Original Article

Optimum time and management for postmyocardial infarction ventricular septal rupture: A systematic review and meta-analysis

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ABSTRACT

Background: Ventricular septal rupture (VSR) is one of the most fatal complications following myocardial infarction with high morbidity and mortality. Usually, the incidence of VSR ranges between 1% to 3% with some studies suggested it was declined to 0.3% with PCI era.

Objective: To systemically assess the evidence regarding the optimum time and management for postmyocardial infarction ventricular septal rupture.

Patients and Methods: The Cochrane Handbook for Systematic Reviews of Interventions was followed in the preparation of this systematic review. Additionally, we followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) criteria.

Results: According to our findings, there was no significant difference in the cardiogenic shock risk ratio between patients who underwent early and late correction for ventricular septal defects after myocardial infarction.

Our findings demonstrated that there was no significant difference ($P=0.57$) in the time of VSD from MI standard mean difference between early and late correction for ventricular septal defect following myocardial infarction.

There was no significant difference in the requirement for the IABP risk ratio between patients who underwent early and late repair for ventricular septal defects following myocardial infarction.

The CPB time standard mean difference between early and late correction for ventricular septal defect, postmyocardial infarction patients significantly differ.

Conclusion: Based on these findings, it can be concluded that shorter time from MI to surgery and from admission to surgery were associated with higher mortality.

Key Words: Coronary artery bypass grafting, percutaneous coronary intervention, ventricular septal rupture.

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INTRODUCTION

One of the most fatal consequences of myocardial infarction, with a high rate of morbidity and mortality, is ventricular septal rupture (VSR)[1]. The incidence of VSR typically is in the range of 1% to 3%; however, certain studies have indicated that after percutaneous reperfusion treatment was introduced, the incidence has decreased to 0.3%[2].

The development of myocardial coagulation necrosis and the dissection of an intramural hemorrhage into the ischemic myocardial tissue are the hallmarks of VSR, which primarily manifests within the first five days following myocardial infarction[3]. Simple and complex VSR ruptures differ in that the former have a straight link between the left and right ventricles, while the latter have a convoluted path that may extend beyond the infarction site[4].

Authorities who create guidelines advise surgical correction of VSR regardless of hemodynamic stability at the time of diagnosis since it has a positive prognostic impact. However, there is continuous disagreement over the best time for surgical repair[5,6]. A growing body of evidence, however, indicates that urgent surgery should come after resuscitation efforts and cardiac care if the patient is experiencing cardiogenic shock as a result of a pulmonary to systemic blood flow ratio shunt rather than the extent of the infarct. Surgery may be done following three to four weeks of medical optimization with inotropic and mechanical cardiac support if the patient's heart rate is stable. Surgery should be performed right away if there is a clinical instability[7].

Another debate was raised in the literature was the reported high postoperative mortality rates reaching to 34–54%[8]. The reason for wide range of mortality between studies may be attributed to confounding factors other

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than VSR nature itself, for example in some studies, cases with emergency surgery usually were hemodynamically unstable and were on mechanical support devices compared to cases who underwent delayed surgery and were hemodynamically stable, this might bias the results of each study, Additionally other differences related to differences in population characteristics and type of technology used may be added factors for heterogeneity between the studies[9,10]. Furthermore, it is not clear if unstable critically ill patients either immediate surgery or extracorporeal membranous oxygenation support and delayed surgery is indicated. In some patients, transcatheter closure may be considered as an alternative to surgery[11].

Therefore, in this article we chose to evaluate previous evidence regarding which time is optimum to repair VSR following myocardial infarction and which management lines is better.

Aim of the work

We aim in this review to systemically assess the evidence regarding the optimum time and management for postmyocardial infarction ventricular septal rupture and if possible, we will provide clear criteria for early and delayed repair.

PATIENTS AND METHODS:

We prepared this systematic review with a careful following of the Cochrane Handbook for Systematic Reviews of Interventions. We also adhered to The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines during the design of our study.

We included studies that met the following inclusion criteria:

(1) Population: Patients with ventricular septal defect, postmyocardial infarction

(2) Intervention: surgical techniques.

(3) Comparator: To active comparator or to each other's

(4) Outcome parameters: Outcomes related to optimum time and management.

(5) Study design: clinical trials whether randomized or nonrandomized, prospective, retrospective, cohort, and case control.

We excluded animal or cadaveric studies, book chapters, studies with incomplete data, case reports, thesis, editorial letters, and papers with overlapped dataset.

Search strategy for identification of studies

An electronic search was conducted since 2003 till December 2022 using PubMed, Scopus, Web of Science, and Cochrane Library: We were used the following keywords; Ventricular septal rupture, Acute myocardial infarction, Optimal Time Repair. We used 'OR' and 'AND' operators during literature search.

Methods of the review

Eligibility screening was conducted in a two step-wise manner (title/abstract screening and full-text screening). Each step was done by two reviewers (MN and MG) independently according to the predetermined criteria. There was no restriction on race, sex, year or age. The duplicated articles were removed primarily using Endnote X8 program (Thompson Reuter, USA) and manually using titles and abstracts screening.

Disagreements at any stage were resolved by consulting senior reviewer AA. Additionally, references/bibliography of the retrieved articles were examined to evaluate any potential further research that could be included in the current study.

Data extraction

We extracted the following data from each of the included study: (1) study characteristics; (2) participants' baseline characteristics; (3) risk of bias domains; and (4) endpoint outcomes.

Study outcomes

Primary outcomes: parameters related to the optimum timing of repair, mortality, residual shunt.

Secondary outcomes: Operative time, blood loss, surgery related complication, pain outcomes, in-hospital morbidity (AKI, chest infection, pulmonary embolism, stroke).

