Saphenous Vein Graft Patency 1 Year After Coronary Artery Bypass Surgery and Effects of Antiplatelet Therapy

Results of a Veterans Administration Cooperative Study*

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To determine whether antiplatelet therapies improve saphenous vein graft patency after coronary artery bypass grafting, we compared 1) aspirin (325 mg once daily), 2) aspirin (325 mg three times daily), 3) aspirin and dipyridamole (325 mg and 75 mg, respectively, three times daily), 4) sulfinpyrazone (267 mg three times daily), and 5) placebo (three times daily). Therapy with dipyridamole and sulfinpyrazone was started 48 hours before bypass graft surgery, and aspirin treatment was begun 12 hours before surgery as a single 325-mg dose. Postoperative treatment was started 6 hours after surgery and continued for 1 year. Graft patency data were obtained early (median, 9 days) and late (median, 367 days) after surgery. The early graft occlusion rate was decreased with all aspirin treatment regimens compared with that of the placebo regimen. At 1 year, in 406 patients with 1,315 grafts, the graft occlusion rate in all of the aspirin groups combined was 15.8% compared with 22.6% for the placebo group (p=0.029). The patients taking aspirin once daily had a lower occlusion rate (13.2%) compared with the patients receiving placebo (p=0.050). At 1 year, in the vein grafts placed to vessels less than or equal to 2.0 mm in diameter (804 distal sites), the graft occlusion rate in all of the aspirin groups was 20.1% compared with 32.3% for the placebo group (p=0.008). In the vein grafts placed to vessels greater than 2.0 mm in diameter (511 distal sites), there was no difference in the occlusion rates between aspirin and the placebo group at 1 year (8.7% vs. 9.0%, p=0.918). For all grafts shown to be patent in the early study (353 patients with 1,043 grafts), there was no difference in occlusion rates at 1 year when aspirin groups were compared with the placebo group (8.2% vs. 9.4%, p=0.763). Thus, graft patency is improved at 1 year after bypass graft surgery by aspirin, and the major benefit occurred in vein grafts placed to smaller vessels. Our data indicate that if a vein graft is patent early after coronary artery bypass graft surgery, aspirin might not improve the chance that the vein graft will remain open at 1 year. (Circulation 1989;80:1190–1197)

The long-term success of coronary artery bypass surgery is dependent on the graft patency after operation. Although the size and quality of the distal vessel, with its resultant runoff, are the most important predictors of postoperative graft patency, some antiplatelet therapies improve graft patency.1–4 With one notable exception,3,4 investigations of antiplatelet agents on

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graft patency have been performed using only a single follow-up angiogram. Although these data have been useful, they have not provided a temporal understanding regarding the pathogenesis of saphenous vein graft occlusion.

The objective of this prospective, centrally directed, randomized, double-blind, placebo-controlled trial was to compare relative graft patencies for placebo and four different antiplatelet regimens initiated before coronary artery bypass surgery and continued for 1 year. The treatment regimens included 1) aspirin 325 mg daily, 2) aspirin 325 mg three times daily, 3) aspirin and dipyridamole 325 mg and 75 mg, respectively, as a combination three times daily, 4) sulfipyrazone 267 mg three times daily, and 5) placebo. The study was designed to compare the effects of these therapies on both early and late vein graft patency. The size of the distal vessel was measured prospectively. Previously, we reported that within 60 days (median, 9 days) after surgery, saphenous vein graft patency was improved by three different aspirin treatment regimens, independent of vessel size, with the greatest benefit occurring in the smaller vessels. The purpose of this communication is to report the effects of these antiplatelet therapies on vein graft patency 1 year after surgery.

Methods

**Study Population**

This trial, organized by the Cooperative Studies Program of the Veterans Administration Medical Research Service, studied male patients undergoing elective coronary artery bypass surgery at 12 participating hospitals from June 1983 to July 1986. The exclusion criteria, definition of the study population, and stratification techniques have been outlined.

