The efficacy of coronary artery bypass grafting (CABG) is well established in patients with coronary artery disease (CAD) (1–6). However, patients undergoing CABG are still at risk for unstable angina, myocardial infarction (MI), and death through the progression of native coronary artery atherosclerosis as well as the occlusion of bypass grafts (7–10). In the post-CABG patient, secondary prevention includes the use of appropriate medical therapy to prevent the occurrence of clinical events. Numerous randomized clinical trials (RCTs) and observational studies have been published on the efficacy of cardiac medical therapy for patients with known CAD who have specific cardiovascular comorbidities (11–26). For example, patients with CAD benefit from antiplatelet and antilipid agents (11–15), whereas patients with depressed left ventricular ejection fraction (LVEF) and diabetes benefit from angiotensin-converting enzyme (ACE) inhibitors. Both aspirin and antilipid agents were found to reduce the progression of atherosclerosis and the occurrence of graft occlusion. Cardiovascular events were decreased with antilipid agents. In small trials, beta-blockers and CCBs failed to decrease the incidence of cardiovascular events. No RCTs examined nitrates, and one small RCT documented a reduction in cardiovascular events among patients treated with ACE inhibitors. We conclude that few RCTs have examined the efficacy of cardiac medical therapy in post-CABG patients. Based on current RCT evidence, aspirin and antilipid agents should be used routinely after CABG. However, current data do not support the use of beta-blockers, CCBs, and nitrates, and more evidence is needed regarding the use of ACE inhibitors. (J Am Coll Cardiol 2005;45:177–84) © 2005 by the American College of Cardiology Foundation

The purpose of this paper is to review the randomized controlled trial (RCT) data investigating cardiac medical therapy for patients after coronary artery bypass grafting (CABG). We identified RCTs with ≥100 enrolled patients that examined the impact of cardiac medical therapy on outcomes ≥1 year after CABG. The MEDLINE database was searched for trials conducted between 1966 and 2004 on the following medications: aspirin, antilipid agents, beta-blockers, calcium channel blockers (CCBs), nitrates, and angiotensin-converting enzyme (ACE) inhibitors. Both aspirin and antilipid agents were found to reduce the progression of atherosclerosis and the occurrence of graft occlusion. Cardiovascular events were decreased with antilipid agents. In small trials, beta-blockers and CCBs failed to decrease the incidence of cardiovascular events. No RCTs examined nitrates, and one small RCT documented a reduction in cardiovascular events among patients treated with ACE inhibitors. We conclude that few RCTs have examined the efficacy of cardiac medical therapy in post-CABG patients. Based on current RCT evidence, aspirin and antilipid agents should be used routinely after CABG. However, current data do not support the use of beta-blockers, CCBs, and nitrates, and more evidence is needed regarding the use of ACE inhibitors. (J Am Coll Cardiol 2005;45:177–84) © 2005 by the American College of Cardiology Foundation

**METHODS**

**Study selection.** We identified RCTs that examined the effects of cardiac medications after CABG conducted between the years 1966 and 2004 and published in the English language. The MEDLINE database was searched for RCTs involving the use of the following medications: aspirin, antilipid agents (specifically using the terms antilipemic and anticholesteremic agents including hydroxymethylglutaryl-CoA reductase inhibitors), beta-blockers, CCBs, nitrates, and ACE inhibitors. We also used “coronary artery bypass graft surgery” as a key term, and limited our search to RCTs and their follow-up studies. Lastly, we reviewed references from these articles for pertinent studies not previously found through the MEDLINE database search.

**Inclusion and exclusion criteria.** Placebo-controlled RCTs that tested the efficacy of the aforementioned cardiac medications were included. We included trials that examined the impact of medical therapy on cardiovascular out-
comes including unstable and stable angina, MI, cardiovascular death, and overall mortality as well as native coronary artery and bypass graft occlusion and the need for further revascularization by percutaneous coronary intervention (PCI) or repeat CABG. Trials that investigated the role of beta-blockers or CCBs on atrial fibrillation were not included, nor were trials that investigated the role of nitrates or CCBs on vasospasm. Only trials that examined native coronary artery and bypass graft occlusion by angiography were included. Trials with mixed outcomes of graft occlusion and cardiovascular events were also included.

