Title: The effects of prophylactic coronary revascularization or medical management on patient outcomes after noncardiac surgery. A meta-analysis

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Purpose: The benefits of prophylactic coronary revascularization for patients undergoing noncardiac surgery are uncertain. The purpose of this study was to systematically evaluate the effect of coronary revascularization and medical management on short- and long-term outcomes after noncardiac surgery.

Method: Ten electronic databases including MEDLINE and EMBASE (1980 to February 2006), and bibliographies of included articles were searched without language restrictions. Studies comparing effects of coronary revascularization and medical management before noncardiac surgery were included. Patient outcome data including perioperative mortality, myocardial infarction, long-term mortality, or late adverse cardiac events were extracted and entered into a meta-analysis.

Results: The quality of published evidence was modest, comprising one randomized controlled trial and six retrospective studies. A total of 3,949 patients undergoing high-risk noncardiac surgery were included in the quantitative analysis. There was no significant difference between coronary revascularization and medical management groups with regards to postoperative mortality and myocardial infarction; the odds ratios (95% confidence intervals) were 0.85 (0.48–1.50) and 0.95 (0.44–2.08), respectively. There were no long-term outcome benefits associated with prophylactic coronary revascularization; the odds ratios (95% confidence intervals) were 0.81 (0.40–1.63) and 1.65 (0.70–3.86) for long-term mortality and late adverse cardiac events, respectively.

Conclusion: In patients with stable coronary artery disease, prophylactic coronary revascularization before high-risk non- cardiac surgery does not confer any beneficial effects, when compared with optimized medical management, in terms of perioperative mortality, myocardial infarction, long-term mortality, or adverse cardiac events.

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Patients with coronary arter y disease (CAD) presenting for noncardiac surgery are at increased risk for perioperative car- diovascular events.[1] These adverse events, including perioperative cardiac death and myocardial infarction, impact greatly on patients' quality of life and cost to the health-care system.[2] Over the last two decades, much effort was spent on preoperative cardiac risk assessment and stratification.[1,3–5] More recently, the paradigm is shifting to therapies, either interventional or medical, to minimize perioperative cardiac events.[6–8]

Coronary revascularization procedures, including coronary artery bypass graft surgery (CABG), percutaneous transluminal coronary angiography, and coronary artery stenting (stent), have been shown to improve survival and quality of life in selected population of patients with CAD.[9–12] However, the efficacy of prophylactic coronary revascularization prior to surgery in reducing perioperative risk is less well studied. Although coronary revascularization is currently part of the American College of Cardiology/American Heart Association (ACC/AHA) guideline for perioperative cardiovascular evaluation for noncardiac surgery algorithms, it is derived primarily from expert opinions and not based on strong evidence.[13,14] Over the last decade, medical therapy such as beta-blockers, alpha-2 adrenergic agonists, calcium channel blockers, statin therapy and antiplatelet therapy have also been associated with reduced perioperative mortality, myocardial infarction or cardiac adverse events.[15–21]

The purpose of this study was to undertake a systematic review and meta-analysis comparing the effect of coronary revascularization and medical therapy on perioperative mortality and myocardial infarction, long-term mortality and late adverse cardiac events after noncardiac surgery.

Methods

With the assistance of an experienced reference librarian, a literature search was undertaken in February 2006 to identify all manuscripts regarding the short- and long-term effect of myocardial revascularization *vs.* medical management as pre-surgical management strategy. Ten electronic bibliographic databases were searched including MEDLINE (1966-2006), Embase (1980-2006) and Cochrane database of controlled trials.

Because only one randomized controlled clinical trial was available in the literature on our review topic,[22] retrospective studies were also included in this review if they met the following criteria: enrolled adult patients with CAD who were undergoing noncardiac surgery; assessed and reported at least one patients' outcomes of concern (perioperative mortality and myocardial infarction, long-term mortality and late adverse cardiac events) following management with coronary revascularization or medical management before noncardiac surgery. Studies were excluded if they were published prior to 1980 due to significant advances in management of CAD disease since that time,[23] or if they were only comparing amongst coronary interventions or medical therapeutic agents. No restriction was applied to the language of publication. One investigator (E.W.) reviewed the title and abstracts of the studies to identify eligible manuscripts. The bibliographies of eligible articles were scanned and hand searched to identify additional articles. The search strategy and database are presented in Appendix A.

Data collection, quality assessment and analysis

All eligible studies were reviewed. The following data were extracted: study design, type of surgery, patient and disease characteristics, preoperative management strategy; and patient outcome measures (pre- and post-noncardiac surgery mortality, post-operative myocardial infarction, long-term mortality, and late adverse cardiac events). Mortality included death due to all causes. The quality of each study was assessed using appraisal tools developed by the Critical Appraisal Skill Program (CASP) (Appendix B)[24] and rated in accordance with the Canadian Task Force on Preventive Health Care's guidelines for grading quality of published evidence (Appendix C).[25] Grading of recommendations was based upon the grading system established by the Canadian Task Force (CTF) for Specific Clinical Preventive Actions (Appendix D).[25]

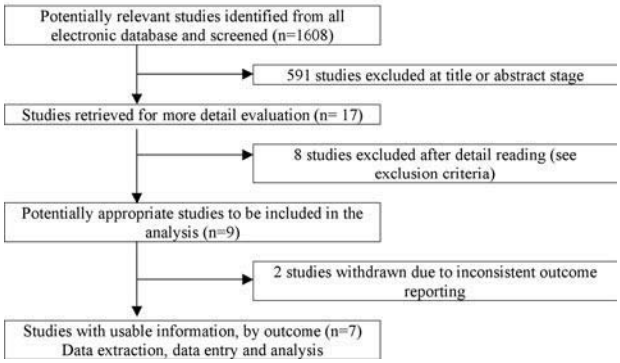

FIGURE 1 Process involved in study selection.

