Preoperative Coronary Revascularization in High-Risk Patients Undergoing Vascular Surgery: A Core Review

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Patients undergoing vascular surgery are at increased risk for cardiac complications related to the presence of underlying coronary artery disease. Preoperative cardiac evaluation may help to identify high-risk patients in whom coronary angiography may be planned with subsequent coronary revascularization for the purpose of improving perioperative and long-term cardiac outcomes. However, the indications and efficacy for type of revascularization for the reduction of cardiac complications compared to medical therapy has been controversial. My aim in this review is to summarize the role of preoperative revascularization compared to conservative medical therapy before elective vascular surgery using current evidence from published studies.

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Patients undergoing vascular surgery are at increased risk for perioperative cardiac complications related to the frequent prevalence of coronary artery disease.[1] Cardiac risk factors and noninvasive test results may often identify patients at increased cardiac risk in whom coronary angiography is often considered. The results of the coronary angiography may occasionally reveal severe coronary artery disease, even though these patients may or may not have a history of chest pain or symptoms related to the coronary artery disease, such as dyspnea. After the presence of severe coronary artery disease is confirmed, coronary revascularization via percutaneous coronary intervention or coronary artery bypass graft (CABG) surgery can be considered for reducing perioperative and long-term cardiac complications. Nevertheless, there has been controversy as to the efficacy for type of coronary revascularization (CABG versus percutaneous coronary intervention) and how coronary revascularization may add to the effect of optimized medical therapy in patients undergoing noncardiac surgery, including vascular procedures. The recommendations of the current guidelines[1] and the results of the published studies in the field are not clearly indicative about the best perioperative and long-term management of these patients undergoing vascular surgery. Therefore, this core review discusses the current state of evidence on preoperative coronary revascularization in patients with extensive coronary artery disease undergoing major vascular surgery.

CABG Surgery Before Vascular Surgery

As early as in the 1980s, Hertzer et al.[2] demonstrated in a consecutive group of 1000 patients at intermediate risk for perioperative cardiac complications that 30% scheduled for aortic aneurysm resection, infrainguinal revascularization, or extracranial reconstruction had severe coronary artery disease, and more than 90% had significant (>70% stenosis) disease in at least one major coronary artery on preoperative coronary angiography (Table 1). This frequent prevalence of coronary artery disease with a subsequently higher perioperative and long-term cardiac complication rate prompted several investigators to study the role of CABG surgery for the reduction of cardiac complications in high risk surgical populations. The results of these studies[3–10] indicated that, in patients with multiple cardiac risk factors and/or with multivessel coronary artery disease, CABG before elective vascular surgery may reduce the risk of perioperative cardiac complications and improve long-term survival. Nonetheless, in these studies no specific criteria for preoperative screening and identification of patients at increased risk was used, the cumulative risks of coronary angiography and myocardial revascularization followed by vascular surgery were not considered and, given the retrospective design of these studies, the effectiveness of cardioprotective medication use such as β-blockers[11–13] and statins[14,15] for the reduction of perioperative and long-term cardiac complications as an alternative or

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Table 1. Summary of Studies About the Role of Coronary Artery Bypass Grafting or Percutaneous Coronary Intervention Before Noncardiac Surgery

