Mediastinitis in cardiac surgery: A review of the literature

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ABSTRACT

Background: Postoperative mediastinitis is a serious complication in cardiac surgery that substantially increases morbidity and mortality. Aim: This study reviews the various prophylactic and therapeutic measures. Material and Method: Literature searches were done to identify relevant studies. Results: Various possible causes and risk factors were identified and prophylaxis such as preoperative disinfection of the skin, non-abrasive preoperative removal of hair, disinfection in the operating room, administration of prophylactic antibiotics, and non-traumatic surgical intervention with sparing use of electrocautery. These, along with wide range of wound-healing modalities have been established for the management of post-sternotomy mediastinitis. Conventional management involves surgical revision with open dressings or closed irrigation, or reconstruction with vascularized soft tissue flap and novel treatment such as vacuum-assisted closure and their overall effect on Morbidity, Hospital stay, Cost and Mortality. Conclusion: Despite advances, there is substantial risk of postoperative mediastinitis. Presently there is no universally acceptable approach regarding the surgical management of mediastinitis.

Key words: Cardiac surgery, mediastinitis, morbidity, mortality, prevention, treatment

INTRODUCTION

Mediastinitis is a dreaded complication of cardiac surgery with incidence varying between 0.9 to 20% and is characterised by retrosternal wound infection with macroscopic sternal osteomyelitis. This leads to prolonged hospital stay and increase health care cost. There is lack of consensus regarding prevention and treatment of mediastinitis. Our aim is to describe various suggestions that have been offered to prevent and treat mediastinitis.

The Centre for Disease Control and Prevention has established a definition of mediastinitis.[1] According to these guidelines, diagnosis of mediastinitis requires at least one of the following: an organism isolated from culture of mediastinal tissue or fluid; evidence of mediastinitis seen during operation; and one of the following conditions: chest pain, sternal instability, or fever (>38°C), in combination with either purulent discharge from the mediastinum or an organism isolated from blood culture or culture of mediastinal drainage.[1]
MICROBIAL AETIOLOGY

The microbial aetiology of sternal wound infections are bacterial, both gram-negative and gram-positive bacteria, as well as fungi. Staphylococcal species continue to be the most common offending organisms. Coagulate negative staphylococci (CONS) have been reported to be one of the significant pathogens in postoperative infections following cardiac operations.\cite{5,6} Reports on causal organisms involved in postoperative infections have shown a shift from gram negative to gram positive bacteria.\cite{7} When there is a foreign material implant, CONS are known to be important pathogens. This is commonest when stainless steels wires are used for closure of sternotomy in cardiac operations.\cite{8} CONS has become the most significant organism in post-sternotomy mediastinitis, accounting for 43% to 64% of all cases in recent studies.\cite{5,6} A large quantity of extracellular polysaccharide is synthesized to form protective biofilm around the colony after the initial colonization, hence, treatment of CONS-associated infections usually requires removal of the infected foreign body. The antibiotic management requires testing for sensitivity, because S. epidermidis strains are frequently resistant to multiple antibiotics. Studies have reported that about 75% of the CONS strains were methicillin-resistant.\cite{5,6} The infections are usually slow and late in onset, with few of the classical symptoms of wound infection.\cite{7} Fever may be absent and the levels of inflammatory markers such as c-reactive protein (CRP) may be normal.\cite{8}

S. aureus is another significant pathogen. It may be more aggressive in nature and shows more classical signs of infection. This organism has been increasingly implicated in the colonization of nasal passages.\cite{9} It has been documented that the incidence of nasal colonization with S. aureus in the normal population ranges from 10-15% and such colonization increases the risk of post-sternotomy mediastinitis.\cite{10} Administration of nasal mupirocin peripheratively has been shown to eradicate 95–100% of S. aureus up to a year postoperatively and demonstrates a 67% reduction of infection.\cite{11}

RISK FACTORS

The pathogenesis of post-sternotomy mediastinitis is complex and multifactorial. Several risk factors have been identified in previous literature, however, there are some inconsistencies regarding the role of individual factors in the pathogenesis of sternal infections.