Statistical analysis

Effects of the two risk reduction strategies, namely prophylactic coronary revascularization and medical management, were analyzed using the odds ratio (OR) the primary outcome measure. Statistical analyses were performed using RevMan 4.2.10 (Cochrane Collaboration, Oxford, UK). The DerSimonian and Laird random effects model was used to calculate the pooled OR [95% confidence interval (CI)]. A sensitivity analysis was then conducted by comparing this pooled OR value with that calculated without the randomized controlled clinical trial. For each outcome measure, between-study heterogeneity was evaluated with the χ^2-based Q statistic and considered significant at $P < 0.10$.[26]

We hypothesized, *a priori*, that factors such as study quality, length of time between preoperative coronary revascularization intervention and noncardiac surgery, and duration of follow-up could explain the differences in outcomes. Subgroup analyses were conducted to examine whether the outcome results were different in studies in which coronary revascularizations were performed after patient enrolment *vs.* those in which coronary revascularizations were performed prior to patient enrolment, and in studies which enrolled patients after 1980 *vs.* studies that enrolled patients before 1980.

TABLE I Patient and disease characteristics in seven included studies

First author, reference location	*Sample CR/MM, (n)*	*Enrolment (yr)*	*Mean Age (yr)*	*DM CR/MM, %*	*Prior MI CR/MM, %*	*Severity of CAD CR/MM*	*Mean LVEF, CR/MM, %*	*Follow-up, (yr)*	*CASP score*	*CTF rating*
Garofalo 2005[31] Italy	83 / 127	1994-2004	68 ± 12	9.6% / 8.6%	67% / 10%	NYHA class 1.4/1.2 CCS class 1.5/1.1	50% / 54%	3.5	7/12	II-3
Godet 2005[32] France	78 / 1060	1996-2002	67 ± 11	14% / 8%	24% / 17%	Clinically symptomatic (%) 36/11	ND	ND	8/12	II-3
McFalls[22] CARP †trial 2004 United States	258 / 252	1999-2003	66 ± 11	19% / 20%	43% / 40%	3-vessel CAD (%) 35.3 / 31.3 Among all included patient revised cardiac risk index: ≥ 2 risk factors 49% ≥ 3 risk factors 13% Eagle's criteria: ≥ 3 risk factors 28%	54% / 55%	2.7	9.5/10	I
Takahashi 2002[30] Japan	21 / 43	1993-2002	66 ± 9	ND	ND	% Stenosis in ≥ one major coronary artery or its main branch: 75 / 50	ND	2.6	7/12	II-3
Back 2002[28] United States	128 / 353	1996-2000	70 ± 1	42% /28%*	54% / 20%*	% Patient with 2 or 3 vessel disease: 19 / 7 Eagle's criteria:	% patient with LVEF < 35%: 19% / 4%		6/12	II-3
Back 2004[29] United States	128 / 353	1996-2000	70 ± 1	42% / 28%*	54% / 20%*	% Patient with ≥ 3 risk factors: 27 / 7		5		
Eagle 1997[27] United States	964 / 582	1974-1979	> 60	ND	ND	ND	ND	ND	4/12	II-3

CR = coronary revascularization; MM = medical management. DM = diabetes mellitus; CAD = coronary artery disease; LVEF = left ventricular ejection fraction; CASP = Canadian Appraisal Skill Program; CTF = Canadian Task Force; ND = no data available; NYHA = New York Heart Association; CCS = Canadian Cardiovascular Society Angina Classification. *P < 0.05 between CR and MM. †CARP trial, the only randomized control trial available. The other six studies are retrospective studies.

TABLE II Number of patients and incidence of events of perioperative outcomes for coronar y revascularization vs medical management groups. The pooled random effect odds ratios, 95% confidence interval and P-values for heterogeneity measure for the three outcomes are provided.