Statistical analysis

In cases where data for specific outcomes were consistently recorded across trials, they were combined into a quantitative synthesis. Mean difference (MD) and 95% confidence interval were used to pool continuous data, and odds ratio (OR) and 95% confidence interval were used to pool dichotomous outcomes. The pooling of studies was done using Review Manager (RevMan, Cochrane Collaboration) version 5.3. The I square value and associated *P value* were utilized to measure the level of heterogeneity. We employed arbitrary

The data was analyzed using Cochrane Collaboration's review Manager Version 5.4 software. The measurement data were described using the standard mean difference (SMD) and 95% CI, and the count data were described using the risk ratio (RR) coefficient and 95% confidence interval (CI).

I2 statistics and the chi-square test were used to evaluate heterogeneity. $P>0.1$ in the chi-square test implies the absence of heterogeneity. For a more thorough assessment of heterogeneity, the I2 statistics were run when $P<0.1$ (I2≥25%, low heterogeneity; I2≥50%, moderate heterogeneity; I2>75%, considerable heterogeneity). When there was little to no heterogeneity in the data, a fixed-effects model made sense; if not, a random effect model was employed.

Plots of funnels were employed to evaluate publication bias. A symmetrical funnel plot indicates the absence of publishing bias. If not, publication bias needs to be taken into account. Effect model when the value of I square exceeds 50%.

Publication bias

We assessed publication bias using Egger test and funnel plot methods[12,13].

RESULTS:

We searched electronic databases from 2003 to 2023. Studies reporting patients undergoing surgical treatment for VSR were analyzed.

First we searched the publications using PubMed, Scopus, Web of Science, and Cochrane Library. The primary research included 1237 papers. Of them 399 were excluded after examining the titles and the abstracts during screening. After monitoring the exclusion criteria, 7 articles met the study criteria and were included in the current meta-analysis (Fig. 1).

General characteristics of the included studied

The current meta-analysis included 7 studies, of them, 6 were retrospective and 1 study was a systematic review. The 7 studies included 3196 ventricular septal defect, postmyocardial infarction patients; 1805 males (56.5%) and 1391 females (43.5%). The mean age ranged from 65.08 to 74.4 years. The general and preoperative characteristics of the included studies are shown in (Table 1).

Quality assessment

For the retrospective studies quality assessment, the Newcastle-Ottawa Scale (NOS) was applied, and the assessment is shown in (Table 2).

Meta-analysis

Mortality rate

Six publications in all published the death rate. Because of the heterogeneity between the studies (I2=69%), the random effect model was used to conduct the meta-analysis. The findings demonstrated a significant difference ($P=0.01$) in the death rate risk ratio between patients who received early and late correction for ventricular septal defects following myocardial infarction (RR=2.53, 95% CI: 1.25–5.11; Fig. 2).

The comparison of the mortality rate indicator's funnel plot analysis reveals that the general symmetry was still there (Fig. 3). Egger's test results indicated that none of the included publications had publication bias ($P>0.05$).

Significant residual shunt

Just two reports described notable residual shunt. The random effect model was used to conduct the meta-analysis because of the high level of heterogeneity (I2=68%). The findings demonstrated that there was no significant difference in the significant residual shunt standard between individuals who underwent early and late repair for ventricular septal defects following myocardial infarction ($P=0.46$) (RR=1.53, 95% CI: 0.50–4.69; Fig. 4).

Overall symmetry was still present, according to the funnel plot analysis comparing the significant residual shunt standard between early and late repair (Fig. 5). Egger's test results indicated that none of the included publications had publication bias ($P>0.05$).

Cardiogenic shock

Only four publications discussed the cardiogenic shock. The random effect model was used to conduct the meta-analysis because of the high level of heterogeneity (I2=98%) across the studies. The findings demonstrated that there was no significant difference ($P=0.17$) in the cardiogenic shock risk ratio between individuals who had early and late correction for ventricular septal defects following myocardial infarction (RR=2.57, 95% CI: 0.67–9.8; Fig. 6).

The general symmetry was still intact, according to the funnel plot analysis of the comparison of the cardiogenic shock indication (Fig. 7). Egger's test results indicated that none of the included publications had publication bias ($P>0.05$).

Timing of VSD from MI in days

Two publications detailed the VSD timing from MI. The random effect model was used to conduct the meta-analysis because of the high level of heterogeneity (I2=97%) among the studies. The findings demonstrated that there was no significant difference (*P=0.57*) in the time of VSD from MI standard mean difference between early and late correction for ventricular septal defect in postmyocardial infarction patients (SMD=-0.29, 95% CI: -1.31 to -0.72; Fig. 8).

The general symmetry was still preserved, according to the funnel plot analysis of the comparison of the time of VSD from MI (Fig. 9). Egger's test results indicated that none of the included publications had publication bias (*P>0.05*).

Need for intraaortic balloon pump (IABP)

IABP was required, according to two reports. The random effect model was used to conduct the meta-analysis because of the high level of heterogeneity (I2=93%) across the studies. The findings indicated that there was no significant difference in the requirement for IABP risk ratio between individuals who underwent early and late repair for ventricular septal defects following myocardial infarction (*P=0.75*) (RR =0.88, 95% CI: 0.42–1.85; Fig. 10).

The general symmetry was still intact, according to the funnel plot analysis of the comparison of the requirement for the IABP indication (Fig. 11). Egger's test results indicated that none of the included publications had publication bias (*P>0.05*).

CPB time (minutes)

Three articles provided CPB time. The fixed effect model was used to conduct the meta-analysis because there was no heterogeneity across the studies (I2=0%). The findings demonstrated a significant (*P<0.00001*) difference in the CPB time standard mean difference between patients who had early and late correction for ventricular septal defect following myocardial infarction (SMD=0.52, 95% CI: 0.41–0.62; Fig. 12).