Major factors include heart failure, diabetes mellitus, obesity, and chronic obstructive pulmonary disease (COPD). It has been documented that the presence of one of these clinical conditions or risk factor for any of these, increases the risk for developing post-sternotomy mediastinitis.\cite{12} The possibly mechanism associated with obesity is not fully understood, although, it might be associated with the poor distribution of perioperative antibiotics in adipose tissue, inadequate preoperative skin preparation as a result of deep skin folds and difficulty in diagnosis in the early phase of the infection.\cite{13} Inadequate sterility is a possible mechanism for the finding of re-exploration for bleeding as a risk factor.\cite{14,15,16} Diabetes mellitus is also a common risk factor.\cite{12} Raised blood glucose levels impairs wound healing and the continuous use of intravenous insulin has been reported to significantly reduce the incidence of deep sternal wound infection in diabetic patients.\cite{17} Heart failure, a high NYHA Class, and a low ejection fraction (<30%) of the left ventricle have also been implicated in mediastinitis.\cite{13,16,18} Prolonged duration of the surgical procedure increases the risk of intraoperative contamination and thus post-sternotomy mediastinitis.\cite{13}

PREVENTION

Mediastinitis is a post-operative infection that is mainly due to intra-operative contamination. The origin of the germ is the patient, the surgical team or the operating room air.\cite{19,20} Among the factors involved in germ pathogenesis in mediastinitis are highly relevant factors such as perioperative disinfection of patient and surgical specialty.

Disinfection in perioperative period

Nasal carriers of staphylococcus aureus are at increased risk for post-operative mediastinitis.\cite{11} but there is no consensus about the efficiency of mupirocin prophylaxis in decreasing post-operative wound infection. Some works have demonstrated a significant reduction in surgical-site infection in mupirocin-treated patients,\cite{21,22} while others failed to show any difference between patients treated with mupirocin nasal ointment and patients treated with placebo.\cite{23} Before mupirocin ointment nasal
therapy, nasal carriage must be identified either by microbiological culture techniques or with real-time polymerase chain reaction. The treatment is prescribed for 5 days (delay consistent with the manufacturer’s recommendations) so emergency patients and neonates, who are usually considered at higher risk for mediastinitis, are not included in many studies. Staphylococcus resistance to mupirocin is rare and mupirocin is safe, however, emergence of high-level resistance to mupirocin has been found in many countries.[23-25] Finally nasal decontamination with mupirocin has been tested for over 20 years without clearly demonstrating an advantage.

Skin disinfection is a major factor in the reduction of post-operative infection. Products used as antiseptic solutions are: povidone-iodine and chlorhexidine. The permeable nature of the skin in small infants allows significant iodine absorption; this is possible and likely to occur in pre-term infants. However, even in neonates, TSH levels may be significantly affected by povidone-iodine and transient thyroid dysfunction may result from topical exposure to iodine-containing antiseptic solutions,[26] acute Wolff-Chaikoff effect, described in 1948, thus iodine containing solution should be avoided in neonates. Furthermore, chlorhexidine-based antiseptic solution is often considered as the best therapy for skin disinfection. Compared to iodine solution, it has a more prolonged action and no known sensitivity. Intra-operative skin disinfection is of the utmost importance, however, it seems that showers or baths with skin disinfectant before surgery are not required.[27]

The rationale for systematic antibioprophylaxis in cardiac surgery is questionable, however, second generation cephalosporin is used for this, in the absence of patient sensitivity. The vast majority of mediastinitis cases are due to staphylococcus and the incidence of resistance to methicillin (varying from one country to another and from one surgical unit to another, with an increase in incidence for US hospitals from 35.9% in 1992 to 64.4% in 2003.[28] Antibiotic prophylaxis induces a change in staphylococcal flora. There is some relation between the efficiency in eradication of carriage of staphylococcus aureus and the emergence of resistant strains of coagulase-negative staphylococci. Staphylococci cultured from the skin of cardiac surgery patients are more resistant after surgery than before surgery and, furthermore, staphylococci causing post-operative infections have the same antimicrobial resistant phenotypes as do colonizing isolates.[29] This supports a modification of patient skin flora induced by antibiotics and is most unlikely due to in-hospital acquired germs. Antimicrobial agents given as prophylaxis may select resistant organisms. In patients who do not receive antibiotic prophylaxis, the staphylococcal flora remains unaffected. In patients receiving cephalosporin prophylaxis, 61% of the sites colonized with a low-level of methicillin-resistant strains before surgery were colonized with high levels of methicillin-resistant staphylococci on the third post-operative day.[30] In this study, the authors also demonstrated that the plasmid profile patterns were identical between pre- and post-operative methicillin-resistant staphylococci. This is in accordance with previous works suggesting that the resistant pathogen is an alteration of patient skin flora rather than a contamination from in-hospital flora. Thus benefit of a prophylactic antibiotic must be balanced with the possible selection of resistant strains that are likely to make up a nosocomial reservoir for new patients and for the hospital staff.