	Pre-NCS death				*Post-NCS death*				*Post-NCS MI*			
	CR		*MM*		*CR*		*MM*		*CR*		*MM*	
Study	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%
Garofalo 2005[31]	0/83	0%	1/127	0%	0/83	0%	2/127	1.6%	0/83	0%	0/127	0%
Godet 2005[32]	0/78	0%	0/1060	0%	4/78	5.1%	44/1060	4.2%	7/78	8.9%	67/1060	6.3%
McFalls CARP† trial 2004[22]	10/258	3.9%	1/252	0.39%	7/225	3.1%	8/237	3.4%	19/225	8.4%	20/237	8.4%
Takahashi 2002[30]	1/21	4.8%	0/43	0%	0/21	0%	2/43	2.3%	ND	ND	ND	ND
Back 2002[28]	ND	ND	ND	ND	4/128	3.1%	4/353	1.1%	6/128	4.7%	8/353	2.3%
Back 2004[29]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Eagle 1997[27]	ND	ND	ND	ND	16/964	1.7%	19/582	3.3%	8/964	0.83%	16/582	2.8%
Total including CARP trial	11/440	2.5%	2/1482	0.13%	31/1499	2.1%	79/2402	3.3%	40/1478	2.7%	111/2359	4.7%
RE odds ratio (95% CI) including CARP trial	8.86 (1.55-50.5) P (heterogeneity) = 0.81				0.85 (0.48-1.50) P (heterogeneity) = 0.27				0.95 (0.44-2.08) P (heterogeneity) = 0.02			
Total excluding CARP trial	1/182	0.55%	1/1230	0.081%	24/1274	1.9%	71/2165	3.3%	21/1253	1.7%	91/2122	4.3%
RE odds ratio (95% CI) excluding CARP trial	6.37 (0.25-163) P (heterogeneity) = NA				0.87 (0.41-1.88) P (heterogeneity) = 0.18				0.95 (0.29-3.14) P (heterogeneity) = 0.006			

CR = coronary revascularization, MM = medical management, NCS = noncardiac surgery; MI = myocardial infarction; ND = no data available. NA = not available; RE = random effects. CI = confidence interval. †CARP trial, the only randomized control trial available. The other six studies are retrospective studies.

Results

Of the 1,608 articles identified, 1,591 articles were rejected at the title and abstract stage; 17 articles were reviewed in detail. After full article readings, seven manuscripts comprising 3,949 patients were included.[22,27–32] Ten articles were rejected due to various reasons: lack of comparison with medical management,[33,34] lack of subsequent noncardiac surgery,[35–41] and outcome report inconsistent with our review criteria[42,43] (Figure 1).

Data were extracted from these seven trials published between 1997 and 2005, one randomized controlled trial,[22] and six retrospective studies.[27–32] Patients from most studies were scheduled for elective major vascular surgery; only one study involved high-risk noncardiac surgery.[27] Duration of long-term follow-up ranged from 31 months to 56 months. The mean age of participants ranged from 60 to 70 yr. Two studies reported short- and long-term outcomes on the same group of patients respectively.[28,29] There were substantial variations in incidence of diabetes, prior myocardial infarction and severity of CAD among the studies (Table I). Moreover, only 28% and 34% of patients from McFalls'[22] and Back's[28,29]studies had three or more Eagle's cardiac risk criteria, suggesting lower cardiac risk study populations.

Quality Assessment

Except McFalls *et al*., which is a randomized controlled clinical trial (CARP trial),[22] the six retrospective studies had inherited flaws in their study design resulting in fair to low CASP scores[24] (Table I).

Pre-noncardiac surgery mortality, postoperative mortality and postoperative myocardial infarction

The number (%) of events for the three perioperative outcomes are shown for the seven studies (Table II). The pooled random effect OR, 95% CI and *P*-values for heterogeneity measure for the seven studies, and for the six studies excluding the CARP trial, are also shown. Except for the pre-noncardiac surgery mortality, pooled data from all studies resulted in similar random effect OR and 95% CI as those from the analyses performed without the CARP trial[22] (Table II).

Four studies[22,30–32] reported death occurring after patient allocation before noncardiac surgery; 11 preoperative deaths occurred among 440 patients receiving prophylactic coronary revascularization, while two

