Influence of patient characteristics and arterial grafts on freedom from coronary reoperation

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Objective: Arteriosclerosis is a progressive disease, and many patients require repeat coronary intervention after coronary artery bypass grafting. We sought to identify patient characteristics and operative factors that predict the need for or bias toward reoperative coronary artery bypass grafting.

Methods: From 1971 to 1998, 48,758 patients underwent primary isolated coronary artery bypass grafting, and 1000 per year were followed every 5 years ($n = 26,927$). A multivariable time-related analysis was performed to model freedom from coronary reoperation and to identify patient and operative variables associated with occurrence of coronary reoperation.

Results: Freedoms from reoperative coronary artery bypass grafting were 99.6%, 98.4%, 93%, 82%, 72%, and 65% at 1, 5, 10, 15, 20, and 25 years, respectively. Risk of reoperation (hazard function) demonstrated a short, rapidly declining early phase, followed by a long, slow-rising late phase. Patient variables that increased the likelihood of coronary reoperation included younger age ($P < .0001$), higher total cholesterol ($P = .0004$) and triglyceride levels ($P = .0005$), lower high-density lipoprotein ($P = .0002$) level, diabetes mellitus ($P < .0001$), and more extensive coronary artery disease ($P = .01$). Increasing extent of arterial grafting performed at primary coronary artery bypass grafting decreased occurrence of coronary reoperation ($P < .0001$).

Conclusion: Patient factors associated with arteriosclerosis progression and type of bypass conduit influence the need for or bias toward repeat coronary artery bypass grafting. Aggressive patient risk-factor reduction and extensive arterial coronary revascularization at primary coronary artery bypass grafting should result in fewer coronary reoperations.

Coronary artery bypass grafting (CABG) is a temporary treatment for a chronic disease. Arteriosclerosis progresses in native coronary arteries and bypass grafts after revascularization, resulting in recurrent ischemic events and need for further intervention. Risk-factor reduction and arterial grafting have been advocated to improve long-term results of myocardial revascularization.¹⁻⁵ For a better understanding of how patient characteristics and operative techniques influence the likelihood of coronary reoperation, we identified factors predictive of the need for or bias toward reoperative CABG.

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
 EF = ejection fraction
 ITA = internal thoracic artery
 LAD = left anterior descending coronary artery
 RCA = right coronary artery

Patients and Methods

Patients

From 1971 to 1998, 48,758 patients underwent primary isolated CABG at The Cleveland Clinic Foundation. Preoperative characteristics, operative procedures, and hospital outcomes were collected prospectively and entered into a registry. The first 1000 patients of each calendar year ($n = 26,927$) were actively followed every 5 years and comprise the study population. Entry into the study was stopped at the end of 1997 to provide a minimum follow-up of 5 years. Mean follow-up was 9.0 ± 6.7 years; 17,829 patients were followed for at least 5 years, 10,913 for at least 10 years, 5102 for at least 15 years, 1867 for at least 20 years, and 237 for at least 25 years. A total of 671 patients were lost to follow-up. Total follow-up was 236,992 patient-years. The outcome investigated was first reoperation for ischemic heart disease. Use of these data for clinical research was approved by the institutional review board.

Statistical Methods

Analysis. Freedom from reoperation was estimated nonparametrically using the Kaplan–Meier method⁶ and parametrically using a multiphase hazard method.⁷ (For additional details, see <http://www.clevelandclinic.org/heartcenter/hazard>.) The parametric method involved determining the number of hazard phases, the equation form for each, and parameters characterizing the distribution of times to reoperation.

To identify preoperative patient characteristics and operative techniques (Appendix) associated with reoperation, multivariable analyses were performed in the hazard-function domain. A directed stepwise entry of variables into the model, including appropriate transformations of continuous and ordinal variables, was performed.⁸ A P value of .05 or less was considered significant for retaining variables in the model. Interactions among significant variables were sought. Bootstrap aggregation (bagging) was used for variable and interaction validation.^{9,10}

Presentation. To simplify graphs, actuarial estimates are presented at yearly intervals. To depict reoperation stratified by patient characteristics or operative technique, actuarial estimates were made of each stratum, and parametric predicted freedom from reoperation, calculated for each patient in each stratum from the risk-factor model, was superimposed. Seventy percent confidence limits equivalent to 1 SE are given for actuarial and parametric estimates.

