Impact of Internal Mammary Artery Conduit on Long-term Outcomes After Percutaneous Intervention of Saphenous Vein Graft

Rajendra H. Mehta, MD, MS; Emily Honeycutt, MBI; Eric D. Peterson, MD, MPH; Christopher B. Granger, MD; Abdul R. Halabi, MD; Linda K. Shaw, MS; Peter K. Smith, MD; Robert M. Califf, MD; Robert A. Harrington, MD; Michael H. Sketch Jr, MD

Background—The influence of an internal mammary artery (IMA) graft on long-term outcomes after percutaneous saphenous vein graft (SVG) intervention is currently unknown.

Methods and Results—To examine the impact of IMA on outcomes in patients undergoing SVG interventions, we analyzed 2119 patients from the Duke Cardiovascular Disease Database (1986–2003) with prior coronary artery bypass surgery undergoing cardiac catheterization who had at least 1 SVG graft. Patients were categorized into 4 groups: group I, SVG intervention and patent IMA; group II, no SVG intervention and patent IMA; group III, SVG intervention without patent IMA; and group IV, no SVG intervention without patent IMA. At a median follow-up of 4.8 years (interquartile range, 2.1 to 8.8 years), adjusted survival rates in groups I, II, III, and IV were 72.8%, 72.3%, 64.5%, and 58.9%, respectively. Multivariate Cox proportional hazards modeling showed similar survival for groups I and II ($P = 0.63$) and for groups III and IV ($P = 0.33$). The presence of IMA graft was related to lower long-term mortality (adjusted hazard ratio [HR], 0.69; 95% CI, 0.58 to 0.82), whereas SVG intervention was not associated with long-term mortality (adjusted HR, 0.94; 95% CI, 0.81 to 1.10). In contrast, the adjusted event-free rates for nonfatal myocardial infarction were lower in the SVG intervention groups (groups I and III) than in the non-SVG intervention groups (groups II and IV) (HR for SVG intervention versus no SVG intervention, 3.19; 95% CI, 2.18 to 4.66), with the presence of patent IMA conferring no significant benefit on this outcome (HR, 1.37; 95% CI, 0.91 to 2.08).

Conclusions—In patients undergoing SVG interventions, survival, but not nonfatal myocardial infarction, is favorably influenced by the presence of patent IMA. In contrast, SVG intervention had no measurable survival benefit but was associated with an increased risk of nonfatal myocardial infarction. (Circulation. 2006;114[suppl I]:I-396–I-401.)

Key Words: coronary artery bypass surgery ■ internal mammary artery ■ percutaneous coronary interventions ■ outcomes

Percutaneous coronary intervention (PCI) of saphenous vein graft (SVG) has been shown to be associated with poor short-term (distal embolization and no-reflow resulting in periprocedural myocardial infarction) and intermediate-term (increased restenosis and repeated target vessel revascularization) outcomes. In addition, SVG intervention has also been shown to be associated with decreased intermediate- and long-term survival. In contrast, the utilization of internal mammary artery (IMA) grafts has not only been shown to improve survival in patients having undergone coronary artery bypass graft (CABG) surgery, but PCI of IMA is associated with an excellent initial success and low incidence of restenosis and need for target-vessel revascularization. Therefore, it is intuitive to expect that among patients undergoing PCI of SVG, the presence of IMA would favorably influence long-term outcomes. However, this hypothesis currently remains untested and unproven. Furthermore, it is not known whether SVG intervention itself would have any impact on long-term patient outcomes.

Accordingly, the purpose of the present study was to examine the impact of IMA graft on long-term outcomes in patients with previous CABG undergoing percutaneous intervention of SVG grafts.

