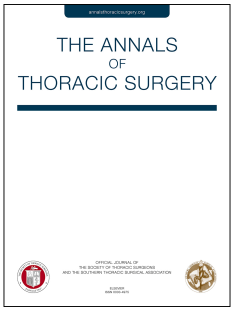


Surgical Repair of Post-Infarction Ventricular Septal Rupture: Systematic Review and Meta-Analysis

Matteo Matteucci, MD, Daniele Ronco, MD, Claudio Corazzari, MD, Dario Fina, MD, Federica Jiritano, MD, Paolo Meani, MD, Mariusz Kowalewski, MD, Cesare Beghi, MD, Roberto Lorusso, MD, PhD

PII: S0003-4975(20)31844-0

DOI: https://doi.org/10.1016/j.athoracsur.2020.08.050

Reference: ATS 34465

To appear in: *The Annals of Thoracic Surgery*

Received Date: 6 May 2020

Revised Date: 28 July 2020

Accepted Date: 3 August 2020

Please cite this article as: Matteucci M, Ronco D, Corazzari C, Fina D, Jiritano F, Meani P, Kowalewski M, Beghi C, Lorusso R, Surgical Repair of Post-Infarction Ventricular Septal Rupture: Systematic Review and Meta-Analysis, *The Annals of Thoracic Surgery* (2020), doi: https://doi.org/10.1016/j.athoracsur.2020.08.050.

Surgical Repair of Post-Infarction Ventricular Septal Rupture: Systematic Review and Meta-Analysis

Running Head: Ventricular Septal Rupture Repair

Matteo Matteucci[a,b,*], MD, Daniele Ronco[a,b,*], MD, Claudio Corazzari[b], MD, Dario Fina[a], MD, Federica Jiritano[a,c], MD, Paolo Meani[a], MD, Mariusz Kowalewski[a,d,e], MD, Cesare Beghi[b], MD, Roberto Lorusso[a], MD, PhD.

[a]*Department of Cardiothoracic Surgery, Heart and Vascular Centre, Maastricht University Medical Centre, Maastricht, The Netherlands*; [b]*Department of Surgical and Morphological Sciences, Circolo Hospital, University of Insubria, Varese, Italy*; [c]*Department of Cardiac Surgery, University Magna Graecia of Catanzaro, Catanzaro, Italy*; [d]*Clinical Department of Cardiac Surgery, Central Clinical Hospital of the Ministry of Interior in Warsaw, Warsaw, Poland;* [e]*Thoracic Research Centre, Collegium Medicum, Nicolaus Copernicus University, Innovative Medical Forum, Bydgoszcs, Poland*

*Drs Matteucci and Ronco contributed equally to this work.

Corresponding Author:

Matteo Matteucci, M.D.

Cardiothoracic Surgery Department – Heart & Vascular Centre

Maastricht University Medical Centre (MUMC)

P. Debyelaan, 12 – 6221 AZ Maastricht, The Netherlands

Email: matteomatteucci87@gmail.com

Word Count: 6,414

Abstract

Background. Ventricular septal rupture (VSR) is a rare but life-threatening complication following acute myocardial infarction. Surgical correction, though challenging and associated with high mortality, remains the treatment of choice. This systematic review and meta-analysis aimed to evaluated the early outcome of surgical VSR repair.

Methods. Electronic databases were searched from January 1998 to February 2020. Studies reporting patients undergoing surgical treatment for VSR were analysed. The primary outcome being assessed was operative mortality. Differences were expressed as odds ratio (OR) with 95% confidence interval (CI) to assess the relationships of predefined surgical variables and clinical prognosis.

Results. A total of 6,361 adult patients from 41 studies were identified. Operative mortality was 38.2%. Pooled ORs showed increased odds of operative mortality in patients with pre/perioperative IABP insertion (OR, 3.48; 95%CI, 3.01 to 4.02; $p < 0.001$), right ventricular (RV) dysfunction (OR, 2.85; 95%CI, 1.47 to 5.52; $p = 0.002$), posterior VSR (OR, 1.73; 95%CI, 1.30 to 2.31; $p < 0.001$), and emergency surgery (OR, 3.79; 95%CI, 2.52 to 5.72; $p < 0.001$). Temporal trend evaluation revealed no difference over time in the operative mortality rate, being 34% in both time-related groups (years 1971-2000 versus years 2001-2018).

Conclusions. VSR repair carries a high operative mortality. Patients with pre/perioperative IABP support, RV dysfunction at presentation, posterior defects, and subjects undergoing VSR correction on emergency basis have increased odds of operative mortality.

Ventricular septal rupture (VSR) is a rare but potentially fatal complication of acute myocardial infarction (AMI), with recent literature reporting an incidence between 0.17% and 0.21%[1,2]. Despite significant improvements over the last two decades in overall mortality for patients with AMI, the outcome of subjects who develop VSR remains dismal[2]. The poor results of medical treatment make surgical intervention the treatment of choice for VSR. However, results of surgical repair are often suboptimal and associated with high mortality due to hemodynamic instability and tissue fragility. Since VSR is uncommon, most published series on surgical outcomes consist of single-center experiences with small sample size, and limited information regarding predictors on management and outcome. Thus, we performed a systematic review and meta-analysis of the available literature in order to provide a current perspective and early postoperative results of the surgical management of VSR.

Material and Methods

This systematic review and meta-analysis were registered with PROSPERO (ID: CRD42020173660) and was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[3].

Data Sources, Search Strategy and Selection Criteria.

PubMed, Embase and Cochrane central register of controlled trials (CENTRAL) were comprehensively searched for relevant studies from January 1, 1998 to the end of February 2020. The search terms were: “ventricular septal rupture” or “ventricular septal defect” or “acquired ventricular septal defect”, and "surgical repair"; “ventricular septal rupture” or “ventricular septal defect” and "cardiac surgery"; “ventricular septal rupture” or “ventricular septal defect” and "surgical treatment"; “ventricular septal rupture” or “ventricular septal defect” and "myocardial infarction". The literature was limited to articles published in English. Studies that provided the outcome for adult patients (> 18 years old) who underwent surgical treatment for VSR were included. Articles were excluded if they satisfied the following criteria: (1) animal studies; (2) ventricular septal defects not AMI-related (e.g. congenital, post-traumatic); (3) studies including < 20 surgical patients. Case reports and systematic reviews were not considered. In case of overlap in some data/patients between studies, the study with the largest population was included in the meta-analysis.

Data Extraction and Endpoint Selection.

A standardised form was used to extract data, including a description of the study population, patient and procedure characteristics, complications, as well as number of clinical events. Two independent reviewers (M.M. and D.R.) selected the articles for inclusion, extracted studies, as well as patient characteristics of interest and relevant outcomes. Discrepancies were resolved by discussion and adjudication by a third reviewer (C.C.). The primary outcome being assessed was operative mortality, defined as any death, regardless of cause, occurring within 30 days after surgery (in or out of the hospital) or after 30 days during the same hospitalization subsequent to the operation. Secondary endpoints were the following in-hospital postoperative complications: cerebrovascular events, major bleeding, renal failure requiring renal replacement therapy, and reoperation for recurrence or residual VSR. Long-term follow-up and out-of-hospital complications were not considered. A meta-analysis was conducted to evaluate risk factors for operative mortality. We assessed also the temporal changes in operative mortality over the study period: for this evaluation two time-frames were used (1971-2000 and 2001-2018), and only studies in which all patients underwent surgery in one of the two frames were considered for such a comparison; if there was overlap between the time frames, studies were excluded from analysis.

Quality Assessment.

Two authors (M.M. and C.C.) independently assessed the trials' eligibility and risk of bias. Risk of bias at the individual study level was assessed using the ROBINS-I tool (Risk Of Bias In Not-randomized Studies of Interventions)[4]. Specifically, all the studies were judged based on these following pre-specified potential sources of bias: confounding bias, information bias, selection bias, reporting bias. Studies were categorized as “Yes”, “No”, or “Unclear” for each of the items. A judgement of “Yes” indicates a small risk of bias, whereas a judgement if “No” indicates a high risk of bias for the specific item. “Unclear” indicates that the risk of bis could not be assessed because of missing data. Any divergences were resolved by a third reviewer (R.L.).

Statistical Analysis.

