Systematic Review

Effects of concomitant coronary artery bypass grafting on early and late mortality in the treatment of post-infarction mechanical complications: a systematic review and meta-analysis

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Background: Mechanical complications of acute myocardial infarction represent life-threatening events, including ventricular septal rupture (VSR), left ventricular free-wall rupture (LVFWR) and papillary muscle rupture (PMR). In-hospital mortality is high, even when prompt surgery can be offered. The role of concomitant coronary artery bypass grafting (CABG) in the surgical treatment of these conditions is still debated.

Methods: A systematic review of the literature, from 2000 onwards, about these complications was performed, analyzing data of subjects receiving versus not-receiving concomitant CABG. Primary outcome was early mortality. Secondary outcome was late mortality for hospital survivors. Subgroup analysis for VSR, LVFWR and PMR was also performed.

Results: Thirty-six studies were identified, including 4,321 patients (mostly VSR-related). Preoperative coronarography was performed in 92.2% of the cases, showing single-vessel disease in 54.3% of patients. Concomitant CABG rate was 49.0%. Early mortality was 32.6% and late mortality was 40.0% with 5.2 years of mean follow-up. The analysis showed no difference in early (OR 0.96; P=0.60) or late mortality (RR 0.91; P=0.49) between CABG and non-CABG group. In subgroup analysis, concomitant CABG was associated with significantly lower mortality at long term for PMR (RR 0.42; P=0.001), although it showed a higher, but not significant, mortality in VSR (RR 1.24; P=0.20).

Conclusions: Concomitant CABG in the treatment for post-infarction mechanical complications showed no significant impact on both early and late mortality, although deserving some distinctions among different types of complication and single versus multiple vessel disease. However, larger, dedicated studies are required to provide more consistent data and evidence.

Keywords: Acute myocardial infarction (AMI); mechanical complications; heart rupture; ventricular septal rupture (VSR); papillary muscle rupture (PMR)

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Introduction

Mechanical complications following acute myocardial infarction (AMI) represent rare, but life-threatening events, typically occurring after ST-segment elevation myocardial infarction (STEMI) (1,2). Over the last decades, the wide diffusion of thrombolysis and percutaneous coronary intervention (PCI) for the early treatment of AMI has significantly led to improved survival for coronary artery disease (CAD) and decreased the incidence of such complications (3-5). Nevertheless, they still bear a high in-hospital mortality, even when prompt surgery can be offered (6). Among post-AMI mechanical complications, we recognize ventricular septal rupture (VSR), left-ventricular free-wall rupture (LVFWR) and papillary muscle rupture (PMR) causing acute mitral regurgitation. Being them all early complications of AMI, the proper timing for surgery and the appropriateness of treating the underlying cause through coronary artery bypass grafting (CABG) have been debated. For instance, the advantage of revascularizing necrotic myocardium during high-risk, emergency procedures, remains controversial. Most importantly, there are still conflicting data on whether concomitant CABG (cCABG) provides early and late survival benefit in these patients (7). Thus, we performed a systematic review and meta-analysis of the available literature in order to evaluate the potential survival benefit of cCABG in patients treated surgically for post-AMI mechanical complications.

Methods

Definitions

'Infarct exclusion' was defined as the VSR repair technique described by David *et al.* or any further modification (8). 'Other techniques' were defined as any other technique to repair VSR different from the David's one, including infarct excision (9).

'Sutureless technique' was defined as LVFWR repair using collagen sponge, or pericardial patch fixed on the epicardium with glues. 'Sutured technique' was defined as LVFWR repair applying sutures to close the myocardial tear or to secure a patch on the epicardium (10).

Early mortality was defined as any death occurred during hospitalization, or within 30 days from surgery. For conflicting data between in-hospital and 30-day mortality, the latter was considered for the survival analysis. Late mortality was defined as any cause-related death after hospital discharge or beyond 30 days from surgery. Reintervention was defined as the need for a further procedure due to failure of repair or rupture recurrence; reoperations for other causes (e.g., bleeding) were not considered.

Literature search strategy

This systematic review and meta-analysis were performed in accordance to the Preferred Recording Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (11). A search of the literature on PubMed, EMBASE and the Cochrane Central Register of Controlled Trials was conducted by three independent researchers, to identify eligible studies published between January 2000 and December 2020, using Medical Subject Headings (MeSH) and free-text terms. The keywords were ('ventricular free-wall rupture' OR 'papillary muscle rupture' OR 'acute mitral regurgitation' OR 'cardiac rupture' OR 'ventricular septal rupture' OR 'ventricular septal defect') AND 'myocardial infarction'. Only publications in English were considered. References of original articles were reviewed manually and cross-checked for other relevant reports that escaped the databases searches.

Eligibility criteria and data extraction

Studies reporting post-operative outcomes of patient receiving repair of LVFWR, VSR or PMR that compared the outcomes of cCABG to the patients who did not undergo concomitant revascularization were included. Exclusion criteria were: (I) animal studies; (II) congenital heart surgery-related studies; (III) studies reporting transcatheter/conservative strategies; (IV) studies not discriminating among mechanical complication types; (V) studies in which outcomes for CABG and non-CABG subgroups were not retrievable. Reviews, case reports or case series reporting <10 cases were not considered. Two independent reviewers (D Ronco and M Matteucci) analyzed the results for eligibility, and extracted studies, as well as relevant patients' characteristics and outcomes, using an appropriate data collection form. Any divergences were resolved by a third reviewer (C Corazzari). For publications analyzing the same population, the most complete study, according to the variables of interest, was selected.

Pre-operative demographics and assessment were recorded, along with the type of rupture for each complication, namely: oozing or blow-out for LVFWR, anterior/apical or posterior for VSR and anterolateral or posteromedial for PMR. Similarly, intra-operative data and surgical techniques were collected. Main post-operative variables included early and long-term mortality, and major complications (e.g., re-rupture requiring reintervention). Data about salvage/emergent/urgent surgery were not collected because of the high variability in definitions among studies.

Quality assessment and endpoint selection

Two independent reviewers (D Ronco and M Matteucci) assessed the risk of bias at individual study level using the ROBINS-I tool (Risk Of Bias In Not-randomized Studies of Interventions) (12). Any divergences were resolved by a third reviewer (R Lorusso).

The primary endpoint of this meta-analysis was early mortality in the CABG and non-CABG groups. The secondary endpoint was late mortality from any cause. Whenever possible, a 5-year follow-up was considered for each enclosed report, otherwise, the longest available follow-up was selected (at least 1 year).

Statistical analysis

When not available from full-text or supplements, late mortality data were extracted from Kaplan-Meier curves using a dedicated software (Plot Digitizer 2.6.8 for Windows). Review Manager 5.3 software, by the Cochrane Collaboration, was used for statistical computations. Calculation of an overall proportion from studies reporting a single proportion was performed using a meta-analytic approach by means of metaprop function of meta package in R. A logit-transformation was performed as suggested by Warton & Hui; to calculate confidence intervals (CIs) for individual study results, Clopper-Pearson approach was used; inverse variance method was used for data pooling. Subgroup analysis was performed using random effect. DerSimonian-Laird estimator was used to estimate the between-study variance. Total proportion with 95% CI was reported. Heterogeneity was reported as I^2. Random-effect model was used to assess difference between early and late death rate among the three different complications. For CABG and non-CABG groups, pooled odds ratios (OR) were reported with 95% CI and a two-tailed $P<0.05$ was considered statistically significant. Results showing low ($I^2<50\%$) to moderate (I^2 50–75%) heterogeneity were analyzed by the fixed-effect model, while those with high heterogeneity ($I^2>75\%$) were analyzed by the random-effect model. Sensitivity analysis was carried out by successfully excluding low-quality studies to assess the outcome stability. Potential publication bias was evaluated by constructing a funnel plot, with asymmetry suggesting possible publication bias.