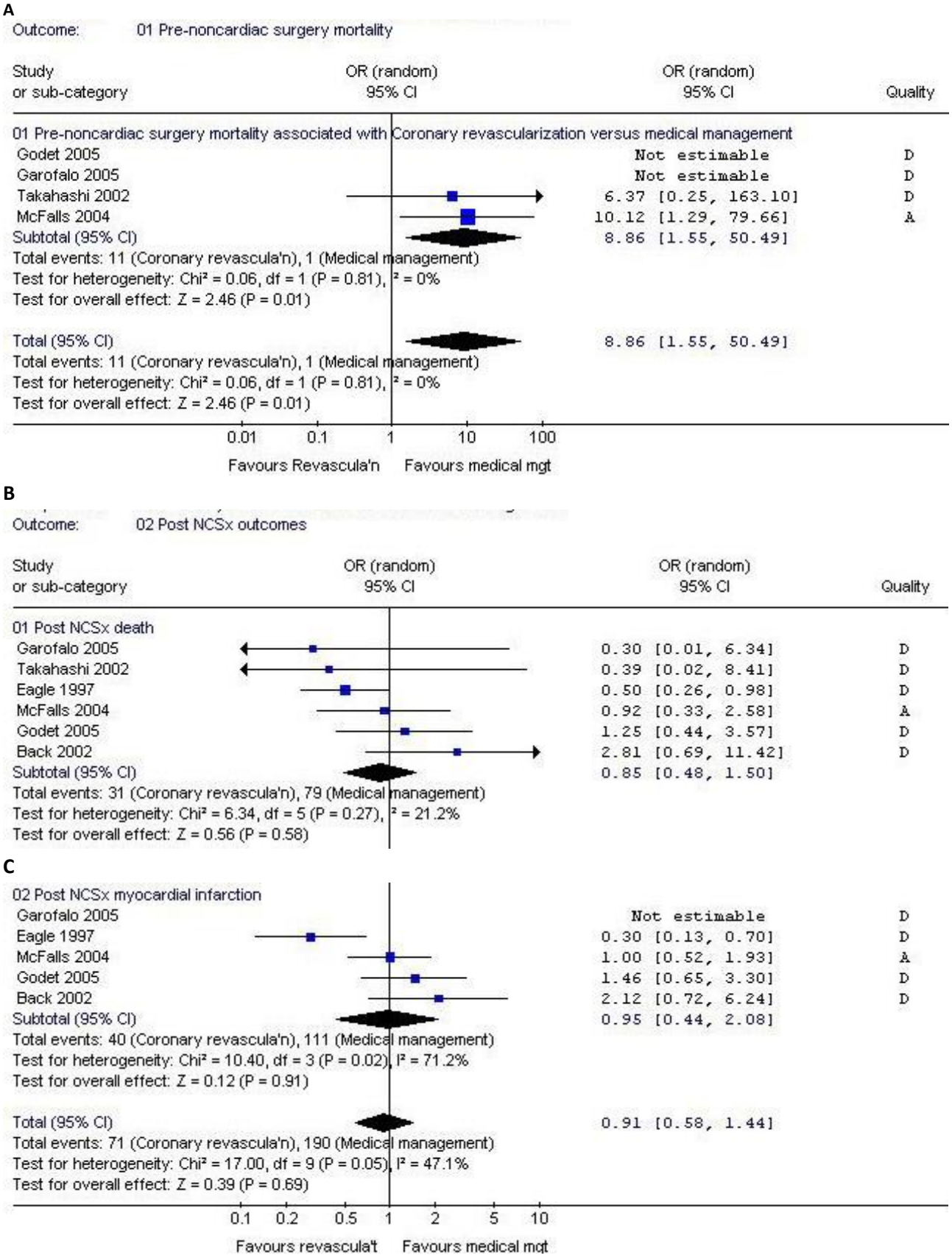

FIGURE 2 Comparison of coronary revascularization *vs* medical management for: (A) preoperative mortality, (B) postoperative mortality, and (C) postoperative myocardial infarction. Each study is shown by name along with point estimate of odds ratios and respective 95% confidence intervals. In each panel, size of box denoting point estimate in each study is proportional to weight of the study.

TABLE III Number of patients and incidence of events of long-ter m outcomes for coronar y revascularization vs medical management groups The pooled random effect odds ratios, 95% confidence intervals and *P*-values for heterogeneity measure for the outcomes are provided.

	Long-term mortality				*Late adverse cardiac event**			
	CR		*MM*		*CR*		*MM*	
Study	n/N	%	n/N	%	n/N	%	n/N	%
Garofalo 2005[31]		5 ± 2.8%		20 ± 11%		11 ± 6.7%		9 ± 6.6%
Godet 2005[32]	ND	ND	ND	ND	ND	ND	ND	ND
McFalls CARP† trial 2004[22]		22%		23%	ND	ND	ND	ND
Takahashi 2002[30]	0/21	0%	0/43	0%	3/20	15%	2/41	4.9%
Back 2002[28]	ND	ND	ND	ND	ND	ND	ND	ND
Back 2004[29]		32%		25.6%	35/111	31.5%	48/285	16.5%
Eagle 1997[27]	ND	ND	ND	ND	ND	ND	ND	ND
Total including CARP trial	96/463	20.7%	158/714	22.1%	45/214	21%	64/453	13.8%
RE odds ratio (95% CI) including CARP trial		0.81 (0.40-1.63) P (heterogeneity) = 0.01				1.65 (0.70-3.86) P (heterogeneity) = 0.10		
Total excluding CARP trial	41/214	19.2%	98/453	21.6%	41/214	19.2%	98/453	21.6%
RE odds ratio (95% CI) excluding CARP trial		0.64 (0.12-3.34) P (heterogeneity) = 0.003				1.65 (0.70-3.86) P (heterogeneity) = 0.10		

CR = coronary revascularization; MM = medical management; NCS = noncardiac surgery; ND = no data available; RE = random effects; CI = confidence interval. *As defined by: Garofalo, 2005: recurrent angina, myocardial infarction, or cardiac ischemia; Takahashi, 2002: patients requiring repeated coronary revascularization during follow-up period; Back, 2004: myocardial infarction, unstable angina, congestive heart failure, ventricular arrhythmia; †CARP trial, the only randomized control trial available. The other six studies are retrospective studies.

Preoperative deaths occurred among 1,482 patients receiving medical management. The odds of mortality during pre-noncardiac surgery period was increased when patients had prophylactic coronary revascularization compared with medical management (OR, 8.86; 95% CI, 1.55–50.5). When the OR was calculated excluding the CARP trial, the 95% CI widened significantly, but the odds of pre-noncardiac surgery mortality remained high (OR, 6.37; 0.25–163) among patients with coronary revascularization.

Meta-analyses of perioperative outcomes from the included studies are shown (Figure 2, A-C). There is non-significant level of heterogeneity for pre-noncardiac surgical mortality, as well as postoperative mortality with and without the CARP trial (Table II). However, a high level of heterogeneity was observed across the studies for postoperative myocardial infarction including or excluding the CARP trial (P = 0.02 and 0.006, respectively).

