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Review

Causes of Mediastinitis and Its Surgical Treatment

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Abstract

Mediastinitis remains a potentially fatal complication of cardiac surgery. This study reviews the risk factors for mediastinitis after cardiac surgery, and discusses current treatment and prevention of this complication. This review explores three major independent risk factors for mediastinitis including individual patient factors, surgical procedures and microbiology. The perioperative period is influenced by the utilization of the internal mammary artery in conjunction with coronary artery bypass grafting, sternal fixation, vacuum-assisted closure, and negative pressure wound therapy. *Staphylococcus aureus* and *Staphylococcus epidermidis* are frequently encountered microorganisms. Additionally, aerobic gram-negative microorganisms and other infrequent microorganisms are also exhibiting a rising trend. Since sternal fixation devices effectively enhance sternal stability, alleviate wound pain, and decrease the occurrence of postoperative mediastinitis, they have been specifically incorporated into certain therapeutic and prophylactic approaches for addressing this complication. Despite the heightened awareness regarding mediastinitis, the large proportion of individuals at risk underscores the crucial need for rigorous monitoring of potential risk factors, posing a significant challenge to the implementation of effective therapeutic and preventative strategies.

Keywords

mediastinitis; risk factors; sternal fixation devices

Backgroud

Mediastinitis, a surgical site infection that typically occurs post-cardiac surgery, is an infection affecting the tissues beneath the sternum [1], causing increased hospital costs [2], morbidity, and mortality with prolonged stay in the intensive care unit (ICU) [3]. The incidence of postoperative mediastinitis varies between 0.4% and 5%, with the majority of cases falling within the range of 1% to 2%. The mortality rate associated with this significant complication is significant, ranging from 14% to 47% [4]. Therefore, it is imperative to understand the risk factors and develop appropriate treatment strategies to mitigate the occurrence of mediastinitis. Previous research has identified numerous preoperative risk factors, including obesity, diabetes, smoking, prior cardiac surgery, prolonged cardiopulmonary bypass time, among others [5]. However, due to the retrospective nature of numerous studies, varying inclusion criteria for subjects, and inconsistent definitions of mediastinitis, there is currently no consensus on the prevalence of these risk factors.

The treatment of mediastinitis necessitates a comprehensive approach encompassing surgical re-exploration, drainage of the affected mediastinal compartments, prompt empirical antibiotic therapy, and rigorous intensive care management [6]. The selection of a surgical approach must be tailored to the unique clinical circumstances of the patient and the surgical expertise of the treating surgeon. Surgical treatment strategies encompass various options such as closed irrigation, radical debridement, and reconstruction techniques using muscles (pectoralis major, rectus abdominis, and latissimus dorsi) or omental flaps (including free flaps, intercostal perforator flaps, breast flaps, and allogeneic bone grafts) [7,8]. The modification of a pectoralis major or omental flap (OF) transposition plays a crucial role [9]. By utilizing negative pressure wound therapy (NPWT) in conjunction with timely sternal revision, significant improvements in outcomes can be achieved [10].

The median sternotomy incision is the standard incision for open-heart surgical procedures, providing rapid access and excellent exposure to all mediastinal structures [11]. Postoperative mediastinitis, a severe complication resulting from sternal wound infection during median sternotomy, poses a significant risk in cardiac surgery [12]. In cardiac surgery, the conventional approach for sternal closure involves the use of wire cerclage (WC), primarily due to its familiarity and simplicity. Nevertheless, a significant drawback of wire cerclage is its tendency to reopen the sternum due to cutting forces, thus failing to offer adequate sternal stability [13]. Rigid fixation has been demonstrated to offer the advantages of enhanced stability and reduced occurrences of non-union, mal-union, and infection [14]. The use of sternal encircling apparatus and peri-sternal cable-ties can effectively reduce the occurrence of postoperative mediastinitis. Therefore, it is becoming increasingly utilized in cardiac surgical procedures [15,16].

The Centers for Disease Control and Prevention (CDC) has revised the diagnostic criteria for postoperative mediastinitis, requiring the presence of at least one of the following: (1) identification of organisms cultured from mediastinal tissue or fluid obtained either during surgery or needle aspiration; (2) confirmation of mediastinitis through gross anatomical or histopathological examination; (3) the presence of at least one of the following symptoms or signs, with no other identifiable cause: fever exceeding 38 °C, chest pain or sternal instability, purulent discharge from the mediastinal area, or radiological evidence of an infectious process in the mediastinum [17,18].