Results

The PRISMA flow diagram is presented in *Figure 1*. After removal of reports not pertinent to the design of the current meta-analysis, 36 studies remained, including 4,321 patients, with a mean age of 69.0±4.0 years and a slight male predominance (58.5%). According to the complication type, patients with VSR accounted for 57.3% of cases, followed by subjects with PMR (37.0%) and LVFWR (5.7%). Pre-operative coronarography was performed in almost all patients (92.2%), most frequently showing single-vessel CAD (54.3%, 1,868/3,440). Pre-operative data are listed in *Table 1*. Most patients presented with cardiogenic shock before surgery (58.2%). Almost two-thirds of subjects had intra-aortic balloon pump (IABP) placed pre-operatively, and 8.6% required extracorporeal membrane oxygenation (ECMO). VSR was more frequent in anterior/apical portion (60.1%, 627/1,043) and infarct exclusion technique was adopted in 40.5% (246/607) of cases. Of the patients with LVFWR, oozing-type was found in most (58.1%, 115/198) and sutured repair was more frequently performed (55.1%). In PMR group, posteromedial muscle rupture was the commonest (83.8%, 109/130); 79.5% of patients underwent mitral valve replacement (Tables S1-S3).

Operative and post-operative data are shown in *Table 2*. Concomitant CABG was performed in 49.0% of patients (43.8% in VSR, 31.7% in LVFWR and 59.7% in PMR). The pooled early mortality was 32.6% (28.5–36.9%) with I^2=79.9% (72.8–85.2%); in VSR patients it was 36.8% (32.4–41.6%), while in subjects with LVFWR it was 26.6% (18.7–36.4%) and in patients with PMR it was 24.0% (18.9–30.1%), P=0.0023 (*Figure 2*). Among individuals who survived the surgery, the commonest cause of in-hospital death was low-cardiac-output syndrome (34.7%, 151/435). Reintervention for residual or recurrent rupture was required in 8.4% of cases.

The pooled late mortality was 40.0% (33.5–46.9%) with I^2=60.9% (41.8–73.7%); in VSR patients it was 37.2% (30.5–44.9%), while in subjects with LVFWR it was 43.4% (25.5–63.3%) and in patients with PMR it was 59.9% (31.9–82.7%), P=0.2870 (*Figure 3*). Mean follow up was 5.2±2.8 years.

Primary endpoint

In the early mortality analysis, there was no difference between CABG and non-CABG groups (OR 0.96; 95% CI:0.84–1.11; P=0.60, I^2=23%; *Figure 4A*). Single complication subgroup analysis accordingly showed that cCABG didn't affect early mortality in any of the three types of mechanical complication: VSR (OR 1.00; 95%

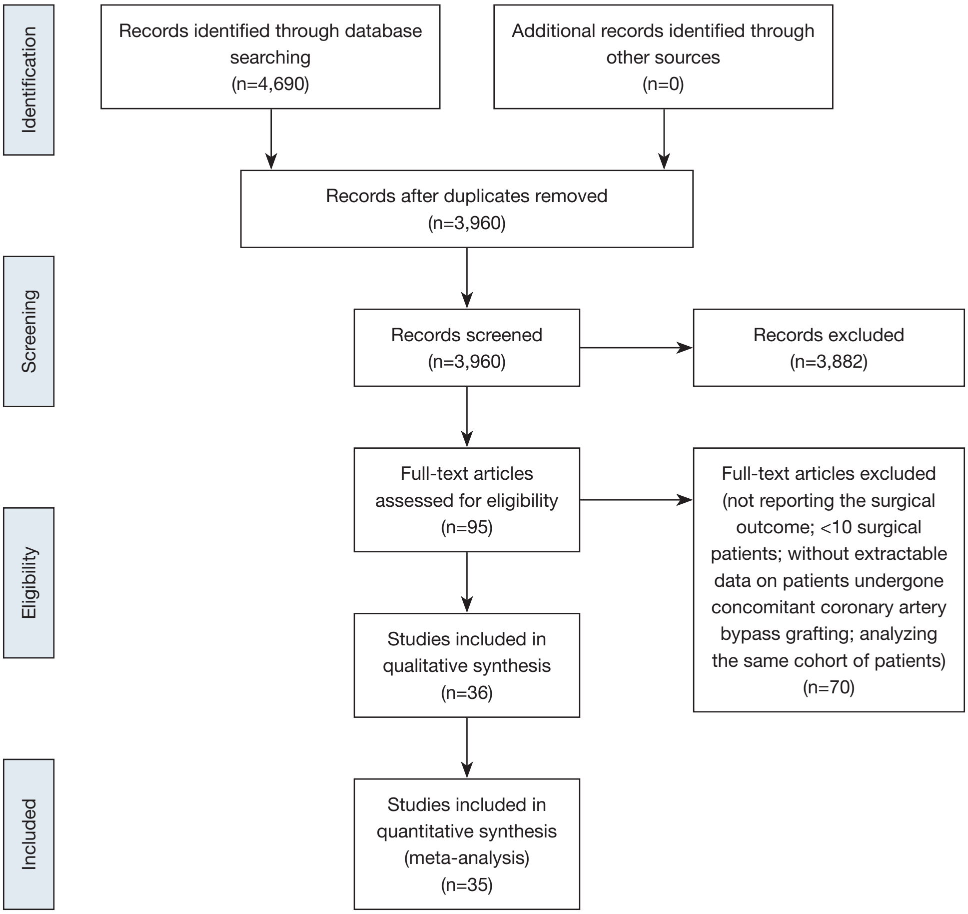

Figure 1 Prisma flow diagram.

CI: 0.84–1.19; P=0.98, I^2=26%; Figure S1A); PMR (OR 0.94; 95% CI: 0.74–1.20; P=0.62, I^2=39%; Figure S1B); and LVFWR (OR 0.73; 95% CI: 0.40–1.33; P=0.30, I^2=0%; Figure S1C).

Secondary endpoint

Long-term survival data of 12 studies could be analyzed, including 496 patients, with a follow-up ranging from 1.5 to 7.2 years. Late mortality was 31.0% in the CABG versus 32.8% in the non-CABG group, hence showing no significant difference (RR 0.91, 95% CI: 0.70–1.19, P=0.49, I^2=35%; *Figure 4B*). However, the single complication analysis showed, for VSR patients, a lower late mortality in the non-CABG group, although not statistically significant (RR 1.24; 95% CI: 0.89–1.73; P=0.20, I^2=0%). Conversely, LVFWR patients showed a slight trend toward a better, but not significant, late survival with cCABG (RR 0.65; 95% CI: 0.11–3.71; P=0.63; I^2=0%). Finally, late mortality appeared significantly lower with cCABG in PMR (RR 0.42; 95% CI: 0.25–0.70; P=0.001; I^2=0%) (Figure S2).

Discussion

The current meta-analysis showed that cCABG in the setting of surgery for post-infarction mechanical complications is not associated with a lower early or late mortality.

The value of cCABG during surgery for post-infarction mechanical complications remains a matter of debate. Despite representing a treatment for the underlying cause of cardiac rupture, the effects of surgical revascularization on early and late mortality have not been clarified yet (7,35).

