

Predictors of Graft Patency 3 Years After Coronary Artery Bypass Graft Surgery

STEVEN GOLDMAN, MD, FACC, KAREN ZADINA, RN, MA, BARBARA KRASNICKA, PhD,*
THOMAS MORITZ, MS,* GULSHAN SETHI, MD, FACC, JACK COPELAND, MD, FACC,
THERON OVITT, MD, WILLIAM HENDERSON, PhD,* FOR THE DEPARTMENT OF VETERANS AFFAIRS
COOPERATIVE STUDY GROUP NO. 297†

Tucson, Arizona and Hines, Illinois

Objectives. The purpose of this analysis was to define the factors that predict 3-year graft patency.

Background. The success of coronary artery bypass graft surgery (CABG) is dependent on vein graft patency after the operation. It has been well established by a series of Department of Veterans Affairs Cooperative Trials that aspirin (325 mg daily) improves saphenous vein graft patency early (7 to 10 days) and at 1 year, but not at 3 years after CABG. This analysis, based on one of these trials, defined factors that predict 3-year graft patency.

Methods. This analysis consisted of 266 patients, with 656 grafts that were patent 7 to 10 days after the operation, who underwent 3-year catheterization. To determine which patient-specific and/or graft-specific factors, or both, predict graft occlusion, a multivariate logistic regression analysis in terms of latent variables was used. It yielded a model that also took into account possible intraclass correlations.

Results. For a vein graft that was patent at 7 to 10 days after the operation, the positive predictors, according to univariate analysis, for that graft being patent at 3 years were cross-clamp time ≤ 80 min ($p < 0.001$), vein preservation solution temperature

$\leq 5^{\circ}\text{C}$ ($p = 0.009$), bypass time ≤ 2 h ($p = 0.042$), number of proximal anastomoses ≤ 2 ($p = 0.018$), operation time ≤ 5 h ($p = 0.044$) and continuous versus intermittent cross-clamp technique ($p = 0.024$). There was also a trend with regard to recipient artery diameter >1.5 mm ($p = 0.063$), serum cholesterol ≤ 225 mg/dl ($p = 0.084$) and single versus sequential or Y vein graft ($p = 0.060$). Factors not predictive of 3-year patency were age, race, smoking history, high density lipoprotein cholesterol, vein source (thigh vs. calf), coronary artery grafted and aspirin treatment. Of all the predictors obtained in the univariate analysis, the only variables that were sufficient to yield a good model within the multivariate analysis were solution temperature ($p = 0.004$), serum cholesterol ($p = 0.024$), number of proximal anastomoses ($p = 0.032$) and recipient artery diameter ($p = 0.034$).

Conclusions. For a patient with patent vein grafts 7 to 10 days after the operation, predictors of 3-year graft patency are more closely related to operative techniques and underlying disease and not to aspirin treatment.

(J Am Coll Cardiol 1997;29:1563-8)

©1997 by the American College of Cardiology

The long-term success of coronary artery bypass graft surgery (CABG) is dependent on graft patency after the operation. It is now well established that aspirin (325 mg daily) improves saphenous vein graft patency early (7 to 10 days) and at 1 year, but not at 3 years after CABG (1-5). This information was established by a series of Department of Veterans Affairs Cooperative Trials designed to determine the effects of aspirin on saphenous vein graft or internal mammary artery (IMA) graft patency after CABG.

From the Department of Veterans Affairs Medical Center and the University of Arizona Heart Center, Tucson, Arizona; and *Department of Veterans Affairs Hospital, Hines, Illinois. †A list of the participants in the Department of Veterans Affairs Cooperative Study Group No. 297 appears in reference 5. This research was supported by the Cooperative Studies Program of the Medical Research Service, Department of Veterans Affairs Central Office, Washington, D.C.

Manuscript received October 9, 1996; revised manuscript received February 4, 1997, accepted February 21, 1997.

Address for correspondence: Dr. Steven Goldman, Cardiology Section (111C), Department of Veterans Affairs Medical Center, 3601 South 6th Avenue, Tucson, Arizona 85723.