Long-term mortality and late adverse cardiac event

The number (%) of events for the long-term outcomes are shown for the relevant studies (Table III). The pooled random effect OR, 95% CI and *P*-values for heterogeneity measure for all relevant studies, and for the retrospective studies excluding CARP are shown. Overall, pooled data from all relevant studies resulted in similar OR as those from the analyses performed without the CARP trial. Meta-analyses of long-term outcomes (Figure 3, A and B) demonstrate that the odds of long-term mortality and late adverse cardiac events did not differ between patients who received prophylactic coronary revascularization and medical management.

In addition, the meta-analyses also showed a high level of heterogeneity across the trials regardless of whether the CARP trial was included or excluded (P = 0.01 and 0.003, respectively); while the meta-analysis for late adverse cardiac events outcome showed a borderline significant level of heterogeneity across the three retrospective studies (P = 0.10), suggesting these follow-up results are too dissimilar to be combined meaningfully.

Bias and subgroup analysis

To help detect any potential biases (e.g., publication bias), a funnel plot was constructed from the post-surgical mortality outcome. Figure 4 revealed an asymmetrical plot of the results from all six relevant studies (including the randomized controlled trial) in

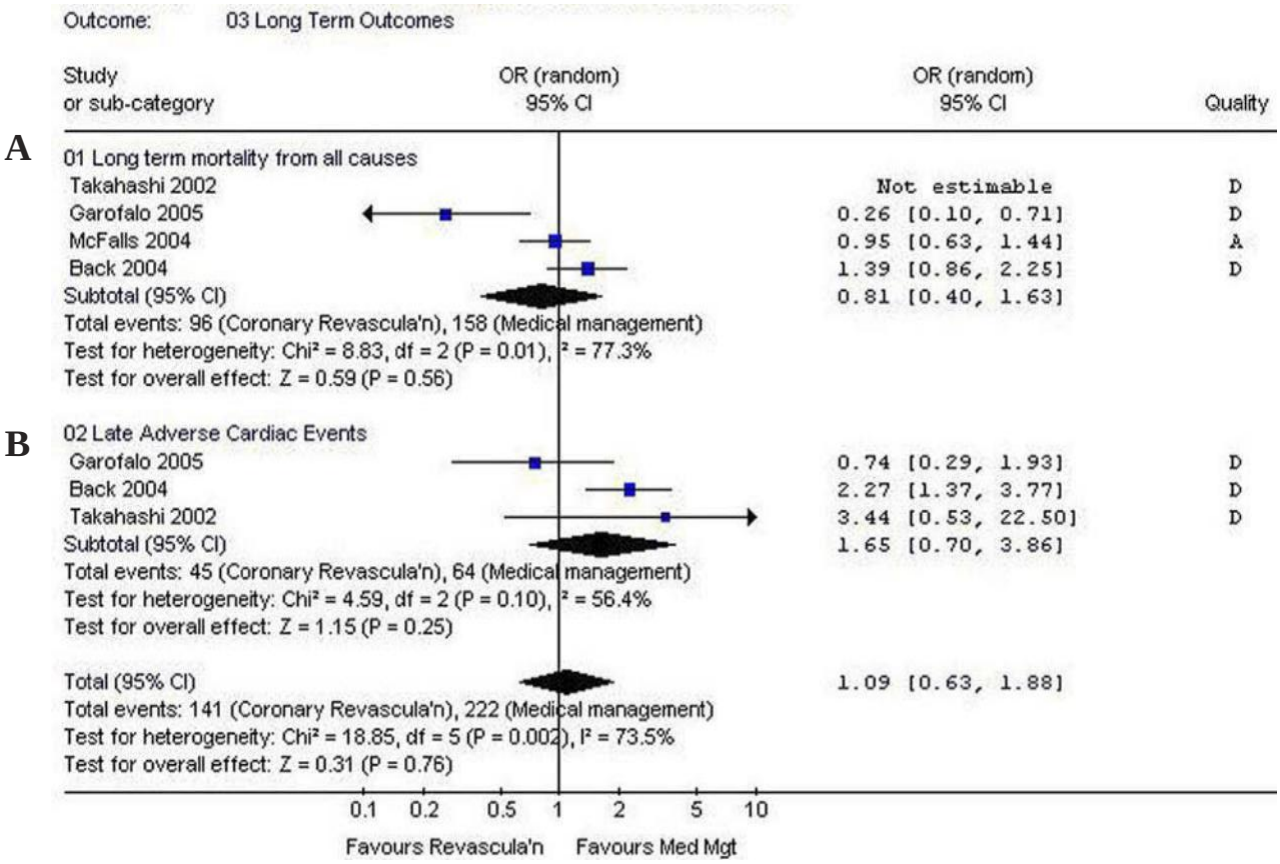

FIGURE 3 Comparison of coronar y revascularization *Vs* medical management for: (A) long-term mortality and (B) delayed adverse cardiac events. Each study is shown by name along with point estimate of odds ratios and respective 95% confidence intervals. In each panel, size of box denoting point estimate in each study is proportional to weight of study.

which the two smaller studies by Takahashi *et al.*[30] and Garofalo *et al.*[31] landed more widely at the bottom left of the plot. For postoperative mortality outcome, these two smaller studies with fewer events showed a more favourable OR with coronary revascularization *vs.* medical management than larger trials with more events (Figure 2A). However, the pooled OR without these two studies did not differ significantly (OR 0.96, 95% CI 0.48–1.91; data not shown).