VSR, LVFWR and PMR are well-known AMI complications, usually occurring within one week of the ischemic episode (1,4). Elbadawi *et al.* recently analyzed

Table 1 Included studies and patient baseline characteristics

First author (Ref.)	Year	Type of complication	Number of patients	Mean age (years)	Male (n)	Preoperative angiography (n)	Multiple CAD* (n)	Single CAD (n)	Previous PCI (n)	Previous thrombolysis (n)	Pre-op IABP (n)	Pre-op ECMO (n)	Pre-op shock (n)	Mean pre-op LVEF (%)
Abu-Omar (13)	2012	VSR	59	N/A	41	N/A	N/A	N/A	3	30	47	N/A	33	N/A
Barker (14)	2003	VSR	65	N/A	40	65	46	19	N/A	31	42	N/A	35	N/A
Bisoyi (15)	2020	VSR	21	N/A	17	21	7	14	0	0	20	0	6	N/A
Bouma (16)	2014	PMR	48	64.9	34	48	25	23	12	N/A	21	N/A	31	N/A
Cinq-Mars (17)	2016	VSR	34	69	19	34	18	16	N/A	11	28	0	24	44
Dogra (18)	2019	VSR	35	61	19	35	N/A	N/A	8	12	16	1	15	33
Formica (19)	2018	FWR	35	68.3	25	27	N/A	N/A	9	N/A	14	12	12	45.7
Fukushima (20)	2010	VSR	68	66.4	49	65	45	20	3	0	28	1	8	N/A
Furukawa (21)	2000	VSR	12	71.3	6	12	7	5	6	0	9	N/A	9	N/A
Huang (22)	2015	VSR	47	68.9	28	47	31	16	17	12	34	6	19	45.8
Iemura (23)	2001	FWR	17	65.4	14	15	N/A	N/A	7	12	N/A	N/A	11	N/A
Jeppsson (24)	2005	VSR	189	69	119	148	N/A	N/A	N/A	64	91	0	N/A	N/A
Kacer (25)	2020	FWR	19	N/A	12	N/A	N/A	N/A	N/A	N/A	1	0	3	N/A
Khan (26)	2018	VSR	31	57.1	21	31	6	25	N/A	N/A	13	0	7	38.4
Kilic (27)	2020	PMR	1,342	65.6	911	1,171	792	379	N/A	N/A	764	41	759	53.1
Kim (28)	2015	VSR	23	68	11	23	7	14	4	N/A	19	1	N/A	42.5
Labrousse (29)	2002	VSR	85	69	51	72	N/A	N/A	N/A	N/A	81	N/A	16	N/A
Lorusso (30)	2008	PMR	126	66.5	40	83	N/A	N/A	N/A	N/A	50	N/A	94	N/A
Malhotra (31)	2017	VSR	40	61.6	26	40	22	18	N/A	N/A	40	N/A	N/A	37
Mantovani (32)	2002	FWR	17	68	11	16	11	5	3	3	7	0	N/A	N/A
Mantovani (33)	2006	VSR	50	66	26	49	24	25	N/A	15	28	0	N/A	N/A
Martinelli (34)	2003	VSR	12	64.4	10	12	7	5	N/A	N/A	6	N/A	N/A	34.6
Matteucci (35)	2020	FWR	140	69.4	91	104	64	40	48	10	51	16	100	41.7
Okada (36)	2005	VSR	10	72	3	10	2	8	4	N/A	10	1	1	43.2
Okamura (37)	2019	FWR	35	71.5	21	32	6	29	19	N/A	13	4	25	N/A
Ozkara (38)	2005	VSR	20	62.1	15	17	7	10	N/A	N/A	19	N/A	4	N/A
Pang (39)	2013	VSR	38	65.7	20	36	22	14	N/A	11	37	0	26	39.7

Table 1 (*continued*)

Table 1 *(continued)*

First author (Ref.)	Year	Type of complication	Number of patients	Mean age (years)	Male (n)	Preoperative angiography (n)	Multiple CAD* (n)	Single CAD (n)	Previous PCI (n)	Previous thrombolysis (n)	Pre-op IABP (n)	Pre-op ECMO (n)	Pre-op shock (n)	Mean pre-op LVEF (%)
Pojar (40)	2018	VSR	39	68.4	19	39	18	21	8	4	17	1	N/A	47.2
Russo (6)	2008	PMR	54	70	40	53	36	17	N/A	N/A	40	N/A	49	56
Sakaguchi (41)	2019	VSR	1,397	74.1	671	1,397	303	1,094	508	N/A	1,075	224†	859	N/A
Schroeter (42)	2013	PMR	28	63.4	22	28	N/A	N/A	9	N/A	12	N/A	15	50.2
Takahashi (43)	2015	VSR	52	67	26	52	33	17	7	0	20	N/A	30	N/A
Thiele (44)	2003	VSR	20	68.5	12	20	11	9	15	N/A	20	3	9	42
Wiemers (45)	2012	VSR	10	65.3	5	8	7	1	3	6	6	N/A	1	N/A
Yalçinkaya (46)	2016	VSR	63	67.2	35	63	N/A	N/A	19	23	57	N/A	N/A	45.2
Yam (47)	2013	VSR	40	N/A	16	38	14	24	N/A	N/A	32	0	11	56
Total			4,321	69.0±4.0	2,526	3,911	1,571	1,868	712	244	2,768	311	2,212	44.2±6.6

*, including patients with left main CAD only; †, including preoperative and intraoperative ECMO. CAD, coronary artery disease; ECMO, extracorporeal membrane oxygenation; FWR, free-wall rupture; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; N/A, not-available; PCI, percutaneous coronary intervention; PMR, papillary muscle rupture; VSR, ventricular septal rupture.

the U.S. National Inpatient Sample database, showing that, from 2003 to 2015, among almost 9 million AMI patients, the incidence of VSR, LVFWR and PMR was 0.25%, 0.02% and 0.06%, respectively (1). Over the last decades, the incidence of cardiac rupture significantly decreased, mainly due to the introduction of early percutaneous revascularization, proving its beneficial effect especially in STEMI patients, who are more at risk for such ominous complications (2-5,18). This important aspect also emerged in the ongoing COVID-19 pandemics, when delayed and difficult access to appropriate treatment has led to a remarkably increased mortality for AMI, paralleled by an increased occurrence of its complications (48).

Thirty-day mortality for these patients can be as high as 90% if left untreated, and urgent surgery with prompt hemodynamic stabilization is often demanded (16,49,50). Nevertheless, surgical in-hospital mortality still ranges from 12% to 60%, depending on reports and type of complication (6,8,17,19). Considering such a high mortality, some authors argued that increasing operative risk and cardio-pulmonary bypass time to restore blood supply to infarcted myocardium wouldn't be justified by a questionable survival advantage (50,51). Our interest was to evaluate if cCABG in these patients is favored for early mortality and if the myocardial protection it provides is maintained beyond the early peri-operative phase.

This meta-analysis shows that cCABG in surgery for post-AMI mechanical complications can be performed safely without significantly increasing early and late mortality, similarly to what Horan *et al.* recently reported for VSR patients only (7). However, it should be noted that our analysis didn't consider percutaneous revascularization, that was carried out in 956 patients and is usually reported to improve survival (4,5). Indeed, Dogra *et al.* identified early thrombolysis as the most important prognostic factor in VSR, decreasing the risk of cardiac rupture (18). Differently, Bouma *et al.* reported that PCI had no effect on long-term survival in PMR patients (52). While considering the favorable contribution of early percutaneous revascularization to risk reduction of cardiac rupture, some authors described that this complication might be accelerated with thrombolysis, causing myocardial hemorrhage during the 'lytic state' of AMI (53). A reduced AMI-to-VSR time-frame in subjects who underwent thrombolysis was also observed in the GUSTO-I trial (4). In our population the mean time from AMI to rupture was 3.5±1.2 days.

