



## Mediastinitis in the intensive care unit patient: a narrative review

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1     **Mediastinitis in the ICU patient: a narrative review.**

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19

20    **Statement:**

21    The abstract is 239 words long

22    The article is 3666 words long.

## **Abstract**

### **Background**

Mediastinitis is a rare but severe infection, defined as an inflammation of the connective tissues and structures within the mediastinum. Due to its proximity with vital structures, mediastinitis represents a highly morbid pathological process associated with a high risk of mortality. In most cases mediastinitis requires treatment in the intensive care unit.

### **Objectives**

The goal of this narrative review is to highlight to the reader the clinical features of mediastinitis, to attempt to define each clinical scenario, to describe the responsible pathogens and finally to depict both the medical and surgical treatment.

### **Sources**

We performed a literature search of the PubMed and Cochrane libraries, limited for articles published between January 2003 and December 2018, reporting on acute mediastinitis.

### **Content**

The term covers different entities of different etiologies including deep sternal wound infection related to sternotomy; esophageal perforation or anastomosis leakage; and finally descending necrotizing mediastinitis often secondary to oropharyngeal abscess. The responsible pathogens and therefore subsequent management depends on the underlying etiology. Empirical antimicrobial therapy should cover the suspected microorganisms while surgery and supportive measures should aim to reduce the inoculum of pathogens by providing adequate drainage and debridement.

### **Implications**

Literature concerning mediastinitis in the ICU is relatively scarce. Here we collated the evidence and reviewed the different causes and treatment options of acute mediastinitis with a particular focus on microbiological epidemiology. Future research in larger cohorts is needed to better understand the treatment of this difficult disease.

## Introduction

An otherwise healthy lumberjack was diagnosed with a tooth abscess. Despite being treated with a course of oral antibiotics and steroids the infection progressed and after two days he developed septic shock caused by descending necrotizing mediastinitis (DNM). This required extraction of the affected tooth, cervico-mediastinal debridement, a prolonged course of intravenous antibiotics and hospitalization in the Intensive Care Unit (ICU) for several weeks. It took almost three months before the patient fully recovered and was able to return to work. Although mediastinitis is rare, this vignette is typical and highlights the high level of morbidity and mortality that this severe infection can cause.

The term “mediastinitis” refers to an infection of the mediastinum which can be caused by a range of different etiologies including deep sternal wound infection (DSWI) following sternotomy, esophageal perforation and DNM which is often secondary to an oropharyngeal abscess. The goal of this narrative review is to define each of these causes of mediastinitis, to describe the associated clinical features and responsible pathogens as well as discuss the medical and surgical treatment options.

## Method

For the purpose of this review, an online literature search of the PubMed and Cochrane libraries was performed using the terms listed in the supplementary file 1. The search was limited to articles that were published in English, between January 2003 and December 2018 and included only human adult subjects. Initially the search was also limited to include only randomized controlled trials, meta-analyses and observational studies. However, as this yielded an insufficient amount of high-quality data the search was subsequently expanded to include expert opinion papers, guidelines, recommendations and case series. Those articles that were not specifically written in the context of the ICU were also included if it was thought to be relevant to this review. Finally, the references of all of these articles identified in this expanded search were screened in order to identify any additional

relevant sources, regardless of publication date. Figure 1 shows the flow chart of the research process. All of the contributing authors had access to electronic versions of all of the articles identified.

## **Definitions, epidemiology and risk factors**

The mediastinum is the area posterior to the sternum and anterior to the thoracic spinal column. It contains the heart and large vessels, trachea, esophagus, thymus and lymph nodes (Figure 2). Mediastinitis describes a process of either inflammation and/or infection of the connective tissues and structures contained within the mediastinum. Due to the vital nature of those structures contained within the mediastinum, mediastinitis is associated with a high degree of morbidity and mortality with most cases requiring admission and treatment in the ICU [1]. The three most common etiologies of mediastinitis are described below and include DSWI, esophageal perforation and DNM.

### **Deep sternal wound infection**

DSWI describes a process by which the mediastinum becomes infected secondary to a deep wound infection following sternotomy. The Center for Disease Control defines DSWI as the presence of fever, chest pain or sternal instability with any one of the following: Purulent discharge from the operative wound; mediastinal widening on imaging studies; identification of micro-organisms cultured from mediastinal fluid or tissues; or histopathological evidence of mediastinitis on tissue samples from the mediastinum[2, 3]. The most recent classification of DSWI is based on the depth and extent of the infectious process and correlates with the severity of the infection. A Type I infection involves the skin and subcutaneous tissues only, Type II either the sternum or ribs, Type III includes bone loss of either the sternum or ribs and finally Type IV, when the mediastinum itself is affected[4].

Recent multi-center cohort studies and meta-analyses have reported that DSWI affects between 0.5% and 2.2% of patients undergoing cardiac surgery [5–7] and is associated with a mortality rate of 14% [5]. Mortality rates of elective cardiac surgery patients are five times higher if postoperative mediastinitis occurs [6]. Risk factors for DSWI can be either patient or procedure-related. The patient-related factors that increase the risk of developing DSWI are old age [2, 7], obesity, elevated preoperative creatinine, peripheral vascular disease [2, 6, 8], diabetes mellitus [2, 5], hyperglycemia in non-diabetic patients [6], pre-operative colonization with *Staphylococcus aureus* [9], chronic obstructive pulmonary disease, smoking, heart failure and female gender [2]. Procedure-related risk factors include the use of a ventricular assist device, transplant surgery [5, 6], the use of bilateral internal mammary artery grafts, prolonged length of surgery, the use of aortic cross clamping, redo surgery and finally on-pump perfusion [2, 8]. Tracheostomy is also considered as a risk factor for DSWI, with early percutaneous tracheostomy being at higher risk. [10, 11]

## Esophageal perforation

As the esophagus is colonized by both commensal and hospital-acquired microorganisms, any loss in the integrity of the esophageal wall may result in mediastinitis. The data relating to esophageal perforation comes from large and recent multi-center cohort studies and systematic reviews. Iatrogenic perforation during endoscopy is responsible for 60% of all esophageal perforations [12, 13] with the risk depending on the type of procedure performed. Pneumatic dilatations are associated with a 2-6% risk of esophageal perforation, stricture dilatation with a 0.09-2% risk and diagnostic procedures with 0.03-0.11% risk [12]. Furthermore, abnormal esophageal tissue is found in half of all of the cases of endoscopic perforation [13]. In the healthy esophagus, perforation usually occurs in areas of natural anatomical weakness such as Killian's triangle, the cricopharyngeal region and the esophagogastric juncture [12]. Spontaneous perforation (including Boerhaave's syndrome) represents between 8 to 33% of all esophageal perforations [12, 14] whilst traumatic and

malignant perforations represent 17% of cases [13, 14]. With an annual incidence of 3.1/million, esophageal perforation is rare with a reported mortality of up to 20% [13]. Whilst late diagnosis is a major factor associated with patient death [12], so elusive is the diagnosis that almost 20% of cases are only diagnosed at autopsy [13].

