

Prognosis following acute coronary syndromes according to prior coronary artery bypass grafting: Meta-analysis

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Abstract

Purpose: Conduct a meta-analysis to study the prognostic influence of a previous coronary artery bypass grafting (CABG) in patients admitted for an acute coronary syndrome (ACS).

Methods: A systematic review of the literature was performed using electronic reference databases through January 2013 (MEDLINE, Cochrane Library, Web of Knowledge, Google Scholar and references cited in other studies). Studies in which ACS outcomes with a previous history of CABG were compared with ACS outcomes with no history of previous CABG were considered for inclusion. The main endpoints of interest were mortality and non-fatal acute myocardial infarction. Data was aggregated at three follow-up times using random-effects meta-analysis models.

Results: Twenty-four studies were included which provided 387,181 patients for analysis. Previous CABG ACS patients were older, more diabetic and had a more frequent history of a previous myocardial infarction. Pooled in-hospital mortality was higher for the previous CABG ACS patients (OR 1.22 [1.04–1.44], $p < 0.01$, I^2 88%). The pooled adjusted OR showed no significant differences for the two groups (adjusted OR 1.13 [0.93–1.37], $p = 0.22$, I^2 92%). Previous CABG ACS patient had a higher pooled 30-day mortality (OR 1.28 [1.05–1.55], $p = 0.02$, I^2 74%); a higher non-adjusted (OR 1.61 [1.38–1.88], $p < 0.01$, I^2 70%) and adjusted (adjusted OR 1.37 [1.15–1.65], $p < 0.01$, I^2 0%) long-term mortality. Both the in-hospital and the long-term re-infarction rates were higher for the previous CABG ACS patients.

Conclusions: According to our data, ACS patients with previous CABG history had a higher risk for short- and long-term adverse events.

Keywords

Acute coronary syndromes, coronary artery bypass grafting, meta-analysis, prognosis

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Introduction

Coronary artery bypass grafting (CABG) has been an established therapy for patients with obstructive coronary artery disease since the 1970s, with a major impact on symptoms¹ and in some subsets on mortality and subsequent cardiovascular events.² Until the late 1990s there had been increasing numbers of CABGs performed annually, in Europe and in the USA.³ This, along with the progression of native coronary atherosclerosis and saphenous vein graft disease during long-term follow-up, has led to an increase in the proportion of patients with an acute coronary syndrome (ACS) who have previously undergone CABG.⁴

Post-CABG patients presenting with acute myocardial infarction (MI) have been shown to be older, with a greater

proportion of diabetes, heart failure, and previous MI.^{5,6} Nonetheless it has been demonstrated that they usually

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have smaller infarcts and a lower incidence of Q-wave MIs.^{7,8} Therefore it has been hypothesized that a prior CABG could exert a protective effect, as a result of the double coronary circulation and ischemic preconditioning.^{6,9,10}

The purpose of this meta-analysis was to systematically review and synthesize existing data on prognosis of patients with ACS and a history of a previous CABG, with respect to in-hospital, short-term and long-term outcomes.

Methods

Search strategy for the identification of studies

We searched electronic databases for articles published in English until January 2013. Databases included MEDLINE, Cochrane Library (Cochrane Central Register of Controlled Trials), Web of Knowledge, Google Scholar and references cited in other studies. The medical subject headings and keyword searches included the terms “acute coronary syndrome”, “acute myocardial infarction”, “prior coronary arterial bypass”. Citations were screened at the title/abstract level and full texts were manually obtained for all potentially relevant articles.

Two evaluators independently extracted all data. Discrepancies were resolved by consensus. Additionally, we signed up with PubMed to receive automated electronic notification for any new articles containing the above search terms.

Criteria for considering studies for this review

All published studies in which ACS outcomes with a previous history of CABG were compared with ACS outcomes with no history of previous CABG, were considered for inclusion in this meta-analysis. Our pre-specified inclusion criteria were as follows: the studies should compare ACS outcomes among patients with and without prior CABG. Moreover, the ACS should not be related to the immediate postoperative period. The study design could have been observational (either single or multicenter and either prospective or retrospective data) or as a post hoc analyses of randomized controlled trials (RCTs). Exclusion criteria were duplicate publication; ongoing/unpublished study and studies published only as an abstract or in conference proceedings.

Identification

The MeSH headings strategy yielded 1969 publications. One additional publication was identified after searching the reference lists of the relevant publications. Over 1473 publications were excluded because it was clear from the title and abstract that they did not fulfil the selection criteria. Two reviewers independently selected the studies to be included, in accordance with the described selection criteria, and read

the remaining 27 articles in full. Three studies were excluded.^{7,11,12} Twenty-four studies were finally included in the meta-analysis, see Table 1 and Supplemental Figure 1.

Methods of review

The following information was extracted from relevant studies: study design, study characteristics, patient characteristics (age, gender, history of diabetes, and previous MI), admission diagnosis, and patient management (invasive/conservative strategy; in-hospital medical therapy; percutaneous coronary intervention (PCI), fibrinolysis). The end-points of interest were in-hospital, short-term and long-term total mortality. Short-term included mortality from discharge to 30 days and long-term included mortality from 90 days to 9.5 years of follow-up.