The Risk Factors and Etiology of Mediastinitis

Identifying risk factors that contribute to the development of mediastinum post-cardiac surgery, as well as enhancing perioperative patient monitoring, can significantly decrease the incidence of postoperative infections. These risk factors are assigned a risk score and are typically categorized into three distinct groups.

A study conducted in 2005 utilized the Society of Thoracic Surgeons (STS) National Cardiac Database to devise a simplified risk scoring system [19], encompassing 12 variables, through logistic regression analysis [19,20]. The calculation of a patient's overall risk score is determined by the aggregation of points assigned to all present risk factors. The aim of this system was to anticipate and subsequently mitigate the occurrence of significant infections.

Baseline Characteristics

Nine variables were significantly associated with an elevated risk of mediastinitis based on univariate analysis, with a significance level of $p < 0.05$. These variables included age, sex, obesity, New York Heart Association (NYHA) chronic heart failure (CHF) class, diabetes mellitus, history of smoking, chronic obstructive pulmonary disease (COPD), renal failure, and prior heart surgery. Notably, over 80% of the patients with mediastinitis were male and older [17]. Across numerous studies, obesity has consistently emerged as the most significant independent predictor of mediastinitis [21]. Although the direct correlation between body mass index (BMI) and the risk of mediastinitis following cardiac surgery remains inconclusive and requires further investigation, a recent study has revealed that patients with extreme obesity (BMI $\geq$40) exhibit a significantly elevated risk of operative mortality. Additionally, these patients are more prone to major perioperative complications, particularly deep sternal wound infection, and are likely to experience a prolonged postoperative hospital stay [22]. In this study, NYHA CHF class emerged as an additional independent predictor of mediastinitis. Furthermore, CHF, a component of the American Society of Anesthesiology score, has been demonstrated to be a crucial factor in predicting postoperative wound infection [23]. The World Health Organization classifies diabetes into several types, including type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), gestational diabetes mellitus (GDM), and certain other specific forms. A study has demonstrated that the occurrence of deep sternal wound infection following bilateral internal thoracic artery grafting is notably elevated among individuals with diabetes [24]. Patients who smoke (within the three months preceding the operation) are at the greatest risk of developing surgical wound infections due to a decrease in pulmonary function, which may affect optimal tissue oxygenation [25], despite the results of a multivariable analysis indicating a decrease in the rate of deep sternal wound infection among patients with diabetes and smoking [26]. COPD defined by the GOLD system and indicated by preoperative medication use, is the most significant preoperative factor associated with the occurrence of deep sternal wound infection [27]. Renal insufficiency, indicated by a plasma creatinine level exceeding 100 µmol/L on the day preceding surgery, and peripheral vascular disease (PVD) both significantly influence prognosis following mediastinitis [28]. Additionally, two separate studies have identified several other factors that increase the risk of post-operative infections. These include unintentional pre-operative weight loss of 10% within 6 months, BMI of less than 21, and a low pre-operative pre-albumin level of less than 20 mg/dL [29,30]. A strong correlation exists between prior heart surgery and postoperative mediastinitis, due to the presence of mediastinal adhesions [17].

Surgical Procedure

Coronary artery bypass grafting is still one of the main treatments for coronary heart disease [31,32]. The use of the internal mammary artery (IMA) for coronary revascularization may increase the incidence of mediastinitis [33]. A recent study evaluated the effectiveness of the vacuum-assisted closure (VAC) technique in comparison to the conventional treatment for patients with post-sternotomy mediastinitis. The results indicate that the VAC technique significantly improves the medical outcome of these patients. Furthermore, it is a safer and more effective treatment modality, as it results in a shorter overall duration of treatment, a reduced time interval from diagnosis to negative culture, and shorter hospital stay for patients with post-sternotomy mediastinitis [34]. By facilitating the formation of healthy granulation tissue and enhancing respiratory function through superior sternal support, VAC effectively promotes wound healing [35,36]. Increasing evidence supports a dose-response relationship between blood transfusions and the development of mediastinitis [37]. Transfusion-associated immunomodulation (TRIM) is a process triggered by allogeneic blood transfusions, which can result in a suppressed immune response. This suppression may lead to postoperative infections, as the host's immune system recognizes a significant amount of foreign antigens [38]. Additionally, there exist numerous risk factors associated with mediastinitis during operative procedures. These factors include the length of the operation, as seen during surgery for aortic dissections [39]. In addition, the duration of cardiopulmonary bypass, the utilization of the intraaortic balloon pump, excessive employment of electrocautery and bone wax, as well as hair removal using a razor instead of clippers are also risk factors [40].

