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Review / Derleme

The risk factors associated with postoperative mediastinitis in cardiac surgery: a systematic review and meta-analysis

Kalp cerrahisinde ameliyat sonrası mediastinitle ilişkili risk etkenleri: Sistematik derleme ve meta analiz

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ABSTRACT

Background: In this review, we aimed to analyze the risk factors of mediastinitis after open cardiac surgery.

Methods: The literature screening was performed at Pubmed, Ovid, and Sciencedirect databases without date limitation. Studies investigating the co-existing diseases were included. The results of trials were evaluated with random or fixed effect model according to the heterogeneity.

Results: A total of 5009 articles were attained after database searching. Thirty five articles were included to the meta-analysis including 131.158 patients who met inclusion criteria. The most possible preoperative risk factors for mediastinitis were atrial fibrillation, pulmonary disease, diabetes mellitus, renal disease, peripheral vascular disease and systemic hypertension ($p<0.05$). Pulmonary hypertension, malignancy, hepatic and neurological diseases, heart failure and dyslipidemia were not found to be risk factors ($p>0.05$). Heterogeneity was not observed for four (renal, hepatic, neurological and peripheral vascular diseases) of 12 factors ($I^2<25\%$).

Conclusion: The results of our meta-analysis showed that preoperative co-existing diseases such as pulmonary hypertension, malignancy, heart failure, hepatic and neurological diseases, and dyslipidemia may not be risk factors for the development of mediastinitis following cardiac surgery.

Keywords: Cardiac surgery; mediastinitis; risk factor.

ÖZ

Amaç: Bu derlemede, açık kalp cerrahisinden sonra mediastinitin risk etkenleri analiz edildi.

Çalışma planı: Literatür taraması tarih sınırlaması olmadan Pubmed, Ovid ve Sciencedirect veritabanlarında uygulandı. Eş zamanlı hastalıkları araştıran çalışmalar dahil edildi. Çalışma bulguları heterojenite durumuna göre rastgele ya da sabit etki modeli ile değerlendirildi.

Bulgular: Veritabanı taramasından sonra toplam 5009 makale elde edildi. Dahil edilme kriterlerini karşılayan 131.158 hastanın yer aldığı 35 makale meta analize dahil edildi. Mediastinit için en olası ameliyat öncesi risk etkenleri atriyal fibrilasyon, pulmoner hastalık, diabetes mellitus, renal hastalık, periferik damar hastalığı ve sistemik hipertansiyon idi ($p<0.05$). Pulmoner hipertansiyon, malignite, hepatik ve nörolojik hastalıklar, kalp yetmezliği ve dislipidemi risk etkeni olarak bulunmadı ($p>0.05$). Heterojenite 12 etkenin dördünde (renal, hepatik, nörolojik ve periferik damar hastalıkları) gözlenmedi ($I^2<\%25$).

Sonuç: Meta analiz sonucu pulmoner hipertansiyon, malignite, kalp yetmezliği, hepatik ve nörolojik hastalıklar ve dislipidemi gibi ameliyat öncesi eş zamanlı hastalıkların kalp cerrahisinden sonra mediastinit gelişimi için risk etkeni olmadığını gösterdi.

Anahtar sözcükler: Kalp cerrahisi; mediastinit; risk etkeni.

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Mediastinitis, also know as deep sternal wound infection (DSWI), is a rare, serious complication often seen after open cardiac surgery which may increase the length of intensive care unit (ICU) and/or hospital stays and also may cause a higher mortality rate. Researchers have reviewed the preoperative, intraoperative and postoperative variables for predicting postoperative mediastinitis development,[1-5] and coexisting diseases, such as diabetes mellitus (DM) and systemic hypertension (HT) along with pulmonary, renal, hepatic, and neurological diseases, were generally examined in those studies. However, we found controversy regarding the association between postoperative mediastinitis and those diseases. Therefore, in this study, we aimed to review and analyze the literature to determine which preoperative variables can be used to predict mediastinitis.

MATERIALS AND METHODS

Search strategy

We performed the database search and analyzed the article in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[6] Two authors searched the PubMed electronic database to determine whether or not coexisting diseases could predict the development of mediastinitis after cardiac surgery. The search concluded on January 5th, 2014, and there were no limitations related to this date.

The search was conducting using the following English keywords or a combination of these words: cardiac surgery, heart surgery, valve surgery, coronary artery bypass grafting (CABG), mediastinitis, and DSWI. The search was limited to English, with articles in other languages being excluded from the study. In addition, the study was limited to clinical trials, comparative studies, multicenter studies, observational studies, randomized controlled trials, controlled clinical trials, and evaluation studies.

Selection of studies

The studies, regardless of sample size, included both retrospective and prospective clinical studies. Inclusion criteria were that it was a clinical study that involved open cardiac surgery with off-pump or extracorporeal circulation and that the article was in English. Experimental studies, articles not in English, and those that focused on non-cardiac surgery were excluded from the study. Furthermore, articles that were associated with our review topic but did not contain information concerning the rate of mediastinitis according to preoperative coexisting diseases were also excluded as well as those that contained data with figures but no numerical values.