With respect to in-hospital management, we also analyzed the pooled data for cardiogenic shock, stroke, and major bleeding rate for both groups. Re-infarction was also analyzed in two separate results: in-hospital and long-term follow-up that included data from 6 months to 9.5 years of follow-up.

Statistical analysis

We used RevMan 5.022 (Nordic Cochrane Centre, København, Denmark) to estimate pooled odds ratio (OR) based on random effects model meta-analysis (inverse variance method). We assumed similarity between the relative risk and OR. Whenever possible we used pooled adjusted relative risk or OR from the primary studies; otherwise, we used raw outcome data to yield unadjusted the ORs. The standard error of the adjusted ORs was calculated according to the formula: $[\ln(\text{upper } 95\% \text{ CI}) - \ln(\text{OR})] / 1.96$. In view of the potential diversity of study designs, we chose to stratify data for in-hospital mortality, based on admission diagnosis and the type of study. The following grouping was elaborated: i) admission diagnosis: studies that included only ST- or only non-ST-elevation ACS patients; ii) study design: stratification was done for post hoc RCTs and post hoc multicenter registries data; and iii) studies publication date: publication before 2000; publication between 2000 and 2010; publication after 2010. Statistical heterogeneity was assessed using the I^2 statistic, and values of 30–60% represented a moderate level of heterogeneity. Publication bias was estimated visually with funnel plots.

Results

The search results yielded 24 relevant studies with 387,181 patients. They comprised nine post hoc analyses of RCTs, 11 multicenter registries, and four single centre studies. The main characteristics of the included studies are described in Table 1.

Table 1. Studies included in the meta-analysis.

Study design	Design	Number patients	% previous CABG	Admission diagnosis	Age (CABG vs no CABG)	Outcome
Al Suwaidi et al., 2001 ²¹	The Mayo Clinic PTCA Registry	1072	11.8	ACS	69.3±9.1 vs 63.8±12.4	Adverse cardiac events (death, MI, CABG, or repeat PCI) were significantly higher in patients with prior CABG (49.2 vs 35.9, $p=0.04$). At 1 year prior CABG was not related with mortality (OR 1.33, 95% CI 0.96–1.84, $p=0.086$) or with the risk for combined cardiovascular events (OR 1.22, 95% CI 0.96–1.56, $p=0.11$). Increased in-hospital mortality for previous CABG patients (5.6 vs 3.5%, $p=0.02$).
Alanbaei et al., 2011 ¹⁶	Retrospective Gulf RACE Registry	8176	5.6	ACS	63 (56–70) vs 55 (47–64)	No significant difference in intra-hospital (4.2 vs 4.6 %, $p=0.74$), at 1 month (6.5 vs 8.2%, $p=0.28$) and 1 year (15.0 vs 12.4%, $p=0.20$) mortality.
Al Aqeedi et al., 2011 ⁵	Prospective Gulf Race-2 Registry	7881	4.2	ACS	63.1±10.8 vs 56.5±12.5	No significant difference in in-hospital mortality (5.8 vs 5.2%, $p=0.52$).
Al Aqeedi et al., 2012 ²²	Retrospective CCU registry	16,750	4.1	ACS	60.5±11 vs 53.7±12	Trends of mortality over 20 years, reduced from 13.2% to 4% ($p<0.01$).
Berry et al., 2009 ²⁰	RCT sub-analysis (VALIANT trial)	14,703	7.0	AMI with HF or LVEF < 35–40%	67±10 vs 65±12	Similar 30-day total mortality (4.6 vs 3.9%). CABG patients were more likely to experience the composite outcome of cardiovascular death, MI, HF, resuscitated cardiac arrest, or stroke (KM 3-year event rate 64 vs 39%, $p<0.01$).
Brilakis et al., 2008 ²³	RCT sub-analysis (PROVE-IT TIMI 22 A to Z)	8655	7.4	ACS	64 ± 10 vs 59± 11	After a median follow-up of 2 years, patients with previous CABG had a higher risk of total (8.1 vs 3.9%, $p<0.01$) and cardiovascular (6.2 vs 2.8%, $p<0.01$) death.
Ditrich et al., 1993 ²⁴	Prospective multicenter	2494	8.8	ACS	62.9±9 vs 63±12	No significant difference in hospital total (7 vs 9%, $p=ns$) and cardiac mortality (6 vs 8%, $p=ns$). Increased 1-year total (16 vs 8%, $p<0.01$) and cardiac (14 vs 7%, $p<0.01$) mortality for previous CABG ACS patients.
Davis et al., 1992 ⁸	CASS Registry	1052	28.3	ACS	–	Lower mortality rates immediately ($p=0.01$), after hospitalization ($p<0.01$) and at 30 days ($p<0.01$) in patients with previous CABG.
Elbarasi et al., 2010 ⁶	Multicenter registry (ACS I, ACS II, GRACE)	10,077	11.8	Non-ST ACS	72 (63–78) vs 67 (56–77)	Lower in-hospital mortality for the previous CABG group (1.7 vs 2.3%).
Kim et al., 2010 ⁹	Multicenter registry	47,557	18.5	Non-ST ACS	72 (63–80) vs 66 (55–78)	Prior CABG patients had a significantly greater unadjusted in-hospital mortality (5.1% vs 4.3%, $p<0.01$); however, there was no difference after adjusting for baseline patient characteristics (OR 0.99, 95% CI 0.87–1.11, $p=0.81$).
Kleiman et al., 1996 ²⁵	Prospective multicentre registry (TIMI III Registry Prospective study)	2048	16.4	Non-ST ACS	64.8 ± 11.5 vs 64.2 ± 14.6	The composite of death, MI, or recurrent ischemia at 42 days was not significantly different among patients with or without previous CABG (20.2% vs 16.4%, $p=0.1$). The same combined result at 1 year was more common in prior CABG patients (39.3% vs 30.2%, $p<0.01$). After adjustments CABG was not associated with the combined outcome either at 42 days or at 1 year.
Labinaz et al., 2001 ¹⁴	RCT sub analysis (GUSTO I)	41,021	4	ST-ACS	64.4 (57–70) vs 61.4 (52–70)	Increased 30-day mortality for the previous CABG patients (10.7 vs 6.7%, $p<0.01$).
Labinaz et al., 2002 ²⁶	RCT sub analysis (PURSUIT)	9455	12	Non-ST ACS	64 (58–72) vs 64 (54–71)	Increased adjusted mortality at 30 days (OR 1.45, 95% CI 1.05–1.90, $p=0.02$) and 180 days (OR 1.32, 95% CI 1.04–1.67, $p=0.02$) for the previous CABG patients.
Kugelmass et al., 2006 ²⁷	RCT sub-analysis (TACTICS TIMI)	2220	22	Non-ST ACS	64.2 vs 61.1	Higher 6 months composite of death, MI or re-hospitalization among patients with prior CABG (22.3% vs 16.4%, $p=0.002$).