Author; year of publication	No. of patients studied; Design	Inclusion/Exclusion criteria	Type of surgery	Type of revascularization	Outcome
Studies of coronary artery bypass grafting/percutaneous coronary intervention					
Hertzer et al.; 1984[2]	1000; prospective	i: consecutive e: refusal, malignancy	Major vascular	CABG	Low rate of perioperative cardiac complications
Hertzer et al.; 1987[3]	246; retrospective	i: consecutive e: refusal, malignancy	Aortic aneurysm	CABG	Late cardiac mortality reduced
Hertzer et al.; 1987[4]	386; retrospective	i: consecutive e: refusal, malignancy	Peripheral vascular	CABG	Late cardiac mortality reduced
Eagle et al.; 1997[5]	3368; retrospective	i: CAG and noncardiac surgery	Abdominal, vascular, thoracic, head and neck	CABG	Perioperative mortality and myocardial infarction rates reduced
Fleisher et al.; 1999[6]	6895; retrospective	i: random sample of Medicare patients	Major vascular	CABG or PCI	Lower rate of cardiac events for aortic patients; reduction in 1 yr mortality
Hassan et al.; 2001[7]	501; retrospective	i: 2-or 3-vessel disease, severe angina, ischemia e: prior CABG/ PCI, advanced age, left main disease	Noncardiac	CABG or PCI	Late cardiac death and myocardial infarction rates reduced
Back et al.; 2002[8]	425; prospective	i: consecutive, elective vascular patients	Major vascular	CABG or PCI	Prior CABG ≤5 yr, PCI ≤2 yr reduced perioperative cardiac events
Landesberg et al.; 2003[9]	502; retrospective	i: elective, consecutive e: previous CABG/ PCI, thallium scan	Major vascular	CABG or PCI	Better late survival
Landesberg et al.; 2006[10]	624; retrospective	The same as above	Major vascular	CABG or PCI	Better late survival for patients at intermediate risk
Poldermans et al.; 2007[29]	101; prospective	i: severe myocardial ischemia	Major vascular	CABG or PCI	No difference in survival compared to medical therapy

CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; CAG = coronary angiography; i = inclusion; e = exclusion.

adjunctive to coronary revascularization was not studied. It should also be noted that patients with peripheral artery disease undergoing CABG surgery can be at substantial risk for perioperative cardiac and cerebrovascular complications compared with patients without peripheral artery disease,[16] which may significantly limit the long-term benefit of coronary revascularization in vascular patients.

Percutaneous Coronary Intervention Before Vascular Surgery

Several small-scale studies have evaluated the role of percutaneous coronary intervention in the reduction of perioperative complications in patients undergoing noncardiac surgery, including vascular surgery[17–21] (Table 2). Most of these studies were retrospective, failed to use adequate control groups, and screening and risk stratification tools to identify high-risk patients who would likely benefit from percutaneous coronary intervention. Therefore, the findings of these studies were not sufficient to prove that the use of preoperative percutaneous coronary intervention may reduce the rate of cardiac complications after noncardiac surgery, including vascular surgery.

Recently, the safety of preoperative percutaneous coronary intervention has been questioned (Table 3). These studies reported perioperative thrombotic complications associated with early termination of dual antiplatelet therapy or bleeding complications when it was continued throughout surgery signifying the unsettled issue of using percutaneous coronary intervention in high-risk cardiac-stable patients for the prevention of perioperative complications.[22–25]

The Coronary Artery Revascularization Prophylaxis (CARP) Trial

This trial was a randomized clinical study in which the issue of whom to screen and how to screen elective vascular patients beyond medical history taking, physical examination and preoperative electrocardiography was not addressed (Table 4).[26] Although the trial was statistically not powered to test the benefit of coronary artery revascularization within 30 days after vascular surgery, there was no difference in the incidence of death and myocardial infarction between the two groups. At a median long-term follow-up time of 2.7 yr, there was also no difference in mortality between revascularized and nonrevascularized patients (Fig. 1). There was also no treatment difference in long-term survival among high-risk clinical subsets including patients with angina, multiple clinical risk variables, and three vessel disease with mild to moderate left ventricular dysfunction.

Thus, the results of this trial suggested that revascularization in cardiac-stable, elective vascular surgery patients may not provide additional benefit in reducing the incidence of perioperative and long-term mortality and cardiac complications. Nevertheless, one of the major limitations of this study was that the indication for coronary angiography was based on the presence of two or more intermediate or minor clinical predictors and/or a positive noninvasive stress test

Table 2. Summary of Studies About the Role of Percutaneous Coronary Intervention Before Noncardiac Surgery