Review Manager 5.3 software, developed by the Cochrane Collaboration (http://tech.cochrane.org/revman/), was used for statistical computations. Pooled odds ratios (OR) were reported with 95% CIs, and a two-tailed $p < 0.05$ was considered statistically significant. The Cochran’s Q test and I^2 test were all performed to judge the heterogeneity among the studies included in the meta-analysis. Heterogeneity was also considered to be significant at $p < 0.1$ for the Q statistic. An I^2 value less 50% indicates low heterogeneity, values between 50% and 75% suggest moderate heterogeneity, and I^2 greater than 75% were considered high heterogeneity. Results showing no significant heterogeneity were analysed by the fixed-effects model and those with significant heterogeneity were analysed by the random-effects model. Sensitivity analysis was carried out by successively excluding the low-quality studies to assess the stability of the outcome. Potential publication bias was evaluated by constructing a funnel plot. The plot was estimated visually, and asymmetric funnel plot suggested possible publication bias.

Results

The literature search identified 41 studies that met explicit inclusion criteria, including a total of 6,361 patients. Of the 41 studies evaluated, all were observational and retrospective in design, with no randomized controlled trials or prospective investigations. The PRISMA flow diagram describing the study selection process is presented in Supplemental Figure 1.

Preoperative Patient Characteristics.

Mean age of the patients was 67.1 ± 4.3 years and men accounted for 55.4% of cases. The rate of individuals in cardiogenic shock was 52.5% at the time of operation, and 68.9% had IABP placed pre- or peri-operatively. The mean time interval from AMI onset to diagnosis of VSR was 5 ± 1.8 days, while time from VSR diagnosis to surgery was 10 ± 13.2 days. Multivessel coronary artery disease was present in 35.6% of subjects. The average left ventricular ejection fraction (LVEF) was 43.9 ± 4.9%. The operation was carried out on emergency bases in 50.8% of cases. Detailed characteristics of studies and patients are listed in Table 1.

Operative Characteristics.

Anterior VSR was the most common location (60.1%). In almost 44% of subjects VSR was repaired with the concept of “infarct exclusion”. Mean duration of cardiopulmonary bypass (CPB) was 143.8 ± 33.8 minutes and aortic cross-clamp time was 87.9 ± 23.3 minutes. Concomitant CABG was performed in 54.3% of patients. Operative data are shown in Table 2.

Postoperative Outcomes.

Overall, the total number of deaths amounted to 2,430, representing an operative mortality rate of 38.2%. Postoperatively, kidney dysfunction requiring renal replacement therapy (RRT) occurred in 15.8% of the subjects, whereas major bleeding and cerebrovascular events in 8.4% and 4.4% of cases, respectively. The rate of recurrent or residual VSR following operative repair was 21%; reoperation was necessary in the 7.4% of patients. The mean intensive care unit (ICU) stay was 9.6 ± 6.8 days, while hospital length of stay was 18.9 ± 11.3 days. Postoperative outcomes are outlined in Table 3. Fifteen articles, comprising 2,312 patients, were included in the temporal trend analysis of operative mortality. There were no substantial changes over time in the operative mortality rate: 34% (time frame 1971-2000) versus 34% (time frame 2001-2018) (Figure 1).

Meta-Analysis.

Odds of operative mortality were significantly increased in patients with pre/perioperative IABP insertion as compared to no IABP (OR, 3.48; 95%CI, 3.01 to 4.02; $p < 0.001$; $I^2 = 0\%$ (Figure 2), corresponding rates of death were 46.5% (1,633/3,515) and 22.4% (352/1,570). Subjects with RV dysfunction at presentation had increased odds of operative mortality as well (OR, 2.85; 95%CI, 1.47 to 5.52; $p = 0.002$; $I^2 = 6\%$) (Figure 2). Operative mortality was increased also when VSR repair was conducted in emergency setting (OR, 3.79; 95%CI, 2.52 to 5.72; $p < 0.001$; $I^2 = 62\%$) (Figure 2). No significant difference was found between VSR repair with concomitant CABG and without concomitant CABG in terms of operative mortality (OR, 1.05; 95%CI, 0.87 to 1.25; $p = 0.62$), with low heterogeneity ($I^2 = 26\%$) (Figure 3). Increased odds of operative mortality were seen in cases of posterior VSR (OR, 1.73; 95%CI, 1.30 to 2.31; $p < 0.001$; $I^2 = 6\%$) (Figure 3), while a non-significant trend towards reduced odds was observed when the repair was performed with the concept of “infarct exclusion” (OR, 0.42; 95%CI, 0.10 to 1.70; $p = 0.22$), with moderate heterogeneity among studies ($I^2 = 68\%$) (Figure 3).

Risk of Bias.

A summary of the risk of biases of included studies is reported in Supplemental Figure 2. Overall, quality assessment revealed a significant risk of bias, especially confounding and selection bias (Supplemental Figure 3). Analysis of the funnel plots showed symmetry and suggested no significant risk of publication bias (Supplemental Figure 4 and Figure 5).

Comment

Although the incidence of VSR has been decreasing with the advent of acute reperfusion strategies, this post-AMI mechanical complication still portends an ominous prognosis[2]. Patients with VSR represent a very high-risk subgroup among those who have suffered an AMI. Clinical and anatomical challenges include the associated hemodynamic instability often leading to cardiogenic shock, the functional/anatomical involvement of the right ventricle, the friable tissue surrounding the infarct area, the complex nature of the defect and its expansion over time. VSR usually occurs after transmural infarction, and can involve any part of the ventricular septum. Most patients develop unpredictable hemodynamic in the hours or days following VSR, and report of long-term survival independent of corrective interventions are extremely rare. The multicenter GUSTO-I trial and the SHOCK registry reported mortality rates of 94% and 96%[5,6], respectively, in medically managed VSR patients, representing numbers estimated to be closed to the natural course of the disease. Surgical repair, therefore, is considered the treatment of choice. Due to the above-mentioned factors, however, the surgical treatment remains a challenging operation with often a complicated course. This systematic review gives an overview of published evidence on the characteristics and outcomes after VSR repair.

Controversies have arisen concerning the optimal timing for surgery. A longer interval before repair has been reported to be associated with better survival[7]. The improved outcome with delayed surgical correction may be related to evolution of the infarct and scar tissue formation, which may facilitate the VSR repair. However, a high proportion of patients are hemodynamically unstable at presentation, and an early intervention is usually required and performed on these individuals. In the acute setting, infarcted myocardium is weak and friable, and holds sutures poorly leading to increased risk of tearing and postoperative residual shunt. Thus, preoperative stabilization of patient status is crucial. Management of compromised subjects should be direct at decreasing left-to-right shunt with afterload reducing agents and IABP insertion. Furthermore, IABP increases the coronary flow and diminishes ventricular wall stress and oxygen demand. The current meta-analysis revealed a significant, yet non-direct, link between the pre/perioperative use of IABP and the risk of operative mortality. A possible explanation for this is related to the critical illness status of patients in whom decision of IABP insertion was made. The lack of specific information in the IABP subgroup prevented us from further exploring this issue.

In the last two decades, in addition to IABP, other forms of short-term temporary mechanical circulatory support (MCS) have emerged as attractive tools in critical patients with persistent hemodynamic instability caused by VSR. Several studies in the literature have documented the use of extracorporeal membrane oxygenation (ECMO) to stabilize patients with VSR until surgery can be performed[8,9]. Other option include the placement of a percutaneous left-ventricular assist device, such as Impella LP 5.0 (Abiomed, Danvers, MA, USA), as a bridge to surgery or transplant[10]. Preoperative MCS may improve hemodynamic and metabolic status, and allow for a delayed surgical correction a few days later, in a more stable condition. However, this improvement occurs at the expense of high rate of complications[11], so the selection and the single center’s experience is important in order to achieve satisfactory results.

Surgical repair of VSR has evolved over time. The two common techniques used for VSR repair are the Daggett and the David procedures[12,13]. The Dagget procedure is a single or multiple patch technique which closes the VSR by placing a patch over the defect and sewing to the LV and RV[12]. On the contrary, the David procedure is an infarct exclusion technique with all sutures placed in the LV[13]. Despite the David method has gained worldwide popularity, if one technique is superior to the other is still not well defined. In our analysis we observed a trend toward lower operative mortality in the “infarct exclusion” group, although this did not reach statistical significance.