**Treatment Regimens**

The treatment regimens previously described were started 48 hours before surgery except for aspirin. When aspirin was one of the active treatment regimens, 325 mg was administered as a single dose 12 hours before operation. Thereafter, aspirin dosing was carried out according to the assigned regimen. The patients were given their first dose of postoperative medication 6 hours after surgery through a nasogastric tube, which was then clamped for 1½ hours. Therapy was continued by nasogastric tube every 8 hours until regular oral administration could be substituted. The dipyridamole and matching placebo were provided by Boehringer Ingelheim Pharmaceuticals, Ridgefield, Connecticut. The sulfipyrazone and matching placebo were supplied by Ciba Pharmaceutical, Summit, New Jersey, and the aspirin and matching placebo were provided by Glenbrook Laboratories, New York, New York. Disalcid (salsalate) was supplied by Riker Laboratories, St. Paul, Minnesota.

All medication was provided in individualized patient kits, each containing a 12-month supply of blistercards. The initial card was designed to accommodate the perioperative dosing schedule, and all cards were identical with this exception. Compliance, which included pill counts and the measurements of urine salicylates, was assessed as noted previously. All patients were seen at 3-month intervals by both their physicians and data coordinators.

**Surgery**

Saphenous vein coronary artery bypass grafting was performed by the usual protocol for each of the study institutions. Although no attempt was made to establish a uniform technique for performing coronary artery bypass surgery, those institutions chosen to participate in the study were selected on the basis of experience and expertise as documented by yearly statistics compiled by the Veterans Administration Central Office. Detailed data forms covering technical aspects of the perfusion, cardiopulmonary solutions, time of operation, arrest period, technical considerations regarding vessel and graft size, cardiac function, postoperative support, and bleeding were maintained for each patient.

**Angiographic Analysis**

The angiographic analysis of the results from the early angiograms has been reported. For the late postoperative angiogram, each aortic anastomosis was selectively engaged and injected. When the origin of a graft was not visualized, an aortic root angiogram was performed. The native coronary arteries were injected, and a left ventriculogram in the right anterior oblique projection was obtained. All angiograms were read at both the participating institution and at the central angiographic laboratory. The data from the central angiographic laboratory were used for this report. In the central angiographic laboratory, each angiogram was read independently by two cardiovascular radiologists without knowledge of the patients' assigned treatment regimen. The analysis was performed with a system that was developed for this study, including a Vanguard projector and a high-resolution television camera to record the images. The images were digitized, and the information was entered into an integrated image processor-computer system. Images were then redisplayed on the integrated memory plane, absolute measurements were obtained, and stenoses were calculated for all vessels 1 mm or greater in diameter. The number, type, and size of all grafts were recorded using an interactive computer program. Images of the cineframes, with the measurements superimposed, were then filmed for storage in hard copy format. The preoperative, 1-week and 1-year postoperative angiograms were analyzed in the same manner.

The size of the distal vessel was analyzed prospectively by measuring the lumen of the vessel from the cinefilm. To determine the absolute lumen diameter of the distal vessel, the diameter of the catheter was measured. The appropriate magnifica-


Table 1. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo</th>
<th>Aspirin daily</th>
<th>Aspirin three times daily</th>
<th>Aspirin+dipyridamole</th>
<th>Sulfapyrazine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>107</td>
<td>104</td>
<td>96</td>
<td>99</td>
<td>96</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>58±8</td>
<td>59±6</td>
<td>59±7</td>
<td>57±8</td>
<td>58±7</td>
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<tr>
<td>Angina (%)</td>
<td>97</td>
<td>95</td>
<td>94</td>
<td>94</td>
<td>96</td>
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<tr>
<td>Hypertension (%)</td>
<td>53</td>
<td>47</td>
<td>36</td>
<td>48</td>
<td>46</td>
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<tr>
<td>Prior myocardial infarction (%)</td>
<td>61</td>
<td>55</td>
<td>57</td>
<td>60</td>
<td>57</td>
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<tr>
<td>Cigarette smoking (pack years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past smokers</td>
<td>30</td>
<td>40</td>
<td>20</td>
<td>45</td>
<td>36</td>
</tr>
<tr>
<td>Current smokers</td>
<td>50</td>
<td>45</td>
<td>48</td>
<td>60</td>
<td>49</td>
</tr>
<tr>
<td>Serum cholesterol (mg/dl)</td>
<td>222±45</td>
<td>228±45</td>
<td>220±49</td>
<td>223±42</td>
<td>220±45</td>
</tr>
<tr>
<td>Serum triglycerides (mg/dl)</td>
<td>186</td>
<td>192</td>
<td>180</td>
<td>194</td>
<td>183</td>
</tr>
<tr>
<td>Serum high-density lipoprotein</td>
<td>32</td>
<td>35</td>
<td>31</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canadian functional class (I-IV)</td>
<td>3.2±0.8</td>
<td>3.2±0.8</td>
<td>3.1±0.9</td>
<td>3.1±0.8</td>
<td>3.2±0.9</td>
</tr>
</tbody>
</table>

- Values are percentages for angina, hypertension, and prior MI, and mean±SD for age, serum cholesterol, and Canadian functional class, and median values for all other characteristics.
- There were no differences in any of these variables among treatment groups.