We excluded all trials that randomized <100 patients. This was done in order to exclude studies conducted with limited power and studies with limited enrollment where the quality of the methodology used may have been questionable and was difficult to assess. We also excluded all trials that examined outcomes <1 year after CABG. This was done for two reasons: first, we were interested in the effects of medications on long-term secondary prevention; and, second, we wanted to exclude all trials that studied events that could be a result of the operation itself. Therefore, we did not review the effect of cardiac medical therapy on early graft patency, although some authors reported both early and late graft patency (≥1 year). Moreover, we excluded all trials that tested the use of cardiac medications before CABG or peroperatively unless the use of the medication continued after hospital discharge. Trials that specifically examined the use of cardiac medications in another subset of cardiac patients, such as post-MI or post-PCI, despite a large majority of these patients having prior CABG, were also excluded. This was done because the study population did not include all patients with previous CABG, and the time since CABG was frequently not reported. Observational studies or in vitro studies were, likewise, not included in this review.

**MEDICAL THERAPY AMONG CAD PATIENTS AND PATIENTS WITH OTHER COMORBIDITIES**

The focus of this paper is to specifically review RCTs of cardiac medical therapy in the post-CABG patient. However, our review would not be complete without the mention of the substantial evidence that exists on the efficacy of these medications among patients with CAD and patients who have other comorbid conditions. The latter often make up a large proportion of patients who undergo CABG, and many of the studies in this section have patient populations that included patients who underwent CABG.

Numerous RCTs have shown aspirin to be beneficial in reducing the risk of adverse cardiovascular events such as MI and death in a wide range of patients. The use of aspirin has been found to significantly decrease the incidence of both nonfatal MI and nonfatal stroke among patients with CAD and among patients with various comorbidities including: atrial fibrillation, prior MI, peripheral vascular disease, post-PCI, and unstable angina (24). Antilipid agents have been found to be efficacious for plaque stabilization in native arteries, and in preventing MI and cardiac death among patients with CAD (12–15).

Beta-blockers have both anti-ischemic and antihypertensive properties. These agents have been found to be of benefit in the prevention of recurrent MI and death among patients with a history of MI as well as post-MI subgroups such as the diabetic elderly (16,17). An improvement in survival has also been found with the use of beta-blockers in patients with congestive heart failure (CHF) (18,19). Both CCBs and nitrates have been found to be beneficial in treating angina among patients with unstable and stable angina who have contraindications to beta-blockers (20). Nitrates have been found to be especially useful among patients with angina who also have left ventricular dysfunction (20). However, because beta-blockers have also been found to reduce mortality in MI patients, beta-blockers are often used as the first-line agents for the treatment of angina. Lastly, both beta-blockers and CCBs are also used in treating hypertension. The ACE inhibitors have been shown to be of benefit in post-MI patients and patients with CHF, diabetes, depressed left ventricular function, and hypertension (21–23). Risk reduction in the composite end point of MI, stroke, or death has also been demonstrated among patients receiving ACE inhibitors with diabetes, peripheral vascular disease, or a history of CAD without heart failure or left ventricular dysfunction (22).

**RCTs OF MEDICAL THERAPY IN THE POST-CABG PATIENT**

A total of 14 RCTs were found that examined the efficacy of aspirin, antilipid agents, beta-blockers, CCBs, nitrates, and ACE inhibitors specifically among patients after CABG.