The results presented in this report are based on an analysis of the factors that predict 3-year vein graft patency, given that the operation has been a success (i.e., there is at least one patent saphenous vein graft 7 to 10 days after CABG). The status of a graft known to be patent at 7 to 10 days was assessed at 1 year and 3 years after the operation. This approach to analysis of vein graft patency eliminates any graft occlusion that occurred as a perioperative event and permits us to examine only those factors that cause vein graft occlusion after the graft has been shown to be patent. A multivariate logistic regression analysis in terms of latent normal variables (6) was used to model the data. The model yielded the most important patient-specific and graft-specific factors predicting graft occlusion.

Methods

Study group. This trial, organized by the Cooperative Studies Program of the Department of Veterans Affairs Medical Research Service, consisted of data from 266 male patients

Abbreviations and Acronyms

CABG	= coronary artery bypass graft surgery
CLAS	= Cholesterol Lowering Atherosclerosis Study
HMG-CoA	= 3-hydroxy-3-methyl-glutaryl-coenzyme A
IMA	= internal mammary artery

entered into the study at 10 participating hospitals from July 1986 to September 1988. Patient follow-up was concluded in 1991. The exclusion criteria, definition of the study group and stratification techniques have been previously described (1-5).

Of the total 374 patients who underwent catheterization 1 year postoperatively, 334 (89%) agreed to participate in the long-term phase of the study and were randomized and prospectively followed for an additional 2 years. Although there were 297 patients, with 779 grafts, who underwent catheterization 3 years postoperatively, the data set for this report consists of the 266 patients, with 656 grafts, who were known to have patent grafts 7 to 10 days after the operation.

Treatment regimens. After receiving aspirin (325 mg daily) for 1 year after the operation and undergoing catheterization 1 year postoperatively, patients were randomized to receive either aspirin (325 mg) or placebo for the next 2 years. The aspirin and matching placebo were provided by Glenbrook Laboratories. All medications were provided in individualized patient kits. Compliance testing was assessed with pill counts, as noted previously (2). To ensure that patients took only their study medications, Disalcid (salsalate) was made available to all patients, and patients were instructed to take either the salsalate or acetaminophen for pain. In addition, to minimize the risks of patients unknowingly taking aspirin-containing compounds, a list of all over-the-counter medications containing aspirin was given to each patient.

Coronary artery bypass grafting. Bypass grafting was achieved by the usual protocol at each of the study institutions. The decision to use the IMA or saphenous vein as a conduit was made by the attending surgeon. If the determination was made preoperatively by the surgeon to use both IMA and saphenous vein grafts, the patient was eligible for the study. If the determination was made preoperatively by the surgeon to use only IMA grafts, the patient was not randomized, because the primary objective of the study was to assess the effect of aspirin on the 3-year patency of saphenous vein grafts. The saphenous vein and IMA grafts were included in separate analyses.

Although no attempt was made to establish a uniform technique for performing the operation, those institutions chosen to participate in the study were selected on the basis of experience and competence as documented by yearly statistics compiled by the Department of Veterans Affairs Central Office. Detailed data forms covering technical aspects of the perfusion, cardioplegic solutions, time of operation, arrest period, technical considerations regarding vessel and graft size, postoperative support and bleeding were maintained for each patient.

Angiographic analysis. The angiographic analysis used in this study was identical to that in our earlier trials (1-5). Briefly, the left IMA and each aortic anastomosis was selectively engaged and injected. When the status of a vein graft could not be determined by graft or stump injection, an aortic root angiogram was performed. Selective angiography of the native coronary arteries was performed during the 1-week and 1-year catheterizations only when a graft was occluded. Selective angiography of the native coronary arteries was routinely performed at the 3-year catheterization. All angiograms were interpreted at both the participating institutions and the central angiographic laboratory. The data from the central angiographic laboratory were used for this report. At the central angiographic laboratory, each angiogram was interpreted independently by two cardiovascular radiologists who had no knowledge of the patients' treatment regimen. The analysis was performed with a system developed for this study, which included a Vanguard projector and high resolution television camera (Vanguard Instrument Corp.) to record the images. The images were digitized and the information entered into an integrated image processor-computer system. The images were then redisplayed on the integrated memory plane, absolute measurements made and stenoses calculated for all vessels ≥ 1 mm in diameter. The number, type and size of all grafts were recorded using an interactive computer program. Images of the cine frames, with the measurements superimposed, were filmed for storage in hard copy format. The angiographic analysis used in this study was prospective. The size of the distal vessel was analyzed by measuring the lumen of the vessel from the cine film. To determine the absolute lumen diameter of the distal vessel, the diameter of the catheter was measured. The appropriate magnification factor was calculated by knowing the actual diameter of the catheter. Actual vessel size was reported using this correction factor.