Variables and Definitions

Values of preoperative patient characteristics and operative techniques used in the multivariable analyses were obtained at primary CABG. Left ventricular function was graded as normal (ejection

Figure 1. Reoperative CABG after primary CABG for all patients. A, Predicted and actuarial estimates for freedom from reoperation. Solid line represents predicted estimates enclosed within dashed 70% confidence limits (1 SE). Symbols represent actuarial estimates at yearly intervals, and error bars represent 70% confidence limits. Numbers in parentheses are numbers of patients at risk. B, Hazard function (instantaneous risk) for reoperation. Dashed lines are 70% confidence limits.

fraction [EF] $\geq 60\%$), mild dysfunction (EF 40%-59%), moderate dysfunction (EF 25%-39%), or severe dysfunction (EF $< 25\%$).

A coronary artery system was considered importantly stenotic if it contained an obstruction at least 50% of the diameter. Incomplete revascularization was defined as failure to graft any system containing at least 50% stenosis, or left anterior descending coronary artery (LAD) and circumflex systems for at least 50% left main trunk stenosis.

Results

Coronary Reoperation

A total of 2637 patients underwent coronary reoperation. Non-risk-adjusted freedoms from reoperation at 1, 5, 10,

TABLE 1. Baseline patient characteristics (n = 26,968 patients)

Characteristic	Reoperation		P value
	No (n = 24,331)	Yes (n = 2,637)	
Demographic			
Age (years, mean $\pm$ SD)	59.6 $\pm$ 10.0	52.7 $\pm$ 8.1	<.0001
Male (No.)	19,823 (82%)	2,352 (89%)	<.0001
Noncardiac comorbidity (No.)			
Diabetes mellitus (medically treated, No.)	3,724 (17%)	120 (5%)	<.0001
History of smoking (No.)	12,028 (54%)	1,130 (51%)	.01
Laboratory values (mean $\pm$ SD)			
Total cholesterol	236.7 $\pm$ 52.1	252.5 $\pm$ 52.3	<.0001
Low-density lipoprotein	149.2 $\pm$ 41.2	56.0 $\pm$ 48.1	.3
High-density lipoprotein	37.2 $\pm$ 10.1	37.2 $\pm$ 12.1	.9
Triglycerides	191.7 $\pm$ 122.6	213.8 $\pm$ 126.3	<.0001
Blood urea nitrogen	18.7 $\pm$ 10.1	17.3 $\pm$ 8.5	.2
Symptoms			
New York Heart Association class (No.)			<.0001
I	4,205 (18%)	287 (11%)	
II	8,294 (34%)	904 (34%)	
III	2,499 (10%)	274 (10%)	
IV	9,316 (38%)	1,170 (44%)	
Cardiac comorbidity			
Left ventricular dysfunction (No.)			<.0001
None	11,132 (47%)	1,542 (59%)	
Mild	7,008 (30%)	743 (28%)	
Moderate	3,684 (15%)	273 (10%)	
Severe	1,886 (8%)	71 (3%)	
Previous myocardial infarction (No.)	13,473 (55%)	1,234 (47%)	<.0001
Coronary artery disease ($\geq$ 50% stenosis, No.)			
Left main trunk	3,502 (14%)	301 (11%)	<.0001
LAD	22,288 (92%)	2,292 (87%)	<.0001
Left circumflex coronary artery	18,282 (75%)	1,854 (70%)	<.0001
RCA	19,748 (82%)	2,033 (77%)	<.0001
No. of diseased systems ($\geq$ 50% stenosis, No.)			<.0001
0	149 (1%)	12 (1%)	
1	2,558 (10%)	408 (15%)	
2	7,088 (29%)	880 (33%)	
3	14,528 (60%)	1,337 (51%)	
Operative procedure (No.)			
Incomplete revascularization	19,386 (80%)	1,960 (74%)	<.0001
Single ITA grafting	13,684 (56%)	1,017 (39%)	<.0001
Bilateral ITA grafting	2,134 (9%)	40 (2%)	<.0001
ITA graft target vessel			
LAD	14,554 (60%)	916 (35%)	<.0001
Left circumflex	2,313 (10%)	45 (2%)	<.0001
RCA	682 (3%)	24 (1%)	<.0001