Location of VSR represents another critical factor. Indeed, posterior VSRs pose technical challenges, as the heart have to be elevated for adequate exposure and posterior descending artery and posteromedial papillary muscle are in close proximity. The current review showed that in almost 40% of cases the VSR was posterior. The posterior location of VSR has been associated with poor surgical outcome due to right ventricular dysfunction, complex ruptures, and difficult repair[14,15]. Our results are in accordance with previous analysis[14,15].

It is controversial whether concomitant CABG improves outcome after VSR repair. This study did not find any significant protective effect of simultaneous CABG in terms of early mortality.

Over the study period, there were no substantial changes over time in the operative mortality. The lack of an improvement in the mortality of patients submitted to cardiac surgery for VSR may account for several reasons: more complex patient profile treated and more liberal indication for surgery as compared to older times, despite enhanced surgical and perioperative management., or an actual lack of substantial changes in more aggressive treatment might be also taken into account, as shown by the limited use of mechanical circulatory support in the reviewed series. Based on the findings, it is clear that ominous outcome is strictly related to patients who have, or develop soon after VSR repair, refractory cardio-circulatory compromise, ultimately leading to multi-organ failure. These observations, therefore, indicate that still more efforts should be devoted to enhance pre- and perioperative management strategies with a more extensive use of temporary MCS, also prophylactically. The data detailing the success of these strategies in patients with acute VSR is currently restricted to case studies[8-10]. However, in the absence of large trial data, these reports provide an interesting, albeit limited, perspective. Future research is needed to examine the potential benefit of such a broader use as well as the actual role and impact of different types of temporary MCS devices in the setting of post-infarction VSR.

In recent years, percutaneous VSR closure has emerged as a promising alternative option for patients with significant risk for surgical closure, either as a definitive therapy, or as a bridge to surgery after initial stabilization. Thiele and colleagues[16] reported a 30-days mortality rate of 65% in 29 patients with VSR underwent primary transcatheter closure, while residual shunting was detected in 13.7% of cases. Based on the operative mortality and reoperation rate for postoperative residual/recurrent shunts observed by the present review the surgical approach remains the standard of care for VSR.

Limitations. The retrospective nature of the reports included represent the major limitations of this study. Retrospective studies are subjects to confounders and bias, possibly affecting the conclusive power of our meta-analysis. The pooled occurrence rates for complications and mortality were based on heterogeneous data and should be treated with considerable reserve. Three national registries provided data for this review. Individual and institutional experience are crucial in determining the likelihood of the success of VSR repair. Although our analysis revealed no evidence of significant reporting bias, such a bias remains still a possibility, with potentially more favourable results being reported from large-volume expert centers that may not be representative of all institutions. Because the timeline of the study period is fairly long, progress in management and operative strategies might have been a confounder, limiting our qualitative and quantitative analysis. Another important limitation of the current review is the considerable amount of missing data. Moreover, we acknowledge the lack of some critical information such as the initial hemodynamic status of patients supported with IABP, the number of distal anastomoses and grafts, defect size, patch materials, and surgeon’s experience. Given these limitations, our results should be interpreted with caution. Finally, because this study is limited by the operative outcomes, it does not provide information on the durability of surgical repair of VSR.

Conclusion

Surgical VSR repair is associated with high operative mortality (38.2%). The results of the present meta-analysis seem to indicate that patients with pre/perioperative IABP support, RV dysfunction at presentation, posterior defects, and subjects undergoing VSR correction on emergency basis have increased odds of operative mortality. Our results also suggest concomitant CABG does not to improve early survival. However, clinical validations studies with larger sample sizes are needed to confirm these findings, particularly to assess whether more aggressive pre- and perioperative management with temporary MCS may improve such still suboptimal early results.

References

1) French JK, Hellkamp AS, Armstrong PW, et al. Mechanical complications after percutaneous coronary intervention in ST-elevation myocardial infarction (from APEX-AMI). Am J Cardiol. 2010 Jan 1;105(1):59-63.
2) Elbadawi A, Elgendy IY, Mahmoud K, et al. Temporal Trends and Outcomes of Mechanical Complications in Patients With Acute Myocardial Infarction. JACC Cardiovasc Interv. 2019 Sep 23;12(18):1825-1836.
3) Moher D, Liberati A, Tetzlaff J, et al; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009 Oct;62(10):1006-12.
4) Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016 Oct 12;355:i4919.
5) Crenshaw BS, Granger CB, Birnbaum Y, et al. Risk factors, angiographic patterns, and outcomes in patients with ventricular septal defect complicating acute myocardial infarction. GUSTO-I (Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries) Trial Investigators. Circulation. 2000 Jan 4-11;101(1):27-32.
6) Menon V, Webb JG, Hillis LD, et al. Outcome and profile of ventricular septal rupture with cardiogenic shock after myocardial infarction: a report from the SHOCK Trial Registry. SHould we emergently revascularize Occluded Coronaries in cardiogenic shocK? J Am Coll Cardiol. 2000 Sep;36(3 Suppl A):1110-6.
7) Arnaoutakis GJ, Zhao Y, George TJ, et al. Surgical repair of ventricular septal defect after myocardial infarction: outcomes from the Society of Thoracic Surgeons National Database. Ann Thorac Surg. 2012 Aug;94(2):436-43; discussion 443-4.
8) Ariza-Solé A, Sánchez-Salado JC, Sbraga F, et al. The role of perioperative cardiorespiratory support in post infarction ventricular septal rupture-related cardiogenic shock. Eur Heart J Acute Cardiovasc Care. 2020 Mar;9(2):128-137.

9) Tsai MT, Wu HY, Chan SH, Luo CY. Extracorporeal membrane oxygenation as a bridge to definite surgery in recurrent postinfarction ventricular septal defect. ASAIO J. 2012;58(1):88□89.

10) La Torre MW, Centofanti P, Attisani M, et al. Posterior ventricular septal defect in presence of cardiogenic shock: early implantation of the impella recover LP 5.0 as a bridge to surgery. Tex Heart Inst J. 2011;38(1):42□49.

11) Cheng R, Hachamovitch R, Kittleson M, et al. Complications of extracorporeal membrane oxygenation for treatment of cardiogenic shock and cardiac arrest: a meta-analysis of 1,866 adult patients. Ann Thorac Surg. 2014;97(2):610□616.

12) Daggett WM, Guyton RA, Mundth ED, et al. Surgery for post-myocardial infarct ventricular septal defect. Ann Surg. 1977 Sep;186(3):260-71.

13) David TE, Dale L, Sun Z. Postinfarction ventricular septal rupture: repair by endocardial patch with infarct exclusion. J Thorac Cardiovasc Surg. 1995 Nov;110(5):1315-22.

14) Pang PY, Sin YK, Lim CH, et al. Outcome and survival analysis of surgical repair of post-infarction ventricular septal rupture. J Cardiothorac Surg. 2013 Mar 9;8:44.

15) Jeppsson A, Liden H, Johnsson P, et al. Surgical repair of post infarction ventricular septal defects: a national experience. Eur J Cardiothorac Surg. 2005 Feb;27(2):216-21.

16) Thiele H, Kaulfersch C, Daehnert I, et al. Immediate primary transcatheter closure of postinfarction ventricular septal defects. Eur Heart J. 2009 Jan;30(1):81-8.

17) Dogra N, Puri GD, Thingnam SKS, et al. Early thrombolysis is associated with decreased operative mortality in postinfarction ventricular septal rupture. Indian Heart J. 2019 May - Jun;71(3):224-228.

18) Li H, Zhang S, Yu M, et al. Profile and Outcomes of Surgical Treatment for Ventricular Septal Rupture in Patients With Shock. Ann Thorac Surg. 2019 Oct;108(4):1127-1132.

19) Sakaguchi G, Miyata H, Motomura N, et al. Surgical Repair of Post-Infarction Ventricular Septal Defect – Findings From a Japanese National Database. Circ J. 2019 Oct 25;83(11):2229-2235.

20) Abbasnejad M, Vand MT, Khamnian Z, Separham A. In-hospital outcome of patients with post-MI VSD: a single-center study. Kardiochir Torakochirurgia Pol. 2018 Dec;15(4):227-232.

21) Khan MY, Waqar T, Qaisrani PG, et al. Surgical Repair of post-infarction ventricular septal rupture: Determinants of operative mortality and survival outcome analysis. Pak J Med Sci. 2018 Jan-Feb;34(1):20-26.