**ASPIRIN**

We found 8 RCTs involving more than 2,500 patients that studied the use of aspirin after CABG (Table 1) (26–33). The number of patients randomized in these trials ranged from 147 to 772 patients, and dosages used in these studies...
Table 1. Randomized Controlled Trials of Aspirin Use in Post-CABG Patients

<table>
<thead>
<tr>
<th>Author, Year (Ref.)</th>
<th>Number Randomized</th>
<th>Medication and Dose</th>
<th>Treatment Onset (No. Days Pre- or Post-Op)</th>
<th>Follow-Up Time (Months)</th>
<th>% With Follow-Up Angiography</th>
<th>% With Angiography Events</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldman et al., 1989 (26)</td>
<td>772</td>
<td>Aspirin 325 mg qd-tid + 75 mg dipyridamole tid*</td>
<td>-1#</td>
<td>12‡</td>
<td>65§</td>
<td>105/299 (35)</td>
<td>47/107 (44)</td>
</tr>
<tr>
<td>Chesebro et al., 1984 (27)</td>
<td>407</td>
<td>Aspirin 325 mg qd + dipyridamole 75 mg tid</td>
<td>0#</td>
<td>12‡</td>
<td>84</td>
<td>12/171 (7)</td>
<td>30/172 (17)</td>
</tr>
<tr>
<td>Goldman et al., 1994 (28)†</td>
<td>334</td>
<td>Aspirin 325 mg qd</td>
<td>365</td>
<td>36</td>
<td>86</td>
<td>(31.4)†</td>
<td>(37.8)†</td>
</tr>
<tr>
<td>Brooks et al., 1985 (29)</td>
<td>320</td>
<td>Aspirin 320 mg + dipyridamole 75 mg tid</td>
<td>2–3#</td>
<td>12</td>
<td></td>
<td></td>
<td>83</td>
</tr>
<tr>
<td>Gavaghan et al., 1991 (30)</td>
<td>237</td>
<td>Aspirin 324 mg qd</td>
<td>0</td>
<td>12‡</td>
<td>92</td>
<td>14/119 (12)</td>
<td>30/100 (30)</td>
</tr>
<tr>
<td>McEnany et al., 1982 (31)</td>
<td>216</td>
<td>Aspirin 600 mg bid</td>
<td>3–4</td>
<td>21.5</td>
<td></td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>Sharma et al., 1983 (32)</td>
<td>176</td>
<td>Aspirin 325 mg tid</td>
<td>3–5</td>
<td>12</td>
<td>81</td>
<td>22/50** (44)</td>
<td>20/44** (46)</td>
</tr>
<tr>
<td>Brown et al., 1985 (33)</td>
<td>147</td>
<td>Aspirin 325 mg tid</td>
<td>2–3</td>
<td>12</td>
<td>86</td>
<td>10/38** (26)</td>
<td>18/44** (41)</td>
</tr>
</tbody>
</table>

Angiographic end point: number of patients with one or more grafts occluded at follow-up angiography

Clinical end point: mean number of patients with MI at follow-up

---

*In this study, patients were randomized to either of four treatment arms (aspirin 325 mg qd, aspirin 325 mg tid, aspirin 325 mg tid + dipyridamole 75 mg tid, sulfinpyrazone 267 mg tid) versus placebo. All aspirin groups have been combined, and the results for the sulfinpyrazone treatment arm were not included. †In this study, the breakdown of patients in each treatment group was not reported and cannot be inferred. ‡Follow-up time occurred at a median of 12 months. §In this study, the breakdown of patients receiving follow-up angiography was not reported, therefore, this percentage includes patients in the sulfinpyrazone treatment arm. ||Follow-up time was reported as a mean. ¶The p value was not explicitly stated in these studies but was reported as nonsignificant. #In these studies, dipyridamole was administered with aspirin. **In these studies, the denominator of both treatment groups do not add up to the total number with follow-up angiography because there were multiple treatment arms, and only aspirin vs. placebo are reported here. Other treatment arms included aspirin and dipyridamole or warfarin.

bid = two times daily; CABG = coronary artery bypass grafting; MI = myocardial infarction; qd = daily; tid = three times daily.
ranged from 325 to 1,200 mg daily. Two of the eight trials that examined the effect of aspirin on graft occlusion found aspirin to be beneficial when administered within one day after CABG (27,30). In contrast, six of the eight trials found graft occlusion to be similar between patients receiving aspirin when compared with patients receiving placebo (26,28,29,31–33). Four of the latter initiated aspirin between 2 and 5 days after CABG (29,31–33), one initiated aspirin before CABG (26), and one initiated aspirin at 12 months after CABG (28). Follow-up times varied between one and three years.