15, 20, and 25 years were 99.6%, 98.4%, 93%, 82%, 72%, and 65%, respectively (Figure 1, A). Two hazard phases were identified: a short, rapidly declining early phase followed by a long, slow-rising late phase beginning 1.5 years after the primary operation (Figure 1, B). One hundred three patients underwent reoperation during the early phase and 2534 during the late phase.

Risk Factors for Reoperation

In univariable analyses, patients who underwent reoperation were younger, were more likely to be male, and had more severe symptoms (Table 1). They also had higher total cholesterol and triglycerides, better left ventricular function, fewer internal thoracic artery (ITA) grafts, and more incomplete revascularization at the primary operation. In multivariable

TABLE 2. Risk factors for reoperation

Factor	Hazard phase	
	Early	Late
Demographic		
Younger age		Increased
Male		Increased
With ITA graft to LAD		Lowered
Symptoms		
Higher New York Heart Association class	Increased	Increased
Noncardiac comorbidity		
History of smoking		Lowered
Diabetes mellitus		Increased
Laboratory values		
Higher total cholesterol		Increased
Lower high-density lipoprotein		Increased
Higher low-density lipoprotein	Increased	
Higher triglycerides	Lowered	Increased
Higher blood urea nitrogen		Lowered
Cardiac comorbidity		
Myocardial infarction		Lowered
Better left ventricular function	Increased	Increased
Coronary artery disease		
Left main trunk stenosis (any) and elevated triglycerides		Increased
LAD stenosis (any)		Increased
Left circumflex stenosis (≥70%)		Increased
RCA stenosis (any) and normal triglycerides		Increased
Operative procedure		
Incomplete RCA revascularization	Lowered	
ITA graft to LAD		Lowered
ITA graft to left circumflex		Lowered
ITA graft to RCA and later date of operation		Lowered
Intra-aortic balloon pump insertion	Increased	
With elevated New York Heart Association class	Lowered	
Experience		
Later date of operation		Lowered

analysis, patient characteristics (including demographic data, cardiac and noncardiac comorbidity, and extent of coronary disease) and operative techniques at primary CABG (including ITA grafting and date of primary operation) influenced need for or bias toward reoperation (Table 2). Because the early phase was small and the late phase large, factors influencing the late phase had a greater impact on likelihood of reoperation.

Demographic data. Men were more likely to undergo reoperative CABG than were women ($P = .002$); however, an ITA-LAD graft neutralized this increased risk ($P = .03$). Younger patients were more likely to undergo reoperation ($P < .0001$; Figure 2).

Figure 2. Predicted and actuarial estimates of freedom from reoperative CABG after primary CABG stratified by age (in years). Solid lines represent predicted estimates enclosed within dashed 70% confidence limits (1 SE). Symbols represent actuarial estimates at yearly intervals, and error bars represent 70% confidence limits.

Noncardiac comorbidity. Diabetes mellitus was associated with higher likelihood of reoperation (Figure 3). Patients treated with insulin and oral medications had equivalent elevated risks of undergoing coronary reoperation ($P < .0001$), but the risk for patients with diet-controlled diabetes was only slightly higher than that for patients without diabetes ($P = .006$). Abnormal lipid profile also increased the risk of reoperation. Specifically, elevated total cholesterol ($P = .0004$), low-density lipoprotein ($P = .01$), and triglyceride ($P = .0005$) levels increased risk, as did lower high-density lipoprotein level ($P = .0002$). Although an elevated triglyceride level appeared to lower early risk of reoperation, overall it increased the risk because of the larger impact of late-phase risk factors. Renal insufficiency lowered the likelihood of reoperation ($P = .03$).