Methods

Patient Population and Data Collection

Using the Duke Cardiovascular Disease Databank, we identified patients with previous CABG who underwent cardiac catheterization between January 1, 1986, and December 31, 2003, who had at least 1 SVG placed during the previous CABG. After their index cardiac catheterization, patients were followed up at 6 months and annually thereafter for mortality status and other adverse events by telephone.
contact, mailed questionnaire, and National Death Index search. The methods used by the Duke Cardiovascular Disease Databank have been described previously.7,8

We excluded patients with prior valve surgery, severe stenosis, or regurgitation of mitral or aortic valves, those with congenital heart disease, and those with completely occluded SVG because in most cases these patients had interventions on their native vessels rather than vein graft. In addition, because the number of IMA interventions was small, we considered patients with successfully intervened IMA to have patent IMA. If IMA was totally occluded at the time of catheterization, we considered these patients as having no IMA. A total of 2119 patients met the study criteria and formed the basis of this analysis. Patients were categorized into 4 groups: group I, SVG intervention and patent IMA; group II, no SVG intervention and patent IMA; group III, SVG intervention without patent IMA; and group IV, no SVG intervention without patent IMA. The non-SVG intervention groups had patients who either had no disease in the graft or had disease but the operator elected not to intervene.

Follow-Up

During follow-up, information was collected on death, cause of death, nonfatal myocardial infarction at follow-up, and date of last known follow-up status. These data were prospectively obtained by mailed questionnaires or telephone interviews at 6 months, 1 year, and annually thereafter. Information from clinic visits and repeated hospitalizations was also evaluated to ascertain follow-up and end point determination. When all time intervals and all patients were considered, follow-up was 98.8% complete. Criteria used to diagnose fatal and nonfatal myocardial infarction and cardiovascular death have been described and validated.9

Statistical Analysis

Summary statistics are presented as frequencies and percentages for categorical variables or as medians with interquartile range (IQR) for continuous variables. The Kruskal-Wallis test for continuous or ordinal variables and the Pearson χ² test for categorical variables were used to test for differences among groups. Unadjusted survival estimates for the 4 groups were generated with the use of the Kaplan-Meier methodology. To adjust for differences in baseline clinical and angiographic characteristics, we used Cox proportional hazards survival models. Variables were assessed for clinical significance in unadjusted models before multivariable testing. Candidate variables for the multivariable survival models included age, gender, dyslipidemia, history of peripheral vascular disease, history of cerebrovascular disease, diabetes, congestive heart failure, hypertension, history of myocardial infarction, left main disease, presence of carotid bruits, ventricular gallop, comorbidity index (including renal insufficiency), mitral regurgitation, left ventricular ejection fraction, and coronary artery disease and graft indices.10,11 The graft indices account for the differences in the target vessels to which the graft is attached as well as the presence or absence of stenosis of the graft.11 After stepwise selection, only variables with a significant (P<0.05) association with long-term end points were included in the final models. Adjusted event-free survival from nonfatal myocardial infarction was similarly generated. Hazard ratios (HRs) and 95% CIs were constructed to provide estimate of risk posed by individual clinical variables on long-term outcomes. End points analyzed include survival, nonfatal myocardial infarction, and the composite of death and nonfatal myocardial infarction. Analyses were performed with the use of SAS statistical software (SAS Institute, Cary, NC).

Statement of Responsibility

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

The baseline characteristics of the 2119 patients in the 4 groups are shown in the Table. The median age was 65 years (IQR, 57 to 72 years). The majority were male (75%) and white (88%), with a history of hypertension and smoking in two thirds and diabetes in one third of the patients. In this post-CABG population, 84% had 2- or 3-vessel native coronary disease, and 58% had previous myocardial infarction. At the median follow-up of 4.8 years (IQR, 2.1 to 8.8 years), overall median survival was 72% (IQR, 53% to 85%).

The number of patients in groups I, II, III, and IV were 855 (40.4%), 975 (46.0%), 119 (5.6%), and 170 (8.0%), respectively. Differences in the baseline clinical features are shown in the Table. At the median follow-up of 4.8 years (IQR, 2.1 to 8.8 years), survival rates in groups I, II, III, and IV were 72.8%, 72.3%, 64.5%, and 58.9%, respectively. Adjusted survival curves were similar for groups I and II (P=0.63) and for groups III and IV (P=0.33) (Figure 1). However, adjusted survival was lower for patients in groups III and IV than for patients in groups I and II (Figure 1). The presence of patent IMA graft at the time of intervention was found to confer an independent main protective effect on long-term mortality (HR, 0.69; 95% CI, 0.58 to 0.82; Wald χ²=18.4; P<0.0001) among patients undergoing SVG interventions. In contrast, SVG intervention was not significantly associated with better adjusted long-term survival (HR, 0.94, 95% CI, 0.81 to 1.10; Wald χ²=0.59; P=0.44). We also examined 3 interactions, ie, IMA×SVG disease, IMA×SVG interventions, and SVG disease×SVG interventions. These interactions were not significant.