A single-vein graft was defined as patent if the origin was visualized and if contrast material was seen to flow through the graft into the distal vessel either by selective injection or by aortic root angiography. When analyzing sequential or Y grafts, a distal anastomosis (either side to side or end to side) was defined as patent if the contrast material was seen to flow from the vein graft into the grafted artery. When the graft was occluded at its origin, all associated distal anastomoses were considered occluded. When one distal anastomosis of a Y or sequential graft was occluded, that site was defined as an occluded graft. When there was a difference of opinion regarding patency, the films were reviewed, and a consensus was reported.

Statistical Analysis

Comparability of treatment groups was tested using the χ² statistic on qualitative variables and the one-way analysis of variance on quantitative variables. Dunnett’s t statistic was used to compare each active treatment group with placebo. The Kruskal-Wallis test was used for quantitative variables that were not normally distributed. The patency data were analyzed two ways: 1) comparison of grafts that were occluded, assuming grafts are not independent, and 2) comparison of the proportion of patients with one or more occluded grafts. Because our previous data showed that there was a dependency of graft patency among individual patients, a cluster sampling approach was used to define the variance for the first analysis. This cluster sampling approach is discussed in depth in the Appendix to our previous publication.

Results

Patient Data

The baseline clinical characteristics for the patients having the 1-year catheterization are shown in Table 1. No differences were observed between the three aspirin groups and the placebo group. The patients who underwent the 1-year postoperative catheterization were compared with those who did not, differences were not found in any of the clinical characteristics. Also, no differences were found in cardiac events or mortality among the treatment groups between the early and late postoperative catheterizations. Of the 299 patients in the aspirin groups who underwent late catheterization, 12 (4.0%) had myocardial infarctions. Of the 107 patients who underwent late catheterization in the placebo group, one (0.9%) had a myocardial infarction (p=0.121). When the entire study population is considered, 12 (2.8%) of 437 patients in the aspirin groups and two (1.4%) of 146 patients in the placebo group had myocardial infarctions (p=0.347). There were two deaths in the placebo group (1.4%) and nine deaths in the aspirin groups (2.1%) (p=0.627). None of the deaths in the aspirin group was related to bleeding or cerebral vascular accidents.

The initial study population consisted of 772 patients who were randomized and had coronary artery bypass surgery with vein grafts. Of these, 555 patients underwent the early catheterization. The late catheterization was performed in 502 patients with 1,618 grafts, for an average of 3.2 grafts per patient. The median time from surgery to catheterization was 367 days, with a range of 62–527 days, with three patients studied at 598, 632, and 798 days. Ninety percent of the catheterizations were
performed between 336 days and 429 days after surgery. No differences were found in the timing of angiography, in relation to surgery, among the treatment groups.

There are no late postoperative catheterization data on 270 patients. The postoperative catheterization was not performed on 259 patients because of patient refusal in 154, lost to follow-up in 32, death in 31, intolerance or discontinuation of study medication in 28, other medical problems in 11, and psychiatric problems in three. The data on 11 patients were not available in the central laboratory.

**Graft Occlusion Data**

The vein graft occlusion rates for all of the treatment groups are shown in Table 2. Because of similar graft occlusion rates in the aspirin groups, these three groups have been combined. In the 406 patients in the aspirin and placebo groups, there were 768 single, 519 sequential, and 28 Y grafts (Table 3). Data on 119 internal mammary grafts were collected, but the internal mammary grafts were not included in this analysis. Overall, the 1-year vein graft occlusion rate, defined for distal anastomoses in all the aspirin groups, was 15.8% compared with 22.6% \( (p=0.029) \) in the placebo group. The graft occlusion rates in each treatment group were 13.2% for the aspirin daily, 16.8% for the aspirin three times daily, and 17.5% for the aspirin and dipyridamole group. These data are displayed in Figure 1. The graft occlusion rate in the sulfinpyrazone group was 18.2%. There was a statistical difference in occlusion rates only for the group receiving aspirin daily compared with the placebo group \( (p=0.050) \). When patients were considered as the units of observation, 34.8% of the patients in the groups receiving aspirin had one or more occluded grafts compared with 43.9% in the placebo group \( (p=0.101) \).