A single vein or IMA graft was defined as patent when the origin was visualized and the contrast agent opacified the graft and the distal vessel, either by selective injection or by aortic root angiography. When analyzing sequential or Y vein grafts, a distal anastomosis (either side to side or end to side) was defined as patent if the contrast medium was seen to flow from the vein graft into the grafted artery. If the graft was occluded at its origin, all associated distal anastomoses were considered occluded. If one distal anastomosis of a Y or sequential vein 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 opinion was reported.

Statistical analysis. The technique used for data collection did not supply continuous information on the occlusion process in time, but only some binary values, occluded or patent, at discrete moments in time. Therefore, analyses based on the logistic regression model (for clustered binary data) with latent normal variables (6) were applied. In such models, the occlusion process is described by a function that determines the outcome of an observable binary variable (occluded or not)—that is, one can assume that the outcome (occlusion of graft) was the realization of an unobservable (latent) continuous

variable and that occlusion occurred only if the latent variable exceeded a certain level. For the *i*th patient ($i = 1, \dots, 266$), the probability π_{ijt} that the *j*th graft ($j = 1, \dots, n_i$) at the time *t* of the 1-year or 3-year angiogram is occluded is equal to the probability that the corresponding (to the given graft) latent variable is greater than zero. The marginal probability π_{ijt} is determined by covariates $x_{ij} = (x_{ij1}, \dots, x_{ijp})'$ (*p* is the number of covariates) in the frame of the generalized linear model logit ($\pi_{ijt} = x_{ij}'\beta$). Vector β has the form $\beta = (\beta_1, \dots, \beta_p)'$, where β_r is the log odds ratio when x_{ijr} is increased by 1. The tetrachoric correlation, which measures the dependence between outcomes (e.g., between y_{ikt} and y_{ijt} [$k \neq j$]) is the correlation between realizations of a pair of relevant latent continuous variables. These variables are assumed to be bivariate standard normally distributed.

First, a univariate analysis was performed to obtain primary information on important predicting factors. Then multivariate analysis was carried out using important factors found in the previous analysis. The model was built in such a way that different variables were forced to be in the model. Model stability (i.e., the influence of each subject on the estimates of covariates) was chosen as the criterion for the final model. For the selection of the model and checking of the model fit to the empiric data, the jackknife method was used.

Results

Patient data. The details of the patient data, including clinical outcomes and complications of the catheterizations, have been reported previously (1-5). Of the original 334 patients who were randomized at 1 year postoperatively, 297 patients underwent 3-year angiography. Of the 37 patients excluded, there were seven deaths and no myocardial infar-

Table 1. Potential Preoperative Patient-Specific Predictors of 3-Year Graft Occlusion by Univariate Analysis

Predictors	No. of Pts (grafts)	Occluded Grafts (%)	p Value
Treatment			
Aspirin	128 (321)	12.5	0.323
No aspirin	130 (313)	15.3	
Age (yr)			
≤50	29 (60)	11.7	0.360
>50	237 (596)	14.8	
Race			
Nonwhite	25 (67)	10.4	0.514
White	241 (587)	14.9	
Smoking			
No	163 (390)	14.1	0.492
Yes	102 (264)	15.2	
Serum cholesterol (mg/dl)			
≤225	144 (349)	10.0	0.084
>225	99 (244)	17.2	
Serum HDL (mg/dl)			
≤30	71 (169)	13.0	0.390
>30	88 (235)	9.8	

HDL = high density lipoprotein; Pts = patients.