Data extraction

Two reviewers independently extracted data from the relevant studies, and any disagreements were resolved by consensus using a third reviewer. At first, we gathered the publication information (first author's name, publication year, patient population, and type of surgery), characteristics of the participants (sample size and type of study methods), and outcome information (mediastinitis rate, number of diseases, number of control cases, and definition of mediastinitis) and then recorded the number of patients with and without mediastinitis (controls).

Statistical analysis

Statistical analysis was carried out using the Comprehensive Meta-Analysis (CMA) Version 2.0 (Biostat, Englewood, New Jersey, USA), and the odds ratio (OR) and 95% confidence interval (CI) (lower-upper limit) was utilized for this analysis. The heterogeneity was evaluated using the statistics of I^2, with it being accepted as significant if $I^2 > 25\%$. In addition, the heterogeneity was classified as low $(25\% < I^2 > 50\%.)$, moderate $(50\% < I^2 > 75\%.)$, or high

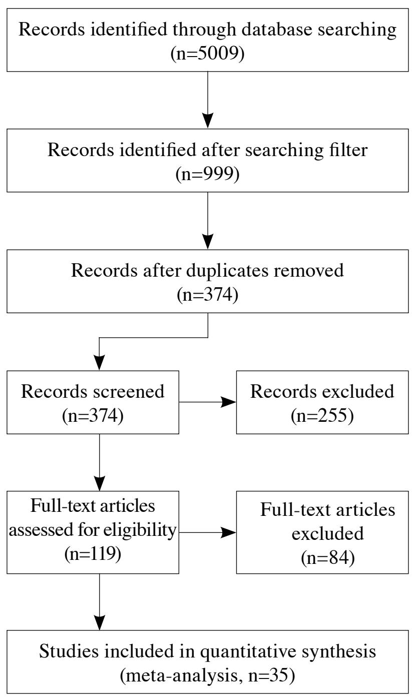


Figure 1. Flow diaphragm of database search.

Table 1. Studies included in the analysis

References	Risk factors in each study	Mediastinitis/control (n)	LE
Abboud et al.[7]	MA: Obesity, smoking, intensive care unit stay of >2 days, infection at another site	39/78	3b
Antunes et al.[2]	Higher incidence of obesity, diabetes, peripheral vascular disease	60/2,452	2b
Ashley et al.[8]	MA: Diabetes, female gender, age >70 years	143/80	3b
Baillot et al.[9]	Significant differences between groups: BMI, diabetes, COPD, renal disease	267/23,232	3b
Bitkover et al.[1]	MA: BMI, use of beta-adrenergic drug before onset of infection	37/74	2b
Braxton et al.[10]	Significant differences between groups: BMI, COPD, renal disease, HF, peripheral vascular disease	193/15,213	3b
Colombier et al.[11]	MA: Smoking, obesity, diabetes	74/148	2b
Dial et al.[12]	UA: Obesity, re-exploration	11/33	3b
Diez et al.[13]	MA: Obesity, COPD, BITA	45/1,643	3b
Eklund et al.[14]	MA: Age, gender, operation type, perfusion time	115/10,598	2b
Elenbaas et al.[15]	UA: Age, diabetes, BMI, atrial fibrillation, peripheral vascular disease, COPD, MA: Age, BMI, atrial fibrillation, diabetes, peripheral vascular disease	100/11,648	2b
Filsoufi et al.[16]	MA: Obesity, previous myocardial infarction, diabetes, COPD, preoperative length of stay >3 days, aortic calcification, aortic surgery, combined procedures, CPB time, re-exploration for bleeding, respiratory failure	106/5,692	3b
Floros et al.[5]	Significant differences between groups: Diabetes, previous surgery, BMI, emergency surgery	34/5,615	2b
Ghotaslou et al.[17]	Significant difference between groups: Mean blood transfusion units, obesity, reoperation, diabetes, HF, hospitalization more than 3 days before surgery	23/1,804	3b
Gualis et al.[18]	MA: Respiratory failure, intensive care unit stay	22/816	2b
Gummert et al.[19]	UA: Diabetes, intensive care unit stay >5 days, mechanical ventilation >72 hours, reexploration, IABP MA: BMI, IABP, diabetes, intensive care unit stay >5 days	134/9,169	2b
Hallam et al.[20]	Significant difference between groups: Smoking, BMI, diabetes	53/7,530	3b
Lin et al.[21]	UA: Previous hospitalization, resternotomy, chronic renal disease, longer operation time, postoperative HF, postoperative renal failure, reoperation MA: Previous hospitalization, reoperation	48/65	3b
Lopez Gude et al.[22]	MA: Obesity, diabetes, COPD, preoperative stay >1 week, pulmonary hypertension, reoperation, myocardial infarction	163/326	3b
Manganas et al.[23]	NS	4/322	3b
Munoz et al.[24]	UA: Emergency surgery, NYHA class IV, CABG, heart transplantation, MA: Reoperation, vasoactive drugs, CABG	73/73	3b
Newman et al.[25]	UA: COPD, prior sternotomy, pyuria, low ejection fraction, high left ventiricular end diastolic pressure (preoperative variables) Logistic regression: COPD, duration of surgery, longer postoperative mechanical ventilation	68/136	3b
Omran et al.[26]	MA: Hypertension, re-exploration, female gender	44/9,157	2b
Parissis et al.[4]	MA: Diabetes, preoperative creatinine >200 µmol/L, prolonged ventilation	52/3,896	2b
Ridderstolpe et al.[27]	MA: Obesity, diabetes, smoking, peripheral vascular disease, high NYHA score	291/2,717	3b