Perforation can also occur due to failure of a surgical anastomosis. This life-threatening post-operative complication occurs in up to 30% of esophageal anastomoses with a mortality rate of 2-12% [15]. The risk of such a failure is associated with a cervical anastomosis, female gender and pre-operative smoking [15]. Anastomotic leak can be graded as follows: Grade I (radiologically evident, no clinical sequelae); Grade II (minor clinical sequelae); Grade III (major clinical sequelae); and Grade IV (necrosis of the conduit) [15]. Whilst there is a paucity of data concerning the success of various treatment options for each grade of leak, it is clear that an anastomotic leak often requires protracted treatment in the ICU, a long hospital stay and multiple interventions. Furthermore, it has a lasting impact on the patients' quality of life, consumes a large amount of hospital resources and is associated with high overall costs [16–19].

#### Descending necrotizing mediastinitis (DNM)

DNM describes a serious infective process that originates from the ears, nose or throat and spreads inferiorly into the mediastinum via connective tissues planes. It can be defined by the presence of a severe oropharyngeal infection with concurrent radiological features that suggest mediastinitis [20, 21]. As with other forms of mediastinitis, DNM can be classified into Type I (localized), Type IIa (diffuse, extending into the lower anterior mediastinum) and Type IIb (diffuse, extending into both the anterior and posterior lower mediastinum) [22] (Figure 3).

DNM is caused by odontogenic (36-47%), pharyngeal (33-45%) or cervical (15%) infections. In 6% of cases, the source of infection is unknown [1, 21]. As listed in Table 1, the main risk factors for DNM include impaired immune function, diabetes, the use of oral glucocorticoids and reduced tissue

oxygenation caused by heart failure, respiratory insufficiency and peripheral artery occlusive disease. As a result, only 13% of DNM patients have no underlying comorbid illness [23]. The regular use of non-steroidal anti-inflammatory drugs is not thought to be a contributing factor [24]. The mortality of DNM is high and reported to be between 15 and 30% [1, 21, 23] with a higher risk of death associated with a delay in diagnosis, inadequate surgical drainage of the mediastinum [23], advanced age, increasing ICU severity scores and higher a grade of DNM [1]. Epidemiology of DNM is also based on recent multi-center cohort studies and systematic review.

#### Acute hematogenous mediastinitis, rare mediastinitis etiologies

A rare cause of acute mediastinitis is primary mediastinitis caused by hematogenous spread from a remote infection. Although typically found in ICU patients, there are only a few case reports that describe this process [25, 26]. As a result, the etiology is poorly understood and treatment modalities not elaborated. Also, any cause of esophageal or broncho-tracheal perforations can be a potential, yet uncommon, cause of mediastinitis.

### **Diagnosis and management**

#### Diagnosis

##### *Clinical presentation*

Signs of mediastinitis are non-specific and largely depend on the underlying etiology. They consist of an infective process causing fever, chills and tachycardia. Although pain is often masked in the ICU patient, if it is present it can often help identify the site and thus underlying cause of the infection. When an ear, nose or throat infection is present, a trismus, or *lockjaw*, can also sometimes be found. A systemic inflammatory response syndrome often develops abruptly although the speed of onset depends on both the underlying etiology and patient characteristics. Early diagnosis of mediastinitis



is critical as it allows for prompt antibiotic therapy to be started and surgical intervention to be performed [21].

#### *Laboratory findings*

Although laboratory findings are non-specific, an elevated leukocyte count, C-reactive protein and procalcitonin level are often found. Additionally, a progressive thrombocytopenia may reflect worsening sepsis. Evidence of disseminated intravascular coagulation may also be present.

#### *Imaging*

When mediastinitis is suspected, contrast enhanced computed tomography (CT) of the neck and chest is the imaging modality of choice in order to confirm the diagnosis. Not only is a CT scan highly sensitive for identifying the underlying cause of the mediastinitis, but the extent of the infectious process can also be gauged. This is vital in planning potential surgical interventions [27] (Figure 4).

Despite the high sensitivity of cross-sectional imaging, it should be noted that in the setting of DSWI diagnosing mediastinitis can be challenging due to the inflammatory changes that occur following surgery. In this situation, a repeat CT scan and/or scintigraphy may be useful in assessing for evidence of disease progression [28].

#### *Microbiological sampling*

In addition to cross-sectional imaging, the microbiological diagnosis of mediastinitis is critical in order to adapt the antimicrobial therapy accordingly. Blood cultures should ideally be taken and either tissue or fluid samples obtained prior to the initiation of antibiotic therapy. This may require aspiration from deep abscess cavities or debridement of infected sternal or mediastinal tissues [29, 30]. In more severe cases, pleural fluid or broncho-alveolar secretions may also be required [31]. When taken alone, superficial wound cultures should be interpreted with caution as they may represent wound colonization rather than infection and lead to inappropriate antibiotic therapy [30].

197

198 Microbiological epidemiology.

199 *Mediastinitis after cardiac surgery -*

200 The majority of patients with postoperative mediastinitis develop monomicrobial infections. In a  
201 French study that included 309 patients admitted to the ICU for post-cardiac surgery mediastinitis,  
202 262 (84.7%) were monomicrobial [32]. The most common bacteria isolated were methicillin  
203 susceptible *Staphylococcus aureus* (MSSA) (31.9%), *Enterobacteriaceae* (25.8%), coagulase negative  
204 *Staphylococcus* (CoNS) (18.7%), *Streptococcus* spp. (8.5%), methicillin resistant *S.aureus* (MRSA)  
205 (6.9%) and non-fermenting Gram negative bacteria (1.9%). In a Chinese study on a similar cohort of  
206 patients, the organisms isolated were Gram negative bacteria (55.4%), MSSA (20.4%), CoNS (14%),  
207 MRSA (5.7%) and fungi (3.8%) [33]. Amongst the Gram negative bacteria, *Acinetobacter baumannii*,  
208 *Pseudomonas aeruginosa*, and *Enterobacter cloacae* exhibited 100%, 15%, and 0% resistance to  
209 ceftazidime respectively, 100%, 22.5% and 40% resistance to piperacillin-tazobactam, and 80%,  
210 17.5%, and 0% resistance to carbapenem [33]. In a Brazilian series including 92 patients with post-  
211 cardiac surgery mediastinitis [34], 33 patients (35.8%) were infected with carbapenem-resistant  
212 *Enterobacteriaceae*, amongst which 15 (45%) were also resistant to colistin. The discrepancy  
213 between the different cultures and sensitivities of the microbiological flora identified may be  
214 explained by local ecologies and institutional antibiotic policies.

215 Sporadic outbreaks of unexpected organisms, such as *Candida* spp. [35] and *Legionella* spp. [36],  
216 have also been found to cause DSWI following cardiac surgery, as have *Nocardia* spp. [37],  
217 *Mycoplasma hominis* and *Mycobacterium tuberculosis* [38, 39]. *Mycobacterium chimaera* as a  
218 causative agent, thought to originate from a contaminated heater-cooler device used in bypass  
219 surgery, has also been described [40].

220 *Mediastinitis secondary to esophageal perforation*

221 The microorganisms responsible for mediastinitis secondary to esophageal perforation depend on  
222 several factors including the site of perforation, the clinical status of patient, the use of enteral  
223 nutrition and of gastric acid suppression, the degree of immunosuppression and a history of recent  
224 antibiotic exposure. In non-intubated, healthy adults who has not recently received antibiotics,  
225 organisms in the upper esophagus are essentially identical to those in the oropharynx and include  
226 streptococci (including *S.salivarius*, *S.mutans*, *S.mitis*, *S.sanguinis* and *S.anginosus*), *Neisseria* spp.,  
227 *Haemophilus* spp. and anaerobes such as *Prevotella* spp. or *Fusobacterium* spp. [41]. In those who  
228 are critically ill and have been exposed to recent antibiotic therapy, the normal oral flora is rapidly  
229 replaced by aerobic Gram negative bacteria, *S. aureus*, and *Candida* spp. [42].