Cardiac comorbidity and coronary artery disease. More extensive coronary artery disease ($P = .01$) and better left ventricular function ($P = .0001$) increased the likelihood of reoperation. Left main stenosis was a risk factor only when associated with elevated triglyceride level ($P = .01$), whereas right coronary artery (RCA) stenosis was associated with reoperation when triglyceride level was normal ($P = .007$). A previous myocardial infarction decreased risk ($P < .0001$), and the more severe symptoms a patient had at primary operation, the greater was the risk of reoperation ($P = .005$).

Operative procedure. More extensive ITA grafting lowered risk of reoperation ($P < .0001$; Figure 4). However, ITA grafts to the RCA were not associated with lower risk until the latter half of the series ($P = .002$; Figure 5).

Figure 3. Predicted and actuarial estimates of freedom from reoperative CABG after primary CABG stratified by diabetes mellitus and its treatment by either diet or medicines. *Solid lines* represent predicted estimates enclosed within *dashed* 70% confidence limits (1 SE). *Symbols* represent estimates at yearly intervals, and *error bars* represent 70% confidence limits.

Intra-aortic balloon pump insertion at primary operation increased risk of early reoperation ($P < .0001$). Patients operated on later in the series were less likely to undergo reoperation ($P < .0001$).

Discussion

Background

Recurrent ischemia after CABG is a serious problem, with only 22% of patients free of ischemic events 15 years after

Figure 4. Predicted and actuarial estimates of freedom from reoperative CABG after primary CABG stratified by use of single or double ITA grafting at primary operation. *Solid lines* represent predicted estimates enclosed within *dashed* 70% confidence limits (1 SE). *Symbols* represent actuarial estimates at yearly intervals, and *error bars* represent 70% confidence limits.

surgery.¹¹ Etiologies include incomplete revascularization, graft failure from technical problems, and arteriosclerosis progression in native coronary arteries or bypass grafts. Treatment includes medical management to control symptoms and surgical or percutaneous reintervention to improve myocardial blood flow and decrease ischemia.

The decision about appropriate treatment must be made for each patient by weighing the risks of treatment against the benefits. Comorbidities and amount of ischemic myocardium are important considerations. Healthy patients with large amounts of myocardium at risk are more likely to undergo reoperation, whereas those with multiple comorbidities, patent arterial grafts, and small areas of ischemic myocardium are more likely to receive medical therapy or percutaneous intervention. To understand what drives the need for or bias toward for coronary reoperation, we identified factors associated with the likelihood of undergoing reoperation.

Principal Findings

Patient characteristics and operative procedures during primary operation each influenced the likelihood of undergoing reoperation. Some patient factors increased risk (eg, risk factors for arteriosclerosis), whereas others decreased it. Operative factors that influenced risk included conduit choice and success of the primary revascularization.

Risk factors for arteriosclerosis. Diabetes mellitus and an abnormal lipid profile were associated with increased risk of undergoing reoperation. These are known risk factors for arteriosclerosis and probably increased the likelihood of reoperation by promoting arteriosclerosis progression in native coronary arteries and arteriosclerosis development in bypass grafts. In contrast, elevated high-density lipoprotein

Figure 5. Predicted 20-year freedom from reoperation for patients with and without an ITA graft to RCA according to year of operation. *Dashed lines* represent 70% confidence limits.

protected against need for reoperation, most probably by lessening the risk of arteriosclerosis.

Comorbidity and symptoms. Smoking, older age, renal insufficiency, and worse left ventricular function decreased the likelihood of reoperation. All these factors elevate mortality and morbidity associated with reoperation and thus may have biased the treatment decision against reoperation and in favor of medical therapy or percutaneous intervention.