When cardiac rupture occurs, it's not always possible

Table 2 Operative and post-operative data

First author (Ref.)	Mean CPB time (min)	Mean aortic cross-clamp time (min)	Concomitant CABG (n)	Post-op IABP (n)	Post-op ECMO (n)	Reintervention (n)	Early mortality (n)	Causes of death (n)*	Late mortality (n)	Mean follow-up (years)
Abu-Omar (13)	110	58	44	N/A	N/A	N/A	23	N/A	12	5
Barker (14)	N/A	N/A	42	42	0	N/A	12	N/A	16	2.4 [4]
Bisoyi (15)	N/A	N/A	17	1	0	0	5	LCOS (n=4)	0	5
Bouma (16)	178	98	24	24	0	0	12	LCOS (n=6), rupture (n=2), bleeding (n=2)	N/A	N/A
Cinq-Mars (17)	141	94	15	2	1	N/A	22	LCOS (n=18), MOF (n=2), sepsis (n=1), respiratory (n=1)	6	[12]
Dogra (18)	172	116	22	0	0	N/A	16	LCOS (n=15), unknown (n=1)	1	[5]
Formica (19)	121.4	52.3	15	10	11	0	12	MOF (n=2), sepsis (n=1), CVA (n=5), arrhythmia (n=1), bowel ischemia (n=2)	6	12.6
Fukushima (20)	N/A	N/A	48	N/A	1	9‡	24	LCOS (n=13), sepsis (n=2), arrhythmia (n=1), bleeding (n=1), anemia (n=2)	16	9.2
Furukawa (21)	127.5	60.1	5	9	N/A	0	0	0	2	5
Huang (22)	193.9	113	27	N/A	N/A	N/A	17	N/A	11	8.3 [6]
Iemura (23)	N/A	60.1	8	15	N/A	0	2	LCOS (n=2)	1	[1.6]
Jeppsson (24)	N/A	N/A	119	55	0	21	77	N/A	38	2.4 [8]
Kacer (25)	N/A	N/A	7	4	1	2	5	Rupture (n=1)	0	[3.8]
Khan (26)	120	61.7	18	N/A	0	0	8	N/A	10	[6]
Kilic (27)	162.4	111.4	796	N/A	N/A	137	268	N/A	N/A	N/A
Kim (28)	194.4	150.1	17	N/A	N/A	3	1	Right ventricular failure (n=1)	5	2.2
Labrousse (29)	N/A	N/A	40	N/A	0	3	36	LCOS (n=22), rupture (n=4), CVA (n=3), arrhythmia (n=2), AKI (n=2), IABP complication (n=2), other (n=1)	31	7.2
Lorusso (30)	N/A	N/A	73	N/A	N/A	N/A	34	N/A	29	[5]
Malhotra (31)	159	105.4	28	N/A	N/A	1	21	LCOS (n=15), sepsis (n=4)	2	1.7
Mantovani (32)	108	61	11	N/A	0	1	3	LCOS (n=1), MOF (n=1), AKI (n=1)	3	3.8

Table 2 (*continued*)

Table 2 (*continued*)

First author (Ref.)	Mean CPB time (min)	Mean aortic cross-clamp time (min)	Concomitant CABG (n)	Post-op IABP (n)	Post-op ECMO (n)	Reintervention (n)	Early mortality (n)	Causes of death (n)*	Late mortality (n)	Mean follow-up (years)
Mantovani (33)	N/A	101	25	N/A	0	4	18	N/A	20	[15]
Martinelli (34)	N/A	N/A	7	6	N/A	3	0	0	1	2.5
Matteucci (35)	104.4	67.1	34	67	11	7	51	LCOS (n=22), rupture (n=9), CVA (n=8), AKI (n=2), Sepsis (n=1), bowel ischemia (n=1)	N/A	N/A
Okada (36)	152.5	88.5	1	N/A	N/A	2	3	LCOS (n=2), MOF (n=1)	N/A	N/A
Okamura (37)	0†	0†	3	N/A	N/A	5	6	LCOS (n=1), rupture (n=1), arrhythmia (n=1), pneumonia (n=3)	11	[10]
Ozkara (38)	98.7	62	14	N/A	N/A	3	6	MOF (n=3), CVA (n=1), arrhythmia (n=2)	1	5.8
Pang (39)	152	82	19	N/A	1	1	15	MOF (n=1), unknown (n=13)	8	[10]
Pojar (40)	146.3	91.8	12	N/A	N/A	0	14	N/A	10	[5]
Russo (6)	89	N/A	42	39	N/A	0	10	LCOS (n=1), rupture (n=2), MI (n=3), other (n=2)	28	6.4
Sakaguchi (41)	198	124	475	125	N/A	N/A	461	N/A	N/A	N/A
Schroeter (42)	151	66	19	20	9	N/A	11	N/A	N/A	N/A
Takahashi (43)	161.5	83.1	33	N/A	N/A	4	19	LCOS (n=19)	8	7.8 [5]
Thiele (44)	N/A	N/A	6	N/A	6	N/A	9	MOF (n=9)	1	3.6
Wiemers (45)	157	115	5	N/A	N/A	1	6	LCOS (n=4)	0	3.4
Yalçinkaya (46)	102.7	65.1	38	48	N/A	2	34	LCOS (n=4), rupture (n=2), unknown (n=28)	10	[5]
Yam (47)	117	87	8	N/A	0	2	8	LCOS (n=2), sepsis (n=4), CVA (n=1), arrhythmia (n=1)	15	5.2 [10]
Total	170.3±32.3	109.3±25.6	2,117	467	41	211	1,269	–	302	5.2±2.8

*, excluding intraoperative deaths; †, all surgeries performed off-pump; ‡, one reintervention performed percutaneously. In parentheses: data extracted from Kaplan-Meier curves. In square brackets: years of follow-up considered for data extraction. AKI, acute kidney injury; CABG, coronary artery bypass grafting; CPB, cardio-pulmonary bypass; CVA, cerebrovascular accident; LCOS, low-cardiac-output syndrome; MI, myocardial infarction; MOF, multi-organ failure.

to perform PCI nor just coronarography either, thereby precluding any possibility of surgical revascularization (20,24,54). Indeed, most patients with post-AMI mechanical complications are admitted to hospital in poor hemodynamic conditions or even in cardiac arrest, as demonstrated by the 58.2% of subjects developing cardiogenic shock pre-operatively and by the 64.3% and 8.6% requiring IABP and ECMO support, respectively (6,18,26,30,41,44). Therefore, emergent surgery might be necessary, thus making any pre-operative assessment unfeasible and time-consuming (55).

