ISOLATED BYPASS GRAFTING OF THE LEFT INTERNAL THORACIC ARTERY TO THE LEFT ANTERIOR DESCENDING CORONARY ARTERY: LATE CONSEQUENCES OF INCOMPLETE REVASCULARIZATION

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Objective: Multiple strategies to achieve some degree of myocardial revascularization are available. In some, less complete revascularization is accepted to limit invasiveness. To examine the issues of incomplete revascularization, we assessed the long-term impact of additional non-left anterior descending coronary artery stenoses in patients undergoing only grafting of the left internal thoracic artery to the left anterior descending coronary artery.

Methods: A total of 2067 patients underwent primary isolated grafting of the left internal thoracic artery to the left anterior descending coronary artery from 1971 to 1997. Of these, 26% and 13% had 2- and 3-system disease, respectively. Multivariable analyses of survival and reintervention were performed in the hazard function domain for 27,683 patient-years of follow-up (mean 14 ± 6.7).

Results: Survival was 99%, 88%, and 62% at 1, 10, and 20 years. Right coronary artery or left circumflex system disease of 50% or more ($P = .02$) and particularly high-grade ($\geq 70\%$) left circumflex ($P = .01$) and proximal right coronary artery disease ($P = .01$), as well as any degree of left main trunk stenosis ($P < .0001$), were associated with reduced long-term survival. Compared with 75% 20-year survival in patients with no non-left anterior descending disease, those with either left circumflex or left main trunk disease experienced a 44% survival, and those with proximal right coronary artery disease, 42%. The most common stated reason for incomplete revascularization was small vessel size. Freedom from reintervention was 89% and 65% at 10 and 20 years, respectively. High-grade left main trunk disease, but, in contrast, mid or distal disease of the right coronary artery, and not left circumflex disease, were risk factors for reintervention.

Conclusions: These findings call into question the long-term appropriateness of interventions whose strategy includes leaving unrevascularized segments in territories not in the distribution of the left anterior descending coronary artery. (J Thorac Cardiovasc Surg 2000;120:173-84)

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Read at the Seventy-ninth Annual Meeting of The American Association for Thoracic Surgery, New Orleans, La, April 18-21, 1999.

Received for publication April 22, 1999; revisions requested Aug 10, 1999; revisions received Feb 22, 2000; accepted for publication March 20, 2000.

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0022-5223/2000 \$12.00 + 0 12/6/107280

doi:10.1067/mtc.2000.107280

One common goal of operations for coronary bypass grafting has been complete revascularization. This goal has been based on logic and on studies from the past that have shown in a general way that *complete revascularization* was associated with better long-term survival.¹⁻⁷ Realistically, it has been difficult to define complete revascularization and to separate the effect of incomplete revascularization as a surgical strategy from the possibility that incomplete revascularization is a marker for worse coronary artery disease or, perhaps, a more rapid rate of progression of coronary artery disease.

Currently, multiple avenues to achieve some degree of myocardial revascularization are available. In some of

Table I. Coronary lesions, cardiac function, symptoms, and comorbidity of patients undergoing LITA-LAD grafting

Variables	No.	% of 2067
Coronary anatomy		
Extent of disease (50% criterion)		
Single-system	1274	62
Two-system	533	26
Three-system	260	13
Left main disease		
None	1902	92
>0	165	8
≥50%	29	2
Coronary dominance		
Right	1469	71
Left	311	15
Codominant	242	12
Unknown	45	2
Left ventricular dysfunction		
None	1352	65
Mild	520	25
Moderate	154	8
Severe	41	2
Angina limitation		
None	302	15
Mild	647	31
Moderate	216	10
Severe	902	44
Comorbidity		
Pharmacologically treated	145	8
diabetes (missing data in 214)		
Smoking history (missing data in 257)	942	52
Previous MI (missing data in 2)	847	41
PVD (missing data in 2)	120	6
Renal failure (missing data in 2)	6	0.3

LITA-LAD, Left internal thoracic artery–left anterior descending coronary artery; MI, myocardial infarction; PVD, peripheral vascular disease.

the strategies, percutaneous and operative, less complete revascularization is accepted to limit the invasiveness of the procedure. Part of the logic behind these strategies is the thought that the left internal thoracic artery to left anterior descending coronary artery (LITA-LAD) graft is so important that revascularization of other areas is relatively unimportant. Our previous studies of patients receiving LITA-LAD grafts have shown that nonsignificant disease in the territories of the right coronary artery (RCA) and left circumflex coronary artery (LCx) system is a predictor of late events.⁸ However, to examine with a larger patient subset the prognostic issues of incomplete revascularization in patients who already have significant stenoses, we studied 2067 patients undergoing operation with an isolated LITA graft solely to the LAD during the years 1971 through 1996, with follow-up extending to 25 years.

Patients and methods

Study group. A total of 2067 patients undergoing isolated grafting of the LITA to the LAD as their sole coronary intervention, for the first time, without concomitant procedures, using a conventional median sternotomy and cardiopulmonary bypass, during the years 1971 through 1996, were identified by means of the Cardiovascular Information Registry (CVIR) at The Cleveland Clinic Foundation. The only patients excluded were those undergoing less invasive surgery and “off-pump” surgery. Demographic, clinical, coronary angiography, surgical, and complication variables were abstracted essentially concurrently with clinical events into the prospective CVIR database. Of the 2067 patients, 1674 (81%) were men and 393 (19%) women. The mean age at operation was 54 ± 9.0 years, ranging from 26 to 83 years. Table I summarizes other characteristics of these patients.