Patients who had more severe symptoms at the primary operation were more likely to undergo reoperation. Such patients may have a greater sensitivity to ischemia. Thus, if ischemia recurs, they may be more likely to have worse angina and to require reoperation to relieve symptoms.

ITA grafts. More extensive ITA grafting lowered the risk of reoperation. ITA grafts have better long-term patency than saphenous vein grafts because of their freedom from arteriosclerosis.¹² It is logical to assume that if grafts that are more likely to remain patent are used at primary operation, important ischemia is less likely to recur, and therefore the need for reoperation will be lower. Incremental benefits of one and then two ITA grafts in terms of both survival and freedom from reoperation have been previously demonstrated.¹⁻³

Sergeant and colleagues¹³ found that the likelihood of reintervention (reoperation and percutaneous therapy) was strongly reduced by increasing the number of ITA grafts at primary operation. However, they noted no decrease in recurrence of angina with arterial grafting.^{11,13} They hypothesized that physicians and surgeons were biased against reintervening in patients with multiple arterial grafts—perhaps appropriately so! The survival benefit from reoperating on patients with patent arterial grafts, particularly to the anterior wall of the left ventricle, is small; thus, reintervention may not be in their best interest because the amount of myocardium at risk may not be large enough to justify reoperation.

ITA grafting to the RCA did not decrease occurrence of reoperation until the latter half of this study. A possible explanation is that percutaneous therapy was not available during the early years, so reoperation was the only way to improve myocardial blood flow. After percutaneous therapy was introduced, there may have been a treatment bias against reoperation in these cases. A second explanation is that with greater surgical experience, it became known that ITA graft patency was lower when used to bypass the RCA than the left-sided coronary arteries.¹² This is due to native blood vessel competitive flow.¹⁴ Use of ITAs to graft RCAs likely became more selective with greater surgical experience, and thus they were more likely to remain patent when used for this purpose later in the study.

Success of primary operation. Insertion of an intra-aortic balloon pump at the primary operation was associated with increased risk of undergoing reoperation within 18

months. Need to place a pump at operation suggests failure of revascularization, possibly from early graft failure or incomplete revascularization. Unsuccessful primary operation would result in failure to relieve symptoms of ischemia, and patients would likely have symptoms early after surgery and require reintervention.

Incomplete revascularization was found by univariable analysis, but not by multivariable analysis, to be associated with reoperation. This may be due to incomplete revascularization being highly correlated with another variable found to be significant in the multivariable analysis (eg, intra-aortic balloon pump); in that case, incomplete revascularization would no longer appear important.

Limitations

Although many patient and operative variables were included in the analysis, important variables may not have been recorded. This is perhaps why some factors identified are difficult to explain. For example, it is hard to understand how incomplete revascularization to the RCA and elevated triglyceride level both lowered the early risk of reoperation. It is possible that these significant variables are correlated with other factors we did not identify or investigate. They also may have been found to be significant by chance alone.

The study period includes three decades of coronary surgery. Both surgical and medical therapy changed during this period, and many treatments available today were not available early in this study. However, using all three decades of data allowed us to evaluate the influence of surgical treatments that were common early in the series but not today, such as saphenous vein grafting to the LAD.

Values of variables used in the analyses were obtained at the primary operation. Thus, we were unable to evaluate how changes in these affected occurrence of reoperation. For example, elevated lipid levels at first revascularization increased the likelihood of undergoing reoperation; however, we do not know whether lowering them after revascularization altered risk.

We evaluated only reoperation; however, during the time of this study, percutaneous intervention became an important treatment for myocardial ischemia, and it is likely that many patients receiving percutaneous therapy today would have undergone reoperation in the past. This may explain why patients later in the series were less likely to undergo reoperation.