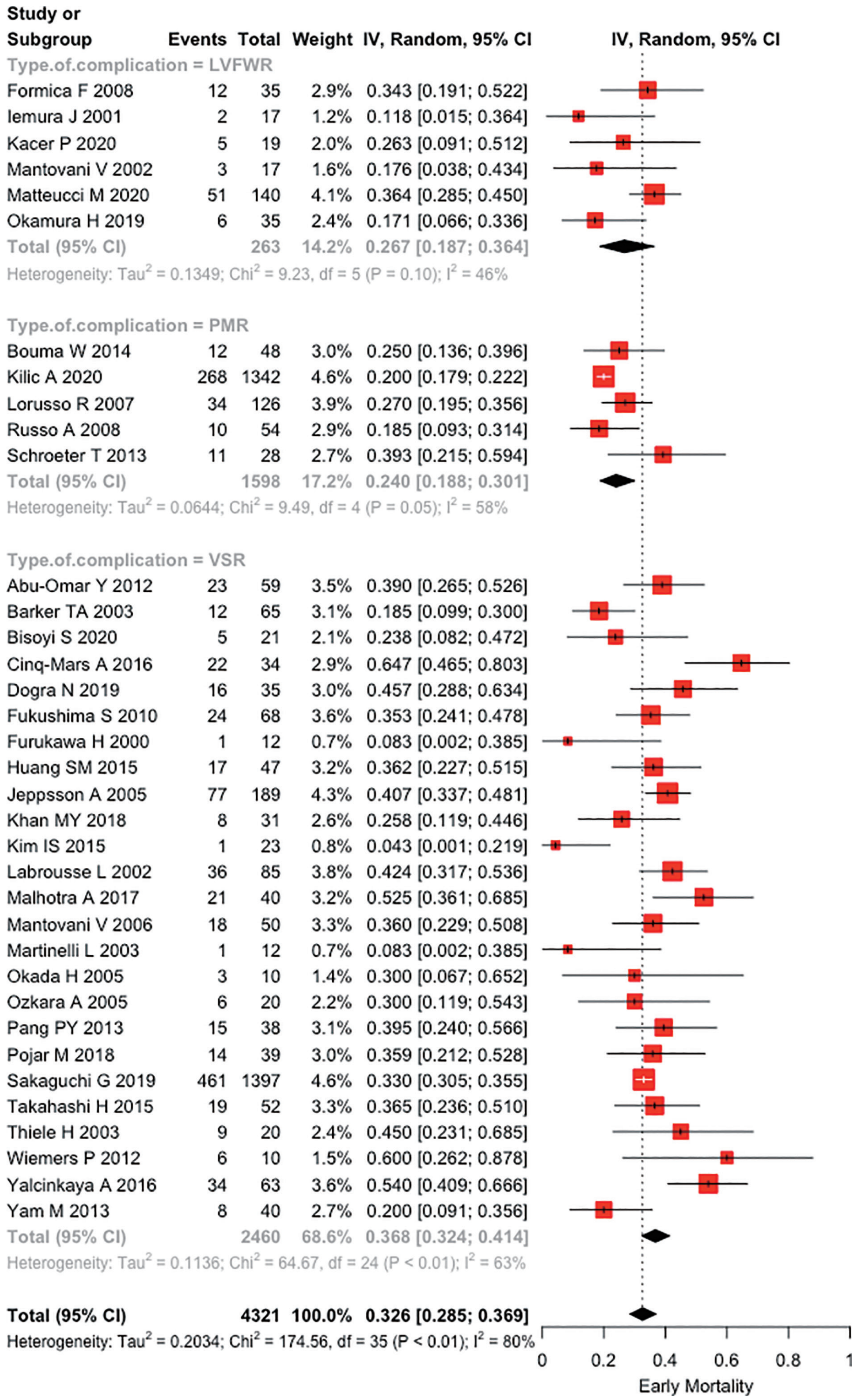

Figure 2 Forest plot of global early mortality. CI, confidence interval; LVFWR, left ventricular free-wall rupture; PMR, papillary muscle rupture; VSR, ventricular septal rupture.

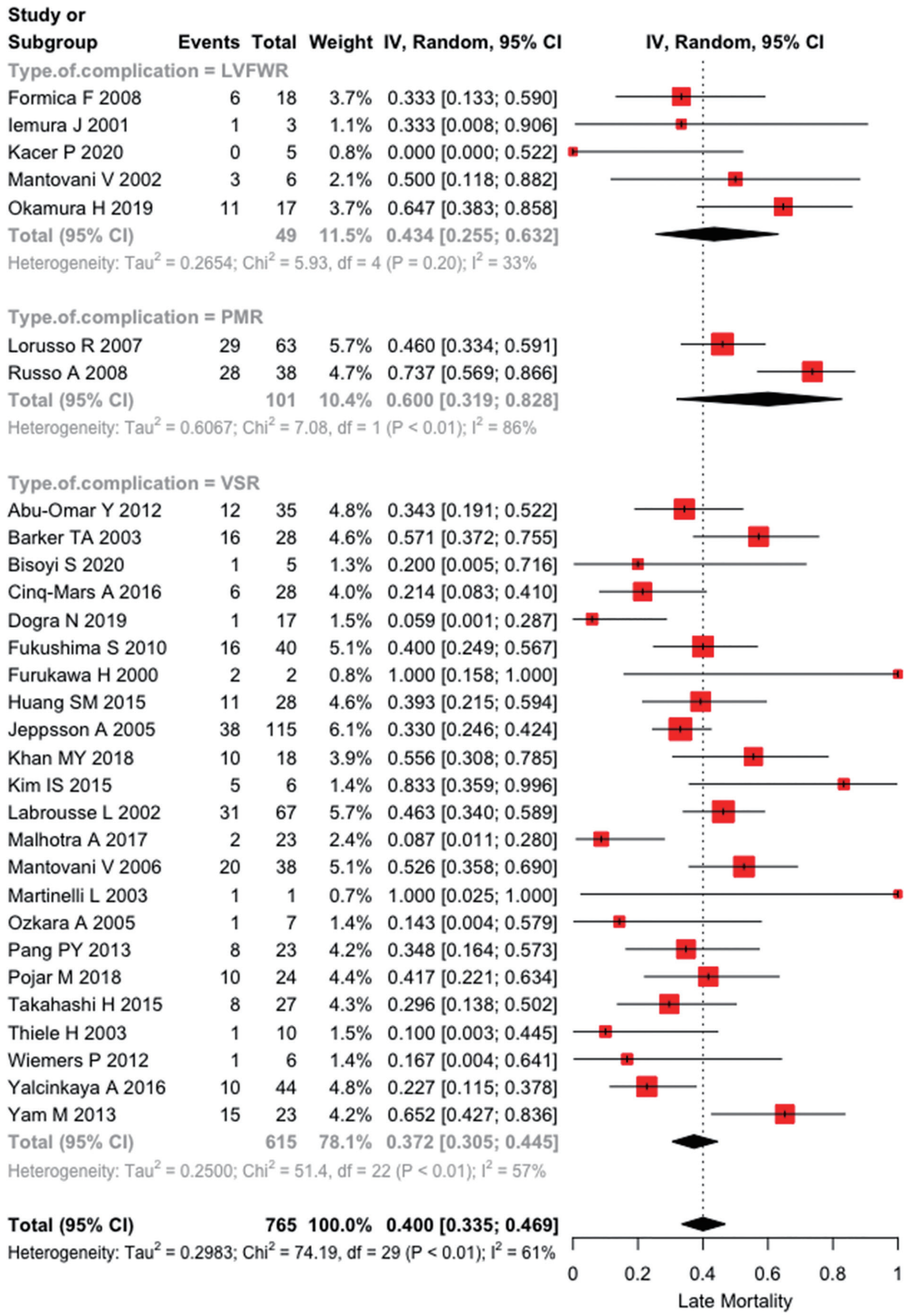

Figure 3 Forest plots of global late mortality. CI, confidence interval; LVFWR, left ventricular free-wall rupture; PMR, papillary muscle rupture; VSR, ventricular septal rupture.

Moreover, Skillington *et al.* pointed out the potentially harmful effect of coronarography on such unstable patients (33,39,47,55). However, many others supported the routine execution of pre-operative coronarography in all patients who don't need a salvage procedure and can be effectively stabilized (20,24,50,51,56). Furthermore, a discussion on the possible advantages of an expanded use of mechanical circulatory supports to achieve patients stabilization has emerged in the last years, in order to complete diagnostic workup and bring the patients to an elective procedure

