surgery found that topical vancomycin (2.5 g in 2 ml of normal saline) applied as a slurry to both edges of the sternum along with perioperative antibiotics and tight glycemic control (<180 mg/dl) resulted in the total elimination of superficial, deep or any type of wound infection in both nondiabetic and diabetic patients.
4. Bone wax (Class III, Level B). Bone wax is not recommended for application to the cut edges of the sternum.

Postoperative prevention

1. Antibiotics (Class I, Level A). Cephazolin or cefuroxime should be routinely administered for 48 hours or less.
2. Continued insulin infusion (Class I, Level A). Should be initiated in the ICU for at least 24

hours to maintain serum glucose level <180 mg/dl (<10 mmol).

3. Early extubation (within first 8 hours of admission in the ICU) may also decrease the incidence of wound complications. (25)
4. Early removal of indwelling urinary and central venous catheters (within first 48-60 hours) have also been found to significantly decreased the incidence of wound infections. (26)
5. Achieving hemostasis with protocols for assessment the bleeding post-op or using thromboelastogram (TEG) if there is bleeding >100 ml (patient over 70 kg) of blood in the first hour after cardiac surgery.
   Boeken V, et al reported that a significant delay of reoperation (11.1±4.2 hours) for bleeding could be also found for patients with postoperative septic complications, e.g. sternal wound infections. (27)

Optimizing use of antimicrobials in the mediastinitis

Empiric antimicrobial treatment

Once DSWI is suspected an empiric therapy should be initiated after adequate sampling for microbiological investigations (tissue samples, blood and eventually sputum). This empiric antibiotic treatment should be including a broad-spectrum coverage against methicillin-resistant gram-positive, gram-negative, and anaerobic organisms. Vancomycin, gentamicin and/or cephalosporin of third generation is an adequate choice.

Suggested targeted antimicrobial treatment

Targeted antimicrobial therapy should be started as soon as possible when the cultures are available. For interpretation, the susceptibility test should be performed better with a medical microbiologist if it is available. If not, an adequate interpretation of the minimal inhibition concentration (MIC) of the sensitivity antibiotics should be enough (**Table 3**).

After sternal closure, switch to oral antibiotics is recommended for a total duration of 6 weeks (if no foreign material is present) or 12 weeks (if any foreign material is present). (7)

During the antimicrobial therapy, laboratory test should be recommended 2 times per week if there is no SIRS or bad distribution (hyperdynamic state) as sepsis and/or septic shock. In this case, the laboratory test should be daily (leukocytes, C-reactive protein [CRP] and/or procalcitonin [PCT], renal function, liver enzymes, etc.). The antimicrobial dose adjustments should be made according to the renal function (creatinine, creatinine clearance, urea, urine output) and the ideal body weight. The nutritional support during the antibiotic's administration is fundamental, supporting an enteral nutrition as soon as possible with supplements of vitamins in patients due to the long-term administration.

De-escalation and switch therapy

Specific improvements in antibiotic use associated with implementation of facility-specific guidelines have included statistically significant increases in likelihood of adequate initial therapy. (28)

De-escalation of the antimicrobial therapy is recommended in severe sepsis guidelines. De-escalation of antimicrobial therapy was defined either by the cessation of a β-lactam or a glycopeptide by the switch to another one with a narrower spectrum or the reduction in the number of antibiotics or the early arrest of antibiotic treatment. Also the switch therapy (29) defined by the switch of a long-acting antimicrobial IV treatment to oral route administration could be observed as future antimicrobial stewardship for the advantages in the patients (avoiding long hospitalization stay among other such as economic). However, an early switch therapy should be avoided to prevent the rapid emergence of resistance.

In addition to hospital-wide activities, such as preauthorization or development of clinical guidelines, a strategy for targeted efforts to improve antibiotic use and clinical outcomes for a specific infectious diseases issue has been shown to be effective. (30)

Conclusion

Post-sternotomy mediastinitis remains a potentially fatal complication of cardiac surgery despite the advancements in the perioperative care in the modern era. However, the institution of pre-operative, intraoperative, and postoperative strategies noted in this review, and from the proposal antimicrobial therapy summarized in **Table 2**, have been shown to significantly decrease the incidence, morbidity, and mortality of this dreaded complication.

An antimicrobial de-escalation and switch therapy adequate can be helpful for avoiding resistances and improve the cost and the long-term hospital staying of these patients.

Table 1. Classification of mediastinitis. Classification of El Oakley and Wright (1966) (11)

Type	Characteristic
I	Presentations within 2 weeks post-op without risk factors
II	Presents within 2 to 6 weeks post-op without risk factors
IIIA	Presents within 2 weeks with one or more risk factors
IIIB	Presents within 2 to 6 weeks post-op with 1 or more risk factors
IVA	Type I, II, or III after one failed therapeutic trial
IVB	Type I, II, or III after more than one failed therapeutic trial
V	Presentation after 6 weeks post-op

Legend: Post-op=post operation.

Table 2. Classification of recommendation and level of evidence

Class I	Procedure/treatment should be performed • Is recommended • Is indicated • Is useful/effective/beneficial
Class IIa	Procedure/treatment is reasonable to perform • Is considered useful/effective/beneficial • Is probably recommended or indicated
Class IIb	Procedure/treatment may be considered • May/might be considered useful/effective/beneficial • Is unclear or not well established
Class III	Procedure/treatment should not be performed • May be harmful • Is not indicated • Is not recommended
Level A: Recommendation based on multiple randomized trials or meta-analyses	
Level B: Recommendation based on evidence from a single randomized trial or nonrandomized studies	
Level C: Recommendation based on expert opinion, case studies, standard of care	

AATS: Expert consensus review for the management of the DSWI. 2016 (10)

Legend: AATS=American Association for Thoracic Surgery; DSWI=deep sternal wound infection.