Table 1. (continued)

References	Risk factors in each study	Mediastinitis/control (n)	LE
Risnes et al.[3]	MA: Age >70 years, male gender, left main stenosis, body mass index ≥30, COPD, diabetes, blood transfusion	107/444	3b
Robinson et al.[28]	MA: Type of surgery, diabetes, preoperative dialysis, respiratory disease, body mass index, ventricular assist device, BITA	153/11,695	3b
Rosmarakis et al.[29]	This study contained only one case of mediastinitis	1/342	2b
Sa et al.[30]*	MA: Obesity, diabetes, smoking, pedicled internal thoracic artery, CPB	28/500	3b
Sa et al.[31]**	UA: Use of pedicled internal thoracic artery, postoperative renal complications, re-operation	11/157	3b
Sakamoto et al.[32]	UA: IABP, emergency operation, operation time >8 hours, intensive care unit stay >5 days, postoperative hyperglicemia		
	MA: Combined CABG, postoperative use of IABP	17/846	3b
San Juan et al.[33]	Significant difference between groups: COPD	17/51	3b
Stahle et al.[34]	UA: Female gender, age, diabetes, hypertension, postoperative renal dialysis, BITA		
	MA: Female gender, diabetes, postoperative renal dialysis, BITA	28/528	2b
Tiveron et al.[35]	MA: Intraaortic balloon pump, hemodialysis, extracardiac vascular intervention	35/2,733	2b
Wouters et al.[36]	UA: Perfusion time, mechanical ventilation >72 hours, length of stay in operating room >5.5 hours		
	MA: Diabetes, smoking, reoperation, mechanical ventilation >72 hours	23/1,345	3b

LE: Levels of evidence; MA:Multivariate analysis; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; HF: Heart failure; UA: Univariate analysis; BITA: Bilateral internal thoracic artery graft; CPB: Cardiopulmonary bypass; IABP: Intra aortic balloon pump; NS: Not Significant; NYHA: New York Heart Association; CABG: Cardiopulmonary Artery Bypass Grafting.

(I^2 >75%) and was evaluated by analyzing subgroups and moderators. The meta-analysis was performed by using fixed or random effect models, with the latter being conducted in the presence of heterogeneity (I^2 >25%) and the former without heterogeneity (I^2 <25%). The overall effect was analyzed via a Z score, and potential publication bias was evaluated using the Begg test.

RESULTS

A flow diagram of the database search is shown in Figure 1. We identified 5,009 records and filtered these down to 999 articles. After duplicates were removed, 374 records remained, and 255 of these were excluded after screening because they were deemed to be unrelated to our topic. Then the full text of 119 articles were assessed for their eligibility, and 83 were excluded because of the absence of detailed data regarding gender in each group. This left 36 articles that were included in the quantitative synthesis.[1-5,7-36] The demographic features of these studies are summarized in Table 1. The ratio of development of mediastinitis was 1.99% (2,619 cases out of 131,158). Results of analysis, heterogeneity and publication bias are shown in Table 2-14.

DISCUSSION

Cardiac surgery is special because of both the individual properties of the patients and the operative procedures. Advanced age and coexisting diseases are common causes of morbidity, with invasive interventions [e.g., arterial cannulation, central venous catheterization, cardiopulmonary bypass (CPB), intra-aortic balloon pumps (IABPs), blood transfusions, and ICU stays being other possible sources of infection. In addition, invasive interventions may lead to the entry of bacterial pathogens.[37]

Kansy et al.[38] found that the ratio of major infections (septicemia, endocarditis, and mediastinitis) was 3.1% after cardiac surgery, and Chen et al.[39] also found a similar ratio for major infections (3.2%), with the risk factors being a high body mass index (BMI), previous CABG, emergency surgery, renal impairment, heart failure, peripheral and cerebrovascular diseases, and immunsuppression.

Many of the coexisting diseases, such as DM,[40] heart failure,[41] pulmonary disease,[23] and malignancy,[42] may decrease a patient's resistance against infection while longer treatment durations of other conditions (AF and systemic HT) can increase the duration of ICU and hospital stays. Hence, the possibility of infection is also higher.