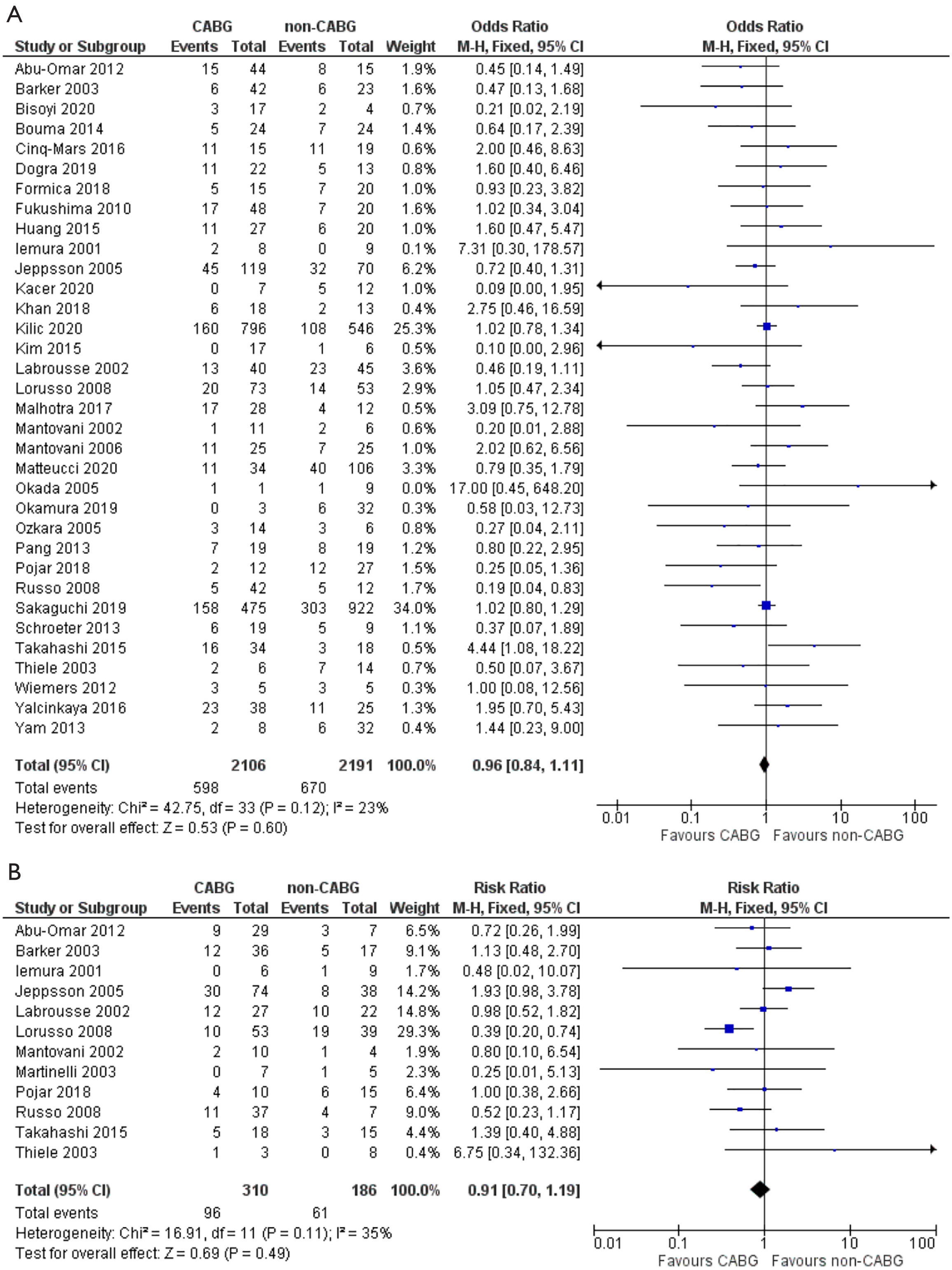

Figure 4 Forest plots of early (A) and late (B) mortality in CABG versus non-CABG groups. CABG, coronary artery bypass grafting; CI, confidence interval; M-H, Mantel-Haenszel.

rather than an emergent surgery (57).

Cardiac rupture usually occurs in single-vessel disease (more frequently LAD) and during the first ischemic episode (24,31,39,47). In the current study, 54.3% of patients had single-vessel CAD (4,7,31). The role of lacking collateral circulation in its pathogenesis may also explain why 83.8% of PMR patients had posteromedial muscle rupture, being it more sensitive to ischemia, because it's usually supplied by terminal branches (58).

In case of single-vessel CAD, PCI of the infarct-related artery (IRA) or thrombolysis is usually performed (22). However, in reports where multivessel CAD was more frequent, CABG was performed more often, showing most of its possible advantage (14). This may explain the survival difference in Barker's and Jeppsson's reports, the latter observing that the extent of CAD predicts late mortality, differently from Yalçınkaya *et al.* (14,24,46).

Concomitant CABG plays a different role in the IRA compared to other stenotic vessels (7). Indeed, some authors argued that revascularization of a coronary supplying infarcted myocardium is of little use, with the disadvantages outweighing the advantages (46,47,50,51). Differently, other reports showed that IRA revascularization may improve early and long-term survival by providing ischemic border perfusion and better control of possible arrhythmias (51). Prêtre *et al.* considered the IRA revascularization only in presence of a large septal or a significant collateral branch reaching viable myocardium (50).

CABG role in patients without viable myocardium has been extensively studied. The STICHES trial showed no significant difference on long-term survival in patients undergone CABG with pre-operative viable versus non-viable myocardium (59).

In multivessel CAD, non-IRA revascularization is considered logical by most authors (14,35,39,60,61). Although Yam *et al.* observed no survival benefit of cCABG in multivessel disease (47), Lundblad *et al.* highlighted that revascularization impacts more significantly on extensive CAD, pointing out the importance of complete revascularization (51). Similarly, Takahashi *et al.* identified incomplete revascularization as an independent risk for early mortality, and Mantovani *et al.* reported a higher mortality for patients left with myocardium at risk of ischemia (33,43). Other authors reported a long-term survival benefit for patients receiving total revascularization, probably for a better myocardial recovery provided by collateral bloodflow (7,22).

Concomitant CABG increases the surgical risk, reflected in EuroSCORE II as an independent predictor of mortality (22,33). Nevertheless, our meta-analysis showed no difference in early mortality between CABG and non-CABG, suggesting that concomitant revascularization doesn't negatively affect patient survival, probably by controlling the added risk of CAD (14,29).

Most studies included in our meta-analysis showed no difference in early mortality between CABG and non-CABG groups, while some authors reported a better survival for patients undergoing CABG (6,14,40,54,62). Takahashi *et al.* observed a higher early mortality for patients undergoing cCABG, explaining such results with a more severe CAD and ventricular dysfunction in that group of patients (43).

Analyzing the three types of complication, in VSR and PMR no difference was found between treatment groups, while LVFWR patients showed a trend slightly favoring cCABG, although not statistically significant. It should be noted, however, that each type of complication has different surgical implications. Indeed, surgery for PMR often requires standard mitral valve repair/replacement and as a result, cCABG is less technically demanding, probably contributing to a better outcome compared to the other conditions, although controversial results have been reported (6,27,63). In VSR, complete revascularization is not always possible, because most techniques require ventricular opening on the infarct area and the closing suture often entraps the culprit vessel that can therefore seldom be grafted (8,51). Similarly, in LVFWR both sutureless and sutured techniques make part of the ventricular wall inaccessible (10). As a matter of fact, Matteucci *et al.* suggested that the real effect of cCABG in LVFWR may be underestimated by the relatively low number of patients undergoing surgical revascularization, thereby possibly justifying the lack of cCABG impact on early mortality (35).

Despite few studies reporting a survival benefit for cCABG, all the authors recommend cCABG whenever possible (14,29,35,43,50,63). Randomized trials would be required to draw better conclusions, but it would be unethical to prevent patients needing CABG from receiving the appropriate treatment (33). The current meta-analysis also showed no survival difference on late mortality between treatment groups. However, in VSR patients there was a trend favoring non-CABG although not statistically significant, differently from the recent observations of Horan *et al.* (7). This result is strongly influenced by the population of Jeppsson *et al.* who reported a higher late mortality in cCABG patients (24). Conversely, Barker *et al.* reported a better long-term survival for cCABG patients after adjustment, although the crude data we analyzed showed no significant difference (14). Other reports showed no difference between treatment groups (29,40,60).