Table 2. Potential Intraoperative and Perioperative Patient-Specific Predictors of 3-Year Graft Occlusion by Univariate Analysis

Predictors	No. of Pts (grafts)	Occluded Grafts (%)	p Value
No. of proximal anastomoses			
≤2	66 (132)	10.6	0.018
>2	200 (524)	15.5	
Operation time (h)			
≤5	199 (492)	12.8	0.044
>5	65 (157)	20.4	
Bypass time (h)			
≤2	167 (376)	12.0	0.042
>2	98 (278)	18.0	
Cross-clamp time (min)			
≤80	225 (535)	11.2	< 0.001
>80	40 (119)	29.4	
Vein preservation solution temp (°C)			
≤5	104 (264)	8.3	0.009
>5	161 (389)	18.8	
Cross-clamp technique			
Continuous	228 (571)	13.5	0.024
Intermittent	37 (83)	21.7	

Pts = patients; temp = temperature.

tions or revascularization procedures. The remaining 30 patients who were excluded either withdrew from the study or refused the 3-year catheterization. Of the 297 patients who underwent 3-year angiography, 31 were excluded from this report because they did not undergo the 7- to 10-day postoperative catheterization, so it was not known whether their grafts were patent after the operation.

In brief, the data are from 266 (80%) of the original 334 patients with patent saphenous vein grafts at 7 to 10 days who had cardiac catheterization at 1 and 3 years after the operation and whose data were available in the central angiographic laboratory. The median time from CABG to 1-year catheterization was 1 year (range 0.2 to 1.5). Ninety percent of the 1-year catheterizations were done between 0.9 and 1.1 years after the operation. The median time from CABG to 3-year catheterization was 3 years (range 1.7 to 4.8). Ninety percent of these catheterizations were done between 2.8 years and 3.2 years after the operation.

The baseline clinical characteristics have been reported previously (1,4,5). The only difference observed in clinical characteristics was related to smoking history. Among patients who underwent the 3-year postoperative catheterization, 18.8% never smoked, compared with 6.5% for patients who were not catheterized ($p = 0.041$). There were no incidences of myocardial infarction, stroke or death during the 3-year postoperative catheterizations.

Vein graft data. In these 266 patients, there were 656 saphenous vein grafts—473 single, 148 sequential and 35 Y grafts.

The results of univariate analysis for vein graft occlusion are presented in Tables 1 to 3. For a saphenous vein graft that was patent 7 to 10 days after CABG, the following were positive predictive factors for that graft being patent 3 years after the

Table 3. Potential Graft-Specific Predictors of 3-Year Graft Occlusion by Univariate Analysis

Predictors	No. of Pts (grafts)	Occluded Grafts (%)	p Value
Diameter (mm)			
≤1.5	77 (110)	22.7	0.063
>1.5	259 (546)	12.8	
Source of vein			
Thigh	117 (204)	12.7	0.449
Calf	206 (441)	15.6	
Type of graft			
Single vein grafts	241 (473)	12.3	0.060
Sequential/Y vein grafts	80 (183)	20.8	
Artery grafted			
RCA/LCx	254 (458)	14.0	0.885
LAD	152 (198)	15.7	

LAD = left anterior descending coronary artery (includes grafts to the diagonal and ramus intermedius); LCx = circumflex coronary artery; RCA = right coronary artery.

operation: cross-clamp time ≤ 80 min ($p < 0.001$), vein preservation solution temperature $\leq 5^\circ\text{C}$ ($p = 0.009$), bypass time ≤ 2 h ($p = 0.042$), number of proximal anastomoses ≤ 2 ($p = 0.018$), operation time ≤ 5 h ($p = 0.044$) and continuous versus intermittent cross-clamp technique ($p = 0.024$). These factors showed a trend: recipient artery diameter >1.5 mm ($p = 0.063$), serum cholesterol ≤ 225 mg/dl ($p = 0.084$) and single versus sequential vein graft ($p = 0.060$). The following were not predictive of 3-year graft patency: age, race, smoking history, high density lipoprotein cholesterol, vein source (thigh vs. calf), coronary artery grafted and aspirin treatment.