Parametric Analysis

To identify time-related risk factors for reoperation, a parametric analysis was used. We believe that this type of analysis has several advantages relative to a Cox-proportional hazards analysis, which assumes the influence of a risk factor is present and of equal importance throughout the period of risk. This may not be true. Some factors may be associated

with early risk; others may not exert an effect until much later. Parametric analysis solves this weakness by identifying (1) different phases of risk, (2) which risk factors are associated with each phase, and (3) the strength of risk factors in each phase. Thus, in this study, many risk factors associated with late reoperation had no effect during the early phase. Rather, they were related to either arteriosclerosis progression or arterial grafts, which would be expected to influence the need for late but not early reoperation.

A second benefit of parametric analysis is that risk prediction can be made for an individual patient. With the risk factors identified in this analysis, an individual's likelihood of undergoing reoperation can be determined. This information may be useful in advising patients about the risks and benefits of revascularization.

Conclusion

Reoperation for myocardial ischemia is common after primary revascularization. Patient characteristics associated with arteriosclerosis progression and type of bypass conduit influence the need for or bias toward repeat CABG. Aggressive patient risk-factor reduction and extensive arterial coronary revascularization should result in fewer coronary reoperations.

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Appendix: Variables Considered in Analyses

Demographic

Gender, age (years), height (cm), weight (kg), body surface area (m^2), body mass index ($kg \cdot m^{-2}$)

Symptoms

New York Heart Association functional class (I, II, III, IV)

Left Ventricular Function

Left ventricular function (normal and mild, moderate, and severe dysfunction), previous myocardial infarction, left ventricular segmental wall motion abnormalities (septal, anterior, inferior, lateral, apical, basilar, none)

Cardiac Comorbidity

Family history of coronary artery disease, atrial fibrillation, complete heart block

Noncardiac comorbidity

History of cigarette smoking, peripheral vascular disease, carotid stenosis, hypertension, diabetes mellitus (diet controlled, orally treated, insulin treated), renal insufficiency

Preoperative Laboratory Values

Total cholesterol level, high-density lipoprotein level, low-density lipoprotein level, triglyceride level, creatinine level, blood urea nitrogen, hematocrit

Coronary Artery Anatomy and Stenosis

Dominance (left, right, codominant), number of coronary artery systems with at least 50% stenosis (one, two, three), left main trunk stenosis (any, $\geq 50\%$ stenosis, $\geq 70\%$ stenosis), LAD stenosis (any, $\geq 50\%$ stenosis, $\geq 70\%$ stenosis), circumflex stenosis (any, $\geq 50\%$ stenosis, $\geq 70\%$ stenosis), RCA stenosis (any, $\geq 50\%$ stenosis, $\geq 70\%$ stenosis)

Procedure

Complete revascularization; incomplete revascularization of LAD, circumflex, or RCA system; any ITA grafting; ITA graft to LAD, circumflex, or RCA; any saphenous vein grafting; saphenous vein graft to LAD, circumflex, or RCA

Experience

Date of operation

Postoperative Management

Postoperative intra-aortic balloon pump

Discussion

Dr Craig R. Smith (*New York, NY*). For more than 20 years, the surgeons at the Cleveland Clinic have been teaching us the benefits of ITA conduits. First, they demonstrated improved survival at 10 years for patients who received a single ITA bypass relative to patients who received vein grafts. In 1999, they demonstrated improved survival, freedom from reoperation, and freedom from percutaneous coronary intervention at 10 years favoring bilateral ITA grafting versus single ITA grafting. In 2004, they did a complex propensity score analysis that demonstrated a similar benefit for bilateral ITA grafting versus single ITA grafting, with follow-up extended to 20 years.

Today, Sabik and coauthors have narrowed their focus to the risk of reoperation and extended the follow-up to 25 years, at which point 65% of their patients have avoided coronary reoperation. Just as important, they have demonstrated that increased use of arterial conduits very significantly increased freedom from reoperation.

I think there are at least three “freedoms” that might be relevant to our understanding of the long-term benefits of CABG. The most comprehensive is freedom from all ischemic events, even those not requiring any kind of intervention. Next in line, at least with respect to frequency, is freedom from any reintervention, followed by its smaller subset, freedom from reoperation, which was the focus of this discussion.