Microbial Etiology

The most common pathogens associated with mediastinitis were *Staphylococcus aureus* and *Staphylococcus epidermidis* [41]. The occurrence of antimicrobial resistance among *S. aureus* has significantly increased [42]. Recently, the Toho University Omori Medical Center conducted a study on 174 pediatric patients who underwent open-heart surgery. Prior to the surgery, all patients underwent nasal culture screening. The study revealed that mediastinitis caused by *methicillin-resistant Staphylococcus aureus* (MRSA) is a critical complication following pediatric cardiac surgery [43]. The most prevalent isolates were *Escherichia coli*, *Klebsiella*, *Pseudomonas*, and *Enterobacteriaceae*. A recent article reports a case report of mediastinitis and sternal osteitis due to M. hominis in an adult patient who underwent cardiac surgery [44]. In a clinical study of adult cardiac surgery patients, the occurrence of postoperative mediastinitis was attributed to the preoperative utilization of chlorhexidine solution contaminated with *Serratia marcescens* [45]. Furthermore, *coagulase-negative staphylococci* and *aerobic gram-negative bacteria* were frequently isolated. Some authors have also suggested that *Aspergillus*, *fungal* and *mycoplasma hominis* infections can lead to mediastinitis, although these cases are exceptionally rare but associated with a high mortality rate [18,44,46].

Surgical Sternal Fixation Technique

The occurrence of mediastinitis following cardiac surgery ranges from 1% to 2%, but it is accompanied by significant adverse effects resulting in increased morbidity. Consequently, the treatment and prevention of mediastinitis are of utmost importance. Various authors have outlined several radical, safe, and reliable methods for treating this condition, including appropriately direct antimicrobial therapy, prompt wound debridement, sternal refixation, closed mediastinal catheter irrigation, partial or complete sternotomy along with the advancement of muscle or omental flaps, the combined use of the bilateral pectoralis major muscle flap (BPMMF) and rectus abdominis flaps or omentum, as well as vacuum-assisted closure (VAC) [9,47–49]. While numerous treatment strategies have been proposed, our primary focus is on evaluating the effectiveness of the sternal fixation device in addressing this specific complication.

Since the reintroduction of Milton's median sternal splitting technique by Julian in 1957 [50], a multitude of alternative approaches for sternal closure have emerged. Presently, the median sternal incision remains the most frequently employed incision for open-heart surgeries [51]. On the basis of the traditional stainless steel wire fixation, the flatwire sternal closure system technique has been developed [52]. Currently, the clinical practice routinely employs three methods for sternum fixation: the Zip Fix system, titanium plates, and sternum plates [53]. The comparison and evaluation of these methods are conducted in a rigorous manner, focusing on both their efficacy and safety (Table 1).

Steel Wire Fixation

Wire cerclage fixation, due to its safety, efficiency, and decreased cost, has established itself as the gold standard technique for sternal closure [54]. Although the procedure may potentially lead to complications, it is important to note that the incidence of sternal healing complications among the general patient population ranges from 0.25% to 5% [55]. Additionally, the mortality rate ranging from 10% to 47% is associated with wound complications situated deeply within the sternum after sternal rewiring [34]. The steel wire ligation fixation exhibits instability, thus elevating the possibility of postoperative complications. These complications encompass, but are not restricted to, deep sternum incision infection, lung dysfunction, sternum nonunion or dehiscence, and chest wall fat liquefaction [52]. The sternum is susceptible to compression of the intercostal vasculature, resulting in a decrease in blood perfusion to the surrounding tissues [11]. The wire cerclage technique encompasses various methods, namely: single wire surround, double wire surround, wire "8" seam legal, Robicsek closure technology, and interlocking multi-twisted wire closure technology [56,57].

Table 1. Comparison of merits and demerits of four Sternal fixation device.