Author; year of publication	No. of patients studied; Design	Inclusion/Exclusion criteria	Type of surgery	Type of revascularization	Outcome
Studies of percutaneous coronary intervention					
Allen et al.; 1991[17]	148; retrospective	i: PCI before vascular surgery	Major vascular	PCI	Lower perioperative cardiac mortality
Elmore et al.; 1993[18]	2452; retrospective	i: PCI before vascular surgery	Major vascular	PCI or CABG	Perioperative rate of myocardial infarction for patients with PCI is lower, higher rate of late events
Gottlieb et al.; 1998[19]	194; retrospective	i: PCI before vascular surgery e: history of CABG/ PCI, missing data	Major vascular	PCI	Low rate of perioperative cardiac events
Posner et al.; 1999[20]	2841; retrospective	i: PCI before surgery e: patients without an index admission ≥30 days	Noncardiac	PCI or no revascularization or normal	Reduced risk of cardiac events compared to no revascularization
Godet et al.; 2005[21]	1152; retrospective	i: consecutive, elective e: emergency, thoracoabdominal, patients with CABG	Abdominal aortic surgery	PCI or no revascularization	No significant reduction in cardiac risk or death
Coronary artery revascularization prophylaxis trial and substudies					
McFalls et al.; 2004[26]	510; prospective	See Table 4	Major vascular	CABG or PCI or medical therapy	No reduction in perioperative and long-term cardiac events
Ward et al.; 2006[27]	222; retrospective	Same as for the original study (see Table 4)	Major vascular	CABG or PCI or medical therapy	CABG associated with reduction in myocardial infarction and hospital stay than PCI
Raghunathan et al.; 2006[28]	307; retrospective	Same as for the original study (see Table 4)	Surgery for critical limb ischemia and intermittent claudication	CABG or PCI or medical therapy	Low perioperative and long-term mortality, no reduction by coronary revascularization

CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

Table 3. Summary of Studies About the Safety of Percutaneous Coronary Revascularization Before Noncardiac Surgery

Author; year of publication	No. of patients studied	Design	Type of surgery	Time elapsed from stenting	Complications
Kaluza et al.; 2000[22]	40	Retrospective	Noncardiac/ vascular	Average 13 days	18% MI; 28% bleeding episodes; 20% death; all deaths, MIs, 73% of bleeding episodes occurred in patients undergoing surgery within 14 days from stenting
Wilson et al.; 2003[23]	207	Retrospective	Noncardiac/ vascular	Within 6 weeks after 7 to 9 weeks	4% death or MI, all events occurred in patients undergoing surgery 6 weeks from stenting; no cardiac events thereafter
Reddy et al.; 2005[24]	56	Retrospective	Noncardiac/ vascular	Within 6 weeks versus after	14% MI, stent thrombosis, bleeding, death in patients undergoing surgery 6 weeks from stenting; no cardiac events thereafter
Schouten et al.; 2007[25]	192	Retrospective	Noncardiac/ vascular	Within 1 to 6 months versus later surgery	higher cardiac event rate in early surgery group compared to late-surgery group (13.3% versus 0.6%)

MI = myocardial infarction.

result, which altogether may have resulted in the selection of patients at lower risk for perioperative cardiac complications resulting in no observed beneficial effect of coronary revascularization. Moreover, for patients with left main coronary artery disease, aortic stenosis, or severe left ventricular dysfunction, the preoperative management, including indication for coronary angiography with subsequent revascularization, has yet to be elucidated.

Two separate studies' *post hoc* subgroup analyses of the CARP study were performed and issues such as superiority of CABG to percutaneous coronary intervention for prevention of perioperative complications were evaluated[27] as well as whether patients with intermittent claudication or those with critical limb ischemia had disparate perioperative and long-term outcomes.[28] Ward et al.[27] found that, although there was no difference in the incidence of mortality after

Table 4. Summary of Recent Studies About the Role of Coronary Revascularization Compared to Optimized Medical Therapy in Patients Undergoing Major Vascular Surgery