Another factor contributing to heterogeneity of effect size was the patients' baseline severity of CAD. The CARP trial studied patients with intermediate or minor cardiac risk factors,[44] while in most of the retrospective studies, patients with more significant CAD were allocated to coronary revascularization group and patients with less significant CAD to the medical management group (Table I). Thus, there is a probable patient selection bias amongst the retrospective studies due to a lack of randomization.

The three studies by Eagle *et al.*[27] and Backe *et al.*[28,29] were rated lower in quality because patients were enrolled after variable periods of time after having received coronary revascularization, contributing to heterogeneity of treatment effects. Subgroup analysis showed that the amount of time between coronary revascularization and subsequent high-risk noncardiac surgery may have caused a difference for the long- term mortality outcome, although not statistically sig- nificant. Patients who had coronary revascularization after being enrolled into the studies tend to have bet- ter long-term survival (OR 0.54, 95% CI 0.15–1.91) than those who had the procedure performed a period of time prior to noncardiac surgery (OR 1.39, 95% CI 0.86–2.25), in comparison with patients who received medical management (Table IV).

TABLE IV Random effect odds ratios (95% confidence interval) for coronary revascularization vs medical management in subgroup analyses

Subgroups	*Pre NCS death*	*Post NCS death*	*Post NCS MI*	*Long-term mortality*	*Late adverse cardiac events*
Total including CARP trial					
Yes	8.86 (1.55-50.5)	0.85 (0.48-1.50)	0.95 (0.44-2.08)*	0.81 (0.40-1.63)*	1.65 (0.70-3.86)
No	6.37 (0.25-163)†	0.87 (0.41-1.88)	0.95 (0.29-3.14)*	0.64 (0.12-3.34)*	1.65 (0.70-3.86)
Patients data from after 1980					
Yes	8.86 (1.55-50.5)	1.18 (0.63-2.20)	1.30 (0.82-2.06)	0.81 (0.40-1.63)*	1.65 (0.70-3.86)
No[27]	NA	0.50 (0.26-0.98)†	0.30 (0.13-0.70)†	NA	NA
CR performed after enrolment					
Yes	8.86 (1.55-50.5)	0.95 (0.47-1.90)	1.16 (0.70-1.94)	0.54 (0.15-1.90)*	1.28 (0.30-5.39)
No[27-29]	NA	1.06 (0.20-5.67)*	0.77 (0.10-5.31)*	1.39 (0.86-2.25)†	2.27 (1.37-3.77)†

NCS = noncardiac surgery; MI = myocardial infarction; CR = coronary revascularization; NA = not applicable. *Statistically significance between-study heterogeneity ($P < 0.10$ for heterogeneity in studies of this subgroup). †Statistically significance between-study heterogeneity cannot be determined due to limited data from one study.

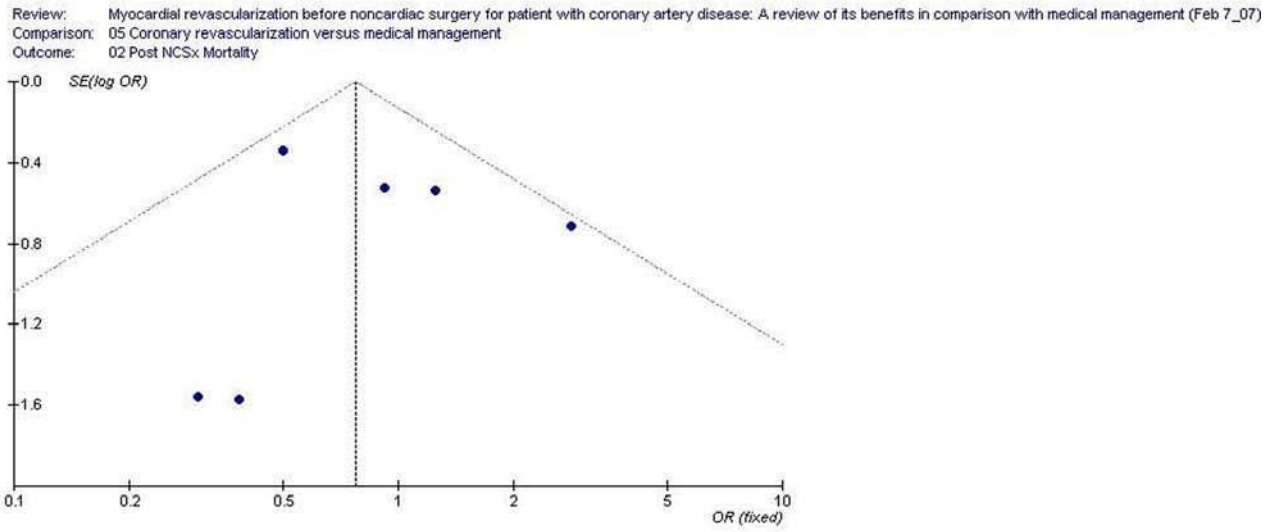

FIGURE 4 Funnel plot for post-noncardiac surgery mortality: results from each of the six relevant studies are represented. The 95% confidence interval line is also displayed.