Many of you will remember a series from Belgium that was published in 1991 by Sergeant and Blackstone, in which freedoms from all ischemic events were 54% at 10 years and a mere 22% at 15 years. This is in contrast to the data that you have just heard, in which freedoms from reoperation were 93% at 10 years and 82% at 15 years. So if we assume, for the sake of argument, that the 1991 figures still apply, this leaves a 50% to 60% gap between ischemic events and reoperation.

I think it is interesting to speculate, as some have, that surgical treatment might actually increase this gap if it produces a stable ischemic syndrome or increases reluctance to reoperate, and there are those who believe that bilateral ITA bypasses have both those effects. Be that as it may, we should certainly hope that improvements in surgery have narrowed the gap by reducing the frequency of nonsurgical ischemic events. With this in mind, Dr Sabik, and understanding that this was not the purpose of your study, do you have any information or opinion regarding the freedom from all ischemic events in this group or the frequency of nonsurgical reinterventions?

According to one of your tables, revascularization was judged to be incomplete in 80% of the group not undergoing reoperation. This seemed improbably high to me and was significantly higher than what you observed in the reoperative group ($P < .0001$). If I understand your analysis, a 50% stenosis is indistinguishable from a 99% stenosis in the tabulation. Is it possible that the group not undergoing reoperation had a higher frequency of debatable 50% to 60% lesions of no surgical significance and that the reoperative group had a higher frequency of lesions more severe than 75%?

I also noticed that bilateral ITA conduits were used in 8% of all patients, and one or two ITAs were used in 71% of all patients. Both figures seem low. I assume this is because ITA use has increased with time. How frequently do you use bilateral ITAs today?

I would also like to know your group's view on the advisability of sequential ITA bypasses. And should the desire to use bilateral ITAs influence the choice of off-pump versus on-pump CABG?

Dr Sabik. Thank you for your insightful comments and questions. We have not determined the freedom from all ischemic events after coronary surgery. However, we have begun to analyze our data to determine freedom from all coronary reinterventions, both reoperation and percutaneous intervention, after CABG. Freedoms from all coronary reinterventions are about 80% at 10 years and about 60% at 20 years. Risk factors for reintervention are similar to those we presented today for reoperation. Risk factors for arteriosclerosis increase the likelihood of reintervention, and arterial grafting lowers the risk. An interesting finding in this analysis is that freedom from percutaneous intervention after coronary surgery is not decreased by ITA grafting at the first operation. We believe that this suggests a bias in treatment of patients with recurrent ischemia and patent arterial grafts. This bias, however, may be appropriate. We are unlikely to reoperate on a patient with recurrent angina from stenosis of a diagonal who has patent ITA grafts to his or her LAD and circumflex. The benefit of reoperation does not outweigh the risk. However, percutaneous intervention to the diagonal to relieve symptoms may be appropriate.

Completeness of revascularization was 80% in the no reoperation group and 74% in the reoperation group. Incomplete revascularization was found by univariable analysis, but not by multivariable analysis, to be associated with reoperation. This may have been due to incomplete revascularization being highly correlated with another variable found to be significant in the multivariable analysis. We defined incomplete revascularization as failure to graft any coronary system containing a stenosis of at least 50% or failure to graft the LAD and circumflex in patients with at least 50% stenosis of the left main trunk. We did not specifically determine whether the grade of coronary lesion was less in the incompletely revascularized no reoperation group than in the reoperation group. However, we did find the degree of coronary stenosis to be directly related to the likelihood of reoperation.

This study covers three decades of surgical revascularization, and our use of ITA during this period changed. In the 1970s, many patients did not receive even single ITA grafting, and few underwent bilateral ITA grafting. This explains the overall low bilateral ITA use. Our bilateral ITA use increased in the latter two decades of the study. However, inclusion in this study of patients operated on early in the series was extremely valuable, because it allowed us to determine how different revascularization strategies affected the likelihood of coronary reoperation.