Characteristics	McFalls et al., 2004[26]	Landesberg et al., 2006[10]	Poldermans et al., 2007[29]
Total number of patients studied	5859	624	1880
No. of patients identified at high-risk	510 (8.7%)	154 (30.2%)	101 (5.4%)
No. of revascularized patients	258 (4.4%)	96 (15.4%)	49 (2.6%)
Study period, year	1997–2004	1990–2002	2000–2005
Type of surgery	Abdominal aortic, lower-extremity bypass	Abdominal aortic, lower-extremity bypass	Thoracoabdominal, abdominal aortic, and lower-extremity bypass
Cardiac symptoms	Stable, no symptoms	Stable, no symptoms	Stable, no symptoms
Risk according to the ACC/AHA guidelines	Minor/intermediate	Minor/intermediate	Minor/intermediate
Type of risk stratification	Eagle risk score, patients classified as low-, intermediate-, and high-risk	Long-term survival score (7 variables), patients classified as low-, intermediate-, and high-risk	Perioperative risk score (5 variables), patients classified as low-, intermediate-, and high-risk
Comparison group	Optimized medical therapy group	Nonrevascularized risk-adjusted patients	Optimized medical therapy group
Preoperative test	Thallium scanning	Thallium scanning	Dobutamine stress echo and thallium scanning
Criteria for coronary angiography	Risk factors and ischemia during testing	Risk factors and moderate-severe ischemia during testing	Risk factors and severe ischemia during testing
Median waiting time between CR and surgery	54 days	36 days	29 days after CABG, 31 days after PCI
Severity of coronary artery disease	91 (35.3%) three-vessel disease	18 (19%) left main, 55 (57%) three-vessel disease	4 (8%) left main, 33 (67%) three-vessel disease
No. of patients with poor left ventricular function/severe valve disease	Excluded	Not indicated	Excluded
Type of CR	141 PCI, 99 CABG	54 PCI, 42 CABG	32 PCI, 17 CABG
Median long-term follow-up, yrs [IQR]	2.7 [1.7–3.9]	5.4 [3.8–8.7]	Only 1-yr follow-up
Preoperative effects of CR	No reduction in postoperative death, myocardial infarction	No reduction in short-term, 6 months, 1 yr mortality	No reduction in 30-day mortality and cardiac events
Long-term effects of revascularization	No difference in long-term mortality	At 3 yr, and long-term intermediate risk patients had survival benefit	No difference in mortality and non-fatal myocardial infarction

ACC/AHA, American College of Cardiology/American Heart Association Guidelines for preoperative risk management before noncardiac surgery[1]; CABG, coronary artery bypass surgery; PCI, percutaneous coronary intervention; CR, coronary revascularization.

the vascular operation between patients who underwent CABG or percutaneous coronary intervention, the incidence of perioperative (6.6% vs. 16.8%, $P = 0.02$) and long-term myocardial infarctions (9.9% vs. 23.7%, $P = 0.009$) after vascular surgery was significantly lower in patients who had CABG compared with patients with percutaneous coronary intervention. In the same study, the investigators also found that, with more complete revascularization, the incidence of postoperative myocardial infarction decreased. Raghunathan et al.[28] found that patients with intermittent claudication had more perioperative myocardial infarctions compared with patients with critical limb ischemia. However, a similar perioperative mortality rate was observed and there were no differences in long-term incidence of myocardial infarctions and mortality. Similarly, as in the original CARP trial, coronary artery revascularization was not associated with a lower risk of perioperative or long-term mortality in either group.

In summary, the results of the CARP trial and the subsequent studies with subgroup analyses indicated that CABG surgery provided more complete revascularization than percutaneous coronary intervention; coronary revascularization before vascular surgery did not improve perioperative and long-term mortality rates,