Two of the eight trials also studied the effect of aspirin on cardiovascular events (Table 1). Neither of these studies found a significant improvement in the incidence of angina, MI, or death among patients treated with aspirin (26,28). In the first of the Goldman et al. (26) studies, aspirin was administered before CABG, and patients were followed for 12 months. In the second Goldman et al. (28) study, aspirin was administered at one year after CABG, and patients were followed for two years.

Several of the trials had study methodologies that differed greatly from each other. All the trials reported both number of bypass grafts and number of patients as their units of analysis. However, the efficacy of aspirin sometimes differed depending on which unit of analysis was used (26,33). In the first of the Goldman et al. (26) studies, aspirin was found to be beneficial on graft occlusion when the number of bypass grafts was reported as the unit of analysis instead of the number of patients (26). At one year, rates of graft occlusion were reduced from 22.6% to 15.8% (p = 0.029) when various aspirin treatment arms were combined and compared with placebo. Similarly, Brown et al. (33) also found reduced graft occlusion among patients treated with aspirin versus patients receiving placebo when grafts were analyzed as the unit of analysis (odds ratio = 0.47, p = 0.04).

Treatment arms also varied between studies. For example, six of the eight trials either had more than two treatment arms (26,31–33) or combined aspirin with dipyridamole or warfarin (26,27,29). As we were only interested in comparisons of aspirin with placebo, other treatment arms were not included in our analysis unless aspirin had been combined with these medications, and separate results were not available (26,27,29). Goldman et al. (26) found similar rates of graft occlusion in all three different treatment arms (325 mg daily, 325 mg three times daily, and 325 mg of aspirin with 75 mg of dipyridamole three times daily) and, hence, combined the results of all three groups into one. In another study, Goldman et al. (28) randomized patients at one year after CABG to continued treatment with aspirin or placebo for an additional two years.

Several of these studies had a significant proportion of patients excluded from the final analyses due to a smaller proportion receiving angiography at follow-up (Table 1). The percent of patients with follow-up angiography ranged from 50% to 92%. Reasons cited by authors were patient refusal, loss to follow-up, death, intolerance or discontinuation of medications, occlusion of grafts early in the study, and medical complications such as psychiatric problems. All authors reported there to be no baseline differences between patients undergoing and not undergoing follow-up angiography. Thus, this suggested that that patients excluded from final analyses did not represent a potential source of bias in the results of these studies. However, it is difficult to infer the generalizability of these results to the larger population of CABG patients without the use of intention-to-treat analyses. It is also possible that the exclusion of patients decreased the power to demonstrate a treatment effect.

In summary, despite the relatively small patient populations included in these studies and the lack of complete angiographic follow-up, current evidence suggests that aspirin may be beneficial in reducing graft occlusion at 12 months after CABG when administered within 1 day after CABG. Evidence is lacking, however, to support the benefit of aspirin in reducing the incidence of cardiovascular events at ≥1 year after CABG. Importantly, aspirin is inexpensive, is associated with few side effects, and is known to be beneficial for patients with CAD (24). Therefore, aspirin should be started immediately after CABG and be continued indefinitely unless contraindications exist.

### ANTILIPID AGENTS

Three RCTs involving over 1,900 patients examined the effect of antilipid agents on graft occlusion and the risk of cardiovascular events (as secondary end points) after CABG: the Post-CABG trial, the Lopid Coronary Angiography Trial (LOCAT), and the Cholesterol Lowering Atherosclerotic Study (CLAS) (34–39) (Table 2). All three RCTs found a significant reduction in the progression of atherosclerosis in bypass grafts. The LOCAT and CLAS trials also reported a significant reduction in the progression of native artery disease (36,37). The Post-CABG and CLAS trials reported long-term follow-up results (35,38,39). Antilipid agents were found to only provide benefit at decreasing the risk of cardiovascular events at ≥7 years after CABG, as demonstrated in the CLAS trial (39). The trials differed in terms of study population, time of treatment initiation, and type and dose of antilipid agent used.