The results of multivariate analysis are presented in Table 4. In the final model we included the following variables that were independent predictors of 3-year graft patency: vein preservation solution temperature ($p = 0.004$), serum cholesterol ($p = 0.024$), diameter of recipient artery ($p = 0.034$) and number of proximal anastomoses ($p = 0.032$). Table 4 also contains the tetrachoric correlations α_1 and α_2 . Only the correlation α_2 is significant. Thus, the occurrence of occlusion or patency of two grafts for the same patient is significantly correlated only for an angiogram performed either at the 1-year or 3-year period.

The following are the data on whether graft narrowing was a predictor of graft occlusion: At 7 to 10 days, 40 grafts were totally occluded and five grafts had stenoses. At 1 year, 102 grafts were totally occluded and 12 grafts had stenoses. With so few cases of graft narrowing, the degree of stenosis is nearly identical to our binary outcome variable.

IMA grafts. There were 167 IMA grafts that were patent at 7 to 10 days. Twelve of these grafts became occluded within 3 years (93% patency). The logistic univariate analysis indicated low body temperature as an important occlusion predictor ($p = 0.0057$). In a second type of univariate analysis (7), significant differences for the occlusion ratio estimates were observed for the following variables: previous myocardial infarction (yes, no), smoking (yes, no) and categorized low

body temperature ($\leq 28^\circ\text{C}$, $>28^\circ\text{C}$). However, there were so few occurrences of occlusions, that the aforementioned results should be treated only as trend indicators.

Discussion

This analysis shows that for a patient who undergoes successful CABG with a patent saphenous vein graft 7 to 10 days after operation, in addition to serum cholesterol being a predictor of 3-year vein graft patency, the other patient-specific predictors are related to operative techniques, such as bypass and cross-clamp times, and vein preservation solution temperature. Recipient artery diameter and use of single versus sequential vein grafts were graft-specific predictors of 3-year patency. Importantly, treatment with aspirin was not predictive of 3-year vein graft patency. Because this report includes only vein grafts that were known to be patent at 7 to 10 days, the factors we identified are the most accurate predictors of long-term vein graft patency. Previous investigators have examined clinical characteristics or operative data and used this information to define predictors of long-term vein graft patency (2,5). This latter approach does not take into account the fact that 7% to 10% of vein grafts occlude within the first week of CABG and another 5% to 10% occlude in the first year after the operation (1,2). The approach outlined here examines prospectively only saphenous vein grafts that were known to be patent at 7 to 10 days. Therefore, the risk factors identified here predict what happens to a vein graft after the patient has undergone "successful CABG."

Causes of graft occlusion. The anatomic descriptions of the causes of saphenous vein graft occlusions are based on clinicopathologic studies that suggest vein graft occlusion in the perioperative period is due to thrombosis resulting from technical problems. Vein graft occlusion within the first year is attributed to intimal proliferation, although after 1 year, atherosclerosis is thought to be the dominant factor (8,9).

Table 4. Multivariate Analysis: Coefficient and Standard Errors for Logistic Regression Equation for Model in Which Patient, Graft and Time Correlation Effects Were Taken Into Account

Variable	Regression Coefficient		p Value
	Estimate	SE	
Intercept	-4.1328	0.7777	< 0.001
Solution temp ($\leq 5^\circ\text{C} = 0$, $>5^\circ\text{C} = 1$)	0.9783	0.3314	0.004
Serum cholesterol	0.0060	0.0028	0.024
No. of prox anastomoses ($\leq 2 = 0$, $>2 = 1$)	0.9724	0.4282	0.032
Recipient artery diameter	-0.3766	0.1770	0.034
Alpha ₁	0.1873	0.1083	0.090
Alpha ₂	0.2811	0.1061	0.009

Alpha₁ = tetrachoric correlation between observations on different grafts for the same patient during different angiographic examinations; Alpha₂ = tetrachoric correlation between observations on different grafts for the same patient during the same angiographic examination; prox = proximal; other abbreviations as in Table 2.