Technology	Merits	Dmerits
Steel wire fixation	safe, rapid, efficient, inexpensive	lower stability, higher risk of postoperative complications
Zipfix cable ties	better strength and fatigue resistance, more stable closure	high cost, can not be reused during reoperation
Rigid plate fixation	minimal allergic reactions, facilitate healing, can be reused during reoperation	troublesome operation, screw tear off the sternum
Sternal encircling device	simple operation, more stable closure	need to select model, high cost

Non-steel-wire Fixation

Zipfix cable ties are precision-engineered implantable plastic devices, meticulously crafted from polyetheretherketone (PEEK). These devices incorporate a blunt-tipped needle at one terminus, and a self-locking ratchet mechanism at the opposing terminus [58]. The sternal ligation band possesses superior width and thickness compared to the sternal wire, exhibiting a rounded and blunt edge. This design ensures optimal strength and fatigue resistance. Additionally, the band minimizes irritation to the soft tissue and internal mammary artery, significantly reducing the risk of inadvertent glove puncture. The enlarged contact surface with the sternum further diminishes the likelihood of sternal dehiscience and reduces the occurrence of chest discomfort [53].

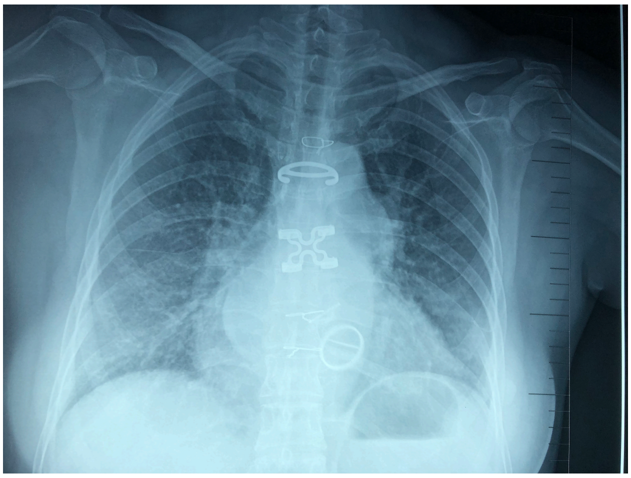

Fig. 1. Rigid plate fixation under X-ray (normal position).

Rigid Plate Fixation

The sternal fixation system, an innovative chest closure device, is made from pure titanium and titanium alloy, ensuring lightness, corrosion resistance, minimal allergic reactions, and compatibility with computed tomography (CT) and magnetic resonance (MR) imaging (Figs. 1,2). After sternotomy, the titanium plate effectively approximates the sternum, facilitating long-term healing, and remains implantable without the need for removal. This significantly minimizes the risk of sternal infection [11]. Experimental findings conducted on animals indicate that the titanium plate fixation method results in a significantly narrower incision gap in comparison to the wire ring fixation technique. Furthermore, this approach facilitates primary bone healing, subsequently expediting the sternal healing process by approximately four weeks [59].

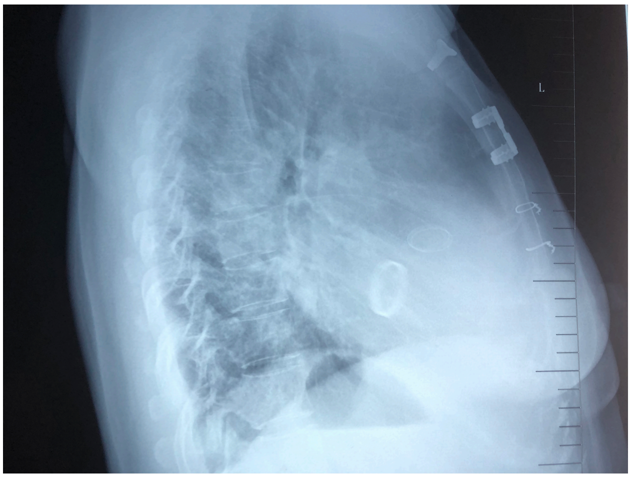

Fig. 2. Rigid plate fixation under X-ray (lateral position).

Sternal Encircling Device

The sternal encircling device is crafted from a nickel-titanium memory alloy, exhibiting a remarkable characteristic: its ability to soften upon exposure to colder temperatures, contract, and subsequently revert to its original condition upon heating. This exceptional material property facilitates a seamless and efficient intraoperative process, significantly shortening the duration of chest closure. The device's design closely aligns with the contour of the sternum, ensuring a precise fit. Once in position, it securely encircles the sternum, preserving its anatomical integrity. Following surgery, patients reported minimal discomfort and pain, and magnetic resonance imaging (MRI) scans were not compromised. Furthermore, a dense coating on the surface of the device mitigates the risk of nickel toxicity [60].