The Post-CABG trial randomized 1,351 patients with prior CABG between 1 and 11 years before randomization to aggressive versus moderate lipid-lowering treatment with lovastatin for an average of 4.3 years (34). Aggressive treatment was 40 mg/day, and moderate treatment was 2.5 mg/day. Doses were doubled if target low-density lipoprotein cholesterol levels of 85 mg/dl in the aggressive treatment group and 140 mg/dl in the moderate treatment group were not reached with the initial doses. In addition, 8 g/day of cholestyramine was added to the treatment regimen if a patient's low-density lipoprotein
level remained above 95 mg/dl and 160 mg/dl in the aggressive and moderate treatment groups, respectively, after two consecutive visits. Of the 1,351 patients randomized in this study, 1,192 or 88% had follow-up angiography. A significantly lower number of patients treated with aggressive antilipid therapy were found to have progression of graft atherosclerosis, new graft lesions, and new graft occlusions at four years. A total of 27% of patients treated with aggressive lipid-lowering treatment were found to have a ≥0.6 mm decrease in lumen diameter when compared with 39% of patients who received less aggressive treatment (p < 0.0001). The composite end point of need for revascularization, MI, stroke, and cardiac death was significantly lower among patients treated aggressively at 7.5-year follow-up but not at 4 years’ follow-up (35).

The LOCAT study randomized 395 men with low high-density lipoprotein at a mean of 22 to 23 months after CABG to 1,200 mg daily of gemfibrozil versus placebo for a mean of 2.7 years (Table 2) (36). Patients with diabetes and low LVEF, two important subgroups of CABG patients, were excluded from the trial. Of the 395 patients randomized in this study, 372 (94%) completed follow-up angiography. Antilipid treatment was found to significantly reduce the number of new lesions in saphenous vein grafts (2.4% in antilipid group vs. 14.3% in placebo group, p < 0.001). The primary end point of change in mean diameter of native arteries was also found to be significantly lower among patients treated with antilipid agents (0.01 ± 0.10 mm in antilipid group vs. 0.04 ± 0.11 mm in placebo group, p = 0.009). The composite end point of repeat revascularization, MI, or death was not significantly different between treatment groups.

The CLAS trial randomized 188 nonsmoking men who underwent CABG at least three months before enrollment to 30 g of colestipol and 3 to 12 g of niacin daily versus placebo (Table 2) (37). Of the 188 patients randomized in this study, 162 (86%) completed follow-up angiography. After treatment with these antilipid agents for two years, the investigators found that the number of subjects with new lesions in both native vessels and grafts was significantly lower among patients treated with antilipid agents than those with placebo. A total of 10% of patients treated with antilipid agents were found to have new lesions within the native vessels compared with 22% of patients treated with placebo (p = 0.03). Likewise, 18% of treated patients had new lesions in bypass grafts compared with 30% of patients treated with placebo (p = 0.04). Cardiac death, MI, and angina were not significantly different between treatment groups at two or four years after CABG (37,38). However, by seven years after CABG, the composite end point of repeat revascularization, MI, or cardiac death was significantly lower among patients treated with antilipid agents (40% vs. 61%, respectively, p = 0.02) (39).

In summary, long-term treatment with antilipid agents in post-CABG patients prevents progression of both native coronary artery and graft atherosclerosis as well as subsequent cardiovascular events. Although the primary end point of these studies was the progression of atherosclerosis, the use of antilipid agents was found to decrease the progression of atherosclerosis as early as two years after CABG. As past research has also demonstrated a benefit of antilipid agents in reducing the progression of atherosclerosis of native arteries among CAD patients without a history of CABG, the routine use of antilipid agents in post-CABG patients appears to be well justified. As none of these studies started treatment onset at the time of surgery and only one of the three trials examined a statin drug, more research is needed to clarify both the time that treatment should be initiated and the types of antilipid agents that might prove beneficial after CABG.