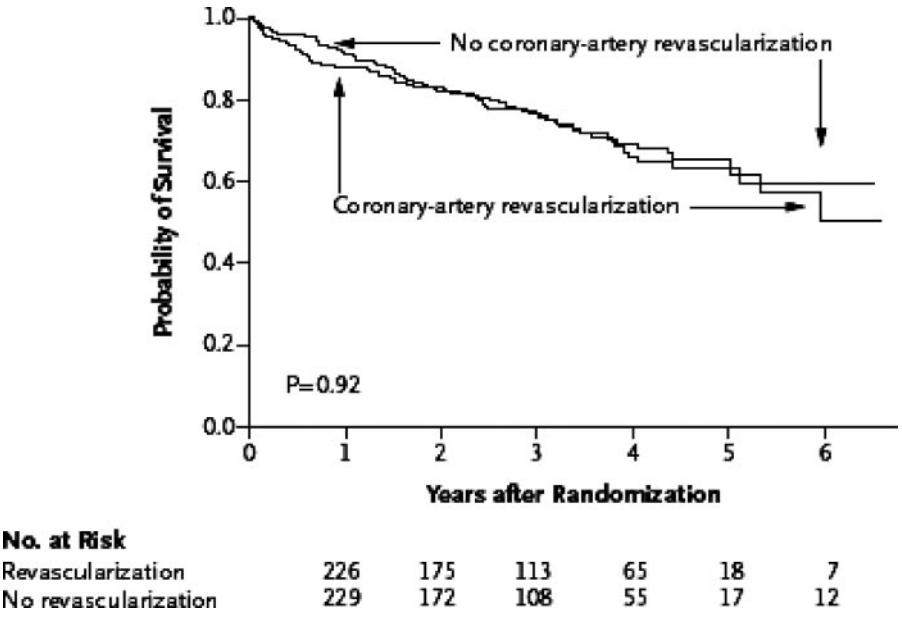

Figure 1. Kaplan–Meier long-term survival curves of patients assigned to undergo coronary artery revascularization or no coronary artery revascularization before elective major vascular surgery [Reproduced from Ref. 26, with permission from the publisher].

possibly because of the additive risk of cardiac and subsequent vascular procedures.

A Clinical Survival Score to Predict Benefit from Coronary Revascularization

In a retrospective observational study that included 502 consecutive patients undergoing major vascular surgery, Landesberg et al.[9] found that patients who had moderate-severe ischemia on preoperative thallium scanning and underwent subsequent coronary revascularization (by either CABG or percutaneous transluminal coronary angioplasty) had better long-term survival than patients with similar preoperative thallium scanning results who did not undergo revascularization. In a subsequent study, Landesberg et al.[10] studied the predictors that could define patients who are most likely to benefit from preoperative cardiac testing and coronary revascularization in a cohort of 624 patients who underwent elective major vascular surgery (Table 4). Patients were stratified into low, intermediate, and high cardiac risk according to the number from 0 to 7 of predictors of long-term survival as follows: age $>$ 65, diabetes mellitus, previous myocardial infarction, congestive heart failure, chronic renal failure, cerebrovascular disease, and ST-segment depression on resting electrocardiogram. Patients with moderate-severe ischemia on thallium scanning were referred to coronary angiography and possible revascularization with percutaneous coronary revascularization or CABG surgery. Coronary revascularization overall was independently associated with improved long-term survival but, in a subgroup analysis at 3 yr, long-term only patients at intermediate risk (two to three of the preoperative risk factors) had significantly better survival with coronary revascularization (Fig. 2).

The findings that coronary revascularization was associated with improved long-term outcome contrasts the results of the CARP trial, probably because only 33% of the enrolled patients in the CARP trial had triple-vessel disease and all patients with left main disease were excluded, compared with 73% with left main and or triple-vessel disease in this study. There are obvious limitations to this study such as its retrospective nature; the results were based on a single institution study without an external validation group; and there was the lack of optimized perioperative and long-term cardioprotective medication use, therefore no data were presented concerning whether optimized medical therapy could have been as protective as coronary revascularization in patients at intermediate risk.

The Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo-V Pilot Study

Poldermans et al.,[29] in a pilot study, investigated the role of preoperative coronary revascularization in high-risk patients undergoing major vascular surgery. Cardiac-stable, elective vascular patients were screened for risk factors, and those with three or more minor/intermediate risk factors underwent cardiac stress testing (Table 4). All patients who experienced extensive stress-induced myocardial ischemia were randomized either for revascularization or for optimized medical therapy. Optimized medical therapy consisted of aspirin, β-blocker, angiotenzin-converting enzyme inhibitor, and statin use. There was no significant difference in 30-day all-cause death or nonfatal myocardial infarction for patients with preoperative revascularization or medical therapy only. There was also no difference in the incidence of perioperative cardiac events in patients treated by CABG surgery or percutaneous coronary intervention. Moreover, there was no difference in the incidence of one-year all-cause mortality or nonfatal myocardial infarction between patients with preoperative revascularization or optimized medical treatment (Fig. 3).