The comparison of the CPB time indication using a funnel plot analysis reveals that the general symmetry was still preserved (Fig. 13). Egger's test results indicated that none of the included publications had publication bias (*P>0.05*).

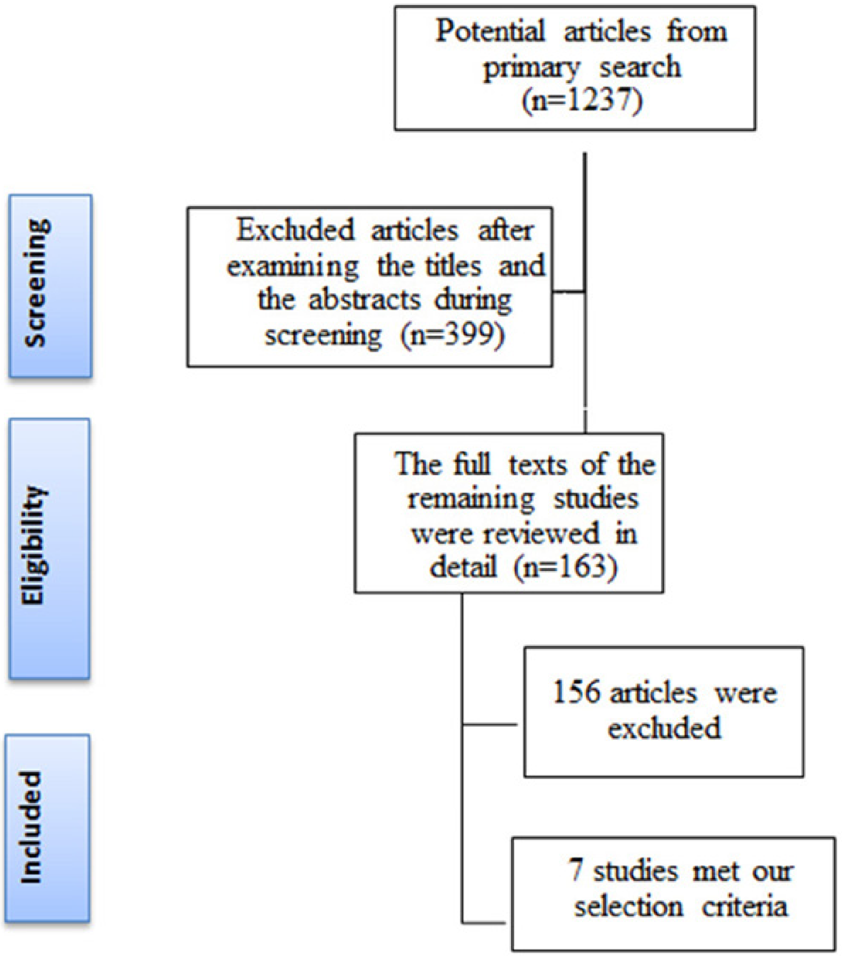

Fig. 1: Flow diagram of the literature search and study selection processes.

Table 1: General characteristics of the included studies

Study	Design	Total patients	Age (years)	M/F	Cardiogenic shock, n	Time to acute myocardial infarction-VSR, d	Time to VSR repair, d	Multivessel coronary artery disease, n	Preoperative left ventricular ejection fraction (%)	Preoperative or perioperative intraaortic balloon pump, n	Preoperative or perioperative extracorporeal life support, n
Mantovani *et al.*[14] (2006)	Retrospective	50 **Early surgery**: 37 (74%) **Late surgery**: 13 (26%)	66	26/24	N/R	N/R	N/R	25	N/R	N/R	N/R
Heckle *et al.*[15] (2020)	A systemic review	126 **≤14 days** (58) **>14 days** (68)	69.8 (8.9)	73/53	64 (50.8%)	3.5 (3.1)	92.5 (308.2)	N/R	0.48 (0.35—0.60)	N/R	N/R
Trivedi *et al.*[16] (2015)	Retrospective	20 **Early closure** (*n*=15) **Late closure** (*n*=10)	67 (range, 52—85)	11/9	12 (60%)	N/R	N/R	The right coronary artery (*n*=11, 55%), left anterior descending artery (*n*=8, 40%) circumflex artery (*n*=1, 5%).	N/R	20 (100%)	N/R
Furui *et al.*[17] (2022)	Retrospective	38 **Early group** *n*=18 **Delay group** *n*=20	74.4±9.0	19/19	Early group: 18 (100) Delay group: 15 (75)	4.6±1.1	N/R	N/R	N/R	33 (84)	IABP 33 (84) ECMO 3 (7.9) Respirator 16 (42)
Fouly & Mousa[18] (2023)	Retrospective	28 **Early repair group** (*n*=12) **Late repair group** (*n*=16)	Early repair: 65.08±5.71 Late repair: 66.25±5.74	23/5	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Arnaoutakis *et al.*[19] (2012)	Retrospective	2876	68	1624/1252	1487	N/R	N/R	966	43.1	1869	84
Cerin *et al.*[20] (2003)	Retrospective	58	73	29/29	24	4	2.8	40	43	12	N/R

N/R, not reported.