In vein grafts placed to distal vessels less than or equal to 1.5 mm in diameter (439 grafts), aspirin compared with placebo decreased the occlusion rate from 37.9% to 27.4% \( (p=0.046) \). In vein grafts placed to distal vessels less than or equal to 2.0 mm in diameter (804 grafts), aspirin compared with placebo decreased the occlusion rate from 32.3% to 20.1% \( (p=0.008, \) Figure 2). Conversely, when the diameter of the recipient vessel was greater than 2.0 mm (511 grafts), no difference was found in the occlusion rates when aspirin was compared with placebo \( (8.7\% \text{ vs. } 9.0\%, p=0.918) \).

The rate of progression of graft occlusion is shown in Figures 3 and 4. These figures compare data from the patients in the aspirin and placebo groups who underwent early and late postoperative catheterizations. If a graft was patent early (353 patients with 1,043 vein grafts), the occlusion rate in the ensuing year in the aspirin groups was 8.7% compared with 9.4% in the placebo group \( (p=0.763) \). In comparing patients with one or more occluded

<table>
<thead>
<tr>
<th>Location</th>
<th>Graft Type</th>
<th>Placebo</th>
<th>Aspirin once daily</th>
<th>Aspirin three times daily</th>
<th>Aspirin/ dipyridamole</th>
<th>Sulfinpyrazone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Single-vein grafts</td>
<td>24.2% 211</td>
<td>14.2% 204</td>
<td>18.4% 185</td>
<td>17.9% 168</td>
<td>13.4% 201</td>
</tr>
<tr>
<td></td>
<td>Sequential grafts</td>
<td>20.6% 126</td>
<td>11.5% 130</td>
<td>15.1% 126</td>
<td>18.2% 137</td>
<td>27.8% 97</td>
</tr>
<tr>
<td></td>
<td>Y grafts</td>
<td>12.5% 8</td>
<td>16.7% 6</td>
<td>0.0% 4</td>
<td>0.0% 10</td>
<td>20.0% 5</td>
</tr>
</tbody>
</table>

Values are percentage of grafts occluded and the number of distal anastomoses. Grafts to the diagonal and ramus intermedius are included under LAD. Each distal anastomotic site is counted as a single graft.

LAD, left anterior descending; RCA, right coronary artery; CX, circumflex.

**Table 2. Frequency of Vein Graft Occlusion According to Type and Location of Graft**

<table>
<thead>
<tr>
<th>Location</th>
<th>Graft Type</th>
<th>Placebo</th>
<th>Aspirin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All grafts</td>
<td>22.6% 345</td>
<td>15.8% 970</td>
</tr>
<tr>
<td></td>
<td>LAD</td>
<td>15.8% 146</td>
<td>10.4% 385</td>
</tr>
<tr>
<td></td>
<td>RCA</td>
<td>27.5% 91</td>
<td>19.2% 255</td>
</tr>
<tr>
<td></td>
<td>CX</td>
<td>27.8% 108</td>
<td>19.4% 330</td>
</tr>
<tr>
<td></td>
<td>Single-vein grafts</td>
<td>24.2% 211</td>
<td>16.7% 557</td>
</tr>
<tr>
<td></td>
<td>Sequential grafts</td>
<td>20.6% 126</td>
<td>15.0% 393</td>
</tr>
<tr>
<td></td>
<td>Y grafts</td>
<td>12.5% 8</td>
<td>5.0% 20</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>0.029</td>
<td>0.161</td>
</tr>
</tbody>
</table>

Values are percentage of grafts occluded and the number of distal anastomoses. Grafts to the diagonal and ramus intermedius are included under LAD. Each distal anastomotic site is counted as a single graft.

LAD, left anterior descending; RCA, right coronary artery; CX, circumflex.
grafts, no difference was found in occlusion rates between aspirin and placebo groups (22.0% vs. 22.1%). If a graft placed to a vessel less than or equal to 2.0 mm in diameter (552 distal sites in 271 patients) was patent early, the occlusion rate in the aspirin groups was 10.0% compared with 9.8% in the placebo group (*p=0.960).