The last three methods all can decrease the risk of postoperative complications, shorten postoperative ventilator weaning time and ICU stay, and relieve the postoperative pain (Table 1) [61].

Prevention of Mediastinitis

The above Four Sternal Fixation Devices to Prevent Mediastinitis

It has been demonstrated that the use of steel wire for chest closure following surgery is an independent risk factor for the development of postoperative sternal infection [51]. Prior research has demonstrated that the fixation of the sternal plate significantly diminishes postoperative discomfort and mitigates the likelihood of wound-related complications among patients undergoing cardiac surgery [62]. Studies conducted by Song *et al*. [63–65] revealed that patients exhibiting various high-risk factors, including pathological obesity (with a BMI exceeding 30), diabetes, chronic obstructive pulmonary disease, renal failure, reoperative surgery, infection, prolonged cardiopulmonary bypass lasting over 2 hours and sternal fracture within the sternal incision, may experience a reduced incidence of mediastinitis after cardiac operation by using rigid sternal fixation. Allen *et al*. [66] randomized 236 patients at 12 US centers at the time of sternal closure to either rigid plate fixation (n = 116) or wire cerclage (n = 120) in a prospective, single-blinded, multicenter trial. They showed that sternotomy closure with rigid plate fixation resulted in significantly better sternal healing, and more sternal complications with wire cerclage 6 months after surgery. Royse *et al*. [67] showed that patients receiving the band and plate system had significantly less sternal edge motion than those receiving wires, 6 and 12 weeks after cardiac surgery and experienced less pain. A recent retrospective, case-control study analyzed morbidly obese patients who underwent open-heart surgery with a median sternotomy between 2011 and 2021, and showed that mediastinitis was significantly less common in the titanium plate group [68]. In Roughton *et al*.'s [69] series of 25 patients with pediatric mediastinitis, the feasibility of rigid sternal fixation was clearly demonstrated.

Other Ways to Prevent Mediastinitis

As can be seen from the above analysis, the sternal fixation device can effectively prevent and treat postoperative mediastinitis. In addition, perioperative prevention and management based on many pre-, intra-, and post-operative risk factors has been reported (Table 2) [70–76].

Studies indicate that inadequate wound drainage is the primary determinant of wound healing. Consequently, maintaining effective wound drainage is imperative for infection control and the facilitation of incisional healing [77]. In recent years, vacuum sealing drainage (VSD) technology has gained widespread acceptance, emerging as a crucial component in the management of complex wounds. This product embodies the integration of negative pressure, sealing, and drainage mechanisms. By maintaining a consistent negative pressure within the enclosed wound environment, it enhances microcirculation, fosters the development of fresh granulation tissue, efficiently eliminates infectious metabolites, speeds up tissue repair, and establishes an optimal foundation for wound healing and subsequent therapeutic procedures [78]. The continuous negative pressure suction serves to prevent contamination of drainage fluids into the mediastinal space and stimulates the development of granulation tissue. By sealing the semi-permeable membrane, the wound is effectively isolated from external factors, thus guarding against bacterial infiltration, containing infection, and optimizing local microcirculation. Additionally, the consistent negative pressure suction enables rapid wound contraction and secure closure, thereby mitigating the potential for dead space formation.

Following extensive research and practical applications, the substitution of the conventional median sternal incision with the intercostal incision in thoracoscopic cardiac surgery (TTCS) [79–82] has demonstrated a substantial reduction in the systemic inflammatory response [83], thereby enhancing surgical outcomes and patient recovery. Minimally invasive procedures, including partial sternotomy [84], can also enhance sternal stability following surgical operations.

Discussion

Multiple retrospective studies have conclusively identified numerous risk factors and have subsequently proposed corresponding therapeutic and preventive measures, which are tailored towards those factors that are amenable to control, including preoperative weight management, detection of blood glucose and protein level levels, prophylactic use of antibiotics, and intraoperative control of blood loss, use of rigid sternal fixation, topical antibiotics, and postoperative vacuum-assisted closure. However, it is worth noting that there remain certain areas of contention that require further exploration. The following points are hereby proposed as potential avenues for consideration in future research.

Despite the established association between RBC transfusion and the occurrence of mediastinitis, there has been a notable absence of further investigations into the relationship between transfusion and mediastinitis in the past decade. It remains undetermined whether the specific components of transfusion products, including RBCs, FFP, PLTs, and cryoprecipitate, as well as the duration of their storage, contribute to the adverse outcomes observed in cardiac surgery. In recent years, a growing number of cases

Table 2. Summary of pre-operative, intra-operative, and post-operative strategies to prevent and manage sternal wound infections.