Although this description is generally well accepted, it does not account for the specific pathophysiologic processes that result in long-term vein graft occlusion. Previous trials from our group (1-5) and others (10-13) have focused on the use of specific antiplatelet agents to improve vein graft patency. The fact that aspirin in the perioperative period, which is continued for 1 year, is effective in reducing vein graft occlusion rates supports the concept that platelet deposition and thrombosis play an important role in vein graft occlusion within 1 year of CABG. Likewise, our previous data showing that aspirin treatment between years 2 and 3 does not result in any improvement in vein graft patency support the pathologic interpretation that the development of atherosclerosis in the vein graft and not thrombosis is the most important factor in determining long-term vein graft patency.

Operative factors. It is interesting that our data demonstrate that operative factors, such as bypass and cross-clamp times, affect long-term graft patency. Our assumption is that the correlation of longer operating times resulting in higher graft occlusion rates at 3 years is due to the fact that the patients with longer operating times were those who required additional revascularization. This is supported by the fact that patients with longer operative times had a larger average number of grafts (cross-clamp time >80 min for 1.98 [average] grafts; cross-clamp time ≤80 min for 1.86 grafts; bypass time >2 h for 2.05 grafts; bypass time ≤2 h for 1.88 grafts).

Vessel diameter. The diameter of the recipient vessel was a determinant in long-term vein graft patency because veins grafted into smaller vessels have higher occlusion rates. We and others have shown this to be true at 1 week, 1 year and 3 years after CABG (1,2,5). In fact, our earlier reports suggest that aspirin is most effective in vein grafts placed to smaller vessels because vein grafts to vessels ≥2.0 mm remain patent even if the patient is not treated with aspirin.

Graft type. The data on single versus sequential or Y vein grafts show a trend for improved 3-year graft patency for those patients who had one aortic anastomotic site for each vein graft. These data are in conflict with the approach taken by surgeons in the 1980s, who promoted the use of a single aortic anastomosis with multiple distal runoff sites to improve flow through the graft so it would remain patent longer. Because the surgeons in the present study did not randomize the patients in terms of single versus sequential or Y grafts, our data should not be regarded as proof that vein grafts with multiple distal sites do poorly. It is possible that the patients with sequential grafts in this study may have had more atherosclerotic disease in their aortas and more distal coronary artery disease as well.

Serum cholesterol. Data now show that treating patients with an elevated serum cholesterol with the 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitors or "statins" is an effective means of secondary prevention of cardiovascular morbidity and mortality in patients with pre-existing coronary artery disease (14). Although studies like these will probably change clinical practice, they do not specifically address patients after CABG and do not examine the effects of

serum cholesterol on vein graft patency. It is interesting to note the conflicting data generated within our own study group in defining the effects of serum cholesterol as a predictor of vein graft occlusion. For example, in our previous analysis, when we attempted to use baseline characteristics to predict 3-year vein graft patency, the baseline serum cholesterol was not useful (5). However, in this vein graft survival analysis, in which the patient had to have one patent vein graft at 7 to 10 days, a serum cholesterol level >225 mg/dl predicted 3-year vein graft occlusion. Because the current report examines only those patients with a patent vein graft, these data are probably a more accurate reflection of the pathophysiology of vein graft occlusion. Other data to support that serum cholesterol may be a predictor of vein graft occlusion are the Cholesterol Lowering Atherosclerosis Study (CLAS) results (15). These investigators showed that colestipol and niacin in combination resulted in a 43% reduction in high density lipoprotein cholesterol, and although this regimen did not alter vein graft patency, this treatment did decrease the development of new lesions in vein grafts. In addition, a 10-year study from the Montreal Heart Institute showed that serum cholesterol levels were significantly higher at the time of CABG and at the 10-year postoperative catheterization in those patients who developed new lesions in their vein grafts (9,16,17).