(Continued)

Table 1. (Continued)

Study design	Design	Number patients	% previous CABG	Admission diagnosis	Age (CABG vs no CABG)	Outcome
Peterson et al., 1999 ¹³	NRMI-2 Multicenter Registry	6351	5.9	ST-ACS	64.7 vs 60.2	Prior CABG patients had a higher hospital mortality rate, either for patients treated with rt-PA (7.7 vs 5.3%, $p<0.01$) or primary angioplasty (8.0 vs 4.4%, $p<0.01$). Prior CABG was a independent predictor of mortality (OR 1.23, 95% CI 1.05–1.44).
Mathew et al., 2002 ⁴	NRMI-3 Multicenter Registry	112,697	14.1	ACS	Non-ST ACS 71.4 ± 10.8 vs 71.9 ± 14.1 ST-ACS 71.4 ± 10.6 vs 68.4 ± 14.7	Unadjusted mortality for ST-ACS was higher in patients with prior CABG (16.2 vs 14.1%, $p<0.01$), whereas in patients with non-ST ACS, prior CABG conferred a lower unadjusted mortality (10.1 vs 12.4%, $p<0.01$). Prior CABG was weakly associated with in-hospital adjusted mortality (OR 1.11, 95% CI 1.00–1.23), but not in patients without ST-ACS (OR 0.99, 95% CI 0.92–1.07).
Mitrovic et al., 2009 ²⁸	Prospective single centre	1828	40.9	ACS	59.6 ± 5.8 vs 61.2 ± 5.2	In-hospital mortality was not significantly different between patients with previous CABG and no previous CABG (4.9 vs 5.9% $p=0.37$). During long-term follow-up (mean follow-up period of 108 ± 14 months), the mortality rate for patients with previous CABG was higher (28 vs 23.6%, $p=0.04$). Clinical outcome at 19 years of follow-up showed that total cardiac events were significantly more common in CABG patients (70.2 vs 50.4%, $p<0.01$), but not the cardiac mortality (83.9 vs 80.4%, $p=0.34$).
Mukherjee et al., 2002 ²⁹	RCT sub-analysis (GUSTO V)	16,458	3.4	ST-ACS	64.9 ± 10.1 vs 61.2 ± 12.1	Unadjusted mortality rate was higher for patients with prior CABG at 7 days (6.0% vs 4.2%, $p=0.04$) and 30 days (8.9% vs 5.6%, $p<0.01$). Adjusted mortality at 30 days was significantly higher in patients with previous CABG (OR 1.64, 95% CI 1.21–2.24, $p=0.001$).
Nikolsky et al., 2012 ³⁰	RCT sub-analysis (ACUITY)	13,764	18	ACS	67 (58–74) vs 62 (53–71)	Higher mortality rate at 30 days (1.8 vs 1.5%, $p=0.18$) in previous CABG patients. At 1 year patients with previous CABG had higher rates of major adverse cardiac events (22.5 vs 15.2%, $p<0.01$ because of greater mortality (5.4 vs 3.9%, $p<0.01$, MI (10.0 vs 6.8%, $p<0.01$ and unplanned revascularization (13.1 vs 8.2%, $p<0.0001$)). History of CABG was an independent predictor of 1-year mortality (OR 1.33, 95% CI 1.03–1.71, $p=0.03$).
Neuman et al., 2011 ³¹	ACSIS Survey (Acute Coronary Syndromes Israeli biennial survey)	9781	10.2	ACS	69.8 vs 62.6	No differences in 30-day mortality in previous CABG patients vs no previous CABG (5.9 vs 5.1 %, $p=0.89$).
Stone et al., 2000 ³²	RCT sub-analysis (PAMI 2)	1100	5.3	ACS	65.4 ± 9.6 vs 59.8 ± 12.3	Unadjusted in-hospital mortality rate was higher for patients with prior CABG (6.9% vs 2.6%, $p=0.05$).
Teixeira et al., 2010 ¹⁰	Prospective single centre	1296	5.6	ACS	69.2 ± 9.4 vs 66.9 ± 12.7	No significant difference for in-hospital mortality (9.5 vs 5.9, $p=0.2$); at 1 month, 6 months or 1 year (9.8 vs 9.1%, log-rank test, $p=0.87$).
Welsh et al., 2010 ¹⁵	RCT sub analysis (APEX-AMI)	5745	2.2	ST-ACS	69 (58.3–76.0) vs 61 (52.0–71.0)	Prior CABG patients had increased 90-day mortality (11.9 vs 4.6%, $p<0.01$) and composite 90-day death/congestive heart failure/shock (16.4 vs 10.1%, $p=0.019$). Adjusted 90-day mortality was also higher in the previous CABG group (OR 1.9, 95% CI 1.08–3.33, $p=0.025$).
Zagher et al., 2003 ³³	Prospective Israeli Thrombolytic Survey	5396	3.2	ACS	—	Crude mortality rates at 7 days, 30 days, and 6 months were higher in patients with prior CABG, although a previous CABG was not an independent predictor after multivariate analysis.