### Table 2. Randomized Controlled Trials of Antilipid Agents in Post-CABG Patients

<table>
<thead>
<tr>
<th>Author, Year (Ref.)</th>
<th>n</th>
<th>Medication and Dose</th>
<th>Treatment Onset (No. Months Post-Op)</th>
<th>Follow-Up (ys)</th>
<th>End Points*</th>
<th>Antilipid Agent† (%)</th>
<th>Control† (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-CABG, 1997 (34)</td>
<td>1,351</td>
<td>Lovastatin‡ 40 mg qd</td>
<td>12–132</td>
<td>4.3</td>
<td>Composite end point‡</td>
<td>85/676 (13)</td>
<td>103/675 (15)</td>
<td>0.12</td>
</tr>
<tr>
<td>Follow-up, 2000 (35)</td>
<td>1,351</td>
<td></td>
<td></td>
<td>7.5</td>
<td>Composite end point‡</td>
<td>207/676 (31)</td>
<td>271/675 (40)</td>
<td>0.001</td>
</tr>
<tr>
<td>Frick et al. (LOCAT), 1997 (36)</td>
<td>395</td>
<td>Gemfibrozil 1,200 mg qd</td>
<td>22–23 ± 13</td>
<td>2.7</td>
<td>Composite end point¶</td>
<td>7/197 (4)</td>
<td>7/198 (4)</td>
<td>&gt;0.05#</td>
</tr>
<tr>
<td>Blankenhorn et al. (CLAS), 1987 (37)</td>
<td>188</td>
<td>Colestipol 30 g qd/niacin 3–12 g qd</td>
<td>3</td>
<td>2</td>
<td>Cardiac death</td>
<td>0/94 (0)</td>
<td>1/94 (1)</td>
<td>&gt;0.05#</td>
</tr>
<tr>
<td>Follow-up, 1990 (38)</td>
<td>103</td>
<td></td>
<td></td>
<td></td>
<td>MI</td>
<td>1/94 (1)</td>
<td>4/94 (4)</td>
<td>&gt;0.05#</td>
</tr>
<tr>
<td>Follow-up, 1996 (39)</td>
<td>162</td>
<td></td>
<td></td>
<td>7</td>
<td>Composite end point**</td>
<td>32/80 (40)</td>
<td>50/82 (61)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

*The clinical end points reported here were not the primary end points of these studies (please see text for more details). †For most studies, the numbers of events were reported as percentages rather than absolute numbers. The numbers reported here have been derived from the percentages given and the initial number of patients cited. ‡In this study, the control group received treatment of 2.5 mg per day of lovastatin versus 40 mg per day in the treatment group with doses doubled in order to reach target levels and colestipol added in certain cases (see text). §Composite end point: death, MI, stroke, CABG, or percutaneous coronary intervention (PCI). ¶Mean follow-up time. ‖Composite end point: cardiac death, MI, CABG, or PCI. #p value not explicitly stated in these studies but was reported as nonsignificant.* **Composite end point: cardiac death, MI, CABG, or PCI. n = number of patients randomized and included in the analyses for clinical end points (please see text for numbers of patients with follow-up angiography); other abbreviations as in Table 1.
BETA-BLOCKERS

Only one RCT examined the effect of beta-blockers after CABG (Table 3). Sjoland et al. (40) conducted a double-blind placebo-controlled RCT of 967 patients undergoing CABG (Table 3). Patients were randomized 4 to 21 days after CABG to 50 mg of metoprolol twice a day for two weeks and 100 mg of metoprolol twice a day thereafter versus placebo for two years. There was no difference between the two arms of the trial with respect to improvement in exercise capacity among the 618 patients who received an exercise test at follow-up. However, patients treated with placebo were found to have a higher (worse) chest pain score when compared with patients treated with metoprolol (Table 3). In another analysis of the total number of patients randomized, none of the end points of repeat revascularization, unstable angina, nonfatal MI, or death were found to be significantly different between the two groups at two-year follow-up (41).

In summary, although the use of beta-blockers is indicated among CAD patients with a history of MI and CHF, only one RCT has examined the use of beta-blockers in a general post-CABG population. There is, therefore, little evidence to suggest that beta-blockers should be used routinely after CABG.