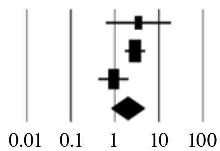
Table 2. Results of analysis

Variables	Results of analysis				Heterogeneity				Publication bias
	OR	95% CI	Z value	*p*	Q value	df	*p*	I^2	tau^2
Pulmonary hypertension	1.9	0.8 4.64	1.52	0.12	5.68	2	0.05	64.7	0.35
Malignancy	2.3	0.3 17.2	0.81	0.4	1.68	1	0.1	40.7	1.06
Hepatic disease	2.8	0.6 12.5	1.3	0.16	1.04	3	0.7	0.0	0.0
Dyslipidemia	1.1	0.7 1.6	0.6	0.5	5.2	3	0.5	43.11	0.07
Neurological disease	1.3	0.9 1.8	1.5	0.12	1.14	2	0.5	0.0	0.0
Atrial fibrillation	2.9	1.0 8.0	2.0	0.03	7.36	2	0.02	72.84	0.55
Peripheral vascular disease	1.7	1.4 2.0	5.7	0.0	10.7	9	0.2	16.57	0.01
Heart failure	1.1	0.8 1.7	0.9	0.3	63.7	11	0.0	82.73	0.3
Renal disease	1.9	1.5 2.3	6.1	0.0	19.2	15	0.2	22.12	0.06
Systemic hypertension	1.3	1.0 1.6	2.2	0.02	25.09	14	0.03	44.21	0.08
Diabetes mellitus	2.1	1.8 2.4	11.0	0.0	38.87	27	0.06	30.54	0.03
Pulmonary disease	2.4	1.8 3.1	6.2	0.0	79.79	25	0.0	68.67	0.26

OR: Odds ratio; CI: Confidence interval; p<0.05 is evaluated as significant; I^2: <25% is accepted as no heterogeneity; df: degree of freedom; tau^2: <0.05 is evaluated as significant.

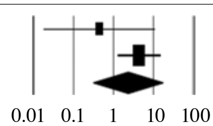
In our meta-analysis, some of the diseases occurred less frequently. Three studies featured pulmonary HT, two focused on malignancy, four had cases of hepatic disease, four included patients with dyslipidemia, three featured neurological disease, and three had cases of AF. The most studied diseases were DM (29 studies), renal disease (16 studies), systemic HT (15 studies), heart failure (12 studies), and peripheral vascular disease (10 studies). We did not observe heterogeneity for the studies that focused on peripheral vascular and renal disease (I^2 <25%). Furthermore, the heterogeneity of the studies that featured DM and systemic HT was low (25%< I^2 <50%), but it was

Table 3. Pulmonary hypertension and mediastinitis

Study name	Statistics for each study					Odds ratio and 95% CI	
	Odds ratio	Lower limit	Upper limit	Z value	*p*		Relative weight
San Juan et al.[33]	3.429	0.622	18.908	1.414	0.157		17.41
López Gude et al.[22]	2.903	1.706	4.939	3.931	0.000		45.24
Tiveron et al.[35]	0.940	0.425	2.079	-0.153	0.879		37.35
	1.961	0.827	4.649	1.529	0.126		

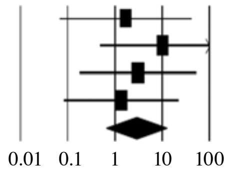
CI: Confidence interval; OR: 1.96, 95% CI: 0.82-4.64; Z value=1.52, p=0.12. Heterogeneity: Q value=5.68, df: 2, p=0.05, I^2: 64.7%.

Table 4. Malignancy and mediastinitis

Study name	Statistics for each study					Odds ratio and 95% CI	
	Odds ratio	Lower limit	Upper limit	Z value	*p*		Relative weight
Lin et al.[21]	0.443	0.018	11.120	-0.495	0.621		27.96
Colombier et al.[11]	4.364	1.269	15.005	2.338	0.019		72.04
	2.303	0.308	17.210	0.813	0.416		

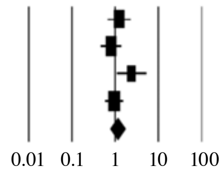
CI: Confidence interval; OR: 2.3; 95% CI: 0.3-17.2; Z value=0.81; p=0.4; heterogeneity: Q value=1.68; df: 1; p=0.19; I^2: 40.7%.

Table 5. Hepatic disease and mediastinitis

Study name	Statistics for each study					Odds ratio and 95% CI	
	Odds ratio	Lower limit	Upper limit	Z value	*p*		Relative weight
Dodds Ashley et al.[8]	1.695	0.068	42.089	0.322	0.748		21.27
Newman et al.[25]	10.263	0.486	216.814	1.496	0.135		23.59
Tiveron et al.[35]	3.066	0.178	52.802	0.772	0.440		27.10
Lin et al.[21]	1.362	0.083	22.331	0.216	0.829		28.05
	2.862	0.651	12.592	1.391	0.164		

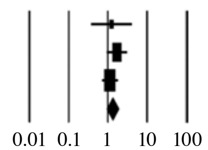
CI: Confidence interval; OR: 2.8; 95% CI: 0.6-12.5; Z value=1.3; p=0.16; heterogeneity: Q value=1.04; df: 3; p=0.78; I^2: 0.0%.