### 230 *Descending necrotizing mediastinitis*

231 Unlike the monobacterial infections of DSWI, mediastinitis caused by DNM is typically polymicrobial  
232 and consists of the normal resident flora found on the mucosal surfaces of the oral cavity, upper  
233 respiratory tract, ears and eyes. However, in those who are critically ill with odontogenic infections,  
234 less than 25% of blood and tissue cultures are positive [43]. This may reflect the finding that the  
235 patients referred from the community to the hospital with odontogenic infections are likely to have  
236 received a course of antibiotics prior to their admission [44].

237 The pathogens found in odontologic infections commonly include *Streptococcus* spp., *S.aureus*,  
238 *P.aeruginosa* and *Escherichia coli* [43]. Most dental abscesses also harbor oral anaerobes including  
239 *Peptostreptococcus* spp., *Fusobacterium nucleatum*, *Prevotella* spp. and *Actinomyces* spp. [45].

240 Infections arising from the pharynx frequently contain oral anaerobes, such as *Fusobacterium*  
241 *necrophorum* and facultative streptococci including *S.pyogenes* [46]. *H.influenzae* may also be found  
242 in parapharyngeal or retropharyngeal abscesses [47].

243 Otogenic infections frequently involve streptococci, obligate anaerobes, *S.aureus* and *P.aeruginosa*  
244 [48]. Infections arising from chronic suppurative sinusitis tend to involve *S.pneumoniae*, *H.influenzae*,

245 *Moraxella catarrhalis*, *S.aureus* and obligate anaerobes [47]. The distribution of these bacterial flora  
246 is described in Table 2.

247

248 General principles of management

249 Although the management of mediastinitis depends on the underlying etiology, several elements of  
250 care are generic to all patients. Mediastinitis is a severe infection that often evolves into septic shock.  
251 In patients with DNM, there is a correlation between both the time to ICU admission and the ICU  
252 severity scores on admission to the unit with the overall mortality [1]. Moreover, septic shock is an  
253 independent predictor of mortality [21].

254 Airway compromise should be anticipated early especially in cases involving the neck and upper  
255 mediastinum. Due to trismus and local swelling, both laryngoscopic visualization and anterior access  
256 to the airway may be compromised. Guidelines dictate that the airway should be managed by an  
257 expert anesthesiologist with an alternative plan for airway control clarified beforehand. Involvement  
258 of an expert otolaryngologist and/or maxillo-facial surgeon in planning intubation is encouraged and  
259 they should also be present at the time of intubation should efforts at endotracheal intubation fail  
260 [49–51].

261

262 Antimicrobial therapy

263 The antimicrobial treatment of mediastinitis should follow the good practice principles of empirical  
264 antimicrobial therapy in ICU patients [52, 53]. Microbiological samples should ideally be collected  
265 prior to the administration of antibiotics although treatment should not be unduly delayed [53]. In  
266 mediastinitis, specific data regarding the efficacy of antimicrobial therapy are scarce and hence the  
267 following recommendations, summarized in Table 3, are based on expert opinions.

268 In mediastinitis secondary to DSWI, empirical antimicrobial therapy should cover MSSA, skin  
269 commensals and gastrointestinal Gram negative bacteria [6, 54]. We recommend a broad-spectrum  
270 beta-lactam penicillin, such as piperacillin/tazobactam, with the addition of a glycopeptid or  
271 oxazolidinone if MRSA or methicillin resistant CoNS stains are suspected.

272 In patients with mediastinitis after esophageal perforation, intravenous broad-spectrum antibiotics  
273 should cover the aerobes and anaerobes that are commonly found in the upper digestive tract and  
274 may include piperacillin/tazobactam or a third-generation cephalosporin with metronidazole [2, 12].  
275 We suggest that this treatment should be continued for at least seven days after the drainage of fluid  
276 collections and repair/healing of the perforation. In more severe infections or complex patients,  
277 although not supported by data from randomized studies, we suggest considering the use of an  
278 empirical anti-fungal. Specifically, we recommend initiating echinocandin if three out of the four  
279 following criteria are present: Septic shock; female gender; previous upper gastrointestinal surgery;  
280 and previous recent antimicrobial therapy lasting more than 48 hours [55].

281 In mediastinitis secondary to DNM, empirical antimicrobial therapy should cover those aerobic and  
282 anaerobic bacteria commonly associated with ear, nose and throat infections. Although there are no  
283 standardized regimens described in the academic literature, a third-generation cephalosporin with  
284 metronidazole [21] or a combination of piperacillin/tazobactam and clindamycin is suggested [56].

285 Once microbiological samples have been obtained, broad-spectrum antimicrobial therapy can be  
286 initiated until such time that it can be tailored according to the subsequent microbiological findings  
287 [57]. The ideal duration of antimicrobial therapy in mediastinitis is not well defined. Nevertheless,  
288 the literature consistently suggests that a long course of treatment lasting between 14 to 21 days is  
289 required [2, 12, 21]. A course of six weeks is recommended when foreign bodies, such as sternotomy  
290 wires, are present [58]. Whilst the use of serial CT imaging and biochemical markers of infection can  
291 be helpful in monitoring the success of antibiotic therapy, the level of evidence supporting this

approach is limited [59]. Therefore, patients require close observation with the dosing, duration and regimen of antimicrobial therapy changed as required.

## Surgery

Control of the infectious source and debridement of affected tissue are the cornerstones of the surgical treatment of mediastinitis. The surgical strategy is determined according to the cause and extent of the underlying disease. This can be best appreciated on cross-sectional imaging. A delay between diagnosis and surgical intervention is known to be associated with poor outcome and as such should not exceed 24 hours [2].

DSWI requires early operative intervention for the debridement of necrotic tissues and the removal of sternal wires. If sternal instability is present and healthy bone stock lacking, surgical closure can be ultimately achieved using muscle or omental flaps [2]. In both DNM and esophageal perforation, priority is given to treating the causative lesion with concurrent generous cervical and mediastinal drainage. Figure 5 shows the classical drainage required for DNM.

Endoscopic management of esophageal perforations or anastomotic leakage with stents has been described in the literature and is an acceptable option if expertise is available [12, 60, 61]. In certain situations, endoscopically placed negative pressure wound therapy has shown promising results [62]. However, due to the small cohorts studied and the clinical heterogeneity of the patients included, no evidence based treatment strategy can be composed based on the existing literature.

For localized infections of the neck and upper mediastinum, fascial planes can often be satisfactorily opened by means of a cervicotomy. Should the anterior mediastinum need to be debrided, a median sternotomy may be required. However, in order to prevent subsequent sternal osteomyelitis, a generous bilateral anterolateral thoracotomy may be more appropriate. If local expertise is available, video assisted thoracic surgery has also been used effectively [63]. Should the patient need

more drastic debridement, a clamshell thoracotomy offers excellent exposure to the entire mediastinum as well as both pleural cavities. If the posterior mediastinum needs to be accessed, a posterolateral thoracotomy may be more appropriate. Any sign of clinical or biochemical deterioration should be identified early as it may indicate the need for subsequent surgical re-intervention.