Table 2: Quality assessment of retrospective studies

Study	Selection	Comparability	Outcome	Score
Mantovani *et al.*[14]	****	*	***	8
Trivedi *et al.*[16]	****	*	**	7
Furui *et al.*[17]	****	*	**	7
Fouly & Mousa[18]	****	*	***	8
Arnaoutakis *et al.*[19]	****	*	***	8
Cerin *et al.*[20]	****	*	**	7

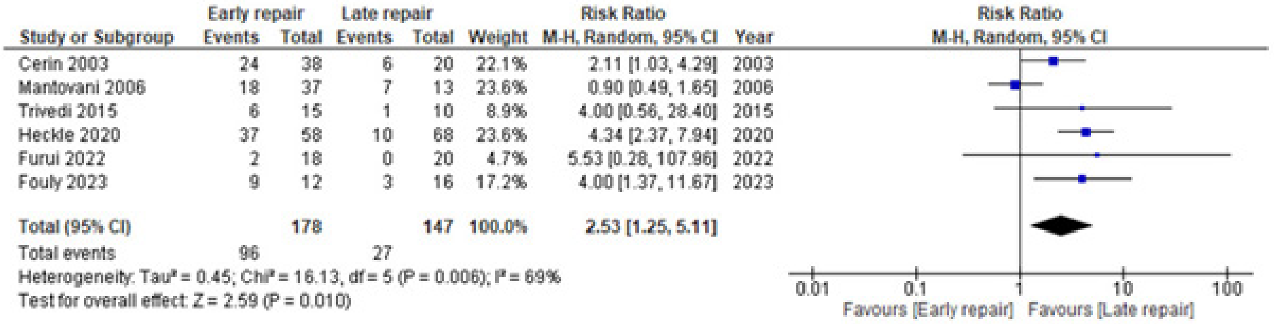

Fig. 2: The forest plot of the comparison of mortality rate between early and late repair for ventricular septal defect, postmyocardial infarction patients. CI, confidence interval.

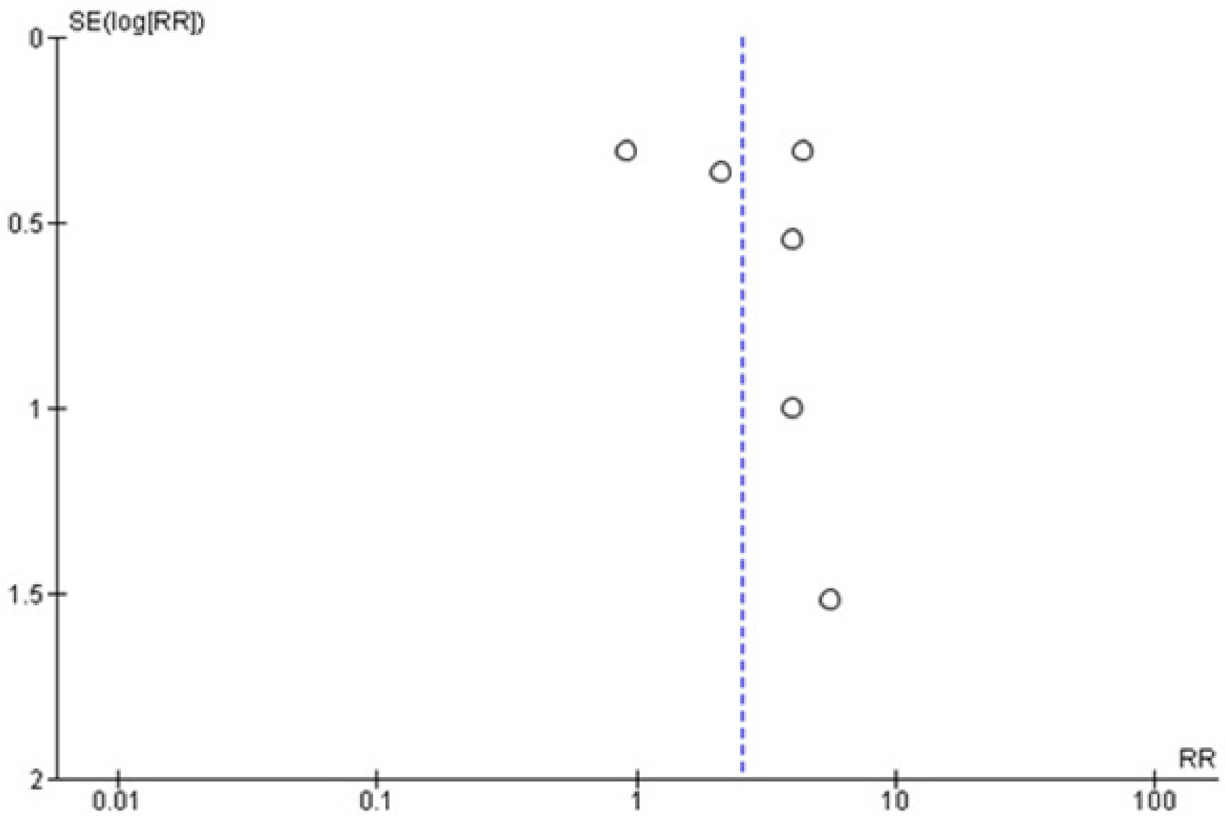

Fig. 3: Funnel plot (mortality rate).

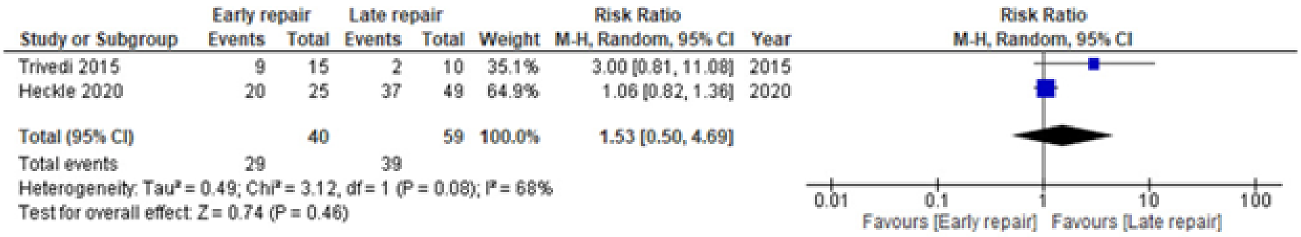

Fig. 4: The forest plot of the comparison of the significant residual shunt between early and late repair for ventricular septal defect, postmyocardial infarction patients. CI, confidence interval.