22) Pojar M, Harrer J, Omran N, et al. Surgical treatment of postinfarction ventricular septal defect: risk factors and outcome analysis. Interact Cardiovasc Thorac Surg. 2018 Jan 1;26(1):41-46.

23) Malhotra A, Patel K, Sharma P, et al. Techniques, Timing & Prognosis of Post Infarct Ventricular Septal Repair: a Re-look at Old Dogmas. Braz J Cardiovasc Surg. 2017 May-Jun;32(3):147-155.

24) Cinq-Mars A, Voisine P, Dagenais F, et al. Risk factors of mortality after surgical correction of ventricular septal defect following myocardial infarction: Retrospective analysis and review of the literature. Int J Cardiol. 2016 Mar 1;206:27-36.

25) Yalçınkaya A, Lafçı G, Diken Aİ, et al. Early Mortality and Long-term Survival after Repair of Post-infarction Ventricular Septal Rupture: An Institutional Report of Experience. Heart Lung Circ. 2016 Apr;25(4):384-91.

26) Huang SM, Huang SC, Wang CH, et al. Risk factors and outcome analysis after surgical management of ventricular septal rupture complicating acute myocardial infarction: a retrospective analysis. J Cardiothorac Surg. 2015 May 4;10:66.

27) Kim IS, Lee JH, Lee DS, et al. Surgical Outcomes of a Modified Infarct Exclusion Technique for Post-Infarction Ventricular Septal Defects. Korean J Thorac Cardiovasc Surg. 2015 Dec;48(6):381-6.

28) Takahashi H, Arif R, Almashhoor A, et al. Long-term results after surgical treatment of postinfarction ventricular septal rupture. Eur J Cardiothorac Surg. 2015 Apr;47(4):720-4.

29) Lundblad R, Abdelnoor M. Surgery of postinfarction ventricular septal rupture: the effect of David infarct exclusion versus Daggett direct septal closure on early and late outcomes. J Thorac Cardiovasc Surg. 2014 Dec;148(6):2736-42.

30) Hu XY, Qiu H, Qiao SB, et al. Clinical analysis and risk stratification of ventricular septal rupture following acute myocardial infarction. Chin Med J (Engl). 2013 Nov;126(21):4105-8.

31) Kettner J, Sramko M, Holek M, et al. Utility of intra-aortic balloon pump support for ventricular septal rupture and acute mitral regurgitation complicating acute myocardial infarction. Am J Cardiol. 2013 Dec1;112(11):1709-13.

32) Park SJ, Kim JB, Jung SH, et al. Surgical Repair of Ventricular Septal Defect after Myocardial Infarction: A Single Center Experience during 22 Years. Korean J Thorac Cardiovasc Surg. 2013 Dec;46(6):433-8.

33) Rohn V, Grus T, Lindner J, et al. Postinfarction ventricular septal rupture - a rare complication remains challenge for cardiac surgical team. Prague Med Rep. 2013;114(1):9-17.

34) Yam N, Au TW, Cheng LC. Post-infarction ventricular septal defect: surgical outcomes in the last decade. Asian Cardiovasc Thorac Ann. 2013 Oct;21(5):539-45.

35) Abu-Omar Y, Bhinda P, Choong CK, et al. Survival after surgical repair of ischemic ventricular septal rupture. Asian Cardiovasc Thorac Ann. 2012 Aug;20(4):404-8.

36) Fukushima S, Tesar PJ, Jalali H, et al. Determinants of in-hospital and long-term surgical outcomes after repair of postinfarction ventricular septal rupture. J Thorac Cardiovasc Surg. 2010 Jul;140(1):59-65.

37) Murashita T, Komiya T, Tamura N, et al. The clinical challenge to reduce the postoperative residual shunt in surgical repair of postinfarction ventricular septal perforation. Interact Cardiovasc Thorac Surg. 2010 Jul;11(1):38-41.

38) Sá MP, Sá MV, Barbosa CH, et al. Clinical and surgical profile of patients operated for postinfarction interventricular septal rupture. Rev Bras Cir Cardiovasc. 2010 Jul-Sep;25(3):341-9.

39) Sibal AK, Prasad S, Alison P, et al. Acute ischaemic ventricular septal defect--a formidable surgical challenge. Heart Lung Circ. 2010 Feb;19(2):71-4.

40) Coskun KO, Coskun ST, Popov AF, et al. Experiences with surgical treatment of ventricle septal defect as a post infarction complication. J Cardiothorac Surg. 2009 Jan 6;4:3.

41) Poulsen SH, Praestholm M, Munk K, et al. Ventricular septal rupture complicating acute myocardial infarction: clinical characteristics and contemporary outcome. Ann Thorac Surg. 2008 May;85(5):1591-6.

42) Sajja LR, Mannam GC, Gutti RS, et al. Postinfarction ventricular septal defect: patch repair with infarct exclusion. Asian Cardiovasc Thorac Ann. 2008 Jun;16(3):215-20.

43) Mantovani V, Mariscalco G, Leva C, et al. Surgical repair of post-infarction ventricular septal defect: 19 years of experience. Int J Cardiol. 2006 Apr 4;108(2):202-6.

44) Barker TA, Ramnarine IR, Woo EB, et al. Repair of post-infarct ventricular septal defect with or without coronary artery bypass grafting in the northwest of England: a 5-year multi-institutional experience. Eur J Cardiothorac Surg. 2003 Dec;24(6):940-6.

45) Cerin G, Di Donato M, Dimulescu D, et al. Surgical treatment of ventricular septal defect complicating acute myocardial infarction. Experience of a north Italian referral hospital. Cardiovasc Surg. 2003 Apr;11(2):149-54.

46) Thiele H, Lauer B, Hambrecht R, et al. Short- and long-term hemodynamic effects of intra-aortic balloon support in ventricular septal defect complicating acute myocardial infarction. Am J Cardiol. 2003 Aug 15;92(4):450-4.

47) Labrousse L, Choukroun E, Chevalier JM, et al. Surgery for post infarction ventricular septal defect (VSD): risk factors for hospital death and long term results. Eur J Cardiothorac Surg. 2002 Apr;21(4):725-31; discussion 731-2.

48) Deja MA, Szostek J, Widenka K, et al. Post infarction ventricular septal defect - can we do better? Eur J Cardiothorac Surg. 2000 Aug;18(2):194-201.

49) Prêtre R, Ye Q, Grünenfelder J, et al. Operative results of "repair" of ventricular septal rupture after acute myocardial infraction. Am J Cardiol. 1999 Oct 1;84(7):785-8.

50) Bouchart F, Bessou JP, Tabley A, et al. Urgent surgical repair of postinfarction ventricular septal rupture: early and late outcome. J Card Surg. 1998 Mar;13(2):104-12.

51) Dalrymple-Hay MJ, Monro JL, Livesey SA, Lamb RK. Postinfarction ventricular septal rupture: the Wessex experience. Semin Thorac Cardiovasc Surg. 1998 Apr;10(2):111-6.

52) David TE, Armstrong S. Surgical repair of postinfarction ventricular septal defect by infarct exclusion. Semin Thorac Cardiovasc Surg. 1998 Apr;10(2):105-10.