## Supportive measures

Several of the supportive measures associated with the treatment of mediastinitis are of particular importance and are described in Table 4. Regarding DSWI, routine pre-operative decolonization of nasal *S. aureus* is beneficial [64] and is included in international guidelines as part of the pre-operative prophylactic care bundle for patients undergoing thoracic surgery [65]. Should debridement result in a wound that is not amenable to surgical repair, negative pressure wound therapy is now well recognized and widely used for the closure of complicated sternal wounds that may still be infected. This strategy is safe and effective for both Type I and Type II DSWI and may also have a role preventing disease progression that could result in gross mediastinitis [2]. Whilst the use of open dressings with granulated sugar [66] and treatment with hyperbaric oxygen therapy [67] have also been described, the quality of the evidence supporting these approaches is either low or very low.

Adequate calorie intake is critical for preventing a catabolic state and is closely related to successful wound healing. However, as those patients with either esophageal perforation or anastomotic leak are often nil by mouth for long periods of time, either an endoscopically or radiologically placed naso-jejunal feeding tube or formal surgical jejunostomy should be used for enteral feeding in stable patients [2, 68]. If enteral nutrition will be contraindicated for a prolonged period of time, total parenteral nutrition should be used. We also recommend intravenous proton pump inhibitor therapy for between two to three weeks [2, 12].

The main supportive measure of DNM is airway management. Due to the difficult nature of the airway in this subset of patients, national and local guidelines regarding difficult airway management must be thoroughly followed. Early tracheotomy should be considered and is both useful for securing the airway as well as opening the fascial planes of the neck [2]. Early airway support is also advantageous as on average patients will need more than three surgical procedures during the course of their illness [21].

## **Conclusion and perspectives**

Mediastinitis is a life-threatening infection with significant associated morbidity and mortality. The diagnosis relies on both thorough clinical examination and early cross-sectional imaging. Subsequent management depends on the underlying etiology and can be divided into DSWI, esophageal perforation and DNM. Identification of the causative bacteria is critical in order to appropriately direct antimicrobial therapy although the responsible pathogens vary according to anatomical location making empirical treatment challenging. Surgery and supportive measures should aim to reduce the inoculum of pathogens by providing adequate drainage and debridement.

As mediastinitis is a relatively rare entity, the literature supporting treatment options is scarce and often focuses on a single etiology or treatment modality. In this article we have collated this evidence and reviewed the different etiologies as well as treatment options of acute mediastinitis with a particular focus on the microbiological epidemiology. Future research in larger cohorts of patients is needed to better understand the treatment of acute mediastinitis in order to reduce both the morbidity and mortality of this difficult disease.



362    **Transparency declaration**

363    Dr. Pastene has nothing to disclose.

364    Dr. Cassir has nothing to disclose.

365    Dr. Tankel has nothing to disclose.

366    Pr. Einav reports personal fees from Zoll, Medtronic, Diasorin, Merck, Artisanpharma, Eisai, Astra  
367    Zenca, outside the submitted work.

368    Pr. FOURNIER has nothing to disclose.

369    Pr. THOMAS has nothing to disclose.

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371    outside the submitted work.

372

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## 376 References

- 377 1. Palma DM, Giuliano S, Cracchiolo AN, Falcone M, Ceccarelli G, Tetamo R, Venditti M (2016)  
378 Clinical features and outcome of patients with descending necrotizing mediastinitis:  
379 prospective analysis of 34 cases. *Infection* 44:77–84
- 380 2. Abu-Omar Y, Kocher GJ, Bosco P, et al (2017) European Association for Cardio-Thoracic Surgery  
381 expert consensus statement on the prevention and management of mediastinitis. *Eur J Cardio-*  
382 *Thorac Surg Off J Eur Assoc Cardio-Thorac Surg* 51:10–29
- 383 3. Goh SSC (2017) Post-sternotomy mediastinitis in the modern era. *J Card Surg* 32:556–566
- 384 4. Anger J, Dantas DC, Arnoni RT, Farsky PS (2015) A new classification of post-sternotomy  
385 dehiscence. *Rev Bras Cir Cardiovasc Orgao Of Soc Bras Cir Cardiovasc* 30:114–118
- 386 5. Filsoufi F, Castillo JG, Rahmanian PB, Broumand SR, Silvay G, Carpentier A, Adams DH (2009)  
387 Epidemiology of deep sternal wound infection in cardiac surgery. *J Cardiothorac Vasc Anesth*  
388 23:488–494
- 389 6. Perrault LP, Kirkwood KA, Chang HL, et al (2018) A Prospective Multi-Institutional Cohort Study  
390 of Mediastinal Infections After Cardiac Operations. *Ann Thorac Surg* 105:461–468
- 391 7. Abdelnoor M, Vengen ØA, Johansen O, Sandven I, Abdelnoor AM (2016) Latitude of the study  
392 place and age of the patient are associated with incidence of mediastinitis and microbiology in  
393 open-heart surgery: a systematic review and meta-analysis. *Clin Epidemiol* 8:151–163
- 394 8. Cotogni P, Barbero C, Rinaldi M (2015) Deep sternal wound infection after cardiac surgery:  
395 Evidences and controversies. *World J Crit Care Med* 4:265–273
- 396 9. Allen KB, Fowler VGJ, Gammie JS, Hartzel JS, Onorato MT, DiNubile MJ, Sobanjo-Ter Meulen A  
397 (2014) *Staphylococcus aureus* Infections After Elective Cardiothoracic Surgery: Observations  
398 From an International Randomized Placebo-Controlled Trial of an Investigational *S aureus*  
399 Vaccine. *Open Forum Infect Dis* 1:ofu071
- 400 10. Tsai Y-C, Phan K, Stroebe A, Williams L, Nicotra L, Drake L, Ryan E, McGree J, Tesar P, Shekar K  
401 (2016) Association between post-sternotomy tracheostomy and deep sternal wound infection:  
402 a retrospective analysis. *J Thorac Dis* 8:3294–3300
- 403 11. Pilarczyk K, Marggraf G, Dudasova M, Demircioglu E, Scheer V, Jakob H, Dusse F (2015)  
404 Tracheostomy After Cardiac Surgery With Median Sternotomy and Risk of Deep Sternal Wound  
405 Infections: Is It a Matter of Timing? *J Cardiothorac Vasc Anesth* 29:1573–1581
- 406 12. Chirica M, Champault A, Dray X, Sulpice L, Munoz-Bongrand N, Sarfati E, Cattani P (2010)  
407 Esophageal perforations. *J Visc Surg* 147:e117-128
- 408 13. Vidarsdottir H, Blondal S, Alfredsson H, Geirsson A, Gudbjartsson T (2010) Oesophageal  
409 perforations in Iceland: a whole population study on incidence, aetiology and surgical outcome.  
410 *Thorac Cardiovasc Surg* 58:476–480
- 411 14. Bhatia P, Fortin D, Inculet RI, Malthaner RA (2011) Current concepts in the management of  
412 esophageal perforations: a twenty-seven year Canadian experience. *Ann Thorac Surg* 92:209–  
413 215