At a median follow-up of 4.8 years (IQR, 2.1 to 8.8 years), event-free rates for nonfatal myocardial infarction in groups I, II, III, and IV were 80.1%, 94.0%, 85.8.8%, and 94.5%, respectively. Cox proportional hazards model showed that event-free rates for nonfatal myocardial infarction were similar for groups I and III (SVG intervention groups, P=0.23) and for groups II and IV (P=0.34) (Figure 2). Adjusted event-free rates from nonfatal myocardial infarction at follow-up were significantly lower for both SVG intervention groups (groups I and III) than for the non-SVG intervention groups (groups II and IV), and this difference remained even when compared with patients in groups II and IV without diseased SVG. The presence of patent IMA graft at the time of SVG intervention had no independent effect on nonfatal myocardial infarction at follow-up (HR, 1.37; 95% CI, 0.91 to 2.08; Wald χ²=2.3; P=0.13). In contrast, SVG intervention was a significant predictor of increased myocardial infarction risk at follow-up (HR, 3.19; 95% CI, 2.18 to 4.66; Wald χ²=35.9; P<0.0001).

Discussion

Our study suggests that the long-term survival of patients undergoing percutaneous intervention of SVG is influenced favorably by the presence of a patent IMA graft. In contrast, SVG intervention in the absence of an IMA graft confers little beneficial effect on long-term survival and in fact increases the risk of subsequent myocardial infarction. Furthermore, our data indicate that although survival in patients undergoing SVG angioplasty is significantly attenuated by the presence of patent IMA conduit, the presence of IMA graft has little impact on the incidence of subsequent nonfatal myocardial infarction after vein graft angioplasty. Thus, our data suggest
that the presence of IMA graft has significant prognostic implications for patients undergoing SVG angioplasty, similar to that seen for patients undergoing CABG.

Our findings, although not reported previously among patients undergoing graft interventions, are not surprising given the relative resilience of IMA grafts to atherosclerosis compared with SVG conduits. IMA grafts have not only been shown to have 5-year patency >90% compared with 50% for vein grafts, but this improved graft patency has been associated with better long-term survival. Furthermore, PCI, whether of native coronary arteries or vein grafts, has not been shown to improve long-term survival but has been shown to improve patient symptoms.

Our data suggest that if long-term survival of patients with CABG is to be improved, in addition to ensuring that a patient receives an IMA conduit, efforts need to be directed toward reducing the incidence of SVG disease by careful selection and harvesting of SVG and by aggressive secondary prevention strategies. This is because once SVG disease occurs, intervention of a diseased vein graft has very little impact on improving survival.

Percutaneous interventions of vein grafts have been shown to be associated with high rates of recurrent ischemia, myocardial infarction, and need for repeated revascularization of the index vein graft. A patent IMA is unlikely to decrease those events, including subsequent myocardial infarction, aggressive restenotic process, or, more commonly, the progression of disease in the intervened vein grafts. Thus, our observation that the incidence of nonfatal myocardial infarction at follow-up is not influenced by IMA seems apparent and merits little further explanation.