Table 1. Studies and Patients' Baseline Characteristics

Author (Reference)	Year	Total Pt (n)	Age* (y)	Male (n)	Cardiogenic Shock (n)	Emergency Surgery (n)	Time (d)* AMI-VSR	Time (d)* VSR-repair	Multivessel CAD (n)	Pre-op* LVEF (%)	Pre/peri-op IABP (n)	Pre/peri-op ECLS (n)
Ariza-Solè (8)	2020	20	67	14	…	…	…	…	11	46	13	5
Dogra (17)	2019	35	61	19	15	…	…	…	…	33	16	1
Li (18)	2019	105	63.1	63	71	24	6.2	47.7	65	46.5	40	…
Sakaguchi (19)	2019	1,397	74.1	671	859	731	…	…	303	…	1,200	224
Abbasnejad (20)	2018	23	67.4	14	14	…	…	…	12	…	16	…
Khan (21)	2018	31	57.1	21	7	4	…	9.3	6	38.4	13	0
Pojar (22)	2018	39	68.4	19	…	16	…	…	18	47.2	17	1
Malhotra (23)	2017	40	61.6	26	…	34	3.2	3.1	22	37	40	…
Cinq-Mars (24)	2016	34	69	19	24	…	3.9	3.4	18	44	28	0
Yalcinkaya (25)	2016	63	67.2	35	…	20	…	…	…	45.2	57	…
Huang (26)	2015	47	68.9	28	19	41	…	…	31	45.8	34	6
Kim (27)	2015	23	68	11	…	20	…	…	7	42.5	19	1
Takahashi (28)	2015	52	67	26	30	29	…	…	33	…	20	…
Lundblad (29)	2014	110	…	80	21	…	…	…	69	…	99	…
Hu (30)	2013	21	…	…	…	…	…	…	…	…	…	…
Kettner (31)	2013	48	…	…	…	…	…	…	…	…	40	…
Pang (14)	2013	38	65.7	20	26	32	…	…	22	39.7	37	0
Park (32)	2013	34	67.1	13	25	9	…	…	18	43.7	23	1
Rohn (33)	2013	25	70.2	12	13	…	…	1.7	…	42.8	20	4
Yam (34)	2013	40	…	16	11	17	…	3	14	56	32	0
Abu-Omar (35)	2012	59	…	41	33	…	…	…	…	…	47	…
Arnaoutakis (7)	2012	2,876	68	1,624	1,487	1,430	…	…	966	43.1	1,869	84^
Fukushima (36)	2010	68	66.4	49	8	…	…	…	45	…	28	1
Murashita (37)	2010	34	79.6	11	21	…	…	…	14	…	31	3
Sà (38)	2010	21	62.8	13	12	…	4.8	7.8	7	50.6	5	…
Sibal (39)	2010	36	70.4	12	28	36	…	…	…	…	22	…
Coskun (40)	2009	41	68	30	29	5	8.7	23.1	24	47.2	19	…
Poulsen (41)	2008	45	68	…	…	…	…	…	…	45	…	…
Sajja (42)	2008	22	57.4	20	15	…	1.9	…	19	…	15	…
Mantovani (43)	2006	50	66	26	…	37	…	…	25	…	28	0
Jeppsson (15)	2005	189	69	119	…	…	…	…	…	…	91	0
Barker (44)	2003	65	…	40	35	…	…	…	46	…	42	…
Cerin (45)	2003	58	73	29	24	18	4	2.8	40	43	12	…
Thiele (46)	2003	20	68.5	12	9	…	…	…	11	42	20	3
Labrousse (47)	2002	85	69	51	16	…	…	3.4	…	…	81	…

Crenshaw (5)	2000	34	…	…	…	…	…	…	…	…	…	…
Deja (48)	2000	110	65.6	69	33	…	5.6	9	44	…	66	1
Pretre (49)	1999	54	…	33	25	…	…	…	28	…	31	…
Bouchart (50)	1998	67	66.3	43	49	58	3.6	6.1	29	…	54	0
Dalrymple-Hay (51)	1998	150	66	90	45	…	…	…	…	…	55	…
David (52)	1998	52	68	25	34	…	…	…	36	…	34	…
Total n/N (±SD)	*/*	*6,361*	*67.1 ±4.3*	*3,444/ 6,213*	*3,038/ 5,789*	*2,561/ 5,037*	*5 (±1.8)*	*10 (±13.2)*	*1,983/ 5,571*	*43.9 (±4.9)*	*4,314/ 6,261*	*335/ 5,177*

Pt = patients; n = number; AMI = acute myocardial infarction; VSR = ventricular septal rupture; CAD = coronary artery disease; LVEF = left ventricular ejection fraction; Pre-op = preoperative; Peri-op = perioperative; IABP = intra-aortic balloon pump; ECLS = extracorporeal life support; * = mean value; SD = standard deviation; d = days; y = years; ^ = ventricular assist device.

Table 2. Operative Data

Author (Reference)	Posterior VSR (n)	Apical/Anterior VSR (n)	CPB Time* (m)	ACC Time* (m)	Concomitant CABG (n)	Infarct Exclusion (n)	Other Techniques (n)
Ariza-Solè (8)	5	15	…	…	7	…	…
Dogra (17)	6	29	172	116	22	26	9
Li (18)	37	68	118.1	78.8	81	94	11
Sakaguchi (19)	…	…	198	124	475	…	…
Abbasnejad (20)	…	…	153	74	15	9	14
Khan (21)	5	26	120	61.7	18	31	0
Pojar (22)	18	21	146.3	91.8	12	39	0
Malhotra (23)	13	27	159	105.4	28	4	36
Cinq-Mars (24)	23	11	141	94	15	…	…
Yalcinkaya (25)	17	46	102.7	65.1	38	9	54
Huang (26)	11	36	193.9	113	27	47	0
Kim (27)	4	19	194.4	150.1	17	21^	2
Takahashi (28)	28	24	161.5	83.1	33	5	47
Lundblad (29)	59	51	120.2	66.7	29	42	68
Hu (30)	…	…	…	…	16	…	…
Kettner (31)	…	…	…	…	30	…	…
Pang (14)	10	28	152	82	19	35	3
Park (32)	6	28	165	85.2	21	34	0
Rohn (33)	8	17	182	94.6	17	25	0
Yam (34)	6	34	117	87	8	0	40
Abu-Omar (35)	27	32	110	58	44	…	…
Arnaoutakis (7)	…	…	…	…	1,837	…	…
Fukushima (36)	33	35	…	…	48	…	…
Murashita (37)	…	…	186	113	13	34	0
Sà (38)	7	14	…	…	0	…	…
Sibal (39)	14	22	…	…	15	18	18
Coskun (40)	14	27	…	…	22	0	41
Poulsen (41)	…	…	…	…	19	…	…
Sajja (42)	14	8	…	…	22	22	0
Mantovani (43)	20	30	…	101	25	16	34
Jeppsson (15)	97	92	…	…	119	…	…
Barker (44)	35	30	…	…	42	…	…
Cerin (45)	19	39	111	68	47	…	…
Thiele (46)	…	…	…	…	6	…	…
Labrousse (47)	35	50	…	…	40	0	85

Crenshaw (5)	…	…	…	…	…	…	…
Deja (48)	34	76	98.2	63.2	40	…	…
Pretre (49)	30	24	…	…	28	0	54
Bouchart (50)	23	44	114	70	22	2	65
Dalrymple-Hay (51)	…	…	…	…	…	0	150
David (52)	26	26	93	65	36	52	0
Total (n/N) (±SD)	*684/ 1,713*	*1,029/ 1,713*	*143.8 (±33.8)*	*87.9 (±23.3)*	*3,353/ 6,177)*	*565/ 1,296*	*731/ 1,296*

VSR = ventricular septal rupture; CPB = cardiopulmonary bypass; ACC = aortic cross-clamp; CABG = coronary artery bypass grafting; m = minutes; n = number; SD = standard deviation; * = mean value; ^ = modified infarct exclusion technique.

Table 3. Main Postoperative Outcomes

Author (Reference)	Major Bleeding (n)	Cerebrovascular Events (n)	RRT (n)	ICU Stay* (d)	Residual/Recurrent VSR (n)	Reoperation (n)	H Stay* (d)	Operative Mortality (n)
Ariza-Solè (8)	6	1	6	…	…	3	…	5
Dogra (17)	…	1	…	…	…	…	…	16
Li (18)	…	…	…	8.8	1	0	31.9	3
Sakaguchi (19)	112	64	295	15.2	…	…	…	461
Abbasnejad (20)	…	…	…	…	…	…	…	13
Khan (21)	1	…	0	2.8	3	0	11	8
Pojar (22)	11	3	13	…	5	0	…	14
Malhotra (23)	3	2	…	…	3	1	…	21
Cinq-Mars (24)	…	3	…	…	9	…	…	22
Yalcinkaya (25)	…	…	…	…	11	2	11.8	34
Huang (26)	11	5	21	24.9	16	…	44.9	17
Kim (27)	1	0	…	5.1	7	3	19.2	1
Takahashi (28)	…	…	…	…	4	4	…	19
Lundblad (29)	15	9	…	…	30	14	…	40
Hu (30)	…	…	…	…	…	…	…	1
Kettner (31)	…	…	…	…	11	4	…	20
Pang (14)	8	…	12	…	9	1	…	15
Park (32)	1	…	3	…	9	5	…	10
Rohn (33)	…	1	7	8.5	4	0	11.4	10
Yam (34)	…	…	16	…	10	2	…	8
Abu-Omar (35)	…	…	…	…	…	…	…	23
Arnaoutakis (7)	224	104	343	…	…	…	…	1,235
Fukushima (36)	6	3	12	…	22	8	…	24
Murashita (37)	…	…	…	19	7	2	…	12
Sà (38)	…	…	…	…	…	…	…	14
Sibal (39)	3	…	8	4.2	11	1	…	19
Coskun (40)	…	…	…	…	15	7	…	14
Poulsen (41)	…	…	…	…	…	…	…	13
Sajja (42)	…	…	…	4.1	…	…	12.6	5
Mantovani (43)	…	…	…	…	13	4	…	18
Jeppsson (15)	22	20	35	…	43	21	…	77
Barker (44)	3	1	10	…	16	…	…	20
Cerin (45)	5	…	…	…	19	9	10.9	30
Thiele (46)	…	…	…	…	…	…	…	9
Labrousse (47)	…	…	…	…	6	3	…	36