- 414 15. Price TN, Nichols FC, Harmsen WS, Allen MS, Cassivi SD, Wigle DA, Shen KR, Deschamps C  
415 (2013) A comprehensive review of anastomotic technique in 432 esophagectomies. *Ann Thorac*  
416 *Surg* 95:1154–1160; discussion 1160-1161
- 417 16. Biere SS a. Y, Maas KW, Cuesta MA, van der Peet DL (2011) Cervical or thoracic anastomosis  
418 after esophagectomy for cancer: a systematic review and meta-analysis. *Dig Surg* 28:29–35
- 419 17. Alanezi K, Urschel JD (2004) Mortality secondary to esophageal anastomotic leak. *Ann Thorac*  
420 *Cardiovasc Surg Off J Assoc Thorac Cardiovasc Surg Asia* 10:71–75
- 421 18. Luketich JD, Pennathur A, Awais O, et al (2012) Outcomes after minimally invasive  
422 esophagectomy: review of over 1000 patients. *Ann Surg* 256:95–103
- 423 19. Blackmon SH, Correa AM, Wynn B, et al (2007) Propensity-matched analysis of three  
424 techniques for intrathoracic esophagogastric anastomosis. *Ann Thorac Surg* 83:1805–1813;  
425 discussion 1813
- 426 20. Estrera AS, Landay MJ, Grisham JM, Sinn DP, Platt MR (1983) Descending necrotizing  
427 mediastinitis. *Surg Gynecol Obstet* 157:545–552
- 428 21. Prado-Calleros HM, Jiménez-Fuentes E, Jiménez-Escobar I (2016) Descending necrotizing  
429 mediastinitis: Systematic review on its treatment in the last 6 years, 75 years after its  
430 description. *Head Neck* 38 Suppl 1:E2275-2283
- 431 22. Endo S, Murayama F, Hasegawa T, Yamamoto S, Yamaguchi T, Sohara Y, Fuse K, Miyata M,  
432 Nishino H (1999) Guideline of surgical management based on diffusion of descending  
433 necrotizing mediastinitis. *Jpn J Thorac Cardiovasc Surg Off Publ Jpn Assoc Thorac Surg Nihon*  
434 *Kyobu Geka Gakkai Zasshi* 47:14–19
- 435 23. Ridder GJ, Maier W, Kinzer S, Teszler CB, Boedeker CC, Pfeiffer J (2010) Descending necrotizing  
436 mediastinitis: contemporary trends in etiology, diagnosis, management, and outcome. *Ann Surg*  
437 251:528–534
- 438 24. Petitpas F, Blancal J-P, Mateo J, et al (2012) Factors associated with the mediastinal spread of  
439 cervical necrotizing fasciitis. *Ann Thorac Surg* 93:234–238
- 440 25. Er F, Nia AM, Caglayan E, Gassanov N (2010) Mediastinitis as a complication of central venous  
441 catheterization. *Infection* 38:509
- 442 26. Chang CH, Huang JY, Lai PC, Yang CW (2009) Posterior mediastinal abscess in a hemodialysis  
443 patient - a rare but life-threatening complication of *Staphylococcus* bacteremia. *Clin Nephrol*  
444 71:92–95
- 445 27. Exarhos DN, Malagari K, Tsatalou EG, Benakis SV, Peppas C, Kotanidou A, Chondros D, Roussos  
446 C (2005) Acute mediastinitis: spectrum of computed tomography findings. *Eur Radiol* 15:1569–  
447 1574
- 448 28. Rouzet F, de Labriolle-Vaylet C, Trouillet J-L, Hitzel A, Benali K, Lebtahi R, Le Guludec D (2015)  
449 Diagnostic value of (9)(9)mTc-HMPAO-labeled leukocytes scintigraphy in suspicion of post-  
450 sternotomy mediastinitis relapse. *J Nucl Cardiol Off Publ Am Soc Nucl Cardiol* 22:123–129
- 451 29. Gottlieb GS, Fowler VG, Kong LK, McClelland RS, Gopal AK, Marr KA, Li J, Sexton DJ, Glower D,  
452 Corey GR (2000) *Staphylococcus aureus* bacteremia in the surgical patient: a prospective

- 453 analysis of 73 postoperative patients who developed *Staphylococcus aureus* bacteremia at a  
454 tertiary care facility. *J Am Coll Surg* 190:50–57
- 455 30. Benlolo S, Matéo J, Raskine L, Tibourtine O, Bel A, Payen D, Mebazaa A (2003) Sternal puncture  
456 allows an early diagnosis of poststernotomy mediastinitis. *J Thorac Cardiovasc Surg* 125:611–  
457 617
- 458 31. Hoffmann M, Kujath P, Vogt F-M, Laubert T, Limmer S, Mulrooney T, Bruch H-P, Jungbluth T,  
459 Schloericke E (2013) Outcome and management of invasive candidiasis following oesophageal  
460 perforation. *Mycoses* 56:173–178
- 461 32. Charbonneau H, Maillet JM, Faron M, et al (2014) Mediastinitis due to Gram-negative bacteria  
462 is associated with increased mortality. *Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol*  
463 *Infect Dis* 20:O197-202
- 464 33. Ma J-G, An J-X (2018) Deep sternal wound infection after cardiac surgery: a comparison of three  
465 different wound infection types and an analysis of antibiotic resistance. *J Thorac Dis* 10:377–  
466 387
- 467 34. Abboud CS, Monteiro J, Stryjewski ME, et al (2016) Post-surgical mediastinitis due to  
468 carbapenem-resistant Enterobacteriaceae: Clinical, epidemiological and survival characteristics.  
469 *Int J Antimicrob Agents* 47:386–390
- 470 35. Arıkan AA, Omay O, Kanko M, Horuz E, Yağlı G, Kağan EY, Ağır H (2018) Treatment of *Candida*  
471 sternal infection following cardiac surgery - a review of literature. *Infect Dis Lond Engl* 1–11
- 472 36. Lowry PW, Blankenship RJ, Gridley W, Troup NJ, Tompkins LS (1991) A cluster of legionella  
473 sternal-wound infections due to postoperative topical exposure to contaminated tap water. *N*  
474 *Engl J Med* 324:109–113
- 475 37. Wenger PN, Brown JM, McNeil MM, Jarvis WR (1998) *Nocardia farcinica* sternotomy site  
476 infections in patients following open heart surgery. *J Infect Dis* 178:1539–1543
- 477 38. Sielaff TD, Everett JE, Shumway SJ, Wahoff DC, Bolman RM, Dunn DL (1996) *Mycoplasma*  
478 *hominis* infections occurring in cardiovascular surgical patients. *Ann Thorac Surg* 61:99–103
- 479 39. Wang LZ, Wei CN, Xiao F, Chang XY, Zhang YF (2018) Incidence and risk factors for chronic pain  
480 after elective caesarean delivery under spinal anaesthesia in a Chinese cohort: a prospective  
481 study. *Int J Obstet Anesth* 34:21–27
- 482 40. Lyman MM, Grigg C, Kinsey CB, et al (2017) Invasive Nontuberculous Mycobacterial Infections  
483 among Cardiothoracic Surgical Patients Exposed to Heater-Cooler Devices1. *Emerg Infect Dis*  
484 23:796–805
- 485 41. Norder Grusell E, Dahlén G, Ruth M, Ny L, Quiding-Järbrink M, Bergquist H, Bove M (2013)  
486 Bacterial flora of the human oral cavity, and the upper and lower esophagus. *Dis Esophagus Off*  
487 *J Int Soc Dis Esophagus* 26:84–90
- 488 42. Safdar N, Crnich CJ, Maki DG (2005) The pathogenesis of ventilator-associated pneumonia: its  
489 relevance to developing effective strategies for prevention. *Respir Care* 50:725–739; discussion  
490 739-741