CCBs AND NITRATES

Only one RCT examined the effect of CCBs after CABG (Table 3) (42), while no RCTs examined the effect of nitrates. Gaudino et al. (42) evaluated the benefits of CCBs beyond the first year after CABG on radial artery graft patency. A total of 120 patients with normal perfusion of the radial artery were randomized after one year of treatment with 120 mg daily of oral diltiazem to either continued or suspended treatment. There were no significant differences at four-year follow-up between the CCB group and the group whose treatment was discontinued with respect to recurrence of angina (10% vs. 12%, respectively, p = 0.85), residual ischemia (by scintigraphy; 17% vs. 18%, p = 0.82), and cardiac death (2% vs. 0%, p = 0.96).

In summary, there is little evidence to support the routine use of CCBs or nitrates after CABG. Although short-term use of CCBs may be useful in patients with radial artery grafts, long-term RCT data for CCBs is limited and is absent for the use of nitrates.

ACE INHIBITORS

Only one RCT involving 149 patients specifically evaluated the benefit of ACE inhibitors after CABG: the Quinapril on Clinical Outcome After Coronary Artery Bypass Grafting (QUO VADIS) study (Table 3) (43). The primary objective of the QUO VADIS study was to evaluate the efficacy of quinapril (40 mg daily) on the change in total exercise endurance at one year. Patients underwent exercise testing both before CABG and at one year after CABG, as...
well as Holter monitoring for 48 h at one year. Quinapril was started one month before CABG and was continued for one year. The treatment had no effect on the primary end point of change in total exercise endurance or the incidence of ischemia on Holter. However, 3.5% of patients receiving quinapril experienced ischemic events such as angina, death, MI, repeat revascularization, stroke, or transient ischemic attacks versus 15% of patients receiving placebo (p = 0.02).

In summary, only one RCT examined the use of ACE inhibitors after CABG. Although evidence from this RCT suggests a beneficial effect of treatment on clinical events at one year, more trials with larger numbers of patients and longer follow-up periods are needed before the routine use of ACE inhibitors after CABG can be recommended.

**Study limitations.** Several potential limitations of our review should be noted. First, as we were interested in the effect of aspirin after CABG, we excluded studies that examined the efficacy of aspirin compared with other anticoagulants or other antiplatelet agents. Therefore, it is possible that other agents such as clopidogrel might provide an added benefit after CABG. Second, most studies that examined the efficacy of aspirin were conducted in the 1980s and only involved saphenous vein grafts. These studies provided little data on arterial grafts. Third, several methodological issues were evident in our review of the literature. For example, the time that treatment was initiated varied substantially between patients enrolled in the various RCTs, making it difficult to draw conclusions as to when treatment with these agents should be started. Agents used, dosages, and study populations also differed between studies. In some RCTs, large numbers of patients were withdrawn from blind treatment because patients in the control group were receiving open-label non-placebo. Many patients also did not complete follow-up angiography. Thus, analyses reported in published reports sometimes presented results for a much smaller group of patients compared with the initial study population. Finally, most patients have a good prognosis for the first several years after CABG. Therefore, studies with small numbers of patients have low power to detect differences in clinical events early after CABG. The fact that most of the RCTs available for review had small numbers of patients and short follow-up times is a major limitation that restricts our ability to make recommendations.

**Conclusions.** Cardiac medical therapy may play a pivotal role in the prevention of angina, MI, repeat revascularization, and death in the post-CABG patient. However, in our review of the literature, very few RCTs were found that specifically examined the efficacy of cardiac medical therapy after CABG. The use of aspirin and antilipid agents seems warranted from the literature. It remains uncertain, however, how long treatment with either of these medications should be continued after CABG, what are the appropriate doses, which antilipid agents should be used, and when treatment with antilipid agents should be initiated. More trials are needed to support the routine use of ACE inhibitors after CABG, and little evidence is available to support the use of beta-blockers, CCBs, and nitrates after CABG. The results of this review point to an urgent need for additional studies investigating cardiac medical therapy in the post-CABG patient.

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