For LVFWR and PMR patients, late mortality data were available in four studies only. In LVFWR, a non-significant trend favoring cCABG was found, with Mantovani *et al.* suggesting a CABG contribution to long-term angina-free survival (32). For PMR, cCABG appeared to provide statistically better late survival (30).

Therefore, from the late-mortality results of this meta-analysis it seems reasonable that cCABG could represent a protective factor preventing patients with a more severe condition from further worsening (14,39). Nevertheless, Sulzgruber *et al.* observed that patients surviving the peri-operative period after cardiac rupture show a long-term mortality comparable to other AMI patients (64). However, the small sample size of most reports and the low incidence of these conditions make it difficult to draw definitive conclusions and advocate larger studies to increase the evidence on this topic.

Limitations

This study contains all the biases inherent to systematic reviews. Particularly, the major limitation is the quality of the included studies (mostly retrospective, with more than half of them analyzing small sample sizes). The included reports may account for a high risk of publication and selection bias. Moreover, some missing data on long-term follow-up were extracted from Kaplan-Meier curves. Data from two national registries were included, but accurate study selection eliminated the potential risk of patient overlapping. We also acknowledge the lack of some useful information for outcome analysis, such as data about emergent/urgent operation and causes of late death. Finally, we couldn't collect data about the need for further revascularization after hospital discharge.

Conclusions

Post-AMI mechanical complications represent rare, but life-threatening events. Surgical treatment constitutes the standard of care, however in-hospital mortality remains high. Concomitant CABG may represent an effective treatment for the underlying cause of these complications, especially in multivessel CAD, albeit increasing the surgical risk. This meta-analysis showed no significant difference between CABG and non-CABG groups in both early and late mortality, with some distinctions among different mechanical complications. However, we believe that cCABG could provide early and long-term advantage by preventing the added risk of CAD progression and should therefore be performed whenever feasible in these patients. Further and dedicated studies are warranted to evaluate the safety and effectiveness of cCABG in this setting.

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Footnote

Conflicts of Interest: RL is a consultant for Medtronic, Getinge and LivaNova, and Member of the advisory board of Eurosets and Fresenius/Xenios. The other authors have no conflicts of interest to declare.

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Supplementary

Table S1 VSR data on rupture location and type of surgery

First author, year	Anterior VSR (n)	Posterior VSR (n)	Infarct exclusion (n)	Other techniques (n)
Abu-Omar (13), 2012	32	27	N/A	N/A
Barker (14), 2003	30	35	N/A	N/A
Bisoyi (15), 2020	17	4	N/A	N/A
Cinq-Mars (17), 2016	11	23	N/A	N/A
Dogra (18), 2019	29	36	26	9
Fukushima (20), 2010	35	33	N/A	N/A
Furukawa (21), 2000	10	2	0	12
Huang (22), 2015	36	11	47	0
Jeppsson (24), 2005	92	97	N/A	N/A
Khan (26), 2018	26	5	31	0
Kim (28), 2015	19	4	21	2
Labrousse (29), 2002	50	35	0	85
Malhotra (31), 2017	27	13	4	36
Mantovani (33), 2006	30	20	16	34
Martinelli (34), 2003	5	7	0	12
Okada (36), 2005	8	2	9	1
Ozkara (38), 2005	13	7	0	20
Pang (39), 2013	28	10	35	3
Pojar (40), 2018	21	18	39	0
Sakaguchi (41), 2019	N/A	N/A	N/A	N/A
Takahashi (43), 2015	24	28	5	47
Thiele (44), 2003	N/A	N/A	N/A	N/A
Wiemers (45), 2012	4	6	4	6
Yalçinkaya (46), 2016	46	17	9	54
Yam (47), 2013	34	6	0	40
Total	627	416	246	361

N/A, not-available; VSR, ventricular septal rupture.

https://dx.doi.org/10.21037/acs-2021-ami-19

Table S2 LVFWR data on type of rupture and type of surgery

First author, year	Oozing LVFWR (n)	Blow-out LVFWR (n)	Sutured (n)	Sutureless (n)
Formica (19), 2018	19	16	19	16
Iemura (23), 2001	14	3	10	7
Kacer (25), 2020	N/A	N/A	14	5
Mantovani (32), 2002	N/A	N/A	16	1
Matteucci (35), 2020	79	61	86	54
Okamura (37), 2019	33	2	0	35
Total	115	83	145	118

LVFWR, left ventricular free-wall rupture; N/A, not-available.

Table S3 PMR data on rupture location and type of surgery

First author, year	Anterolateral PMR (n)	Posteromedial PMR (n)	MVR (n)	MVr (n)
Bouma (16), 2014	5	43	38	10
Lorusso (30), 2007	N/A	N/A	96	30
Kilic (27), 2020	N/A	N/A	1,071	271
Russo (6), 2008	5	49	41	13
Schroeter (42), 2013	11	17	25	3
Total	21	109	1,271	327

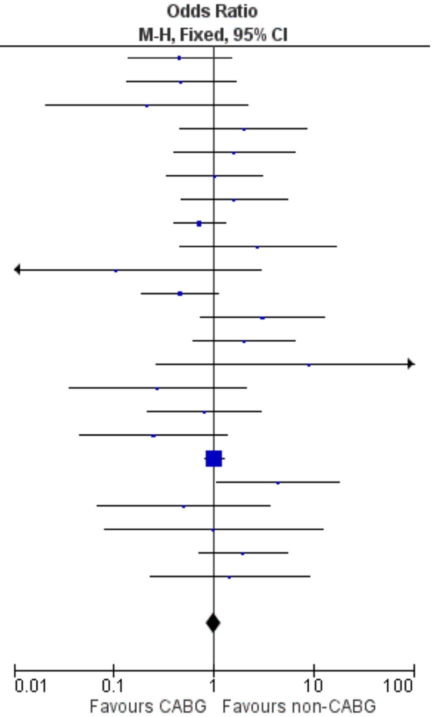
MVR, mitral valve replacement; MVr, mitral valve repair; N/A, not-available; PMR, papillary muscle rupture.

https://dx.doi.org/10.21037/acs-2021-ami-19

A

Study or Subgroup	CABG VSR Events	CABG VSR Total	non-CABG VSR Events	non-CABG VSR Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Abu-Omar 2012	15	44	8	15	3.2%	0.45 [0.14, 1.49]
Barker 2003	6	42	6	23	2.7%	0.47 [0.13, 1.68]
Bisoyi 2020	3	17	2	4	1.1%	0.21 [0.02, 2.19]
Cinq-Mars 2016	11	15	11	19	1.0%	2.00 [0.46, 8.63]
Dogra 2019	11	22	5	13	1.3%	1.60 [0.40, 6.46]
Fukushima 2010	17	48	7	20	2.6%	1.02 [0.34, 3.04]
Huang 2015	11	27	6	20	1.6%	1.60 [0.47, 5.47]
Jeppsson 2005	45	119	32	70	10.1%	0.72 [0.40, 1.31]
Khan 2018	6	18	2	13	0.6%	2.75 [0.46, 16.59]
Kim 2015	0	17	1	6	0.8%	0.10 [0.00, 2.96]
Labrousse 2002	13	40	23	45	5.9%	0.46 [0.19, 1.11]
Malhotra 2017	17	28	4	12	0.9%	3.09 [0.75, 12.78]
Mantovani 2006	11	25	7	25	1.6%	2.02 [0.62, 6.56]
Okada 2005	1	1	2	9	0.1%	9.00 [0.27, 299.86]
Ozkara 2005	3	14	3	6	1.3%	0.27 [0.04, 2.11]
Pang 2013	7	19	8	19	2.0%	0.80 [0.22, 2.95]
Pojar 2018	2	12	12	27	2.5%	0.25 [0.05, 1.36]
Sakaguchi 2019	158	475	303	922	55.4%	1.02 [0.80, 1.29]
Takahashi 2015	16	34	3	18	0.8%	4.44 [1.08, 18.22]
Thiele 2003	2	6	7	14	1.1%	0.50 [0.07, 3.67]
Wiemers 2012	3	5	3	5	0.5%	1.00 [0.08, 12.56]
Yalcinkaya 2016	23	38	11	25	2.1%	1.95 [0.70, 5.43]
Yam 2013	2	8	6	32	0.7%	1.44 [0.23, 9.00]
Total (95% CI)		**1074**		**1362**	**100.0%**	**1.00 [0.84, 1.19]**
Total events	383		472			