- 491 43. Qu L, Liang X, Jiang B, Qian W, Zhang W, Cai X (2018) Risk Factors Affecting the Prognosis of  
492 Descending Necrotizing Mediastinitis From Odontogenic Infection. *J Oral Maxillofac Surg Off J*  
493 *Am Assoc Oral Maxillofac Surg* 76:1207–1215
- 494 44. Sandner A, Börgermann J, Kösling S, Silber R-E, Bloching MB (2007) Descending necrotizing  
495 mediastinitis: early detection and radical surgery are crucial. *J Oral Maxillofac Surg Off J Am*  
496 *Assoc Oral Maxillofac Surg* 65:794–800
- 497 45. Brook I (2009) Current management of upper respiratory tract and head and neck infections.  
498 *Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-*  
499 *Rhino-Laryngol - Head Neck Surg* 266:315–323
- 500 46. Ehlers Klug T, Rusan M, Fuursted K, Ovesen T (2009) *Fusobacterium necrophorum*: most  
501 prevalent pathogen in peritonsillar abscess in Denmark. *Clin Infect Dis Off Publ Infect Dis Soc*  
502 *Am* 49:1467–1472
- 503 47. Brook I (2004) Microbiology and management of peritonsillar, retropharyngeal, and  
504 parapharyngeal abscesses. *J Oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg* 62:1545–  
505 1550
- 506 48. Laulajainen Hongisto A, Aarnisalo AA, Lempinen L, Saat R, Markkola A, Leskinen K, Blomstedt G,  
507 Jero J (2017) Otogenic Intracranial Abscesses, Our Experience Over the Last Four Decades. *J Int*  
508 *Adv Otol* 13:40–46
- 509 49. Apfelbaum JL, Hagberg CA, Caplan RA, et al (2013) Practice guidelines for management of the  
510 difficult airway: an updated report by the American Society of Anesthesiologists Task Force on  
511 Management of the Difficult Airway. *Anesthesiology* 118:251–270
- 512 50. Frerk C, Mitchell VS, McNarry AF, Mendonca C, Bhagrath R, Patel A, O’Sullivan EP, Woodall NM,  
513 Ahmad I, Difficult Airway Society intubation guidelines working group (2015) Difficult Airway  
514 Society 2015 guidelines for management of unanticipated difficult intubation in adults. *Br J*  
515 *Anaesth* 115:827–848
- 516 51. Langeron O, Bourgain J-L, Francon D, et al (2018) Difficult intubation and extubation in adult  
517 anaesthesia. *Anaesth Crit Care Pain Med*. doi: 10.1016/j.accpm.2018.03.013
- 518 52. Champion M, Scully G (2018) Antibiotic Use in the Intensive Care Unit: Optimization and De-  
519 Escalation. *J Intensive Care Med* 885066618762747
- 520 53. Pastene B, Duclos G, Martin C, Leone M (2016) Antimicrobial therapy in patients with septic  
521 shock. *Presse Med* 45:e111-117
- 522 54. Lemaigen A, Birgand G, Ghodhbane W, et al (2015) Sternal wound infection after cardiac  
523 surgery: incidence and risk factors according to clinical presentation. *Clin Microbiol Infect Off*  
524 *Publ Eur Soc Clin Microbiol Infect Dis* 21:674.e11–18
- 525 55. Montravers P, Dupont H, Leone M, et al (2015) Guidelines for management of intra-abdominal  
526 infections. *Anaesth Crit Care Pain Med* 34:117–130
- 527 56. Gunaratne DA, Tseros EA, Hasan Z, Kudpaje AS, Suruliraj A, Smith MC, Riffat F, Palme CE (2018)  
528 Cervical necrotizing fasciitis: Systematic review and analysis of 1235 reported cases from the  
529 literature. *Head Neck* 40:2094–2102

- 530 57. McDanel JS, Perencevich EN, Diekema DJ, Herwaldt LA, Smith TC, Chrischilles EA, Dawson JD,  
531 Jiang L, Goto M, Schweizer ML (2015) Comparative effectiveness of beta-lactams versus  
532 vancomycin for treatment of methicillin-susceptible *Staphylococcus aureus* bloodstream  
533 infections among 122 hospitals. *Clin Infect Dis Off Publ Infect Dis Soc Am* 61:361–367
- 534 58. Yusuf E, Chan M, Renz N, Trampuz A (2018) Current perspectives on diagnosis and management  
535 of sternal wound infections. *Infect Drug Resist* 11:961–968
- 536 59. Zhang T, Wang Y, Yang Q, Dong Y (2017) Procalcitonin-guided antibiotic therapy in critically ill  
537 adults: a meta-analysis. *BMC Infect Dis* 17:514
- 538 60. Vogel SB, Rout WR, Martin TD, Abbitt PL (2005) Esophageal perforation in adults: aggressive,  
539 conservative treatment lowers morbidity and mortality. *Ann Surg* 241:1016-1021 ;discussion  
540 1021-1023
- 541 61. Brinster CJ, Singhal S, Lee L, Marshall MB, Kaiser LR, Kucharczuk JC (2004) Evolving options in  
542 the management of esophageal perforation. *Ann Thorac Surg* 77:1475–1483
- 543 62. Bludau M, Hölscher AH, Herbold T, Leers JM, Gutschow C, Fuchs H, Schröder W (2014)  
544 Management of upper intestinal leaks using an endoscopic vacuum-assisted closure system (E-  
545 VAC). *Surg Endosc* 28:896–901
- 546 63. Son HS, Cho JH, Park SM, Sun K, Kim KT, Lee SH (2006) Management of descending necrotizing  
547 mediastinitis using minimally invasive video-assisted thoracoscopic surgery. *Surg Laparosc*  
548 *Endosc Percutan Tech* 16:379–382
- 549 64. Bode LGM, Kluytmans JAJW, Wertheim HFL, et al (2010) Preventing surgical-site infections in  
550 nasal carriers of *Staphylococcus aureus*. *N Engl J Med* 362:9–17
- 551 65. Engelman R, Shahian D, Shemin R, Guy TS, Bratzler D, Edwards F, Jacobs M, Fernando H, Bridges  
552 C, Workforce on Evidence-Based Medicine, Society of Thoracic Surgeons (2007) The Society of  
553 Thoracic Surgeons practice guideline series: Antibiotic prophylaxis in cardiac surgery, part II:  
554 Antibiotic choice. *Ann Thorac Surg* 83:1569–1576
- 555 66. De Feo M, Gregorio R, Renzulli A, Ismeno G, Romano GP, Cotrufo M (2000) Treatment of  
556 recurrent postoperative mediastinitis with granulated sugar. *J Cardiovasc Surg (Torino)* 41:715–  
557 719
- 558 67. Mills C, Bryson P (2006) The role of hyperbaric oxygen therapy in the treatment of sternal  
559 wound infection. *Eur J Cardio-Thorac Surg Off J Eur Assoc Cardio-Thorac Surg* 30:153–159
- 560 68. Doddoli C, Trousse D, Avaro J-P, Djournio X-B, Giudicelli R, Fuentes P, Thomas P (2010) [Acute  
561 mediastinitis except in a context of cardiac surgery]. *Rev Pneumol Clin* 66:71–80

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**INITIAL** PubMed and Cochrane search :  
RCT, meta-analyses and observational studies