Surgical speciality

Many risk factors of mediastinitis could be decreased with a high-quality level of care. Immunomodulation and an increase in gut mucosal permeability, induced by cardiopulmonary bypass and increased by hypothermia or deep hypothermic circulatory arrest, are also considered as predisposing factors.[31,32] They can be minimized with a more physiological cardiopulmonary bypass and warm surgery. In paediatric patients younger than 1-year-old, length of surgery, redo for bleeding, post-operative open-chest, ECMO and blood transfusion are also classical risk factors for deep wound infection.[33]

Optimal thoracic blood drainage is important as stagnant blood in the mediastinum is a perfect growth medium for microorganisms, hematoma collected in the supra- sternal space is clearly the origin of an abscess that may diffuse in the retrosternal space.

It is noteworthy that the association of red blood cell transfusion with infection is dose-dependent. In neonates and young infants, blood-free surgery is unrealistic but efforts have to be taken to decrease blood use. Blood conservation with a miniaturized bypass circuit, vacuum-assisted venous drainage and microplegia is effective[34] and, thus, is likely to
decrease the risk of paediatric post-operative mediastinitis.

Skin closure with cyanoacrylate glue, initially used for treatment of sternal instability, was also described as a protective factor against deep wound infection.\[^{39}\]

Finally, the human factor is probably the most difficult to assess and the most difficult to control but not the least important. An optimal protocol is the first step of an efficient prophylaxis and its practical application is crucial, which depends on the motivation and quality of the medical staff.

One particularity of open heart surgery is the need for cardiopulmonary bypass. In this technique, the sucker system drains blood into the cardiotomy from the mediastinum or from cardiac cavities to the venous reservoir of the bypass circuit. In the sucker system tubing, room air is mixed with blood and thus potentially contaminated air enters into the bypass circuit. There is some evidence of transmission of fungal infections through contaminated air-handling systems,\[^{36}\]\ and air filtration as well as radiation were considered efficient ways to protect from mediastinitis. Gram negative bacilli may also be transmitted from the environmental flora but contamination with coagulase negative staphylococci is probably only due to patient or surgical team flora.\[^{37}\]

**DIAGNOSIS**

Erythematous painful incisions, wound dehiscence, purulent discharge along with sternal instability are typical features. Besides these, leukocytosis, raised C-reactive protein and positive blood culture are often present. Culture and sensitivity of purulent discharge upon which antibiotic treatment is based should be immediately initiated followed by surgical drainage. Culture of epicardial pacing wire is not satisfactory. CT scan is useful for localization of infected tissue and to some extent in early diagnosis.\[^{38}\]

**TREATMENT**

Treatment of mediastinitis is based on surgery and antibiotic therapy, but there is still controversy about the best strategy to help speed-up wound healing. There is consensus on surgical revision with careful debridement of the infected areas, removal of foreign material and curettage of sternal edges till normal bleeding; Culture and sensitivity of purulent fluids; and intravenous antibiotics, based on empiric probability, need to be injected before surgery and modified according to germ sensitivity.

Open dressing and closed irrigation are two conventional treatments. Open dressing has disadvantages, namely, thoracic instability requiring mechanical ventilation and prolonged immobilization, increasing risk of muscular weakening and patient discomfort. Heavy sedation for change of dressing. Cytotoxicity of classical antiseptic and lethal iodine toxicity following povidone-iodine irrigation in a 34-month-old patient has been described.\[^{39}\]\ For this problem, topical treatment with granulated sugar was also proposed and was considered by several authors as a simple, efficient and inexpensive alternative to irrigation during open chest management.\[^{40}\]