Table 6. Dyslipidemia and mediastinitis

Study name	Statistics for each study					Odds ratio and 95% CI	
	Odds ratio	Lower limit	Upper limit	Z value	*p*		Relative weight
Salehi Omran et al.[26]	1.236	0.662	2.308	0.665	0.506		24.03
Colombier et al.[11]	0.805	0.460	1.409	-0.759	0.448		27.21
Abboud et al.[7]	2.368	1.074	5.223	2.137	0.033		17.74
Risnes et al.[3]	0.951	0.582	1.555	-0.198	0.843		31.01
	1.138	0.764	1.697	0.636	0.525		

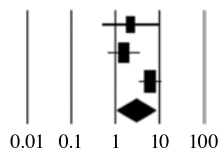
CI: Confidence interval; OR: 1.13; 95% CI: 0.7-1.6; Z value=0.6; p=0.5; heterogeneity: Q value=5.2; df: 3; p=0.5; I^2: 43.11%.

Table 7. Neurological disease and mediastinitis

Study name	Statistics for each study					Odds ratio and 95% CI	
	Odds ratio	Lower limit	Upper limit	Z value	*p*		Relative weight
Tiveron et al.[35]	1.234	0.374	4.066	0.345	0.730		8.73
Filsoufi et al.[16]	1.702	0.945	3.066	1.771	0.077		35.85
Robinson et al.[28]	1.131	0.704	1.815	0.508	0.612		55.41
	1.319	0.927	1.876	1.540	0.123		

CI: Confidence interval; OR: 1.3; 95% CI: 0.9-1.8; Z value=1.5; p=0.12; heterogeneity: Q value=1.14; df: 2; p=0.56; I^2: 0.00%.

Table 8. Atrial fibrillation and mediastinitis

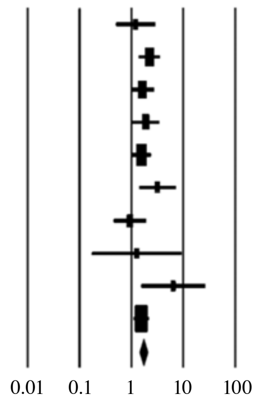
Study name	Statistics for each study					Odds ratio and 95% CI	
	Odds ratio	Lower limit	Upper limit	Z value	*p*		Relative weight
Gualis et al.[18]	2.167	0.488	9.628	1.016	0.310		23.29
Risnes et al.[3]	1.550	0.670	3.584	1.025	0.305		35.83
Elenbaas et al.[15]	6.111	3.371	11.078	5.965	0.000		40.88
	2.936	1.073	8.033	2.097	0.036		

CI: Confidence interval; OR: 2.9; 95% CI: 1.0-8.0; Z value=2.0; p=0.03; heterogeneity: Q value=7.36; df: 2; p=0.02; I^2: 72.84%.

Table 9. Peripheral vascular disease and mediasitinitis

Study name	Statistics for each study					Relative weight
	Odds ratio	Lower limit	Upper limit	Z value	*p*	
Diez et al.[13]	1.199	0.501	2.870	0.407	0.684	4.25
Elenbaas et al.[15]	2.230	1.395	3.565	3.350	0.001	14.73
Filsouf et al.[16]	1.627	0.962	2.752	1.815	0.070	11.73
López Gude et al.[22]	1.896	1.045	3.440	2.104	0.035	9.13
Ridderstolpe et al.[27]	1.566	1.030	2.380	2.097	0.036	18.46
Antunes et al.[2]	3.171	1.406	7.155	2.780	0.005	4.89
Parissis et al.[4]	0.934	0.453	1.925	-0.184	0.854	6.20
Salehi Omran et al.[26]	1.267	0.173	9.258	0.234	0.815	0.82
San Juan et al.[33]	6.409	1.541	26.657	2.555	0.011	1.60
Braxton et al.[10]	1.550	1.105	2.176	2.535	0.011	28.19
	1.702	1.421	2.037	5.787	0.000	

Odds ratio and 95% CI



CI: Confidence interval; OR: 1.7; 95% CI: 1.4-2.0; Z value=5.7; p=0.00; heterogeneity: Q value=10.7; df: 9; p=0.2; I^2: 16.57%.

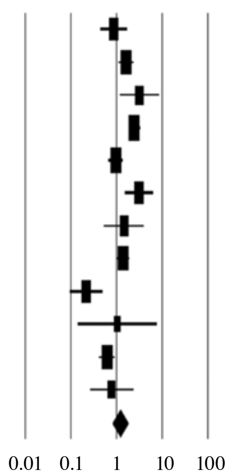
high for those that included patients with heart failure (I^2 >75%).

The ratio of mediastinitis development was approximately 2%. However, future studies are needed because only nine of the 35 studies had a large sample size (>5,000) (23,499 in Baillot et al.,[9] 15,406 in Braxton et al.,[10] 11,848 in Robinson et al.,[28] 11,748 in Elenbaas et al.,[15] 10,713 in Eklund et al.,[14] 9,303 in Gummert et al.,[19] 7,583 in Hallam et al.,[20] 5,798 in Filsoufi et al.,[16] and 5,649 in Floros et al.[5] However, none of these included the majority of the factors we wanted to assess in their analyses. When we excluded[5,9,10,14-16,19,20,28] those results from our analysis, the present results changed as opposite for pulmonary HT, hepatic and neurological disease, AF, and heart failure.