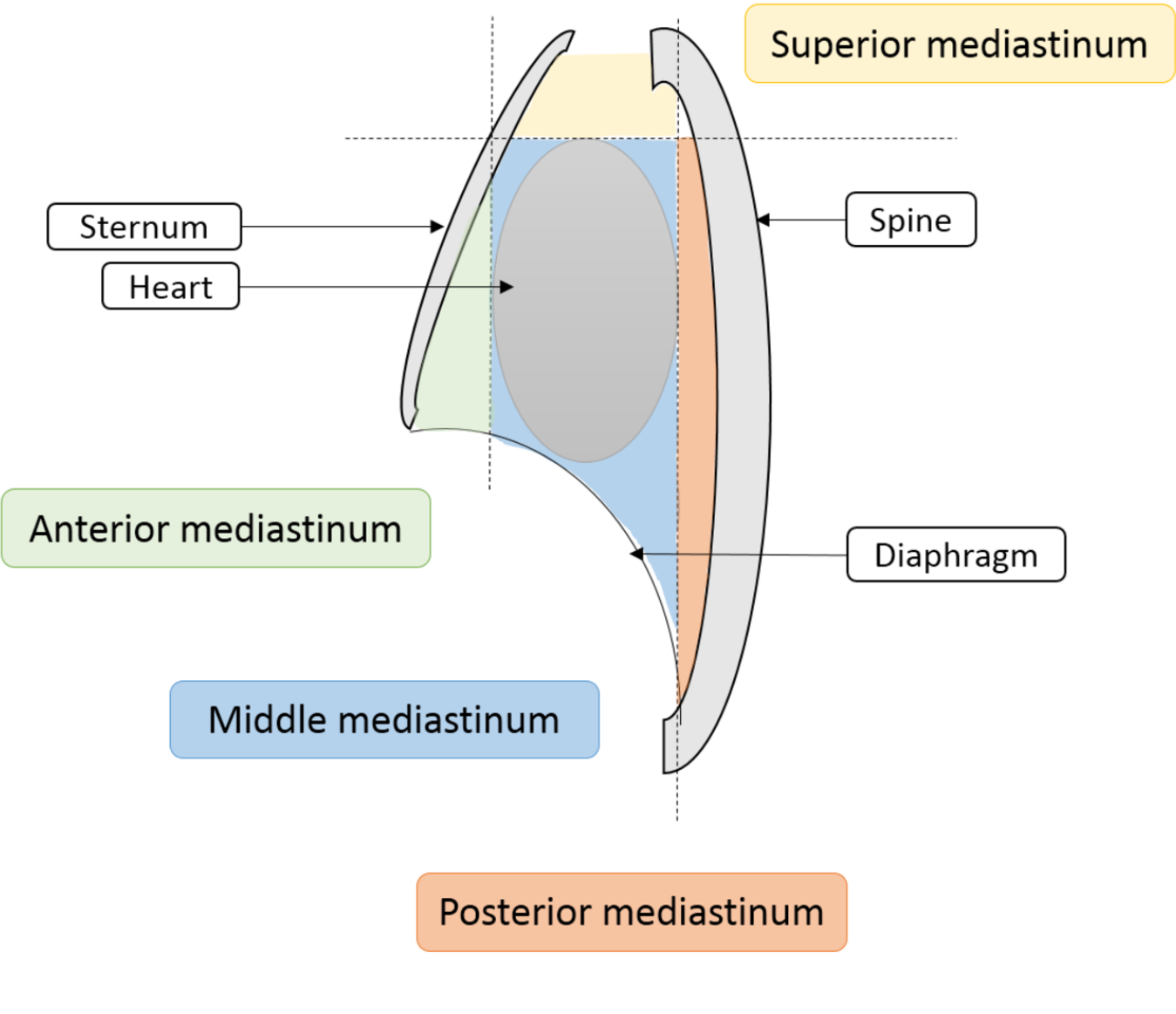
Insufficient amount of data

**EXTENDED** PubMed and Cochrane search :  
expert opinion papers, guidelines, recommendations  
and case series

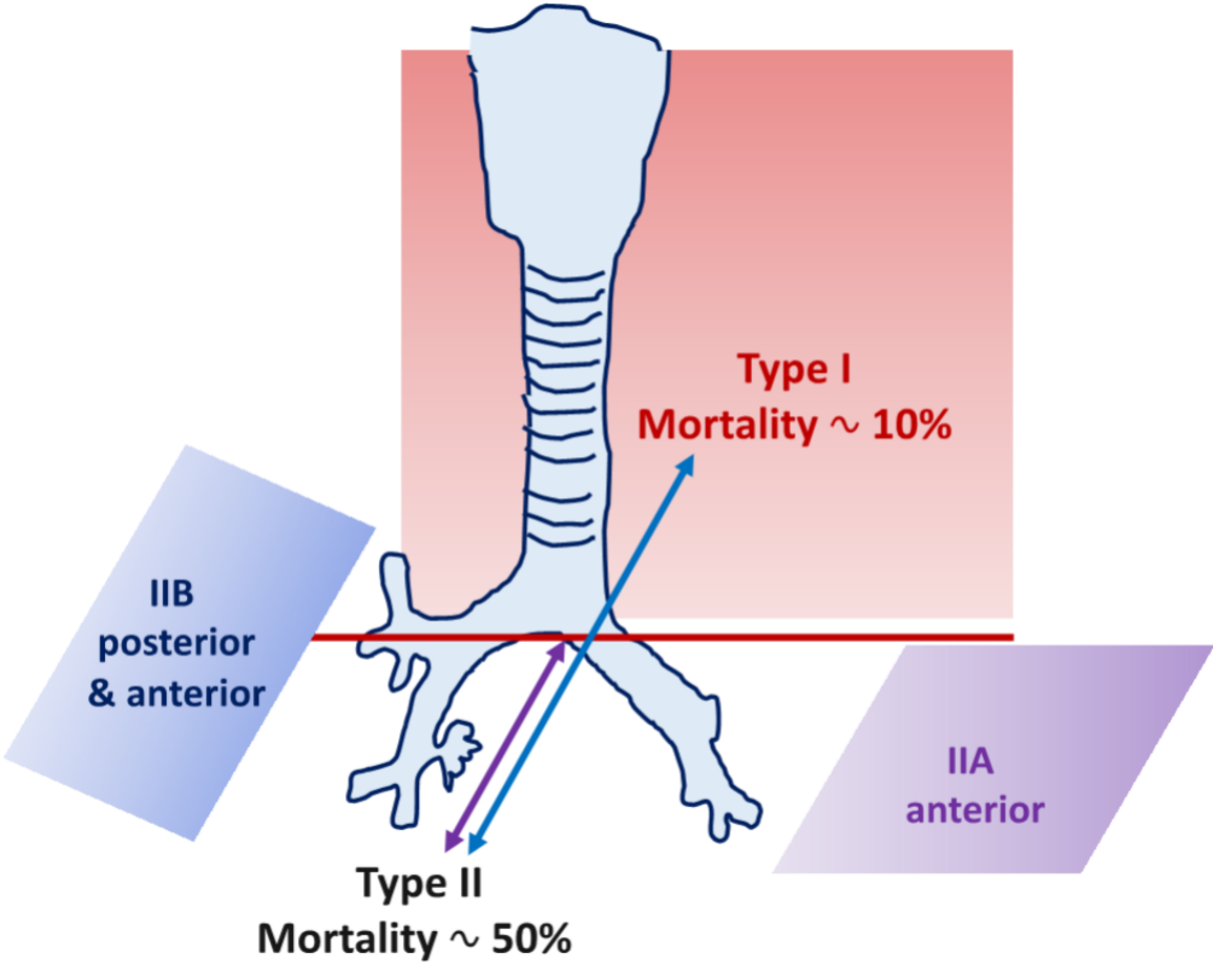
**n = 66**

Inclusion of non ICU-specific papers

Inclusion of relevant references







SC 250mm

R

L

C1 66  
W1 193

30509-52

-145.7mm

120kV, 199mAs

ST 21.1s

SW 5.5mm

Widening of the mediastinum

Mediastinal collection

Pneumomediastinum

5  
cm

37.3mm

73.3mm

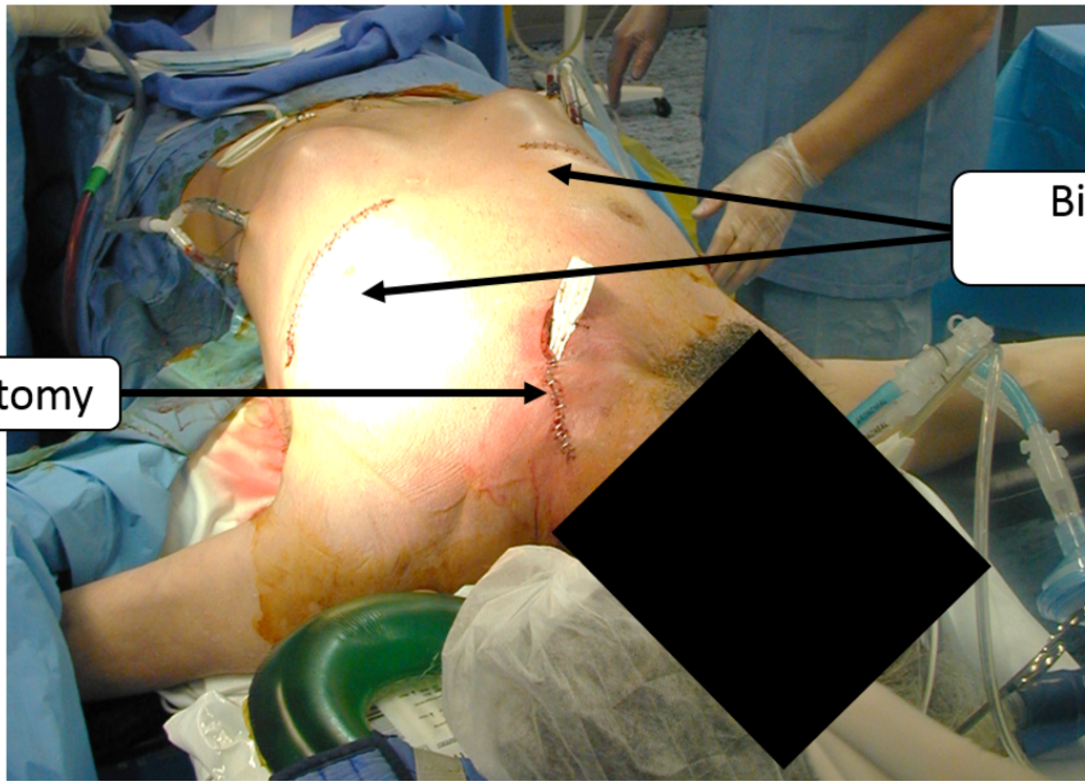
Z 2.24

SC 430mm

R

L

C1 84  
W1 238



Cervicotomy

Bilateral anterolateral  
thoracotomy

**Table 1.****Risk factors for mediastinitis**

<b>Etiology</b>	<b>Patient related risk factors</b>	<b>Procedure related risk factors</b>
<b>DSWI</b>	Old age	Use of ventricular assist device
	Obesity	Transplantation surgery
	Elevated creatinine	Redo surgery
	Peripheral vascular disease	Bilateral internal mammary artery graft
	S.aureus colonization	Length of surgery
	Diabetes mellitus	Aortic cross clamping
	Hyperglycemic episodes	Length of on-pump perfusion
	Chronic obstructive pulmonary disease	
	Smoking	
	Heart failure	
	Female gender	
<b>Esophageal perforation</b>	Abnormal esophageal tissues	Pneumatic dilatation
<b>Anastomotic leakage</b>	Female gender	Cervical anastomosis
<b>DNM</b>	Smoking	Circumference and surface of defect
	Sepsis	Extent of the defect
	Time from diagnosis	
	Impaired immune function	
	Reduced tissue oxygenation	
	Oral intake of glucocorticoids	

Table 2.

## Microbiological flora of mediastinitis according to disease etiology

Type of infection	Deep sternal wound infection	Descending necrotizing mediastinitis	Esophageal perforation
Gram positive	Methicillin-susceptible <i>S. aureus</i>	<i>Streptococcus</i> sp. <i>S. aureus</i>	<i>Viridans streptococci</i> including <i>S. salivarius</i> , <i>S. mutans</i> , <i>S. mitis</i> , <i>S. sanguinis</i> , <i>S. anginosus</i>