Clinical Implications

The findings of our study have several clinical implications. Prior studies have reported that survival after vein graft intervention and among patients with prior CABG in general has improved significantly in recent years compared with the 1980s and early 1990s. Much credit for this improved outcome typically has been attributed to technological advances in coronary interventions (ie, increased use of co-
nary stents, improved drug therapy, use of distal protection devices, and increasing experience of interventional cardiologists).\textsuperscript{1–4,13,15–17,19,20} Our data suggest a need for caution in conferring the entire benefit of improved survival after SVG intervention to progress in technology or increasing operator experience alone, as suggested by these studies. Both of these prior studies\textsuperscript{4,18} failed to account for the increasing use of IMA conduits during recent years as a result of growing awareness on the part of the surgical community of the importance of IMA graft during CABG and widespread dissemination of public report cards that recognize the use of IMA as an important quality of care indicator for patients undergoing CABG.\textsuperscript{21–23} Thus, as suggested by our findings, it is possible that a significant portion of the improved survival after SVG intervention observed in recent years could be the result of increasing IMA use by our surgical colleagues rather than predominantly related to improvement in PCI technology. In fact, none of the randomized clinical trials evaluating technological advances in interventional cardiology (stents and distal protection devices) have shown significant survival benefit of these innovations after intervention of SVG.\textsuperscript{4,19,20} Thus, it is quite likely that the favorable effect on survival in these prior observational studies\textsuperscript{4,18} may not only be related to factors such as changes in technology and expertise alone but rather may also be attributable to other factors including the increasing use of an IMA. Our data suggest that observational investigations studying outcomes of SVG graft interventions should at the very least account for any differences in the proportion of patients with IMA conduits in the comparison arms.

Alternatively, it is also possible that studies evaluating various newer devices (stents, distal protection devices) may have failed to reveal any incremental survival advantage because of the similar and high proportion of patent IMA in the comparison arms.\textsuperscript{1–4,13,15–17,19,20} This is despite the fact that these devices were effective in reducing SVG intervention–related events such as periprocedural myocardial infarction, recurrent ischemia, and target vessel revascularization.\textsuperscript{1–4,13,15–17,19,20} Although most such studies were underpowered to specifically assess survival, it is also possible that the impact on survival of a patent IMA in patients with prior CABG is so strong that it eclipses any of the relatively small advantages of newer technologies observed during vein graft intervention on survival.

The finding that nonfatal myocardial infarction after SVG interventions was not reduced by the presence of an IMA graft is not surprising. Most of the patients in our study predated the routine use of distal protection devices. Although the rates of periprocedural myocardial infarctions have been shown to be reduced significantly by these devices in the acute phase,\textsuperscript{19,20} the incidence of myocardial infarction at follow-up as reported in our study is unlikely to be influenced by the acute use of distal protection devices. Furthermore, stents have significantly reduced the number of recurrent ischemic events compared with balloon angioplasty in patients undergoing SVG interventions.\textsuperscript{3} Although reduction in these events has not improved survival among patients undergoing SVG interventions, it is likely that the improvement in anginal symptoms and the reduction in myocardial infarction may affect left ventricular systolic function and/or the patient’s functional status and/or quality of life. Data on these outcome domains are currently less available.
Limitations
Our analysis is retrospective and subject to ascertainment bias. We only examined survival and survival free of subsequent nonfatal myocardial infarction. Thus, the influence on other outcome domains, eg, repeated revascularization, recurrent ischemia, angina, or quality of life, cannot be ascertained from our data. It is likely that SVG intervention may improve these outcomes, although this remains to be proven. Our study focused on a subset of patients undergoing SVG interventions and should be generalized with caution to other post-CABG patients. Similarly, our data do not provide information on whether other arterial conduits (radial or gastroepiploic arteries) would confer survival benefit similar to that observed with IMA in patients undergoing SVG intervention. Finally, the influence of unmeasured variables and adherence to medications and goals of lifestyle changes (smoking cessation, exercise, weight reduction, dietary modification) after discharge could not be assessed because these data were not collected. Although these factors and variations in adherence to treatment goals are likely to have a significant influence on long-term mortality, it remains to be shown whether they significantly attenuate the observed beneficial effect of an IMA graft on long-term survival among patients undergoing SVG interventions.

Conclusions
In patients undergoing SVG interventions, survival, but not subsequent nonfatal myocardial infarction, is favorably influenced by the presence of patent IMA. In contrast, SVG intervention not only did not have any measurable survival benefit but in fact increased the risk of subsequent nonfatal myocardial infarction. Furthermore, studies are needed to evaluate whether SVG intervention may be beneficial in improving recurrent ischemia, angina, functional status, and quality of life.

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Disclosures
None.

References


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