Crenshaw (5)	…	…	…	…	…	…	…	16
Deja (48)	6	5	18	4.8	44	13	…	38
Pretre (49)	…	…	…	…	10	4	…	14
Bouchart (50)	2	3	4	8	2	1	14	17
Dalrymple-Hay (51)	…	…	…	…	…	…	…	48
David (52)	…	…	10	10	3	0	21	10
Total (n/N) (±SD)	*440/ 5,248*	*225/ 5,145*	*813/ 5,134*	*9.6 (±6.8)*	*343/ 1,638*	*112/ 1,512*	*18.9 (±11.3)*	*2,430/ 6,361*

RRT = renal replacement therapy; ICU = intensive care unit; VSR = ventricular septal rupture; n = number; d = days; H = hospital; * = mean value; SD = standard deviation.

Figure Legends

Figure 1. Temporal trend evaluation of operative mortality for post-infarction VSR repair.

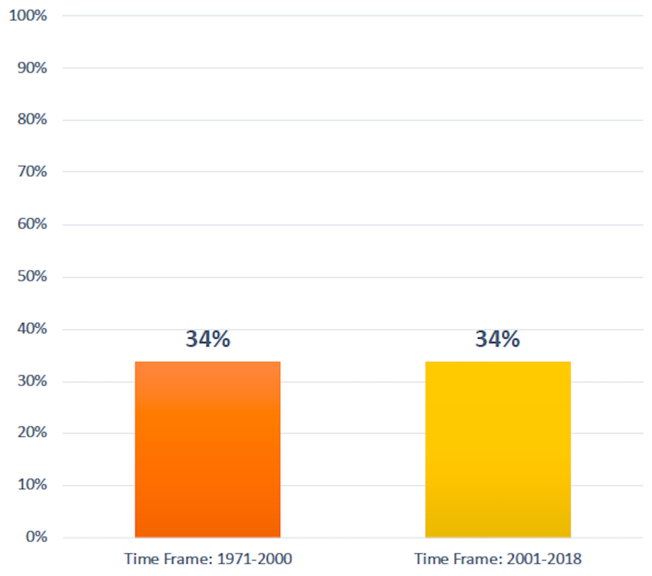
VSR = ventricular septal rupture.

Figure 2. Forrest plots of comparison (from above to below): IABP support (A), RV function (B), timing of surgery (C).

IABP = intra-aortic balloon pump; RV = right ventricular.

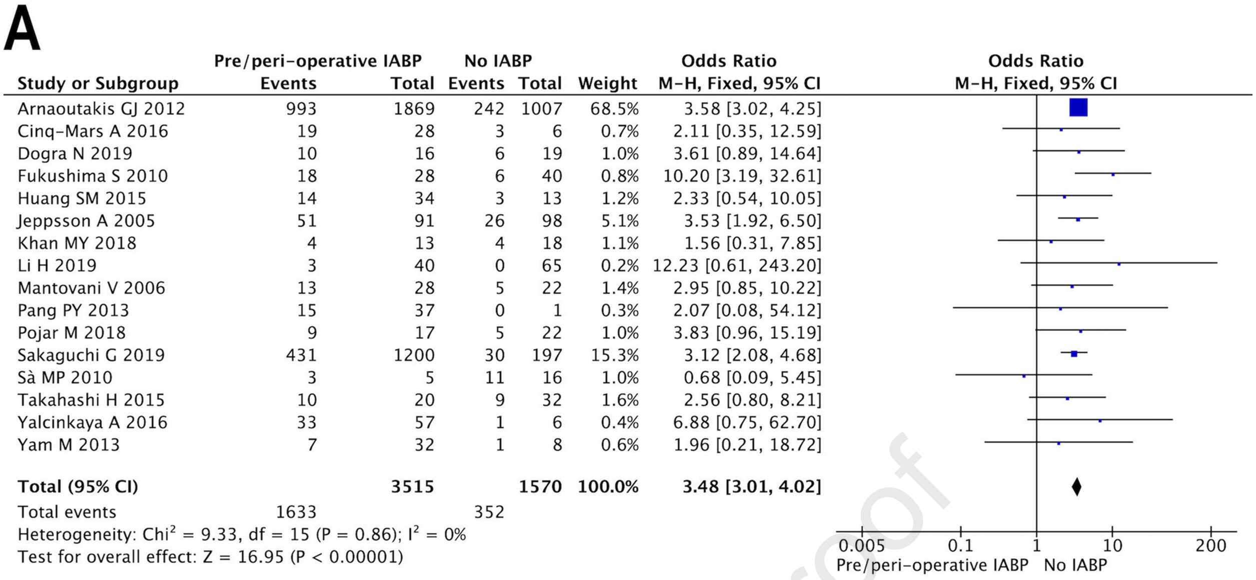
Figure 3. Forrest plots of comparison (from above to below): concomitant CABG (A), VSR location (B), surgical technique (C).

CABG = coronary artery bypass grafting; VSR = ventricular septal rupture.



Time Frame (Reference)	N. of Patients	Operative Mortality
1971-2000 (5,15,47-52)	741	256
2001-2018 (8,17,19-21,23,33)	1,571	534

A

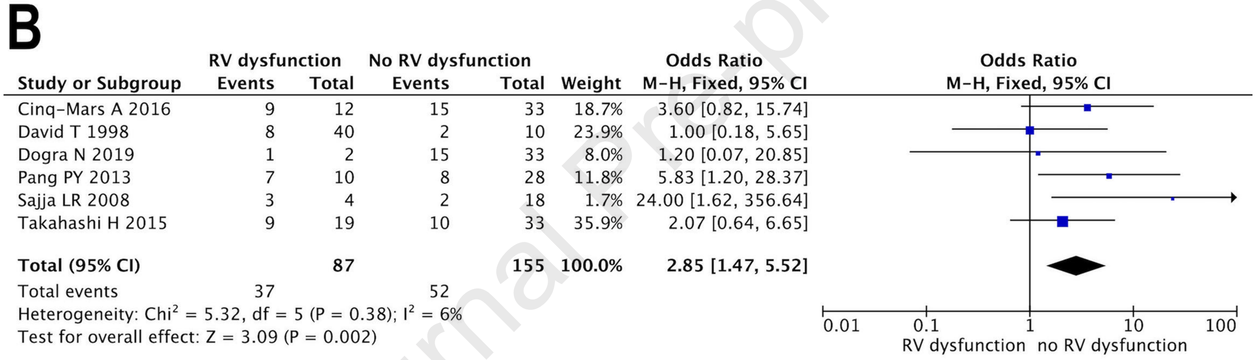


Study or Subgroup	Pre/peri-operative IABP Events	Total	No IABP Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Arnaoutakis GJ 2012	993	1869	242	1007	68.5%	3.58 [3.02, 4.25]
Cinq-Mars A 2016	19	28	3	6	0.7%	2.11 [0.35, 12.59]
Dogra N 2019	10	16	6	19	1.0%	3.61 [0.89, 14.64]
Fukushima S 2010	18	28	6	40	0.8%	10.20 [3.19, 32.61]
Huang SM 2015	14	34	3	13	1.2%	2.33 [0.54, 10.05]
Jeppsson A 2005	51	91	26	98	5.1%	3.53 [1.92, 6.50]
Khan MY 2018	4	13	4	18	1.1%	1.56 [0.31, 7.85]
Li H 2019	3	40	0	65	0.2%	12.23 [0.61, 243.20]
Mantovani V 2006	13	28	5	22	1.4%	2.95 [0.85, 10.22]
Pang PY 2013	15	37	0	1	0.3%	2.07 [0.08, 54.12]
Pojar M 2018	9	17	5	22	1.0%	3.83 [0.96, 15.19]
Sakaguchi G 2019	431	1200	30	197	15.3%	3.12 [2.08, 4.68]
Sà MP 2010	3	5	11	16	1.0%	0.68 [0.09, 5.45]
Takahashi H 2015	10	20	9	32	1.6%	2.56 [0.80, 8.21]
Yalcinkaya A 2016	33	57	1	6	0.4%	6.88 [0.75, 62.70]
Yam M 2013	7	32	1	8	0.6%	1.96 [0.21, 18.72]
Total (95% CI)		**3515**		**1570**	**100.0%**	**3.48 [3.01, 4.02]**
Total events	1633		352			