ACS: acute coronary syndrome; HF: heart failure; CABG: coronary artery bypass grafting; KM: Kaplan-Meier; MI: myocardial infarction; ST-ACS: ST-elevation ACS; non-ST-ACS: non-ST elevation ACS; RCT: randomized controlled trial.

Table 2. Pooled baseline characteristics and in-hospital medical therapy.

	Mean difference	Number of patients included		I ²
		Previous CABG ACS patients	No previous CABG ACS patients	
Age (years)	2.88 (1.35–4.41)	20,746	166,236	99
LVEF (%)	−6.46 (−8.71 to −4.21)	17,206	101,539	98
	Pooled OR	Previous CABG ACS patients		I ²
		Previous CABG ACS patients	No previous CABG ACS patients	
ST-elevation ACS	0.22 (0.11–0.43)	4880 / 18,444	52,547 / 129,998	99
Non-ST-elevation ACS	3.45 (1.96–6.09)	13,458 / 18,444	77,312 / 129,998	98
Male gender	1.56 (1.43–1.71)	29,818 / 40,392	222,812 / 336,592	90
Diabetes	1.75 (1.57–1.95)	15,373 / 39,344	84,118 / 334,743	94
Previous MI	5.70 (4.69–6.94)	21,715 / 39,279	65,685 / 332,165	98
Aspirin	0.96 (0.74–1.23)	15,841 / 19,364	135,515 / 157,612	95
Second AAP	0.88 (0.71–1.09)	14,070 / 17,627	101,510 / 134,918	94
IIb/IIIa inhibitors	0.94 (0.61–1.44)	1635 / 16,137	16,498 / 97,984	97
Beta-blockers	0.95 (0.81–1.10)	9767 / 19,236	80,129 / 151,995	93
ACEi / ARA	1.05 (0.82–1.36)	1116 / 2198	23,556 / 45,094	83

AAP: antiplatelet therapy; ACEi: angiotensin converting enzyme inhibitors; ACS: acute coronary syndrome; ARA: angiotensin II receptor antagonist; CABG: coronary artery bypass grafting; MI: myocardial infarction; LVEF: left ventricular ejection fraction; I²: study heterogeneity.

Regarding baseline characteristics, the pooled data associated previous CABG ACS patients with an older age (mean difference +2.88 years [1.35–4.41], I² 99%) and with male gender (OR 1.56 [1.43–1.71], I² 90%). Regarding admission diagnosis, non-ST-elevation ACS was more frequent for patients with a previous CABG history. The pooled data identified a higher prevalence of diabetes (OR 1.75 [1.57–1.95], I² 94%) and of previous MI (OR 5.70 [4.69–6.94], I² 98%) in the CABG ACS patients. Moreover, the previous CABG ACS patients also had a lower pooled left ventricular ejection fraction (mean difference −6.46% [−8.71–4.21], I² 98%) (Table 2).