Table 10. Heart failure and mediastinitis

Study name	Statistics for each study					Relative weight
	Odds ratio	Lower limit	Upper limit	Z value	*p*	
Tiveron et al.[35]	0.866	0.434	1.727	-0.409	0.682	8.55
Filsouf et al.[16]	1.615	1.094	2.383	2.413	0.016	10.54
Ghotaslou et al.[17]	3.154	1.155	8.619	2.240	0.025	6.52
Braxton et al.[10]	2.434	1.811	3.270	5.902	0.000	11.05
Eklund et al.[14]	0.960	0.661	1.394	-0.215	0.830	10.64
Muñoz et al.[24]	3.106	1.511	6.383	3.083	0.002	8.34
Sakamoto et al.[32]	1.461	0.534	3.996	0.738	0.460	6.52
Ridderstolpe et al.[27]	1.405	1.023	1.931	2.097	0.036	10.94
Abboud et al.[7]	0.216	0.095	0.490	-3.663	0.000	7.67
Diez et al.[13]	1.035	0.139	7.707	0.033	0.973	2.79
López Gude et al.[22]	0.616	0.412	0.920	-2.369	0.018	10.47
San Juan et al.[33]	0.788	0.261	2.374	-0.424	0.671	5.97
	1.199	0.817	1.760	0.929	0.353	

Odds ratio and 95% CI

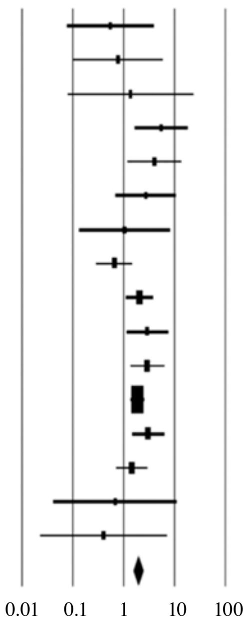


CI: Confidence interval; OR: 1.1; 95% CI: 0.8-1.7; Z value=0.9; p=0.3; heterogeneity: Q value=63.7; df: 11; p=0.00; I^2: 82.73%.

Table 11. Renal disease and mediastinitis

Study name	Odds ratio	Lower limit	Upper limit	Z value	*p*	Relative weight
Dodds Ashley et al.[8]	0.553	0.076	4.004	-0.586	0.558	1.12
Gualis et al.[18]	0.779	0.103	5.918	-0.241	0.809	1.07
Sakamoto et al.[32]	1.354	0.078	23.429	0.209	0.835	0.54
Tiveron et al.[35]	5.476	1.619	18.527	2.734	0.006	2.95
Lin et al.[21]	4.013	1.175	13.706	2.217	0.027	2.90
Abboud et al.[7]	2.721	0.687	10.772	1.426	0.154	2.31
Ridderstolpe et al.[27]	1.038	0.131	8.219	0.035	0.972	1.02
Filsoufi et al.[16]	0.650	0.284	1.489	-1.018	0.309	6.37
Diez et al.[13]	2.028	1.078	3.813	2.194	0.028	10.98
Sá et al.[30]	2.899	1.115	7.535	2.183	0.029	4.80
Robinson et al.[28]	2.888	1.335	6.248	2.693	0.007	7.35
Baillot et al.[9]	1.858	1.341	2.575	3.723	0.000	41.14
Braxton et al.[10]	3.007	1.433	6.314	2.910	0.004	7.96
Gummert et al.[19]	1.437	0.698	2.957	0.984	0.325	8.40
Hallam et al.[20]	0.677	0.042	11.044	-0.274	0.784	0.56
Sá et al.[31]	0.400	0.022	7.117	-0.624	0.533	0.53
	1.918	1.556	2.365	6.103	0.000	

Odds ratio and 95% CI

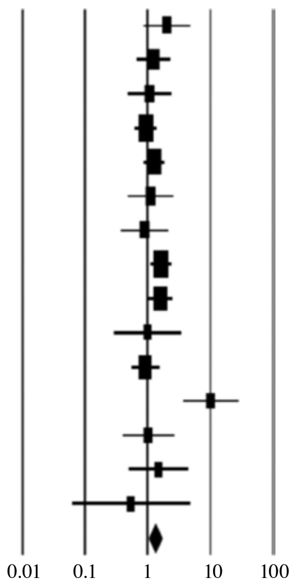


CI: Confidence interval; OR: 1.9; 95% CI: 1.5-2.3; Z value=6.1; p=0.00; heterogeneity: Q value=19.2; df: 15; p=0.2; I^2: 22.12%.