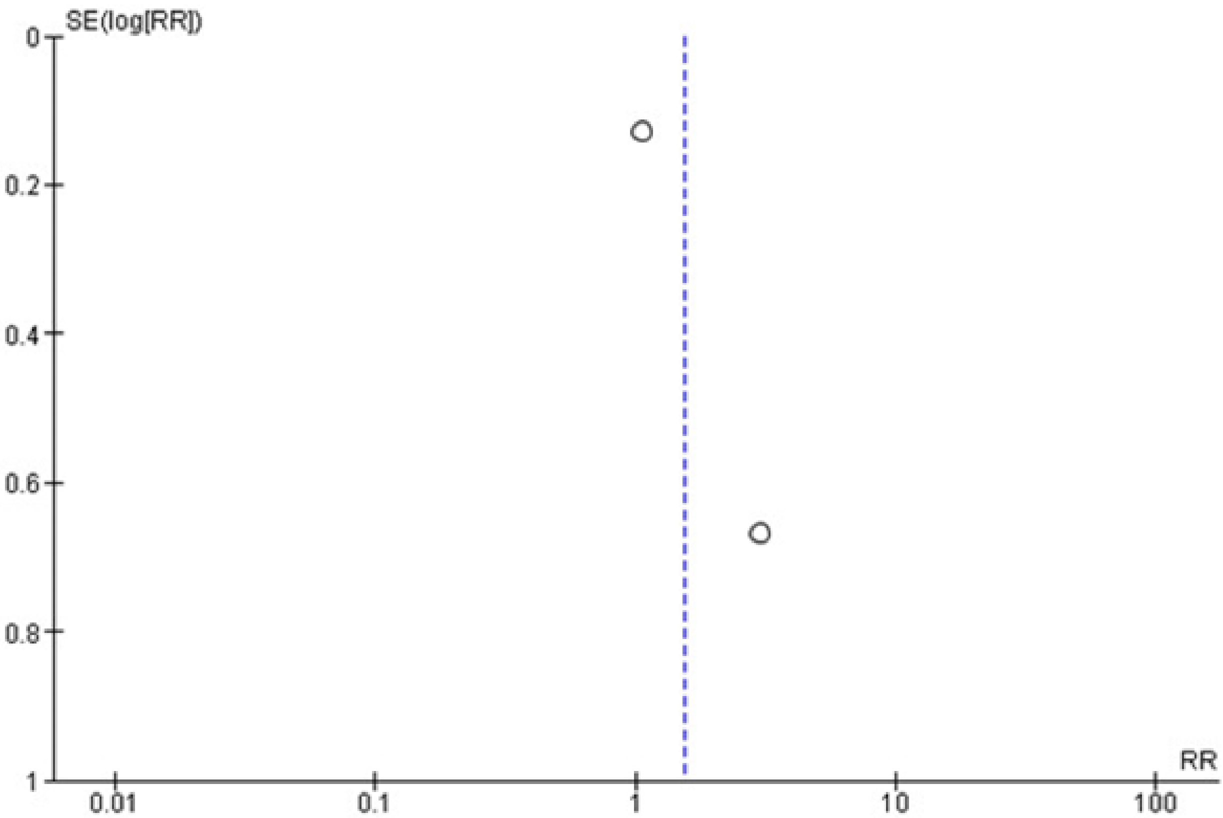

Fig. 5: Funnel plot (significant residual shunt).

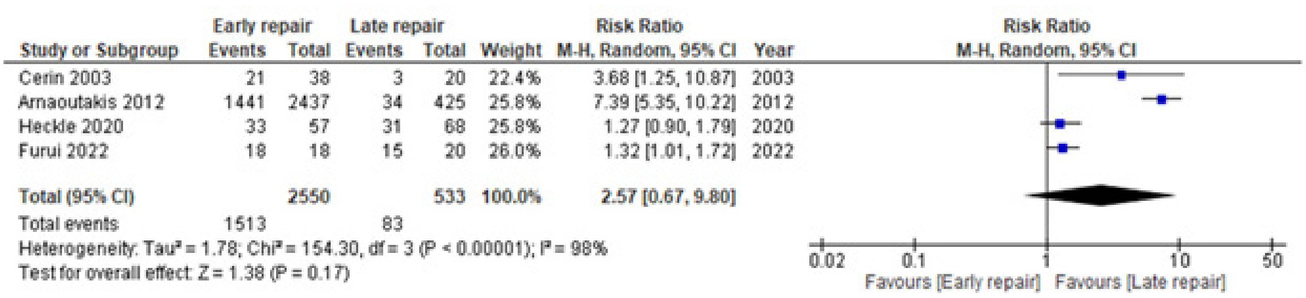

Fig. 6: The forest plot of the comparison of the cardiogenic shock between early and late repair for ventricular septal defect, postmyocardial infarction patients. CI, confidence interval.