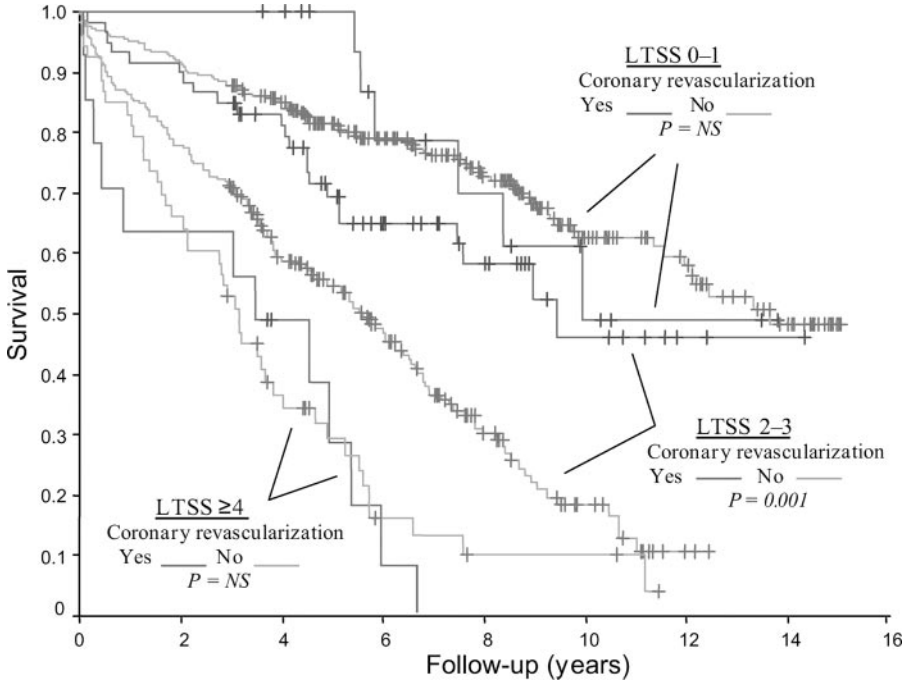

Figure 2. Kaplan–Meier long-term survival curves of patients with and without preoperative coronary artery revascularization in each one of the three groups: low-risk, intermediate-risk, high-risk. Only the intermediate-risk patients had significantly better long-term survival with preoperative coronary revascularization [Reproduced from Ref. 10, with permission from the publisher].

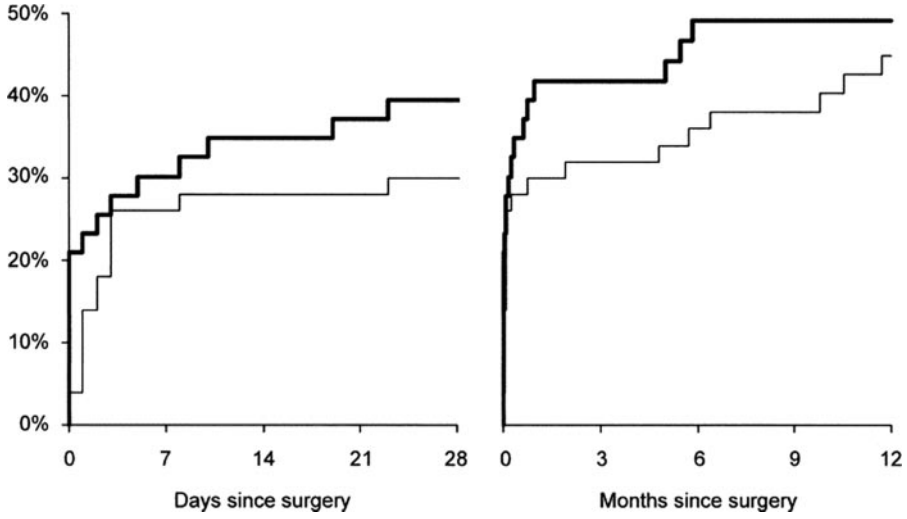

Figure 3. Incidence of all-cause death or myocardial infarction during 1-yr follow-up according to the allocated treatment strategy [Reproduced from Ref. 30, with permission from the publisher]. Light line: best medical treatment only; Dark line: best medical treatment and preoperative coronary revascularization.