However, the numerous drawbacks of open chest management have stimulated the emergence of new therapies, such as primary closed sternum with continuous irrigation and drainage. This approach was described in 1963 and had theoretical advantages.\[^{41}\]\ Mechanical ventilation was not required and length of treatment is shorter. However, the results were disappointing and far from the expected progress, with a high rate of failure and mortality. Cardiac tamponade induced by imbalance between irrigation and drainage, or even cardiac rupture, were reported.\[^{42}\]\ A combination of two techniques, primary open chest management followed by delayed closed chest irrigation, was also proposed but was also less than satisfactory. However, irrigation is still used and is considered a cost-effective therapy.\[^{43}\]

Procedures using reconstructive plastic surgery with vascularized soft tissue flaps were described in 1980. Pectoral muscle flap obliterate the dead space with well-vascularized tissue is probably the major positive aspect of this approach.\[^{44}\]\ By eliminating any residual cavity and by filling all of the space with healthy tissue, from an infectious point of view, this treatment represents real progress. The mediastinal cavity is anfractuous, thus failure of irrigation and drainage is probably due to incomplete irrigation and drainage with persistence of one or several septic residual cavities. Unfortunately, drawbacks of plastic procedures are also numerous. Morbidity associated with the muscle flap technique includes
pain, weakness, hernia and an esthetic prejudice, which is of great significance in paediatric patients and more specifically in young girls.\textsuperscript{[46]} Chest wall instability, bleeding, recurrence of infection were noticed and omental transfer was proposed as an alternative to the pectoral flap.\textsuperscript{[47]} On the other hand, the omental flap has been credited to alter respiratory function by decreasing the percent vital capacity and oxygen consumption at the anaerobic threshold.\textsuperscript{[48]}

When compared to closed mediastinal irrigation, the benefit of muscle flap reconstruction is not obvious. Plastic procedures may have short-term and long-term results equivalent to irrigation, but the length of stay in intensive care is longer for patients treated with muscle flap closure.\textsuperscript{[49]}

Latest developments in mediastinitis surgical treatment are the introduction of vacuum-assisted closure therapy. The application of negative pressure has several advantages: Such as enhance Wound drainage by negative pressure; avoids any residual mediastinal cavity so that the mediastinum is fill with healthy tissue; Better approximation of the wound edges and favours stabilization of the chest; and some benefits in local microcirculation have been described.\textsuperscript{[50,51]} Vacuum-assisted closure was also used following continuous irrigation, when irrigation was ineffective or in patients with low cardiac output syndrome after a successful treatment of their hemodynamic instability.\textsuperscript{[52]}

The benefit obtained with vacuum-assisted wound closure over classical management is unquestionably accepted by the medical community. However, there are constraints for the patient: the vacuum-assisted closure system must be changed every 2 or 3 day, positive results are seen after a long time and confinement in bed is necessary for days or weeks; following vacuum device therapy, a delayed closure is necessary and, thus, the intensive care stay is prolonged. Cardiac ruptures were described in adults during topical negative pressure\textsuperscript{[53]} and the best negative pressure in paediatric patients is still to be determined. There is also a real concern about the risk of hemodynamic instability during negative pressure application in patients with Fontan- or Rastelli-type procedures; experimental data remains conflicting, and the precise location of the foam placement is important.\textsuperscript{[54]} Magnetic resonance imaging has confirmed a reduction in cardiac output and stroke volume after initiation of vacuum therapy at the levels currently used in clinical human applications. This hemodynamic effect can be minimized by interposition of paraffin gauze dressing over the heart during application of negative pressure.\textsuperscript{[55]}

Early primary closure over a single chest tube is more comfortable with a high success rate. Another method of primary closure with high vacuum drainage had been described using conventional debridement of infected and necrotic tissue, sternal edge revision and drainage using high vacuum Redon’s catheters with a negative pressure of 90 kPa. Benefits were need less mechanical ventilation thus shorter intensive care unit stay, well tolerated in both paediatric and adult patient, high avoid any residual cavity thus filling mediastinum with healthy vascularised tissue, acceptable healing rate, shorter duration of IV antibiotics, early mobilization, usually well tolerated in Fontan, Rastelli type of operation with the exception of Norwood Stage 1.

**CONCLUSION**

Prevention of mediastinitis is still a difficult challenge. Prognosis is different in adult as compared to paediatric patients, with mortality being very rarely related to mediastinal infection. Primary sternal closure with vacuum-assisted suction drainage is better option in both adult and paediatric cases.

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