	Coagulase-negative <i>Staphylococcus</i>	<i>Streptococcus pyogenes</i> <i>Streptococcus pneumoniae</i>	
	<i>Streptococcus</i> sp.	<i>Peptostreptococcus</i>	
	Methicillin-resistant <i>S. aureus</i>		
Gram negative	Enterobacteriaceae	<i>Hemophilus influenza</i>	<i>Neisseria</i> sp.
	Non-fermenting bacteria including <i>Pseudomonas</i>	<i>Pseudomonas aeruginosa</i> <i>Escherichia coli</i>	<i>Hemophilus</i> sp. <i>Prevotella</i> sp.
	<i>aeruginosa</i> and <i>Acinetobacter baumannii</i>	<i>Moraxella catarrhalis</i> <i>Fusobacterium</i> sp.	<i>Fusobacterium</i> sp.
		<i>Prevotella</i> sp.	
Others	<i>Candida</i> sp.	<i>Actinomyces</i>	

**Table 3.**

**Suggested antimicrobial therapy for mediastinitis according to disease etiology**

Type of infection	Deep sternal wound infection	Descending necrotizing mediastinitis	Esophageal perforation
<b>First line</b>	<p>“Piperacillin/Tazobactam”</p> <p>or</p> <p>“Third-generation cephalosporin”</p> <p>+</p> <p>“Glycopeptid or Linezolid”</p>	<p>“Third-generation Cephalosporin</p> <p>+</p> <p>Metronidazole”</p>	<p>“Piperacillin/Tazobactam”</p> <p>or</p> <p>“Third-generation Cephalosporin</p> <p>+</p> <p>Metronidazole”</p>
<b>Optional</b>	.		Antifungals

**Table 4.****Main Supportive measures for the treatment of mediastinitis**

<b>Etiology</b>	<b>Action</b>	<b>Management</b>
<b>Deep Sternal Wound Infection</b>	Prevention	Pre-operative antibiotic prophylaxis
		Routine S.aureus eradication
		Perioperative glycemic control
	Wound Management	Negative pressure wound therapy
<b>Esophageal perforation</b>	Nutrition	Early enteral nutrition when feasible
		Total parenteral nutrition if needed
	Pharmacological	Proton pump inhibitors
	Interventional	Endoscopic management
		Negative pressure wound therapy
<b>Descending necrotizing mediastinitis</b>	Airway Management	Early tracheotomy