The implications of this study compared to the CARP trial and the study of Landesberg et al. are that a previously validated risk score[30] was used for selection of high-risk patients and noninvasive stress testing for further risk stratification and identification of patients who were more likely to benefit from coronary revascularization. Although under-powered, this pilot study showed that optimized medical therapy alone in these high-risk patients was sufficiently effective for reduction of perioperative and one-year complications, highlighting the issue of whether cardiac-stable vascular surgery patients should be screened with additional stress testing. Nevertheless, the risk of perioperative and one-year event rate in patients with revascularization and in patients with medical therapy was still very high, stressing the importance for finding less invasive surgical methods for the treatment of abdominal aortic aneurysm and peripheral vascular disease.[31] Moreover, compared with the CARP trial, 43% of the patients had a reduced left ventricular function (left ventricular ejection fraction <35%) and the majority (67%) of patients had triple-vessel disease. There are also limitations to this pilot study: it was a multicenter study but no center effect was measured, different classifications were used to detect myocardial infarction after coronary revascularization and after vascular surgery, two different noninvasive testing modalities were used to select high-risk patients, patients with significant valve disease were excluded, and a shorter follow-up period was used as compared to the CARP trial and the study of Landesberg et al.

In their decision making about opting for coronary revascularization in addition to optimized medical therapy, clinicians could only rely on data from studies about the role and type of coronary revascularization in patients with stable coronary artery disease from nonoperative settings. The findings of these studies show that CABG surgery offers long-term survival benefit in

asymptomatic or mildly symptomatic patients and in patients with double or triple vessel disease.[32] Moreover, CABG surgery compared to percutaneous coronary intervention was associated with a reduced rate of angina pectoris, the need for repeat revascularization and 5-yr mortality in patients with chronic stable angina[33,34] or in patients with diabetes mellitus after 10-yr of follow-up.[35]

A current meta-analysis of 2950 patients in 11 trials also failed to show the benefit of percutaneous coronary intervention compared with medical therapy in patients with stable coronary artery disease.[36] Recently, the COURAGE trial research group also reported in a multicenter, randomized trial of 2287 cardiac-stable patients with multivessel coronary artery disease that percutaneous coronary intervention compared with optimized medical therapy did not reduce the risk of death, myocardial infarction, or other major cardiovascular events during an average observation period of 4.6 yr.[37] Although, the recent introduction of drug-eluting stents may offer additional benefit in the treatment of in-stent restenosis with a subsequent reduction in cardiac complications compared with bare metal stents. Their use was also shown to be less cost effective for treating patients with stable coronary artery disease.[38]

Additionally, there is still a lack of firm consensus in a perioperative scenario about the issue of delaying noncardiac surgery for the completion of antiplatelet therapy or, in case of drug-eluting stents, the lack of consensus about the timing of noncardiac surgery after stenting. It should also be noted that there is a higher rate of recurrent events in patients undergoing percutaneous coronary revascularization, which is almost always due to progressive disease rather than restenosis.[39] The likely reason for the lack of long-term beneficial effect of percutaneous coronary intervention compared with CABG surgery is that percutaneous coronary revascularization is for treatment of current culprit lesions, whereas CABG surgery may also bypass future culprit lesions.[40]

Finally, patients with concomitant peripheral artery disease and coronary artery disease who undergo coronary revascularization have reportedly increased periprocedural and long-term complications.[16,41] Several investigators have noted that the risk of any major complication (death, myocardial infarction, stroke, coma, or emergency revascularization) after CABG surgery,[16] and after percutaneous coronary intervention[16,41] was substantially higher for patients with peripheral artery disease than those without, probably because these patients have more systemic atherosclerotic burden, which culminates in cardiovascular and cerebrovascular complications. Furthermore, patients with peripheral artery disease undergoing percutaneous coronary intervention are also more likely to develop vascular complications, such as retroperitoneal hemorrhage, femoral hematoma, critical limb ischemia, and requirement for blood transfusion.[42]

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