Table 12. Systemic hypertension and mediastinitis

Study name	Odds ratio	Lower limit	Upper limit	Z value	*p*	Relative weight
Abboud et al.[7]	2.017	0.863	4.714	1.621	0.105	5.26
Colombier et al.[11]	1.218	0.655	2.263	0.623	0.534	7.80
Diez et al.[13]	1.073	0.474	2.428	0.169	0.865	5.55
Elenbaas et al.[15]	0.933	0.625	1.392	-0.341	0.733	11.51
Filsoufi et al.[16]	1.245	0.841	1.845	1.094	0.274	11.65
Ghotaslou et al.[17]	1.117	0.481	2.595	0.257	0.797	5.31
Gualis et al.[18]	0.886	0.374	2.095	-0.276	0.782	5.15
López Gude et al.[22]	1.617	1.108	2.362	2.488	0.013	11.93
Risnes et al.[3]	1.605	1.020	2.524	2.047	0.041	10.51
Sá et al.[30]	0.988	0.289	3.384	-0.019	0.985	2.97
Antunes et al.[2]	0.921	0.549	1.544	-0.313	0.754	9.38
Salehi Omran et al.[26]	10.121	3.618	28.310	4.410	0.000	3.96
Sakamoto et al.[32]	1.020	0.390	2.668	0.040	0.968	4.39
San Juan et al.[33]	1.483	0.493	4.463	0.701	0.483	3.56
Sá et al.[31]	0.537	0.061	4.727	-0.560	0.575	1.08
	1.313	1.040	1.657	2.291	0.022	

Odds ratio and 95% CI

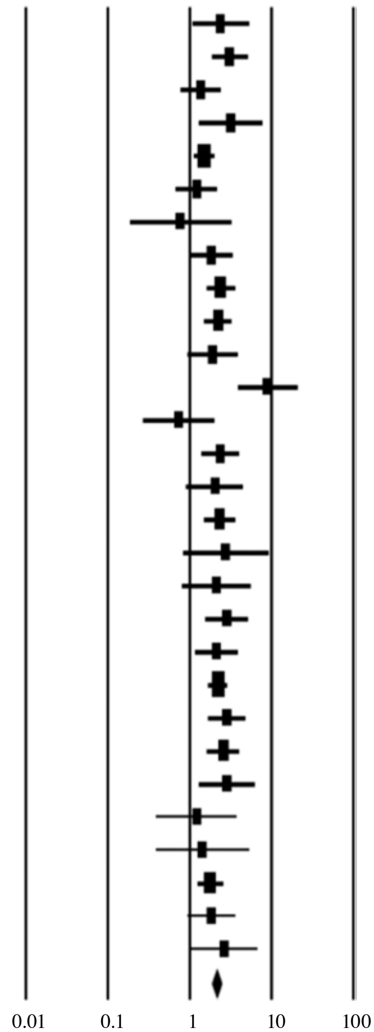


CI: Confidence interval; OR: 1.3; 95% CI: 1.0-1.6; Z value=2.2; p=0.02; heterogeneity: Q value=25.09; df: 14; p=0.03; I^2: 44.21%.

Table 13. Diabetes mellitus and mediastinitis

Study name	Statistics for each study					Relative weight
	Odds ratio	Lower limit	Upper limit	Z value	*p*	
Abboud et al.[7]	2.400	1.060	5.433	2.099	0.036	2.12
Antunes et al.[2]	3.087	1.830	5.208	4.225	0.000	4.24
Dodds Ashley et al.[8]	1.353	0.764	2.396	1.036	0.300	3.73
Bitkover and Gårdlund[1]	3.145	1.269	7.793	2.475	0.013	1.77
Braxton et al.[10]	1.482	1.104	1.990	2.615	0.009	8.05
Colombier et al.[11]	1.206	0.664	2.191	0.615	0.539	3.50
Dial et al.[12]	0.776	0.189	3.174	-0.354	0.724	0.79
Diez et al.[13]	1.829	1.010	3.310	1.994	0.046	3.53
Elenbaas et al.[15]	2.390	1.595	3.581	4.225	0.000	5.88
Filsoufi et al.[16]	2.233	1.514	3.293	4.050	0.000	6.14
Floros et al.[5]	1.898	0.923	3.905	1.741	0.082	2.60
Ghotaslou et al.[17]	8.950	3.897	20.555	5.166	0.000	2.06
Gualis et al.[18]	0.745	0.272	2.042	-0.572	0.567	1.47
Hallam et al.[20]	2.349	1.367	4.037	3.092	0.002	4.03
Lin et al.[21]	2.017	0.909	4.475	1.725	0.085	2.21
López Gude et al.[22]	2.308	1.488	3.580	3.737	0.000	5.33
Muñoz et al.[24]	2.738	0.817	9.171	1.633	0.102	1.06
Newman et al.[25]	2.153	0.813	5.702	1.542	0.123	1.56
Salehi Omran et al.[26]	2.842	1.556	5.191	3.397	0.001	3.45
Parissis et al.[4]	2.114	1.153	3.874	2.421	0.015	3.42
Ridderstolpe et al.[27]	2.227	1.694	2.927	5.741	0.000	8.54
Risnes et al.[3]	2.846	1.661	4.877	3.806	0.000	4.06
Robinson et al.[28]	2.561	1.623	4.040	4.042	0.000	5.08
Sá et al.[31]	2.839	1.284	6.279	2.577	0.010	2.22
Sakamoto et al.[32]	1.206	0.388	3.744	0.324	0.746	1.19
San Juan et al.[33]	1.436	0.379	5.440	0.532	0.594	0.88
Ståhle et al.[34]	1.774	1.226	2.566	3.041	0.002	6.49
Tiveron et al.[35]	1.843	0.943	3.602	1.789	0.074	2.93
Wouters et al.[36]	2.652	1.030	6.825	2.022	0.043	1.65
	2.119	1.862	2.411	11.385	0.000	

Odds ratio and 95% CI



CI: Confidence interval; OR: 2.1; 95% CI: 1.8-2.4; Z value=11.3; p=0.00; heterogeneity: Q value=38.96; df: 28; p=0.08; I^2: 28.10%.