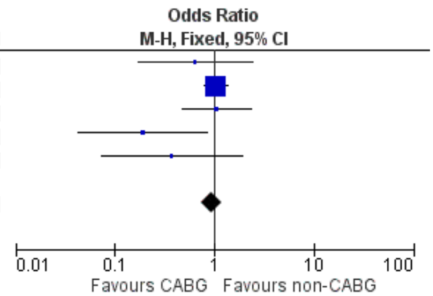
Heterogeneity: Chi² = 29.77, df = 22 (P = 0.12); I² = 26%
Test for overall effect: Z = 0.03 (P = 0.98)



B

Study or Subgroup	CABG PMR Events	CABG PMR Total	non-CABG PMR Events	non-CABG PMR Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Bouma 2014	5	24	7	24	4.2%	0.64 [0.17, 2.39]
Kilic 2020	160	796	108	546	78.0%	1.02 [0.78, 1.34]
Lorusso 2008	20	73	14	53	9.0%	1.05 [0.47, 2.34]
Russo 2008	5	42	5	12	5.2%	0.19 [0.04, 0.83]
Schroeter 2013	6	19	5	9	3.5%	0.37 [0.07, 1.89]
Total (95% CI)		**954**		**644**	**100.0%**	**0.94 [0.74, 1.20]**
Total events	196		139			

Heterogeneity: Chi² = 6.52, df = 4 (P = 0.16); I² = 39%
Test for overall effect: Z = 0.49 (P = 0.62)



C

Study or Subgroup	CABG FWR Events	CABG FWR Total	non-CABG FWR Events	non-CABG FWR Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Formica 2018	5	15	7	20	16.0%	0.93 [0.23, 3.82]
Iemura 2001	2	8	0	9	1.4%	7.31 [0.30, 178.57]
Kacer 2020	0	7	5	12	15.7%	0.09 [0.00, 1.95]
Mantovani 2002	1	11	2	6	9.4%	0.20 [0.01, 2.88]
Matteucci 2020	11	34	40	106	52.6%	0.79 [0.35, 1.79]
Okamura 2019	0	3	6	32	4.9%	0.58 [0.03, 12.73]
Total (95% CI)		**78**		**185**	**100.0%**	**0.73 [0.40, 1.33]**
Total events	19		60			

Heterogeneity: Chi² = 4.84, df = 5 (P = 0.44); I² = 0%
Test for overall effect: Z = 1.04 (P = 0.30)

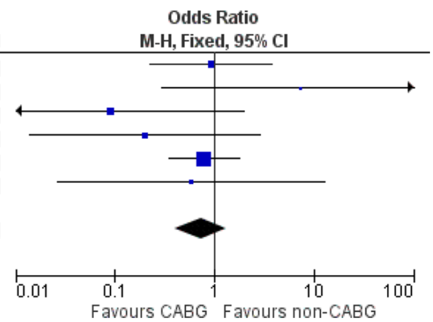


Figure S1 Subgroup analysis of early mortality for VSR (A), PMR (B) and LVFWR (C). CABG, coronary artery bypass grafting; CI, confidence interval; LVFWR, left ventricular free-wall rupture; M-H, Mantel-Haenszel; PMR, papillary muscle rupture; VSR, ventricular septal rupture.

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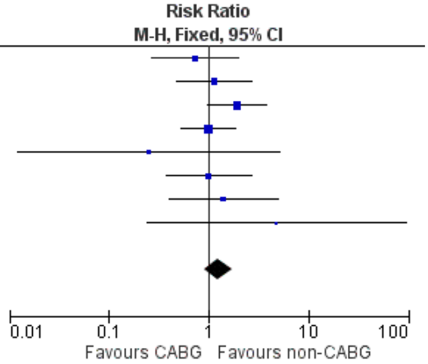
A

Study or Subgroup	CABG VSR Events	CABG VSR Total	non-CABG VSR Events	non-CABG VSR Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Abu-Omar 2012	9	29	3	7	11.1%	0.72 [0.26, 1.99]
Barker 2003	12	36	5	17	15.7%	1.13 [0.48, 2.70]
Jeppsson 2005	30	74	8	38	24.4%	1.93 [0.98, 3.78]
Labrousse 2002	12	27	10	22	25.4%	0.98 [0.52, 1.82]
Martinelli 2003	0	7	1	5	4.0%	0.25 [0.01, 5.13]
Pojar 2018	4	10	6	15	11.1%	1.00 [0.38, 2.66]
Takahashi 2015	5	18	3	15	7.5%	1.39 [0.40, 4.88]
Thiele 2003	1	4	0	7	0.9%	4.80 [0.24, 96.34]
Total (95% CI)		**205**		**126**	**100.0%**	**1.24 [0.89, 1.73]**
Total events	73		36			

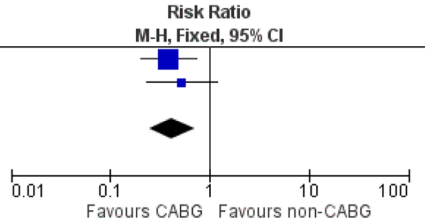
Heterogeneity: $Chi^2 = 5.41$, df = 7 (P = 0.61); $I^2 = 0\%$
Test for overall effect: Z = 1.28 (P = 0.20)



B

Study or Subgroup	CABG PMR Events	CABG PMR Total	non-CABG PMR Events	non-CABG PMR Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lorusso 2008	10	53	19	39	76.5%	0.39 [0.20, 0.74]
Russo 2008	11	37	4	7	23.5%	0.52 [0.23, 1.17]
Total (95% CI)		**90**		**46**	**100.0%**	**0.42 [0.25, 0.70]**
Total events	21		23			

Heterogeneity: $Chi^2 = 0.33$, df = 1 (P = 0.56); $I^2 = 0\%$
Test for overall effect: Z = 3.29 (P = 0.001)



C

Study or Subgroup	CABG FWR Events	CABG FWR Total	non-CABG FWR Events	non-CABG FWR Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Iemura 2001	0	6	1	9	46.4%	0.48 [0.02, 10.07]
Mantovani 2002	2	10	1	4	53.6%	0.80 [0.10, 6.54]
Total (95% CI)		**16**		**13**	**100.0%**	**0.65 [0.11, 3.71]**
Total events	2		2			

Heterogeneity: $Chi^2 = 0.08$, df = 1 (P = 0.78); $I^2 = 0\%$
Test for overall effect: Z = 0.49 (P = 0.63)

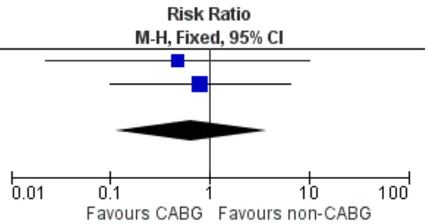


Figure S2 Subgroup analysis of late mortality for VSR (A), PMR (B), and LVFWR (C). CABG, coronary artery bypass grafting; CI, confidence interval; LVFWR, left ventricular free-wall rupture; M-H, Mantel-Haenszel; PMR, papillary muscle rupture; VSR, ventricular septal rupture.

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