Solution temperature. The predictive effects of using a lower temperature for preparation of the vein graft is interesting. To our knowledge, this is the first report suggesting that the temperature of the vein perfusate solution has an effect on long-term patency. Most other investigators who studied vein graft preparation techniques examined short-term patency and looked at factors that result in mechanical damage (i.e., using low vs. high pressure distention or different vasodilating solutions) (18). The general conclusions from these studies were that endothelial damage and vasospasm during the preparation of the saphenous vein for bypass grafting may be an important cause of graft failure. One report suggested that these factors may be responsible for 12% to 20% of venous grafts that occlude during the first year (19). Because of this, current surgical practice emphasizes improvement in surgical handling techniques, lower inflation pressure during the leak testing and different preservation media to improve graft patency. More recent data showed improvement in endothelial preservation in vein grafts when perfused with cold (4°C) saline or the University of Wisconsin solution compared with heparinized blood (20). Interestingly, the importance of the temperature of the perfusion fluid is also thought to be important during donor heart preservation before heart transplantation, because vessel endothelium tends to degenerate if preserved in normal saline at room temperature, although it can be well preserved in cold saline (4°C) for 4 to 6 h (21).

IMA grafts. The number of IMA graft occlusions (12 in 167 patients) were too few to analyze. Nevertheless, these data are interesting and demonstrate that although IMA graft occlusion may be rare, our 3-year IMA occlusion rate of 7.2% shows that some of these grafts do occlude. Although previous reports suggest 10-year patency rates of 90% to 95% for IMA

grafts (22), it is important to note that this information was not obtained from prospectively designed trials. In addition, the patients who were operated on in the 1970s, before the use of IMA grafts became widespread, were probably better candidates than those who receive IMA grafts today (i.e., larger distal left anterior descending coronary arteries and better runoff). Most importantly, when patients operated on in the 1980s are studied prospectively, the 10-year patency rate will probably be lower than 90%.

Statistical model. In our statistical analysis we concentrated on the problems of finding the most important predictors of long-term saphenous vein graft patency and possible correlations at the patient, graft and time levels. The baseline information on patient-specific and graft-specific covariates was utilized. We based the analysis on the concept of latent variables for clustered data (6). Such an approach was used because catheterization supplies information on graft patency only at discrete moments of time, whereas graft occlusion is a continuous process, and we could simultaneously take into account both types of covariates and multilevel correlations.

By means of univariate analysis, we carried out the first selection of predictors and then we tried to build an adequate multivariate logistic regression. The data were modeled in such a way that the marginal outcome probabilities were determined by means of covariates in the frame of a logistic linear model. Therefore, the coefficients in the regression equation could be interpreted as population-average logarithms of adjusted odds ratios.

For selection of a final model and checking of its stability, we applied the jackknife diagnostic tool. In this method, we looked for the change of beta estimates by recomputing the model for a data set with the *i*th patient deleted. Among the results, the jackknife method indicated that the recipient artery diameter applied as a continuous variable yielded more stable models than the use of categorized diameter. The final model chosen included solution temperature, number of proximal anastomoses, serum cholesterol and recipient artery diameter. It is worth noting, however, that the cross-clamp time was not included in the model because of its high correlation with the number of proximal anastomoses. Finally, we tried to obtain information on possible intraclass correlations and their origins. From Table 4, we can conclude the existence of some correlations among the observations from an individual patient for different times after CABG and different grafts, but the main correlation is the one among observations taken for a given patient but different grafts either at the 1-year or 3-year postoperative angiogram. A detailed description of the statistical analysis performed by us will shortly be published (23).

References

1. Goldman S, Copeland J, Moritz T, et al. Improvement in early saphenous vein graft patency after coronary artery bypass surgery with antiplatelet therapy. *Circulation* 1988;77:1324-32.
2. Goldman S, Copeland J, Moritz T, et al. Saphenous vein graft patency one