Heterogeneity: $Chi^2 = 9.33$, df = 15 (P = 0.86); $I^2 = 0\%$

Test for overall effect: Z = 16.95 (P < 0.00001)

B

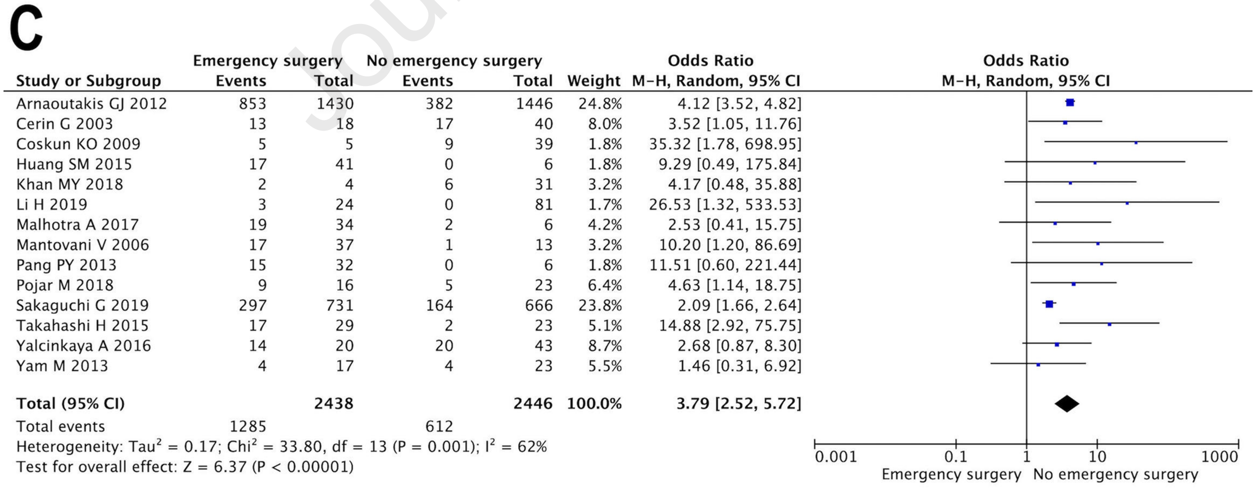


Study or Subgroup	RV dysfunction Events	Total	No RV dysfunction Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Cinq-Mars A 2016	9	12	15	33	18.7%	3.60 [0.82, 15.74]
David T 1998	8	40	2	10	23.9%	1.00 [0.18, 5.65]
Dogra N 2019	1	2	15	33	8.0%	1.20 [0.07, 20.85]
Pang PY 2013	7	10	8	28	11.8%	5.83 [1.20, 28.37]
Sajja LR 2008	3	4	2	18	1.7%	24.00 [1.62, 356.64]
Takahashi H 2015	9	19	10	33	35.9%	2.07 [0.64, 6.65]
Total (95% CI)		**87**		**155**	**100.0%**	**2.85 [1.47, 5.52]**
Total events	37		52			

Heterogeneity: $Chi^2 = 5.32$, df = 5 (P = 0.38); $I^2 = 6\%$

Test for overall effect: Z = 3.09 (P = 0.002)

C

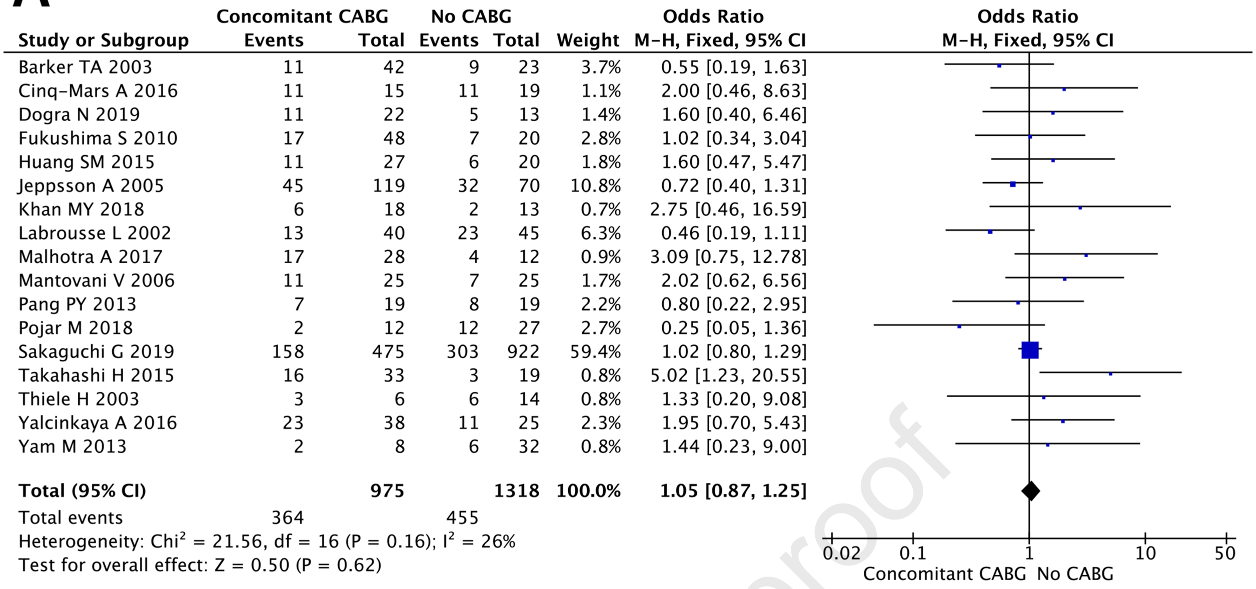


Study or Subgroup	Emergency surgery Events	Total	No emergency surgery Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Arnaoutakis GJ 2012	853	1430	382	1446	24.8%	4.12 [3.52, 4.82]
Cerin G 2003	13	18	17	40	8.0%	3.52 [1.05, 11.76]
Coskun KO 2009	5	5	9	39	1.8%	35.32 [1.78, 698.95]
Huang SM 2015	17	41	0	6	1.8%	9.29 [0.49, 175.84]
Khan MY 2018	2	4	6	31	3.2%	4.17 [0.48, 35.88]
Li H 2019	3	24	0	81	1.7%	26.53 [1.32, 533.53]
Malhotra A 2017	19	34	2	6	4.2%	2.53 [0.41, 15.75]
Mantovani V 2006	17	37	1	13	3.2%	10.20 [1.20, 86.69]
Pang PY 2013	15	32	0	6	1.8%	11.51 [0.60, 221.44]
Pojar M 2018	9	16	5	23	6.4%	4.63 [1.14, 18.75]
Sakaguchi G 2019	297	731	164	666	23.8%	2.09 [1.66, 2.64]
Takahashi H 2015	17	29	2	23	5.1%	14.88 [2.92, 75.75]
Yalcinkaya A 2016	14	20	20	43	8.7%	2.68 [0.87, 8.30]
Yam M 2013	4	17	4	23	5.5%	1.46 [0.31, 6.92]
Total (95% CI)		**2438**		**2446**	**100.0%**	**3.79 [2.52, 5.72]**
Total events	1285		612			

Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 33.80$, df = 13 (P = 0.001); $I^2 = 62\%$

Test for overall effect: Z = 6.37 (P < 0.00001)