When graft occlusion rates for different locations and types of grafts were compared between the active treatment groups and placebo group, no significant differences were found (Table 2). However, when all grafts were considered, a benefit was found with aspirin treatment once daily. By combining all of the aspirin groups, a significant improvement was also found in graft patency for single-vein grafts (Table 3). Moreover, the aspirin groups always had lower occlusion rates than did the placebo group.

Complications

The most frequent complication found on the late angiogram was ventricular tachycardia or ventricular fibrillation requiring direct-current countershock in seven patients. There was dissection of a graft

Figure 1. Bar graph of percentage of occluded grafts in each treatment group. P, placebo; A1, aspirin once daily; A3, aspirin three times daily; A/D, aspirin/dipyridamole; S, sulfinpyrazone. A1 vs. P, 9.4% difference (95% CI: 0.0, 18.7); A3 vs. P, 5.8% difference (95% CI: −3.6, 15.2); A/D vs. P, 5.1% difference (95% CI: −4.2, 14.5); S vs. P, 4.6% difference (95% CI: −4.9, 13.8). n=1,618 grafts. *p=0.050 compared with placebo.

Figure 2. Bar graph of percentage of occluded grafts in each treatment group to distal vessels less than or equal to 2.0 mm in diameter. The aspirin group includes all patients on aspirin (aspirin once daily, aspirin three times daily, aspirin/dipyridamole). Placebo vs. aspirin, 12.3% difference (95% CI: 3.3, 21.3). n=804 distal vessels ≤2.0 mm in diameter.

Figure 3. Bar graph of percentage of new occlusions in all vein grafts that were patent early (9 days) compared with those grafts that were patent at 1 year. The aspirin group includes all patients on aspirin (aspirin once daily, aspirin three times daily, aspirin/dipyridamole). Placebo vs. aspirin, 0.7% difference (95% CI: −3.8, 5.2). n=1,043 vein grafts.

Figure 4. Plot of progression of disease between 9 days and 367 days after surgery represents data from the patients (353) who had both catheterizations. ○, placebo; ●, aspirin.
without occlusion in one patient that resolved in 24 hours, subintimal tear of the femoral artery in one patient, and myocardial infarction in one patient.

Compliance

When patient compliance, between 60 days and 1 year after surgery, was assessed by pill counts, the patients were found to have taken 85% of their study medications. There were no differences in compliance among treatment regimens. The following percentages of patients in the treatment groups had detectable urine salicylates at the outpatient visit before the 1-year catheterization: 66% of patients in the aspirin daily, 88% in the aspirin three times daily, 81% in the aspirin with dipyridamole, 8% in the sulfipyrazone, and 19% in the placebo group.

Discussion

This study shows that aspirin improves saphenous vein graft patency at 1-year after surgery and that the major benefit occurs in vessels less than or equal to 2.0 mm in diameter. However, the frequency of new graft occlusions in the patients with patent grafts at 9 days was not improved by aspirin administration during the subsequent year (Figure 3). According to the early postoperative angiographic data, each of the three different aspirin regimens significantly improved patency compared with the placebo regimen. Because the occlusion rates at 1 year were similar for each of the aspirin-treatment groups (Figure 1), the rates were combined in the 1-year analysis (Figure 2). We conclude from these results, together with previous findings from the early postoperative angiogram,1 that the benefit of aspirin treatment is achieved early after surgery in the vein grafts placed to smaller vessels. We postulate that aspirin inhibits acute platelet thrombus formation immediately after mechanical and surgical injury to vein grafts and anastomotic sites but that aspirin probably fails to modify the occlusive process after the vein graft and anastomoses become reendothelialized.

The benefit from aspirin observed in both the early and late studies occurred primarily in the grafts placed to smaller vessels, that is, in the grafts placed to vessels less than or equal to 1.5 or 2.0 mm in diameter. Undoubtedly, this finding reflects the increased frequency of acute platelet-dependent thrombotic occlusion in grafts placed to smaller vessels. Probable factors contributing to this greater thrombogenicity include 1) surgically induced hemodynamic compromise resulting in stenotic, disturbed, and reduced flow, and 2) relative increased ratio of the platelet-active exposed endothelium to luminal diameter leading to a greater likelihood of occlusion by the resultant platelet thrombus. Aspirin inhibition of platelet recruitment would reduce the local platelet accumulation.