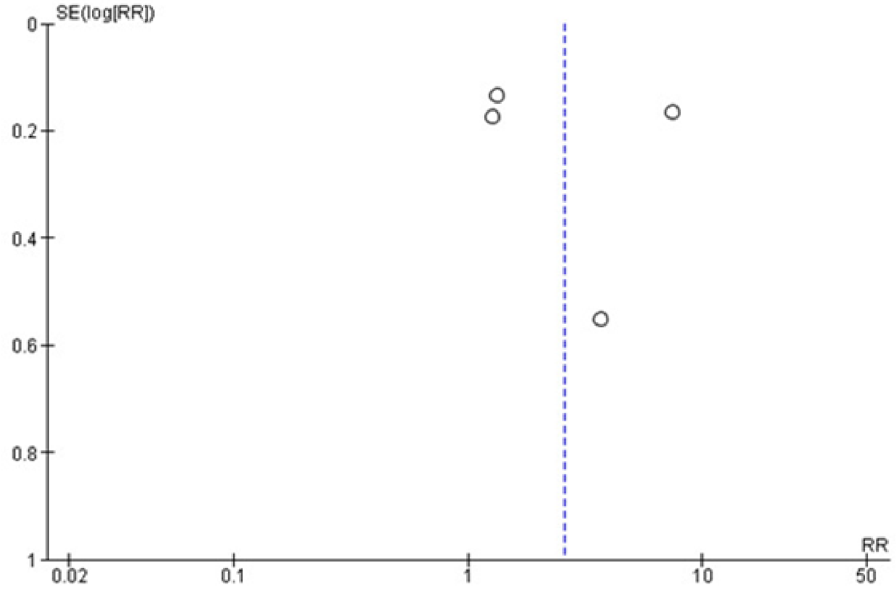

Fig. 7: Funnel plot (cardiogenic shock).

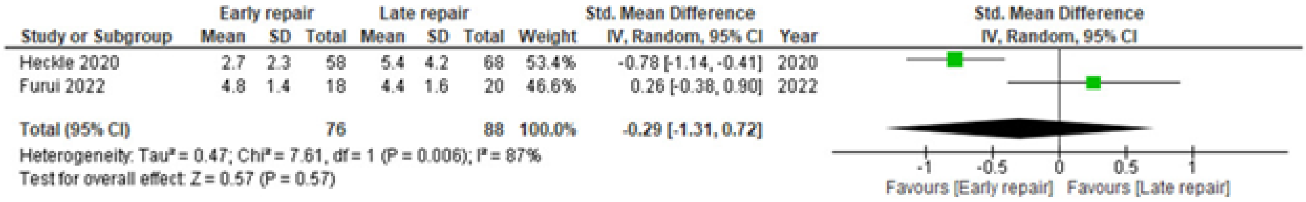

Fig. 8: The forest plot of the comparison of timing of VSD from MI between early and late repair for ventricular septal defect, postmyocardial infarction patients. CI, confidence interval; SD, standard deviation; SMD, standard mean difference.

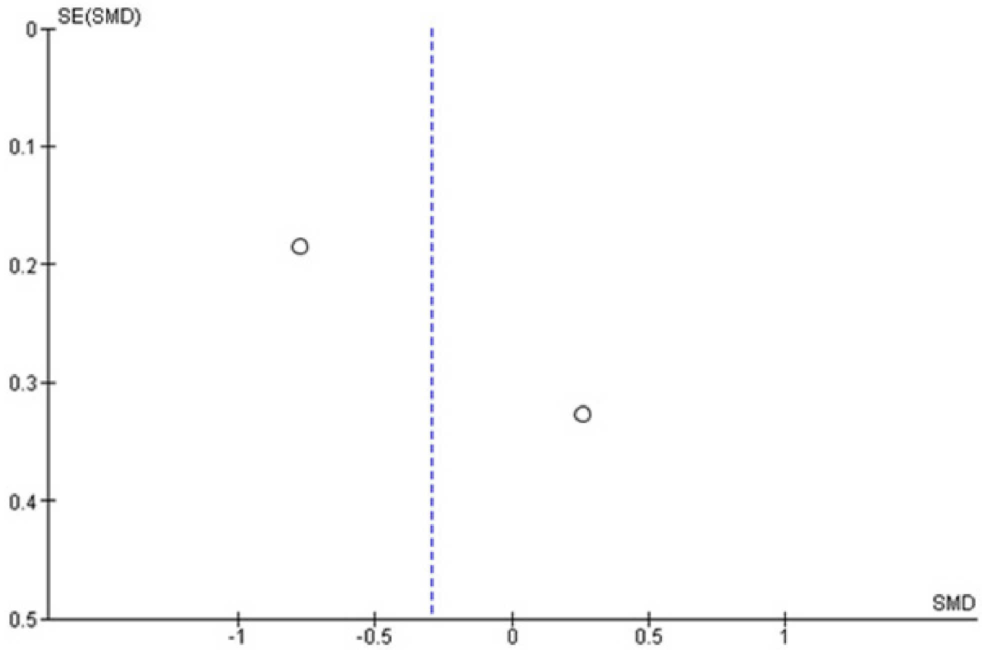

Fig. 9: Funnel plot (timing of VSD from MI).

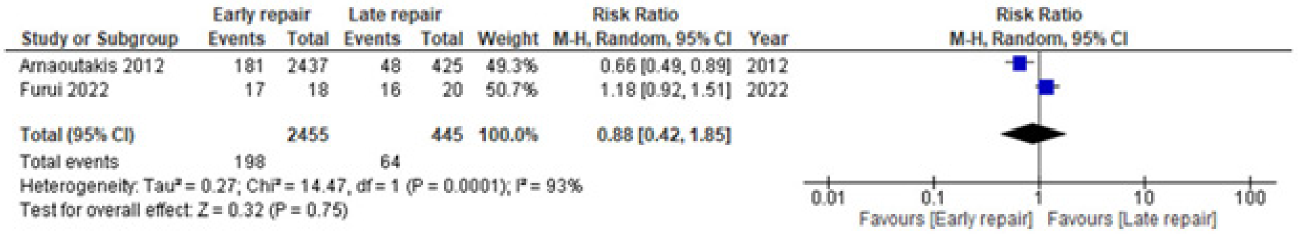

Fig. 10: The forest plot of the comparison of the need for IABP between early and late repair for ventricular septal defect, postmyocardial infarction patients. CI, confidence interval; RR: risk ratio.