In-hospital mortality

Fourteen studies were included in the pooled analysis of in-hospital all-cause mortality. During hospital stay 2854 (8.8%) of 32,060 previous CABG patients died, compared with 21,354 (7.6%) of 282,603 in the no previous CABG history patients (OR 1.22 [1.04–1.44], $p < 0.01$, I² 88%) (Figure 1(a)). The difference remained significant for the studies that included only ST-elevation ACS patients (OR 1.39 [1.17–1.65], $p < 0.01$, I² 68%). For studies that included only non-ST-elevation ACS patients, there were no significant differences between the groups (OR 1.01 [0.70–1.44], $p = 0.97$, I² 94%) (Supplemental Figure 2(a)). With respect to the design of the study, the pooled data from RCTs identified a worse prognosis for the previous CABG ACS patients (OR 1.36 [1.06–1.73], $p = 0.01$, I² 16%), that was in contrast with data from observational multicenter registries (OR 1.22 [0.96–1.54], $p = 0.1$, I² 92%) (Supplemental Figure 2(b)). Regarding publication date, we noted a worse prognosis for

the previous CABG ACS patients in studies published before 2000 (OR 1.44 [1.04–2.00], $p = 0.03$, I² 58%). A similar in-hospital mortality was noted for studies published between 2000 and 2010, and after 2010 (Supplemental Figure 2(c)). Finally the pooled adjusted OR available for only six trials, with a total of 173,826 patients, concluded that there were no significant differences for the two groups regarding in-hospital adjusted mortality (adjusted OR 1.13 [0.93–1.37], $p = 0.22$, I² 92%) (Figure 1(b)).

In-hospital management and morbidity

With respect to in-hospital management, ACS patients with a history of a previous CABG had a lower pooled probability of a percutaneous coronary intervention during hospital stay (OR 0.75 [0.63–0.90], $p < 0.01$, I² 96%) (Figure 2(a)); and a lower pooled rate of in-hospital fibrinolysis (OR 0.44 [0.34–0.57], $p < 0.01$, I² 93%) (Supplemental Figure 3(a)). Cardiogenic shock was significantly more frequent in the previous CABG history patients (OR 1.52 [1.34–1.74], $p < 0.01$, I² 0%) (Figure 2(b)). Previous CABG patients had a higher rate of in-hospital re-infarction (OR 1.41 [1.09–1.83], $p < 0.01$, I² 31%) (Figure 2(c)). There were no significant differences between groups with respect to stroke and in-hospital major bleeding rates (Supplemental Figure 3(b) and (c), respectively).

Short and long-term data

With respect to 30-day mortality, data was available from 12 studies including 130,099 patients. Over 570 of 9374 (6.1%) previous CABG patients died, in comparison with 6436