Discussion

Results of the only randomized controlled trial available, the Coronary Artery Revascularization Prophylaxis Trial (CARP trial),[22] demonstrated that there is no reduction in postoperative myocardial infarction, mortality, or long-term mortality among patients randomized to prophylactic coronary revascularization compared with patients allocated to optimized medical management before major vascular surgery. Our quantitative analyses of this CARP trial,as well as six retrospective studies, suggest a similar result: for patients with CAD scheduled for noncar- diac surgery, prophylactic coronary revascularization does not reduce the odds of postoperative mortality, myocardial infarction, long-term mortality or late adverse cardiac events when compared with medical therapy. In fact, patients in the coronary revascular- ization group had increased odds of pre-noncardiac surgery mortality compared to those in the medical management group (OR 8.86, 95% CI 1.55–40.5), highlighting the additional risks associated with the

pre-surgical noncardiac surgery coronary revascularization intervention. These results, however, are based on a small number of perioperative mortality and cardiovascular events reported from the included studies.[22,27–32] Patient selection bias limits the strength of our conclusion, as well as its generalizability to patients with unstable or moderately-severe CAD. For example, the OR of pre-noncardiac surgery mortality among patients with coronary revascularization and those with medical management becomes non-significant when meta-analysis is performed excluding data from the CARP trials (OR 6.37, 95% CI 0.25–163.1). This is likely caused by the differences in quality of study design and availability of complete patient data.

Eagle *et al.*[13] found that prior CABG, compared with medical management, significantly reduce perioperative cardiac events (myocardial infarction and death) after high-risk noncardiac surgery. Results from more recent studies failed to show prophylactic coronary revascularization to have cardiovascular/survival benefit[22,28–32] (Table IV). This may be partly explained by improved perioperative medical therapy towards risk reduction,[21,45] advances in surgical technology[46] and reduced noncardiac surgical risk.[47] However, one may argue that patients with worse prognosis were more likely to have been allocated to the revascularization group (selection bias); and that this particular subgroup of patients with more severe CAD may benefit from prophylactic coronary revascularization procedure before high-risk noncardiac surgery. Yet, due to the limited sample size and other potential biases, any subgroup statistical significance was not detected. In a recent retrospective study, Landesberg *et al.*[48] examined records of 502 consecutive patients who underwent vascular surgery; patients with mod- erate-severe reversible ischemic disease on thallium scanning were referred for coronary angiography and, if appropriate, coronary revascularization before hav- ing high-risk vascular surgery. Multivariate analysis showed prophylactic coronary revascularization was associated with significant five-year survival (OR, 0.52; $P = 0.018$). When our meta-analysis was repeated including data from Landesberg's selective (group III and IV) patients, the pooled OR (95% CI) for post- operative mortality was 0.81 (0.50–1.32), and that for long-term mortality was 0.68 (0.35–1.30). However, the between-study heterogeneity for long-term mortality remained highly significant ($P = 0.003$).

As suggested in the decision-making guideline by Fleisher *et al.*[49] for major vascular surgery, recommendation to perform coronary revascularization prior to major vascular repair should involve weighing both the risks associated with coronary revascularization and the risk of the surgical procedure performed without preoperative interventions. The possibility exists for subgroups of patients with severe CAD in whom the risk of the vascular surgery, if performed without preoperative interventions, outweighs the combined risk of coronary revascularization and the surgical procedure. However, with advances in vascular procedural technology,[47,50,51] and improvements in perioperative medical management,[15,19–21,52] it is unlikely that prophylactic coronary revascularization will benefit patients undergoing noncardiac surgery except for patients in the highest risk category.

Lastly, from a health-economic standpoint, the cost-effectiveness of recommending prophylactic revascularization must also be considered when alternative medical management is as effective. The cost of performing both coronary intervention and then major vascular surgery, as suggested by Mason *et al.*,[53] was over $40,000 in the 1990s; a figure significantly higher than the alternative strategy of proceeding to vascular surgery with close monitoring of cardiac status ($24,300). Thus, medical therapy as a risk reduction strategy in patients with stable CAD is probably as effective as, and more cost-effective than, prophylactic coronary revascularization.–

A recent review by Kertai *et al.*[44] qualitatively summarized the role of preoperative revascularization before elective vascular surgery using current evidence from the CARP trial and relevant studies, and their findings were similar to ours in that the perioperative management of patients undergoing high-risk vascular surgery should involve weighing the risk benefit of extensive preoperative evaluation and risk management. The main differences between our systematic reviews relate to our more selective inclusion criteria and the methods adapted from Meta-analysis of Observational Studies in Epidemiology (MOOSE guideline)[54] to quantitatively determine if prophylactic coronary revascularization is beneficial in patients undergoing noncardiac surgery.

This study has several limitations. The strength of the conclusion is limited by the quality of reported studies. The systematic review comprised one randomized controlled trial and six retrospective studies. Although we are able to perform a quantitative analysis, the test for heterogeneity suggests significant differences in clinical population or methodological design amongst the studies. Secondly, six of seven studies enrolled vascular patients for elective high cardiac risk vascular surgeries, limiting the validity to extrapolate the result to other noncardiac surgeries. Outcomes for patients scheduled for urgent surgery of low to moderate cardiac risk are not

considered in this review. Thirdly, among studies included in the meta-analyses, none randomly compared prophylactic CABG *vs* percutaneous coronary intervention in their effects on the primary outcomes of interest. Therefore, we could not comment on their relative efficacy.