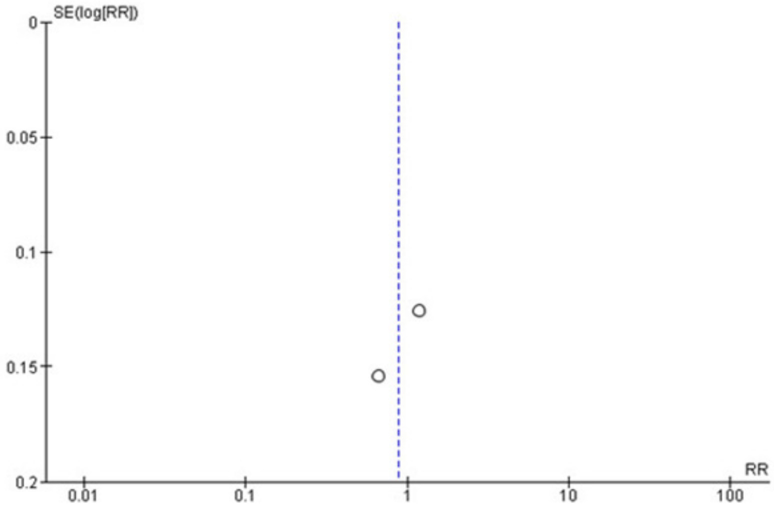

Fig. 11: Funnel plot (the need for IABP).

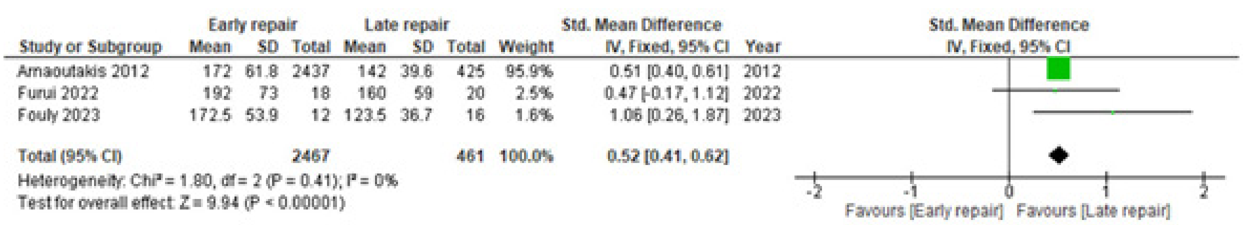

Fig. 12: The forest plot of the comparison of CPB time between early and late repair for ventricular septal defect, postmyocardial infarction patients. CI, confidence interval; SD, standard deviation; SMD, standard mean difference.

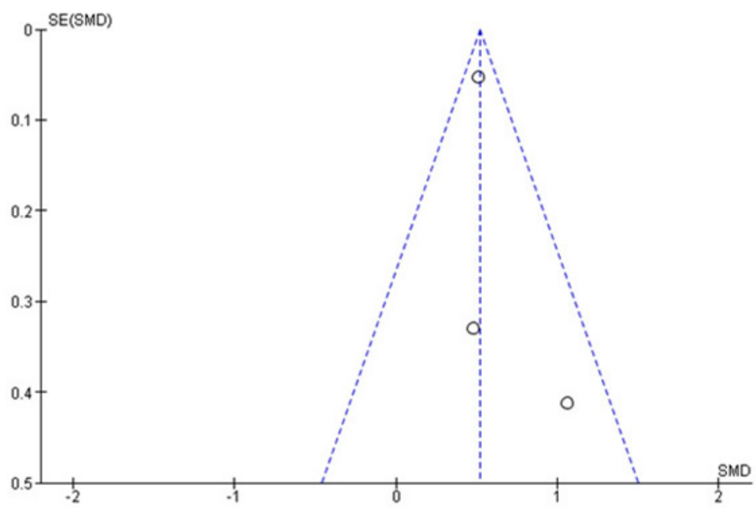

Fig. 13: Funnel plot (CPB time).

DISCUSSION

After an acute myocardial infarction (AMI), ventricular septal rupture (VSR) is an uncommon but very severe disease. The incidence of VSR has dropped to less than 1% since the percutaneous reperfusion era began. Nevertheless, there has been no discernible improvement in mortality, which is still quite high and ranges from 38% to 88% in the first 30 days[21].

Moreover, current research has not revealed any appreciable shifts in these death rates. Furthermore, the current COVID-19 epidemic has caused delays in medical care, which has raised the risk of mechanical problems following myocardial infarction, which have significant death rates[22].

The most common outcome of ventricular septal rupture is a rapid onset of cardiogenic shock and multiorgan failure, which makes it challenging to compare various treatment approaches and prevents the availability of randomized trial data. The best use of mechanical circulatory support (MCS) for patients with ventilator-associated respiratory distress (VSR) and its timing, as well as how to handle problems, remain controversial despite recent increases in its usage[23].

Furthermore, even though VSR closure is thought to be the only viable treatment for most patients, there are still significant information gaps in this challenging situation regarding the best time to do surgery and the best bridging therapy between diagnosis and intervention[24].

In a recent publication, our group indicated a trend toward lower mortality in recent years, but we did not specify which characteristics were associated with improved survival[25].