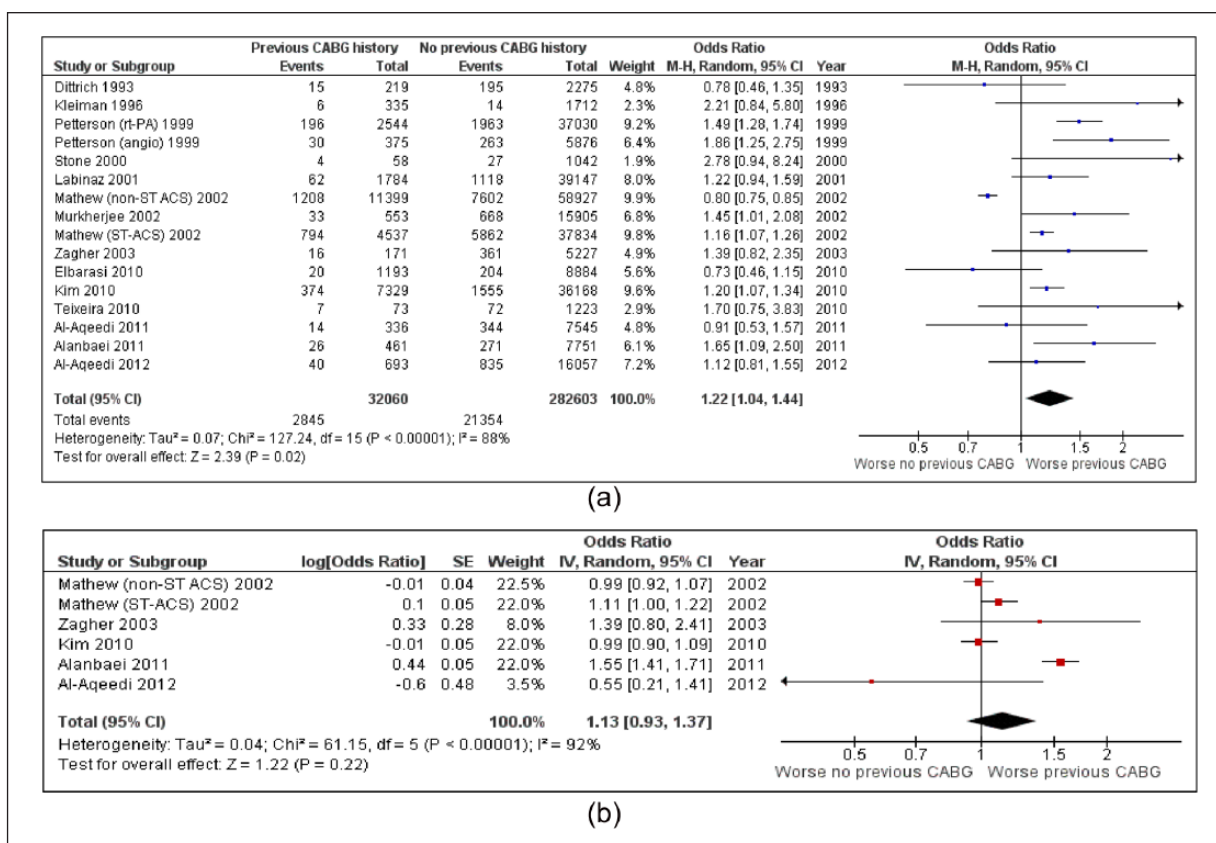


Figure 1. In-hospital outcome. (a) Forrest plot for in-hospital mortality. (b) Forrest plot for adjusted in-hospital mortality.

from 11,4619 (5.6%) with no previous CABG ACS patients. These pooled data was statistically significant (OR 1.28 [1.05–1.55], $p=0.02$, I^2 74%) (Supplemental Figure 4(a)). Long-term mortality data was available from 12 studies, with a total of 8590 events. Previous CABG history was associated with a significant worse long-term mortality (OR 1.61 [1.38–1.88], $p<0.01$, I^2 70%) (Figure 3(a)).

Adjusted data was available for four studies, which allowed an estimation of an adjusted pooled OR. Even after adjustment, previous CABG was associated with a higher rate of long-term mortality (adjusted OR 1.37 [1.15–1.65], $p<0.01$, I^2 0%) (Figure 3(b)).

With respect to long-term re-infarction rate, data was available for 33,160 patients with a total of 2536 events. Previous CABG history patients were more likely to have a re-infarction during follow-up (OR 1.88 [1.44–2.46], $p<0.01$, I^2 80%) (Supplemental Figure 4(b)).

Discussion

According to our pooled data, previous CABG patients admitted for an ACS had a worse prognosis, especially for the long-term.

The impact of prior CABG on survival after an ACS is a controversial subject. Previous studies from the 1990s¹³

and the 2000s^{6,9} have suggested that patients with prior bypass surgery have an increased in-hospital mortality, which was likely because of more adverse baseline characteristics in the post-CABG cohort. Our data seem to be in agreement. First, our baseline pooled data associated previous CABG ACS patients with an older age, and with higher risk variables such as diabetes, previous MI, and a lower LVEF. Second, our pooled adjusted OR did not confer an increased in-hospital mortality. This probably means that the higher non-adjusted in-hospital mortality of previous CABG patients was likely the result of older age and multimorbidity, and not the previous surgery itself.

We improved the inconsistency of the data regarding in-hospital mortality by stratifying the population. In this way, we were able to conclude that ST-elevation previous CABG ACS patients had higher in-hospital mortality. It has been suggested that post-CABG MIs tend to be smaller in relationship with a number of factors: small vessel disease; collateral circulation or native vessel disease distal to a graft.⁴ Nevertheless, the presence of an ST-segment elevation is suggestive of a larger lesion in a form of transmural myocardial injury and usually represents an acute occlusion of an epicardial coronary artery or of a graft. Contrary to previous reports,¹⁴ recent data regarding prior CABG ST-elevation ACS patients, reported a nearly equal distribution of the