Table 3. Suggested targeted

Empiric antibiotic started once DSWI is suspected. Dose per day	Microorganism result after culture	Switch therapy	New antibiotic proposed	Time	Route
Gram-positive					
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Staphylococcus spp. Oxacillin/methicillin susceptible		Cloxacillin or flucloxacillin	2 weeks	IV IV
		YES FOLLOWED	Rifampicin + levofloxacin, TMX, doxycycline	4 weeks	PO
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Oxacillin/methicillin resistant		Vancomycin	2 weeks	IV
		YES FOLLOWED	Rifampicin	4 weeks	PO
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Streptococcus spp.		Ceftriaxone	2 weeks	IV
		YES FOLLOWED	Levofloxacin or amoxicillin	4 weeks	PO
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Enterococcus Penicillin susceptible		Amoxicillin + gentamicin	2 weeks	IV
		YES FOLLOWED	Amoxicillin	4 weeks	PO
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Penicillin resistant		Vancomycin + gentamicin	2 weeks	IV
		YES FOLLOWED	Linezolid	4 weeks	PO
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Vancomycin resistant		Individual Removal implant Lifelong suppression necessary		
Gram-negative					
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Enterobacteriaceae Escherichia coli Klebsiella Enterobacter		Ciprofloxacin	6 weeks	PO

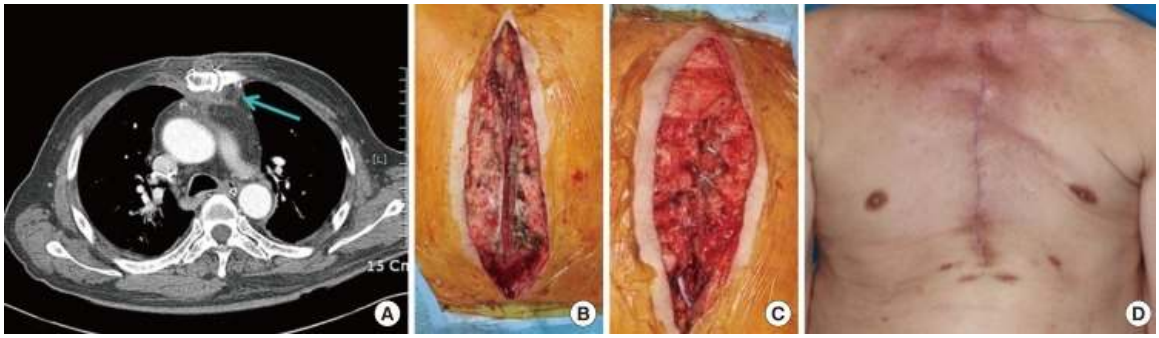
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Non-fermenters Pseudomonas aeruginosa Acinetobacter spp.		Piperacillin-tazobactam Meropenem Ceftazidime + gentamicin	2 weeks	IV
		YES FOLLOWED	Ciprofloxacin	4 weeks	PO
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Ciprofloxacin resistant		Meropenem + colistin and/or fosfomycin	2 weeks	IV
		FOLLOWED	Oral long-term suppression	1 year	PO
Anaerobes					
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Gram-positives Cutibacterium Peptostreptococcus Finegoldia magna		Ceftriaxone	2 weeks	IV
		YES FOLLOWED	Rifampicin + levofloxacin or amoxicillin	4 weeks	PO
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Gram-negatives Bacteroides		Ampicillin-sulbactam	2 weeks	IV
		YES FOLLOWED	Metronidazole	4 weeks	PO
Candida spp.					
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Fluconazole susceptible		Caspofungin or anidulafungin	2 weeks	IV
		YES FOLLOWED	Fluconazole for suppression	1 year	PO
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Fluconazole resistant		Voriconazole		PO
		FOLLOWED	Removal implant Long-term suppression	1 year	
Culture negative					
Vancomycin (2x1 g) Gentamicin (1x3-5 mg/kg) Ceftriaxone (1x2 g)	Culture negative		Ampicillin-sulbactam	2 weeks	IV
		YES FOLLOWED	Rifampicin + levofloxacin or amoxicillin	4 weeks	PO

Total duration of therapy: 6-12 weeks. Start for 2 weeks usually IV (except in case of Enterobacteriaceae using oral. If there is not able oral administration, could be treated IV). Switch therapy after 2 weeks, following new antibiotic proposed, usually for 4 weeks. Some patients could be treated by oral long-term suppression.

Laboratory test twice per week: Check white blood cells, discard thrombocytopenia, procalcitonin (or C-reactive protein), liver enzymes and renal function by creatinine/eGFR (estimated glomerular filtration rate). This table has been modified from Yusuf E, et al. Current perspectives on diagnosis and management of sternal wound infections. (7) The doses of antibiotic listed here must be followed and recommended by pharmacist and/or infectologist.

Legend: DSWI=deep sternal wound infection; IV=intravenous; PO=per oral.

Figure 1. Immediate debridement and reconstruction with a pectoralis major muscle flap for post-sternotomy mediastinitis (20)



Legend: (A) Preoperative CT post sternal fluid collection (blue arrow) was noted when mediastinitis was diagnosed. (B) Intraoperative view of the sternal wound, which was debrided of foreign material and necrotic tissue. (C) Intraoperative view of the advanced pectoralis major muscle for coverage of the defect. (D) Two weeks after surgery.

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