A retrospective study by Arnaoutakis *et al*.[19] of 2876 patients from the STS database (mean age 68 years, 56.5% men) aimed to characterize post-MI VSD repair patients and identify risk factors for operative death. 65.0% were supported preoperatively with an IABP and 63.9% underwent concomitant CABG. Operative mortality was 54.1% if repair was within 7 days of MI and 18.4% if more than 7 days after MI. Multivariable analysis identified several factors associated with increased odds of operative death, including urgent/emergent surgical status, preoperative IABP support, and concomitant CABG. Overall, this study found extremely high operative mortality for post-MI VSD repair, particularly when performed soon after MI and with other complicating factors.

A retrospective study by Cerin *et al*.[20] of 58 postinfarction VSD patients (mean age 73 years) aimed to evaluate clinical outcomes and risk factors for mortality after surgical repair. The overall operative mortality rate was 52%, with higher mortality (75%) for surgery within 1 week of MI versus 16% for surgery >3 weeks after MI. Shorter time from MI to surgery and from admission to surgery were associated with higher mortality. Other preoperative risk factors were cardiogenic shock, pulmonary hypertension, and larger VSD diameter. Concomitant procedures like LV reconstruction (in 13 patients) and CABG (in 81%) appeared safe.

Fouly and Mousa[18] compared early (n=12) versus late (n=16) VSR repair in 28 patients. They reported that, there were no differences in baseline characteristics between groups. Anteroapical VSR was most common. Ischemic and cardiopulmonary bypass times were shorter with delayed repair. Operative mortality was 75% for early repair versus 18.75% for late repair ($P=0.006$). Among survivors, there were no differences in blood loss, stroke, infection rates, ICU/ward stay between groups.

A retrospective study by Furui *et al*.[17] of 38 post-AMI VSR patients undergoing surgery examined outcomes of a delayed (n=18) versus early (n=20) surgical repair strategy. Delayed repair was associated with higher preoperative infection rates but lower reoperation rates, operative mortality ($P=0.04$), 30-day and hospital mortality compared to early repair. Although VSR severity (defect diameter, Qp/Qs) worsened in both groups during waiting periods, the rate of increase was greater for the early group ($P=0.05$). Despite risks of waiting, including defect enlargement and hemodynamic compromise, the benefits of lower mortality with delayed repair appeared to outweigh these risks.

Heckle *et al*.[15] compared early (within 14 days) versus late (after 14 days) transcatheter repair for post-MI VSD in 126 patients from published case reports and series. Overall 30-day survival was 62.7%, but was significantly lower with early (36.2%) versus late (85.3%) repair ($P<0.01$). No differences were seen in age, gender, shock, VSD/infarct characteristics between groups, though early repair patients had higher Qp:Qs ratios, larger occluder sizes, and lower success rates.

Mantovani *et al*.[14] examined outcomes of surgical postinfarction VSD repair in 50 patients over a 20-year period. Mean age was 66 years, 60% had anterior and 40% posterior infarcts. Median time from rupture to surgery was 2 days. Preoperative IABP was used in 56% and angiogram in 98%. Patch repair was performed in 90% and CABG in 50%. Operative mortality was 36% overall, 26.7% for anterior and 50% for posterior infarcts ($P=ns$). Emergency surgery and rupture-to-surgery interval <3 days predicted early mortality. 5-year survival was 76% for hospital survivors.

A multicenter study by Trivedi *et al*.[16] of 20 patients (mean age 67 years) evaluated a combined surgical and transcatheter strategy for post-MI VSD closure. Median time from MI to VSD was 6 days, 60% had cardiogenic shock. Median defect size was 18 mm. Total of 27 closure procedures were performed (14 surgical, 6 percutaneous). Percutaneous patients were older with higher EuroSCOREs than surgical patients but had no procedural complications. Residual shunt and mortality rates were similar between surgical and percutaneous groups. Early closure (<21 days) was associated with higher rates of residual shunt and mortality, regardless of procedure type, though this mortality association was significant only for early percutaneous closure. Overall hospital mortality was 30% compared to mean predicted EuroSCORE mortality of 75%.

Our study included 3196 ventricular septal defect, postmyocardial infarction patients; 1805 males (56.5%) and 1391 females (43.5%). The mean age ranged from 65.08 to 74.4 years.

Our results showed that the mortality rate risk ratio among early and late repair for ventricular septal defect, postmyocardial infarction patients significantly differ (*P=0.01*)) (RR=2.53, 95% CI: 1.25–5.11).

The results showed that the significant residual shunt standard among early and late repair for ventricular septal defect, postmyocardial infarction patients did not significantly differ (*P=0.46*) (RR=1.53, 95% CI: 0.50–4.69).

Our results showed that cardiogenic shock risk ratio among early and late repair for ventricular septal defect, postmyocardial infarction patients did not significantly differ (*P=0.17*) (RR=2.57, 95% CI: 0.67–9.8).

Our results showed that timing of VSD from MI standard mean difference among early and late repair for ventricular septal defect, postmyocardial infarction patients didn't significantly differ (*P=0.57*) (SMD =-0.29, 95% CI: -1.31 to -0.72).

Our results showed that the need for IABP risk ratio among early and late repair for ventricular septal defect, postmyocardial infarction patients did not significantly differ (*P=0.75*) (RR=0.88, 95% CI: 0.42–1.85).

Our results showed that CPB time standard mean difference among early and late repair for ventricular septal defect, postmyocardial infarction patients significantly differ (*P<0.00001*) (SMD =0.52, 95% CI: 0.41–0.62).

CONCLUSION

Based on these findings, it can be concluded that shorter time from MI to surgery and from admission to surgery were associated with higher mortality, while other outcomes such as residual shunt, cardiogenic shock, timing of VSD from MI, and the need for IABP are not significantly influenced by the timing of repair. However, it is important to consider individual patient characteristics and clinical factors when determining the optimal timing for VSD repair postmyocardial infarction.

CONFLICT OF INTEREST

No conflict of interest.

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