A

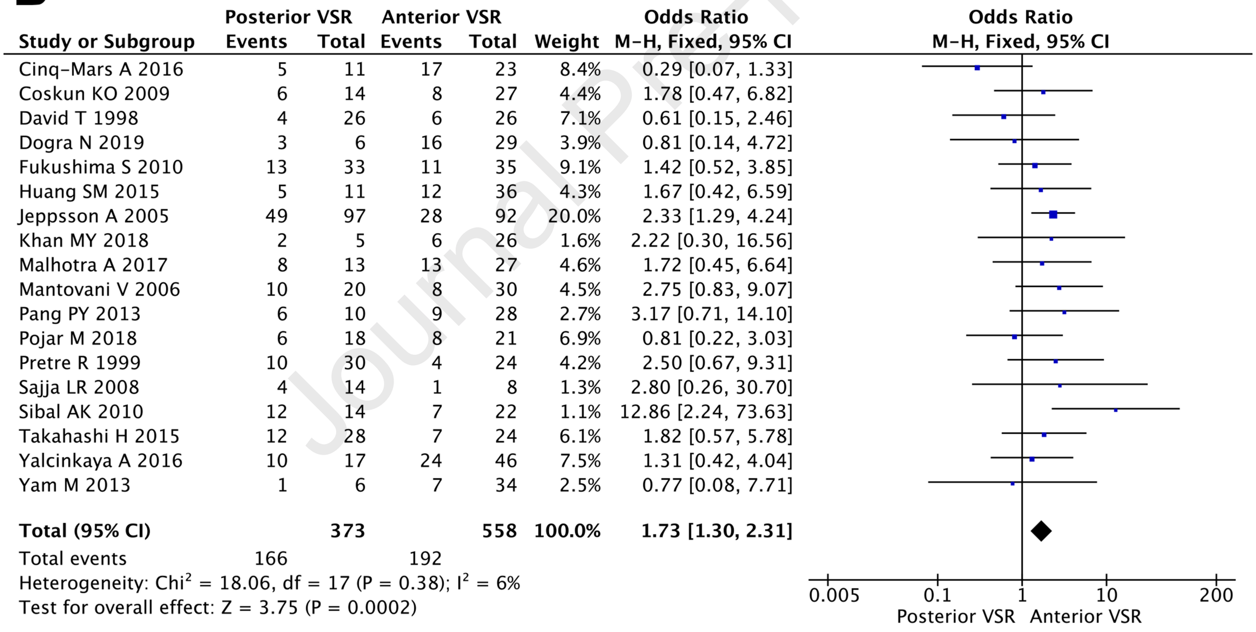


Study or Subgroup	Concomitant CABG Events	Concomitant CABG Total	No CABG Events	No CABG Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Barker TA 2003	11	42	9	23	3.7%	0.55 [0.19, 1.63]
Cinq-Mars A 2016	11	15	11	19	1.1%	2.00 [0.46, 8.63]
Dogra N 2019	11	22	5	13	1.4%	1.60 [0.40, 6.46]
Fukushima S 2010	17	48	7	20	2.8%	1.02 [0.34, 3.04]
Huang SM 2015	11	27	6	20	1.8%	1.60 [0.47, 5.47]
Jeppsson A 2005	45	119	32	70	10.8%	0.72 [0.40, 1.31]
Khan MY 2018	6	18	2	13	0.7%	2.75 [0.46, 16.59]
Labrousse L 2002	13	40	23	45	6.3%	0.46 [0.19, 1.11]
Malhotra A 2017	17	28	4	12	0.9%	3.09 [0.75, 12.78]
Mantovani V 2006	11	25	7	25	1.7%	2.02 [0.62, 6.56]
Pang PY 2013	7	19	8	19	2.2%	0.80 [0.22, 2.95]
Pojar M 2018	2	12	12	27	2.7%	0.25 [0.05, 1.36]
Sakaguchi G 2019	158	475	303	922	59.4%	1.02 [0.80, 1.29]
Takahashi H 2015	16	33	3	19	0.8%	5.02 [1.23, 20.55]
Thiele H 2003	3	6	6	14	0.8%	1.33 [0.20, 9.08]
Yalcinkaya A 2016	23	38	11	25	2.3%	1.95 [0.70, 5.43]
Yam M 2013	2	8	6	32	0.8%	1.44 [0.23, 9.00]
Total (95% CI)		**975**		**1318**	**100.0%**	**1.05 [0.87, 1.25]**
Total events	364		455			

Heterogeneity: Chi^2 = 21.56, df = 16 (P = 0.16); I^2 = 26%

Test for overall effect: Z = 0.50 (P = 0.62)

B

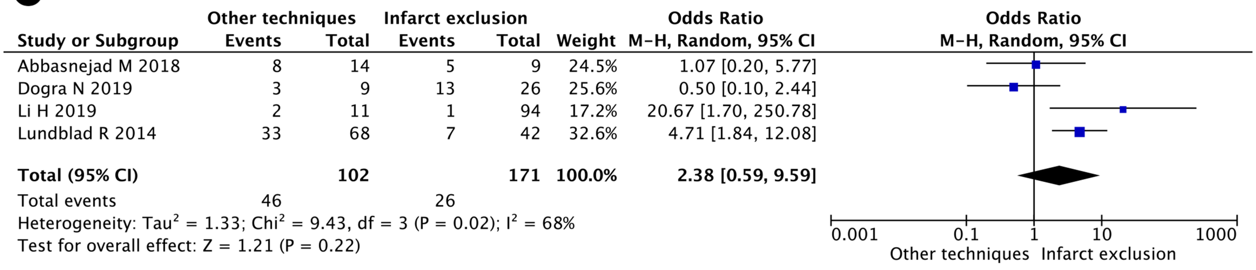


Study or Subgroup	Posterior VSR Events	Posterior VSR Total	Anterior VSR Events	Anterior VSR Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Cinq-Mars A 2016	5	11	17	23	8.4%	0.29 [0.07, 1.33]
Coskun KO 2009	6	14	8	27	4.4%	1.78 [0.47, 6.82]
David T 1998	4	26	6	26	7.1%	0.61 [0.15, 2.46]
Dogra N 2019	3	6	16	29	3.9%	0.81 [0.14, 4.72]
Fukushima S 2010	13	33	11	35	9.1%	1.42 [0.52, 3.85]
Huang SM 2015	5	11	12	36	4.3%	1.67 [0.42, 6.59]
Jeppsson A 2005	49	97	28	92	20.0%	2.33 [1.29, 4.24]
Khan MY 2018	2	5	6	26	1.6%	2.22 [0.30, 16.56]
Malhotra A 2017	8	13	13	27	4.6%	1.72 [0.45, 6.64]
Mantovani V 2006	10	20	8	30	4.5%	2.75 [0.83, 9.07]
Pang PY 2013	6	10	9	28	2.7%	3.17 [0.71, 14.10]
Pojar M 2018	6	18	8	21	6.9%	0.81 [0.22, 3.03]
Pretre R 1999	10	30	4	24	4.2%	2.50 [0.67, 9.31]
Sajja LR 2008	4	14	1	8	1.3%	2.80 [0.26, 30.70]
Sibal AK 2010	12	14	7	22	1.1%	12.86 [2.24, 73.63]
Takahashi H 2015	12	28	7	24	6.1%	1.82 [0.57, 5.78]
Yalcinkaya A 2016	10	17	24	46	7.5%	1.31 [0.42, 4.04]
Yam M 2013	1	6	7	34	2.5%	0.77 [0.08, 7.71]
Total (95% CI)		**373**		**558**	**100.0%**	**1.73 [1.30, 2.31]**
Total events	166		192			

Heterogeneity: Chi^2 = 18.06, df = 17 (P = 0.38); I^2 = 6%

Test for overall effect: Z = 3.75 (P = 0.0002)

C



Study or Subgroup	Other techniques Events	Other techniques Total	Infarct exclusion Events	Infarct exclusion Total	Weight	Odds Ratio M-H, Random, 95% CI
Abbasnejad M 2018	8	14	5	9	24.5%	1.07 [0.20, 5.77]
Dogra N 2019	3	9	13	26	25.6%	0.50 [0.10, 2.44]
Li H 2019	2	11	1	94	17.2%	20.67 [1.70, 250.78]
Lundblad R 2014	33	68	7	42	32.6%	4.71 [1.84, 12.08]
Total (95% CI)		**102**		**171**	**100.0%**	**2.38 [0.59, 9.59]**
Total events	46		26			

Heterogeneity: Tau^2 = 1.33; Chi^2 = 9.43, df = 3 (P = 0.02); I^2 = 68%

Test for overall effect: Z = 1.21 (P = 0.22)