We use ITAs to perform both sequential grafts and composite T or Y grafts. The technique used depends on the quality of the ITA, the coronary anatomy, and the preference of the surgeon. If the ITA is small, we use it as a single graft. If it is of good quality, we may use it as a sequential graft if the coronary anatomy allows sequential grafting without kinking of the ITA.

We do not believe that the quality of surgical revascularization should be compromised to avoid cardiopulmonary bypass, unless bypass poses an important risk to the patient. If the same quality of revascularization can be performed off pump as on pump, and the morbidity of the operation can be lowered by performing it off

pump, then off-pump revascularization may be the best way to proceed.

Dr Joan Ivanov (Toronto, Ontario, Canada). This was a typically excellent presentation from your group, Dr Sabik. Reoperation, to me, seems to be a very difficult outcome at which to look, because it is probably the one outcome that is most subject to any kind of selection bias. So can you discuss your predictors, such as age and gender, in that domain?

Second, we have noticed quite a significant reduction, a temporal trend, in the numbers of patients coming back for reoperative CABG. Did you use any kind of temporal marker in your models to try and adjust for time?

Dr Sabik. I agree that the decision to reoperate is highly dependent on selection bias, and that is why in our presentation we stated that our objective was to determine how patient characteristics and the primary operation influence the need for or bias toward coronary reoperation.

How is younger age a risk factor for the likelihood of having a reoperation? We believe it is a surrogate for a patient characteristic, such as a gene that predisposes one toward aggressive arteriosclerosis. Or it may be a surrogate for level of activity. Younger people are more likely to be active than older patients, and they are therefore more likely to have recurrent angina and to be referred for reoperation. An older patient may have had similar arteriosclerosis progression but be less active and without symptoms and therefore not be referred for surgery. We believe that male gender is similarly a surrogate for a patient characteristic not included in our analysis.

Dr Ivanov. And a temporal trend?

Dr Sabik. We used date of surgery to determine the influence of time on the need for or bias toward reoperation. We found that patients operated on in the 1970s and 1980s had a much higher likelihood of undergoing reoperation than those operated on in the 1990s, and we believe this was due to the introduction of percutaneous coronary therapy in the late 1980s.

Dr Harold L. Lazar (Boston, Mass). In your large database, did you have any evidence to suggest that the use of statins or angiotensin-converting enzyme inhibitors in these patients might have prolonged the time to revascularization?

Dr Sabik. We do not have that information in our database.

Dr Brian Buxton (Heidelberg, Austria). Thank you for a lovely article and for drawing our attention to the 20-year results. I would like to follow up Dr Smith's comments on the right ITA by asking you a few more details about its use during the period of the study and what your current recommendations are. Specifically, do you use left or right coronary targets in situ or free grafting?

Dr Sabik. We believe that ITAs should be used preferentially to graft left-sided coronary arteries. We know that their patency—and therefore effectiveness—is greater when they are used to bypass left-sided coronary arteries. We use the left ITA routinely to bypass the LAD and the right ITA to bypass the next most important left-sided coronary artery. We use a radial artery to graft any remaining left-sided coronary artery and a saphenous vein graft to bypass the RCA.

Dr Buxton. What about the proximal attachment to the right ITA? Currently, do you leave it in situ, do a Y graft, or do an aortic anastomosis?

Dr Sabik. We use all three techniques, depending on the quality of the ITAs and the coronary anatomy.

Dr John D. Puskas (Atlanta, Ga). Just to reiterate what Dr Smith asked, the overall series had 8% bilateral ITA use. What is your current use?

Dr Sabik. Overall, we use bilateral ITAs in about 25% of our patients undergoing primary coronary revascularization. This overall percentage is influenced by the characteristics of our patient population. We are unlikely to use bilateral ITAs in obese, insulin-treated patients with diabetes and are very likely to use them in non-insulin-treated patients younger than 70 years.

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