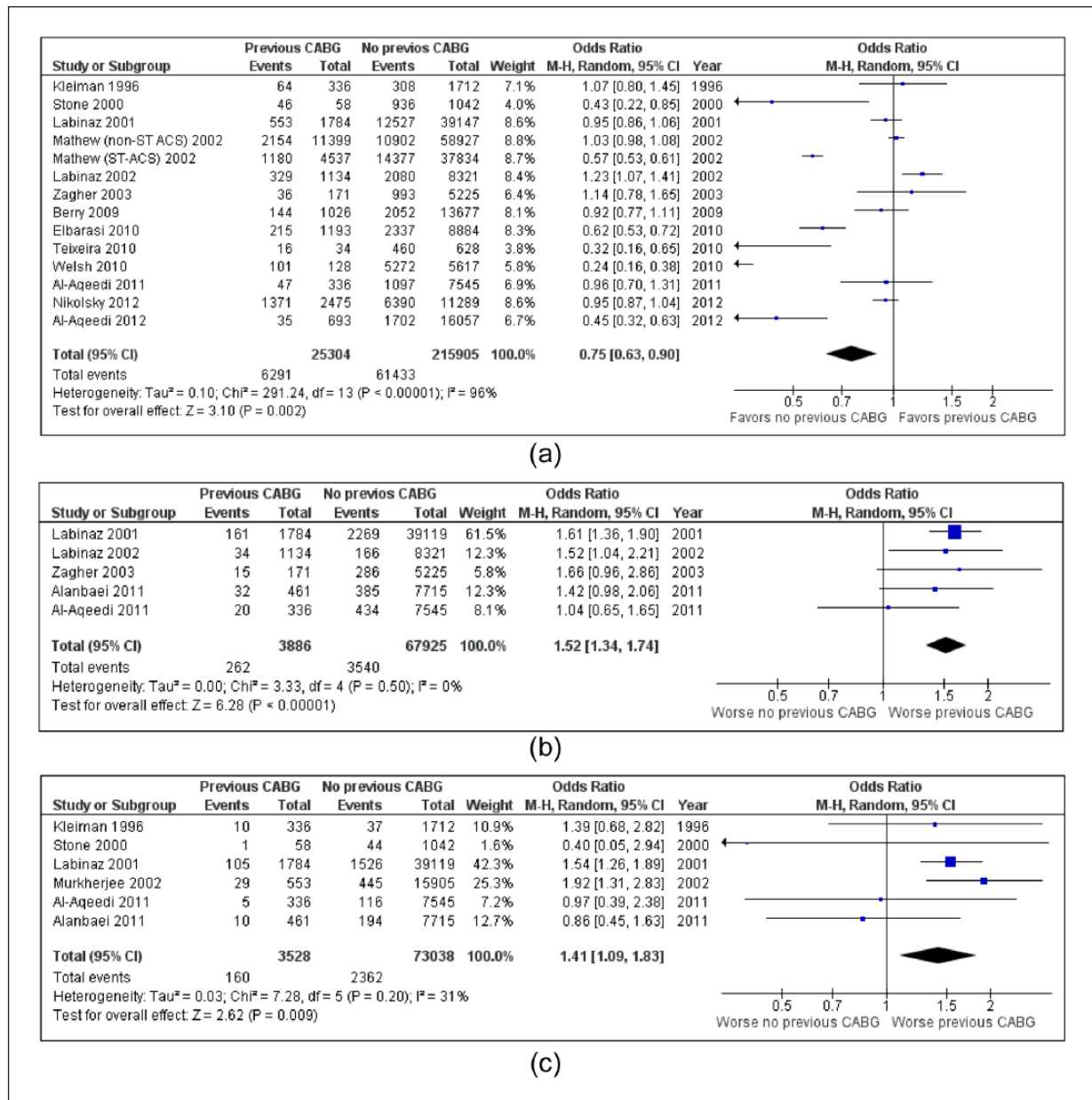


Figure 2. In-hospital management. (a) Forrest plot for in-hospital PCI. (b) Forrest plot for cardiogenic shock. (c) Forrest plot for in-hospital re-infarction.

infarct related artery, between bypass grafts and native coronary vessels.¹⁵ Moreover, the graft culprit patients had a lower success of primary PCI, and a significantly higher rate of clinical events. In that same trial, over 20% of prior CABG patients planned for primary PCI, failed to receive reperfusion, mainly because of technical limitations and for the inability to identify a culprit vessel. Those 20% of patients also had a significantly higher short-term mortality supporting the concept that there is no evidence of a protective effect of a dual coronary circulation in patients who failed to receive primary PCI.¹⁵ Underutilization of reperfusion therapies in ST-elevation post-CABG patients has also been reported since the lytic era¹⁶ with significant prognostic

implications.¹⁴ It has also been demonstrated that previous CABG patients have an increased total atherosclerotic burden and more advanced disease overall, as well as a greater clot burden, and longer lesions, which are factors associated with a higher resistance to thrombolytic therapy.¹⁴ We believe our data indirectly corroborate this worse prognosis of ST-elevation ACS patients, not only because of the higher in-hospital mortality, but also the lower rate of percutaneous intervention and fibrinolysis in the previous CABG ACS patients.

Of interest was that in the non-ST-elevation ACS group of patients, in-hospital mortality was similar between the previous CABG and the rest of the ACS cohort. That was