According to the 2002 ACC/AHA guidelines for perioperative cardiovascular evaluation for noncardiac surgery,[13] it is recommended that patients with intermediate risk undergoing high-risk surgery or with poor functional capacity, should undergo noninvasive testing and possibly prophylactic preoperative coronary revascularization. The rationale behind this recommendation is that prophylactic coronary revascularization may reduce perioperative mortality and morbidity. Our findings suggest that prophylactic coronary revascularization does not offer survival or cardiac protective benefit over medical management to patients, 60–70 yr of age, with stable CAD before high-risk noncardiac/vascular surgery (Grade D recommendation, Appendix D). A paradigm shifting towards preoperative medical therapy including beta- blockers, statin and aspirin therapy may be more cost- beneficial compared to prophylactic revascularization. The 2006 ACC/AHA guideline[15] update focusing on perioperative beta-blocker may reflect a shift in perioperative strategy in favour of perioperative medical management over prophylactic coronary revascularization. Our systematic review, comprising one randomized controlled trial and six retrospective stud- ies, has a limited ability to extrapolate to our current patient population. It also highlights the urgent need for adequately powered randomized controlled trials to provide the answer to the question: Does prophy- lactic coronary revascularization improve patient out- come compared to medical management in patients undergoing noncardiac surgery? If so, which patient subset(s) will derive significant benefit in outcome?

Acknowledgement

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APPENDIX A Search strategy

Electronic search of bibliographical databases

Source searched: ten electronic bibliographic databases were searched:

- Ovid Medline (1966-2006 Feb, in-process & other non-indexed citations),
- EMBASE (1980-2006),
- Cumulative Index to Nursing & Allied Health Literature (CINAHL),
- Evidence Based Medicine of Cochrane Central Register of Controlled Trials,
- Cochrane Database of Systematic Reviews.
- Database of Abstracts of Reviews of Effects(DARE)
- The Cochrane Central Register of Controlled trials (CENTRAL)
- NHS Economic Evaluation Database (NHS EED)
- Conference Paper Index
- ISI proceedings

EMBASE search strategy included noncardiac surgical or noncardiac surgery or [surgery (exp) AND statis- tics (exp)] or [surgery (exp) AND surgical mortality (exp)] or intraoperative period (exp) or postoperative complication (exp) or preoperative period (exp)

AND

(coronary artery surgery or coronary artery bypass graft or coronary artery bypass surgery or coronary artery recanalization or coronary reperfusion or heart muscle revascularization) or angioplasty (exp)

AND

Heart muscle ischemia (exploded to drug therapy) or coronary artery atherosclerosis (exploded to drug therapy) or coronary artery obstruction (exploded to drug therapy) or coronary artery spasm (exploded to drug therapy) or (medical management AND (heart muscle ischemia (exploded) or coronary artery ath- erosclerosis (exploded) or coronary artery obstruction (exploded) or coronary artery spasm (exploded))

Medline search strategy included noncardiac surgical or noncardiac surgery or surgical procedures (explod- ed to subcategory adverse effect, contraindications, statistics & numerical data, mortality) or periopera- tive care or postoperative care (subcategory adverse effects, mortality, rehabilitation, statistics & numerical data, therapy), or postoperative period (exploded) or preoperative care

AND

Myocardial revascularization (exploded) or angio- plasty (exploded)

AND

Myocardial ischemia (exploded to subcategory drug therapy) AND (medical management or medical therapy or drug therapy)

APPENDIX B Critical Appraisal Skills Program (CASP) - Critical appraisal tools[24]

The CASP appraisal tools are provided and produced by the Critical Appraisal Skills Program (CASP), part of the Public Health Resource Unit (PHRU) based in Oxford, England. http://www.phru.nhs.uk/casp/critical_appraisal_tools.htm

One mark is given to each question. Total score for CASP critical appraisal – cohort study is 12. Total score for CASP critical appraisal – randomized control trial is 10.

Copy of the two CASP appraisal tools employed is available as Additional Material at www.cja-jca.org.

APPENDIX C[55] (http://www.ctfphc.org/)

Canadian Task Force for Preventive Health Care

Level of evidence – Research quality rating

- I Evidence from randomized controlled trial(s)
- II Evidence from controlled trial(s) without randomization
- II-2 Evidence from cohort or case-control analytic studies, preferably from more than one centre or research group
- II-3 Evidence from comparison between times or places with or without the intervention; dramatic results in uncontrolled experiments could be included here
- III Opinions of respected authorities, based on clinical experience; descriptive studies or reports of expert committees

APPENDIX D[55] (http://www.ctfphc.org/)

Canadian Task Force (CTF) for Preventive Health Care

Recommendation grades for specific clinical preventive actions

- A The CTF concludes that there is good evidence to recommend the clinical preventive action.
- B The CTF concludes that there is fair evidence to recommend the clinical preventive action.
- C The CTF concludes that the existing evidence is conflicting and does not allow making a recommendation for or against use of the clinical preventive action, however other factors may influence decision-making.
- D The CTF concludes that there is fair evidence to recommend against the clinical preventive action
- E The CTF concludes that there is good evidence to recommend against the clinical preventive action.
- I The CTF concludes that there is insufficient evidence (in quantity and/or quality) to make a recommendation, however other factors may influence decision-making.

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