Stages	Prevention
Preoperative	(1) Nasal colonization of bacteria and nasal decontamination with mupirocin (NDM) (2) The use of chlorhexidine skin wash before the surgery (3) Patient counseling and education involving a registered dietitian to promptly perform a thorough nutrition assessment, manage obesity and smoking, and tailor an individualized plan of care (4) Proper monitoring of perioperative blood glucose level, patients with increased serum glucose levels >180 mg/dL should have their blood glucose level optimized prior to surgery using intravenous insulin infusions (5) Albumin levels are detected preoperatively, and patients with hypoalbuminemia should be reoperated after receiving 7–10 enteral nutrition (6) Screening is performed to confirm existing infection, followed by prophylactic antibiotic treatment with a first or second-generation cephalosporin (the addition of vancomycin in *methicillin-resistant Staphylococcus aureus* (MASA) patients) for at least 24 hours (7) The hair removal of the surgical site on immediately before surgery rather than the previous day, the use of mechanical clippers rather than razors
Intraoperative	(1) An adequately ventilated sterile operating room and close monitoring of hospital equipment and personnel (2) Use of diathermy to control bleeding, the risk of sternal infection increases if the bleeding volume is greater than 800 mL (3) Internal mammary artery (IMAs) are taken down in a skeletonized fashion rather than in pedicled fashion (4) Sternal closure with (interlocking) figure-of-eight stainless steel wires, sternal screws, stainless steel plates, and bone staples to cerclage wires (5) The use of biomaterials present in the form of sponges, gels and powder instead of bone wax can avoid impeding bone healing (6) The topical solution is made of 1 g cephazolin and 40 mg gentamicin in 40 mL of normal saline which is sprayed multiple times over the sternal edges intraoperatively (7) Topical application of vancomycin and gentamicin collagen sponges for hemostasis
Post-operative	(1) Chest support using a corset or vest (2) The platelet rich plasma (PRP) and calcium thrombin enhance bone healing (3) Leaving the closed wound covered for at least 48 h with an impermeable wound dressing to prevent surgical site infection (4) Vacuum-assisted closure leads to a promptly and moderately stable sternal repair, provides evacuation of wound fluid, stimulates granulation tissue, and reduces the morbidity of dressing changes (5) Prophylactic negative pressure wound therapy (NPWT) significantly reduces surgical site infections (6) Early extubation and day-to-day attention to indwelling central venous arterial and pulmonary artery catheter (7) Intensive care unit and recovery room environment should be thoroughly cleaned and disinfected

of mediastinitis have been attributed to *non-Gram-positive bacteria*. However, there remains a dearth of extensive, high-quality randomized controlled studies that delve into the antimicrobial drug selection, dosage, and treatment duration for *gram-negative bacteria*, fungi, and other uncommon pathogens. Currently, sternal fixation devices such as titanium plates are popularly studied. However, the initial cost remains prohibitively high, hindering widespread acceptance. Therefore, it is imperative to use a personalized approach to strike a balance between surgical costs and the management of wound complications arising from sternotomy procedures. A number of novel hemostatic agents and bone wax substitutes have been devised in recent times, yet there remains a lack of unequivocal reports indicating the existence of materials capable of concurrently addressing sternal healing, postoperative bleeding, and the occurrence of infection. The principal challenge arises from the infrequency of mediastinitis occurrences, coupled with the brevity of postoperative follow-up among numerous patients. Consequently, numerous studies conducted have been retrospective in nature, and a prospective study remains elusive, hampering our ability to comprehensively capture delayed mediastinitis.

Conclusion

In summary, mediastinitis remains a devastating complication that occurs infrequently among patients undergoing cardiac surgery, yet its prognosis is exceedingly grim and mortality rates are alarmingly high. Therefore, it is imperative to possess a comprehensive and profound understanding of the etiology of mediastinitis, along with the meticulous execution of surgical techniques, precise alignment of the sternum, and secure closure, as these factors constitute the fundamental pillars of preventing the occurrence of mediastinitis.

Author Contributions

YY, JX and QJ contributed to the conception and design of the review. QJ contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Both images were from one patient in Sichuan Provincial People's Hospital and this patient's informed consent was obtained.

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Conflict of Interest

The authors declare no conflict of interest.

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