We used the definition of mediastinitis, type of surgery, and study design as moderators to analyze the reason for heterogeneity and found that the heterogeneity did not change based on the definition of mediastinitis or type of surgery. However, study design was a primary cause of heterogeneity.

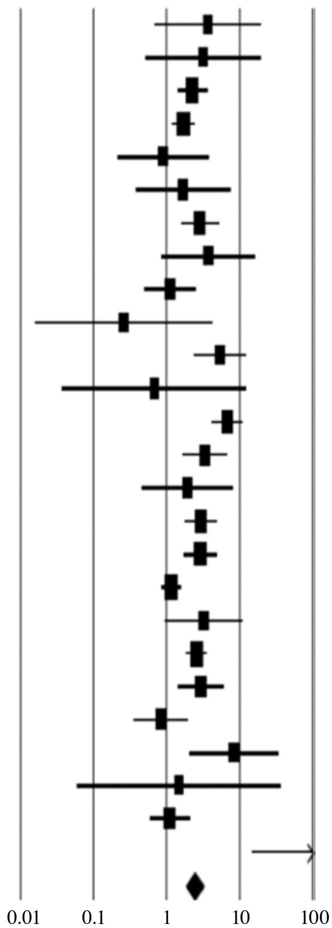
In the literature, there were many studies that discussed the presence of mediastinitis after cardiac surgery. However, the main limitation of our meta-analysis was that we excluded studies because of their design and the absence of needed data. Another limitation was that we excluded the patients' individual demographic characteristics, such as age and gender, along with the intraoperative variables (e.g., the presence or absence of CPB and aortic cross-clamp time) because we focused on coexisting diseases.

Conclusion

The results of our meta-analysis showed that preoperative coexisting diseases, such as pulmonary HT, malignancy, heart failure, hepatic and neurological diseases, and dyslipidemia, may not be risk factors for the development of mediastinitis after cardiac surgery. However, there is still a need for large, randomized, controlled studies to decrease the heterogeneity of analysis.

Table 14. Pulmonary disease and mediastinitis

Study name	Statistics for each study					Odds ratio and 95% CI
	Odds ratio	Lower limit	Upper limit	Z value	*p*	Relative weight
Lin et al.[21]	3.663	0.679	19.752	1.510	0.131	1.96
Abboud et al.[7]	3.167	0.507	19.792	1.233	0.218	1.73
Elenbaas et al.[15]	2.271	1.430	3.605	3.478	0.001	6.17
Robinson et al.[28]	1.696	1.163	2.472	2.747	0.006	6.55
Ghotaslou et al.[17]	0.892	0.207	3.837	-0.153	0.878	2.41
Sakamoto et al.[32]	1.686	0.377	7.540	0.684	0.494	2.32
Risnes et al.[3]	2.876	1.554	5.324	3.364	0.001	5.43
Dial et al.[12]	3.750	0.853	16.477	1.750	0.080	2.36
Colombier et al.[11]	1.128	0.493	2.585	0.286	0.775	4.45
Wouters et al.[36]	0.258	0.016	4.280	-0.945	0.345	0.85
Sá et al.[30]	5.355	2.336	12.271	3.966	0.000	4.45
Sá et al.[31]	0.680	0.037	12.431	-0.260	0.795	0.80
Ridderstolpe et al.[27]	6.787	4.118	11.186	7.513	0.000	5.99
Newman et al.[25]	3.348	1.632	6.868	3.296	0.001	4.94
Tiveron et al.[35]	1.935	0.457	8.199	0.896	0.370	2.44
Filsoufi et al.[16]	2.934	1.748	4.924	4.074	0.000	5.90
López Gude et al.[22]	2.903	1.706	4.939	3.931	0.000	5.84
Baillot et al.[9]	1.174	0.855	1.611	0.989	0.322	6.79
Bitkover et al.[1]	3.220	0.946	10.962	1.871	0.061	3.01
Braxton et al.[10]	2.565	1.852	3.553	5.670	0.000	6.76
Diez et al.[13]	2.929	1.422	6.035	2.914	0.004	4.92
Hallam et al.[20]	0.839	0.358	1.968	-0.403	0.687	4.35
San Juan et al.[33]	8.225	2.017	33.533	2.939	0.003	2.53
Rosmarakis et al.[29]	1.467	0.059	36.435	0.234	0.815	0.67
Gummert et al.[19]	1.110	0.580	2.125	0.315	0.753	5.27
Manganas et al.[23]	160.000	14.472	1768.928	4.140	0.000	1.11
	2.419	1.837	3.184	6.298	0.000	



CI: Confidence interval; OR: 2.4; 95% CI: 1.8-3.1; Z value=6.2; p=0.00; heterogeneity: Q value=79.79; df: 25; p=0.00; I^2: 68.67%.

Declaration of conflicting interests

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