One previous study from the Mayo Clinic also reported serial angiographic analyses in which a higher patency rate for the treated group was found at 1 year, with the major benefit occurring in grafts placed to smaller vessels.3,4 There are a number of important differences in that study compared with the present data. First, in the Mayo Clinic trial, treatment was with aspirin and dipyridamole. By comparing aspirin only with aspirin plus dipyridamole, the present study established the efficacy of aspirin without the additional benefit from dipyridamole. Second, in the present study, a relatively conservative statistical approach was used consisting of a cluster method of analysis because patency rates for distal anastomotic sites within individual patients are dependent.1,2 Whereas, the Mayo Clinic study recognized the dependency of graft patency within patients, no statistical methods were used in analyzing patency rates for distal anastomotic sites other than the inefficient comparison of patients with one or more occluded grafts. A third difference between the two studies is the progression of graft occlusion. Although the Mayo Clinic study reported a decreased incidence (p=0.048) of new occlusion rates (between 1 week and 1 year), the present study found no benefit of therapy in terms of reduction in new occlusion rates.

A possible explanation for the differences between these studies may relate to a difference in the extent to which risk factors were modified after coronary artery bypass graft surgery. Data from the CLAS study suggest that if risk factors are controlled, there will be fewer adverse changes and a decreased appearance of new lesions in vein grafts.5

Although the effects of aspirin in this study were defined without using the subgroup analyses outlined in Tables 2 and 3, there may be a benefit in the aspirin groups. The important observation is the overall benefit to the aspirin groups, and the failure to demonstrate benefits in a variety of subgroups is most probably related to relatively small numbers of patients in each subgroup. Increasing the number of patients could have improved the subgroup analysis, but the observed differences were so small that an important difference would be unlikely to appear even if all patients received both postoperative angiograms. For this database, we obtained the second angiogram in 90% (502 of 555) of the eligible patients or 65% (502 of 772) of the patients initially enrolled in the study.

In the present study, patient compliance based on pill counts was excellent. Although urine salicylate levels were measured to assess compliance objectively, salicylates appear in the urine only when aspirin has been ingested within 12 hours of obtaining the sample. Thus, although a positive urine test for salicylates is evidence of taking aspirin, a negative test might not necessarily indicate poor compliance.

That the patients taking aspirin tended to have a higher incidence of myocardial infarction and death is puzzling. The differences were not significant, and the numbers were small. Because the deaths in the aspirin groups were not due to cerebral vascular
accidents or related to bleeding, it does not seem appropriate to incriminate aspirin as a cause.

On the basis of these results, we conclude that the administration of aspirin (325 mg daily) improves vein graft patency at 1 year and that the major benefit occurs in grafts placed to smaller vessels (≤2.0 mm in diameter). Combining diprydramide with aspirin provides no added benefit. However, because our earlier data showed that preoperative aspirin increased surgical blood loss and the reoperation rate for bleeding, we do not recommend giving aspirin before surgery. The necessity of beginning aspirin treatment before surgery has not been established. If the benefit of aspirin is related to the inhibition of platelet cyclooxygenase, smaller and less frequent doses could also be efficacious. Although our data do not show a benefit to continuing aspirin between the 1-week and 1-year postoperative periods, this does not necessarily imply that aspirin should be stopped 1 week after surgery. Stopping aspirin could create a rebound effect causing the occlusion rate to increase. Also, aspirin could have a long-term beneficial effect on vein graft patency that is not observed after just 1 year of therapy. These questions are being addressed in a second study that the VA Cooperative Studies Group is conducting currently.

Acknowledgments

We acknowledge the important contributions made by the staff cardiologists and cardiovascular surgeons whose names do not appear as authors. We also thank both the medical and surgical housestaff at each hospital. This study could not have been performed without the assistance and enthusiastic cooperation of these individuals. We would also like to express our appreciation to the patients who participated in this study.

Appendix

*The Veterans Administration Study Group consisted of the following:

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References


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S Goldman, J Copeland, T Moritz, W Henderson, K Zadina, T Ovitt, J Doherty, R Read, E Chesler and Y Sako

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