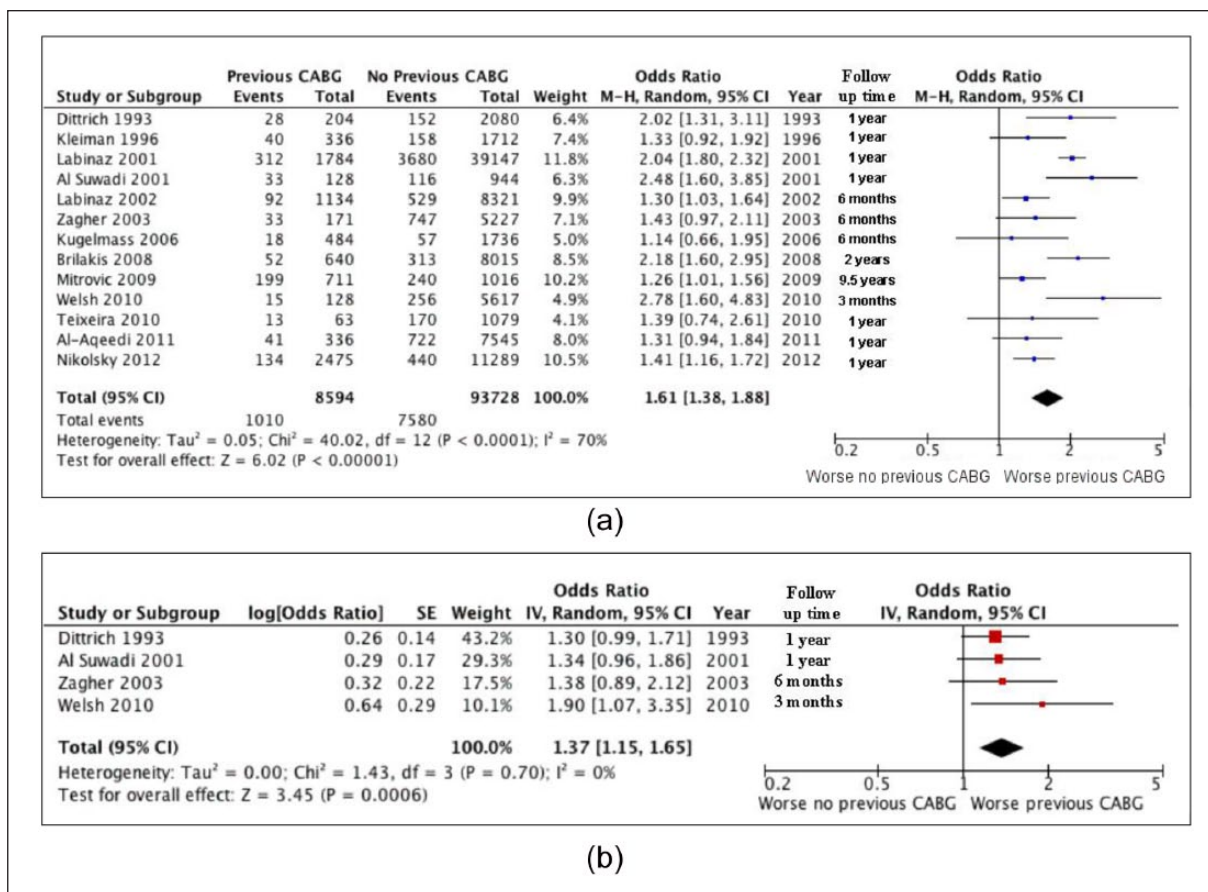


Figure 3. Long-term outcomes. (a) Forrest plot for long-term mortality. (b) Forrest plot for long-term adjusted mortality.

true despite the older age, the higher risk profile, and the more conservative approach. It is certainly plausible that the effect of the dual coronary circulation, the presence of collaterals, and the ischemic preconditioning could be protective. This seems especially important in the context of small non-transmural myocardial ischemic lesions.

Regarding in-hospital major bleeding we concluded, although with a high level of heterogeneity, that major bleeding was not significantly increased for previous CABG patients. Although in the past 20 years optimized medical therapy has improved significantly in the post-CABG subset of patients,¹⁷ recent reports from the present decade concluded for a less aggressive antiplatelet and anticoagulation therapy in those patients, probably protecting them from an increased bleeding.⁹ Moreover, a lower rate of percutaneous intervention and lytic therapy could also have influenced this result.

Our pooled data also demonstrated that percutaneous revascularization was less common in post-CABG patients, in both ST- and non-ST-elevation cohorts. The reasons for this are probably diverse. Previous authors have reported that CABG patients during an ACS are less referred for an invasive strategy⁴ despite their increased ischemic risk,

supporting a concept of a paradoxical strategy allocation.¹⁸ The lower referral could be because of older age, multimorbidity, and previously known coronary anatomy, considered not to be amenable to further revascularization. Also, post-CABG patients referred for an invasive strategy often may not receive such therapy because of complex anatomy and the problems associated with interventions on diseased saphenous vein grafts.¹⁵ This conservative management, associated with a lower rate of arterial and saphenous graft patency at 10 years after surgery,¹⁹ and a lower use of medical therapy,²⁰ could also be important factors to explain the higher short- and long-term re-infarction rates, and consequently a higher long-term mortality of post-CABG patients after an ACS. Unfortunately the majority of the studies did not report time from CABG to the coronary event. This would be important to further stratify data, as the different age of the grafts at the time of infarction could likely exert either a beneficial or deleterious effect.

Post-CABG ACS patients are a complex group of patients, with respect to multimorbidity, coronary anatomy, and revascularization. Our data was consistent with a worse prognosis for this ACS subset of patients, but the outcomes also seem to be influenced by the more adverse baseline

variables, for which adjustments are not complete. Whether the events in this ACS subset of patients can be prevented by a repeat revascularization procedure is still uncertain. Strategies should continue to be developed to minimize the adverse outcome of this ACS subset of patients, with emphasis on medical therapy, innovative percutaneous treatments, and minimally invasive surgical procedures.

Limitations

Our analysis is based on studies from the 1990s to 2012. Methodologies across the studies were not uniform regarding ACS definition, medical therapy, revascularization, and even the surgical technique. We have included in our analysis RCTs sub-analysis and observational (single and multi-center) studies. All of these factors contributed to the heterogeneity in various endpoints, which influenced the consistency of our results. We also suspect the existence of publication bias, as the Funnel plots (Supplemental Figure 5) are not symmetric.

Conclusions

Post-CABG patients had a worse outcome after an ACS, especially regarding long-term mortality, short- and long-term re-infarction.

Conflict of interest

None declared.

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