- year after coronary artery bypass surgery and effects of antiplatelet therapy. *Circulation* 1989;80:1190-7.
3. Goldman S, Copeland J, Moritz T, et al. Internal mammary artery and saphenous vein graft patency: effects of aspirin. *Circulation* 1990;82 Suppl IV:IV-237-42.
4. Goldman S, Copeland J, Moritz T, et al. Starting aspirin therapy after operation: effects on early graft patency. *Circulation* 1991;84:520-6.
5. Goldman S, Copeland J, Moritz T, et al. Long term graft patency (3 years) after coronary artery surgery: effects of aspirin. Results of a VA Cooperative Study. *Circulation* 1994;89:1138-43.
6. Qu Y, Williams GW, Beck GJ, Mendendorp SV. Latent variable models for clustered dichotomous data with multiple subclusters. *Biometrics* 1992;48:1095-1102.
7. Henderson W, Moritz T, Goldman S, et al. The statistical analysis of graft patency data in a clinical trial of anti-platelet agents following coronary artery bypass grafting. *Control Clin Trials* 1988;9:189-205.
8. Bourassa MG, Campeau L, Lesperance J, Grondin CM. Changes in grafts and coronary arteries after saphenous vein aortocoronary bypass surgery: results at repeat angiography. *Circulation* 1982;65 suppl II:II-90-7.
9. Campeau L, Enjalbert M, Lesperance J, et al. The relation of risk factors to the development of atherosclerosis in saphenous-vein bypass grafts and the progression of disease in the native circulation. *N Engl J Med* 1984;311:1329-32.
10. Chesbro JH, Fuster V, Eleveback LR, et al. Effects of dipyridamole and aspirin on late vein graft-patency after coronary artery bypass operations. *N Engl J Med* 1984;310:209-24.
11. Sanz G, Pajaron A, Algegría E, et al. Prevention of early aortocoronary bypass occlusion by low-dose aspirin and dipyridamole. *Circulation* 1990;82:765-73.
12. Gavaghan TP, GebSKI V, Baron DW. Immediate postoperative aspirin improves vein graft patency early and late after coronary artery bypass surgery. *Circulation* 1991;83:1526-33.
13. Van der Meer J, Hillege HL, Ascoop CAPL, Pfisterer M, van Gilst WH, Lie KI, for the CABADAS Research Group. Prevention of one year vein-graft occlusion after aortocoronary-bypass surgery: a comparison of low-dose aspirin, low-dose aspirin plus dipyridamole, and oral anticoagulants. *Lancet* 1993;342:257-64.
14. Scandinavian Simvastatin Survival Study Group. Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994;344:1383-9.
15. Blankenhorn DH, Nessim SA, Johnson RL, Sanmarco ME, Azen SP, Cashin-Hemphill L. Beneficial effects of combined colestipol-niacin therapy on coronary atherosclerosis and coronary venous bypass grafts. *JAMA* 1987;257:3233-40.
16. Grondin CM, Campeau L, Lesperance J, Enjalbert M, Bourassa MG. Comparison of late changes in internal mammary artery and saphenous vein grafts in two consecutive series of patients 10 years after operation. *Circulation* 1984;70 suppl I:I-208-12.
17. Grondin CM, Campeau L, Thornton JC, Engle JC, Cross FS, Schreiber H. Coronary artery bypass grafting with saphenous vein. *Circulation* 1989;79 suppl I:I-24-9.
18. LoGerfo FW, Quist WC, Crawshaw HM, Haudenschild C. An improved technique for preservation of endothelial morphology in vein grafts. *Surgery* 1981;90:1015-24.
19. Cantinella FP, Cunningham JN, Srungaram RK, et al. The factors influencing early patency of coronary artery bypass grafts. *J Thorac Cardiovasc Surg* 1982;83:686-700.
20. Santoli E, Mattia DD, Boldornini R, Mingoli A, Tosoni A, Santoli C. University of Wisconsin solution and human saphenous vein graft preservation: preliminary anatomic report. *Eur J Cardiothorac Surg* 1993;7:548-52.
21. Manciet LH, Poole DC, McDonagh PF, Copeland JG, Mathieu-Costello O. Microvascular compression during myocardial ischemia: mechanistic basis for no-reflow phenomenon. *Am J Physiol* 1994;266:H1541-50.
22. Lytle BW, Loop FD, Cosgrove DM, Ratliff NB, Easley K, Taylor PC. Long-term (5-12 years) serial studies of internal mammary artery and saphenous vein coronary artery bypass grafts. *J Thorac Cardiovasc Surg* 1990;15:15-20.
23. Krasnicka B, Moritz T, Henderson W, et al. Modeling clustered dichotomous data with multiple subclusters. *J Am Statistical Assoc*. In Press.