Follow-up. CVIR personnel follow up the first 1000 patients per year undergoing primary elective isolated coronary bypass grafting at 5-year intervals. Those patients in the present study group not part of this routine follow-up were contacted by telephone in the summer of 1998. Twenty-seven (1.3%) were lost to follow-up, most of whom were foreign patients. Total follow-up was 27,683 patient-years, mean 14 ± 6.7 years. The longest follow-up was 25.8 years. Among survivors, 89% have been followed up for 5 years or more, 71% for 10 years or more, 54% for 15 years or more, 32% for 20 years or more, and 2% for 25 years or more.

Angiographic data. Stenoses were recorded by CVIR abstractors from the catheterization report for each coronary system as follows. For the LAD system, the maximal stenosis was recorded in the proximal, mid, and distal portions of the LAD, the diagonal branches, a major septal artery, and the ramus intermedius coronary artery if it originated from the LAD. For the LCx system, the maximal stenosis was recorded in the proximal LCx, the lateral branches, posterolateral segments, in the ramus intermedius if it came off the circumflex, and in the posterior descending coronary artery if it originated from the LCx in a left dominant pattern. For the RCA system, the maximal stenosis was recorded in the proximal, mid, and distal RCA, right marginals, and posterior descending coronary artery and posterolateral segments in right dominant patterns.

Incomplete revascularization. We defined incomplete revascularization as the presence of stenosis in the LCx or RCA systems of 50% or greater. This definition assumes that (1) the LITA-LAD graft allows complete perfusion of the LAD system and (2) stenosis of the left main trunk is managed separately in the analyses. In addition to this arbitrary, global dichotomous variable, we investigated the overall maximal LCx and RCA system stenoses, as well as stenosis in each of the segments cited above. For this we used both the “continuous” percent stenosis and variables representing three discrete criteria: (1) stenosis greater than 0 (any stenosis), (2) stenosis of 50% or greater diameter reduction, and (3) stenosis of 70% or greater diameter reduction.

To verify the quality of this information, and to ascertain the recorded reasons non-LAD lesions were not bypassed, we selected a 10% random sample of cases with lesions in the RCA or LCx system greater than or equal to 50% for detailed study. For this, the uniform pseudorandom number generator in the SAS system software (SAS Institute, Inc, Cary, NC) was used. Because of systematic discard of angiograms by the institution and missing records, a total of 268 random records were randomized to obtain the requisite 206 complete records. All coronary angiography reports were reviewed, which in most cases included prints of representative angiographic frames rather than original angiographic films that had been destroyed or returned to the referring institution. For patients catheterized elsewhere, both the outside catheterization report and the report of its review by Cleveland Clinic Foundation cardiologists were examined. Recommendations made by cardiologists preoperatively were recorded. Each operative report was reviewed, along with any other records, such as letters to referring physicians, to record reasons for incomplete revascularization.

Data analysis. The end points for this study were two: (1) all-cause mortality from the time of LITA-LAD grafting and (2) reintervention, either by percutaneous revascularization of any kind (generically designated percutaneous transluminal coronary angioplasty [PTCA]) or reoperation. The primary objective of the data analysis was to determine the association, if any, between unbypassed lesions in the non-LAD coronary systems (left main, LCx, RCA) and these time-related events. Secondary objectives included investigating the pattern of incomplete revascularization across time and identifying the reasons for incomplete revascularization.

Nonparametric estimates of survival and freedom from reintervention were obtained by the method of Kaplan and Meier.⁹ A parametric method* was used to resolve the number of phases of instantaneous risk of death (hazard function) and to estimate their shaping parameters.¹⁰

The potential risk factors (variables) obtained from the CVIR database were organized for analysis as in Appendix Table I. Exploratory analyses of these variables included correlation analysis, stratified life table analyses, and decile risk analysis of ordinal and continuous variables to determine possible transformations of scale needed to properly calibrate the variables to outcome.

Multivariable analyses were performed with particular attention to the details of the unbypassed coronary stenoses. Specific so-called interaction analyses were conducted of the coronary lesions identified as risk factors with the pattern of coronary artery dominance, left ventricular function, age, and diabetes. Interaction analysis was also performed of incomplete revascularization (see below). The analyses used a directed technique of entry of variables into the multivariable models.¹¹ The *P* value criterion for retention of variables in the final models was .05.

Multivariable logistic regression analysis was used to identify the characteristics of patients with incomplete revascularization. For this, all patient variables were examined, but the only coronary artery variables incorporated into the analysis were those related to the pattern of coronary dominance.

Presentation. Because few patients were followed up longer than 25 years, graphical presentations were truncated at 25 years. *Nonparametric* Kaplan-Meier time-related estimates are presented as discrete symbols accompanied by asymmetric confidence limits (CL) equivalent to 1 SE.¹² Smooth, solid curves, which are superimposed on the symbols, are completely independent *parametric* estimates of the distribution of intervals to death or reintervention. These are accompanied by confidence limits equivalent to 1 SE.¹⁰

For informal survival comparison and reference, a predicted US population life table was generated for each patient, specific to his or her sex and age at the time of the operation. These tables were averaged to portray an age-sex-matched population life table. For some comparisons, individual curves were generated for each patient from the multivariable equations and averaged within strata.¹³ These were compared with stratified Kaplan-Meier estimates.

For comparisons of survival in patients with disease other than in the LAD system, a cohort of 682 patients was identified with no recognized obstruction of *any degree* (not just nonsignificant obstruction) in the left main trunk, LCx system, or RCA system. For clarity, only parametric estimates of this cohort are portrayed.

Results

Incomplete revascularization. The prevalence of incomplete revascularization (50% or greater lesions in either the RCA or LCx systems) fell from about 60% to 20%-25% by the early 1980s and remained at those levels (Fig 1). The most common reason recorded for not grafting non-LAD vessels was that the arteries were too small (Table II). In a few cases, specific problems with conduit availability or unavailability of a site for aortic graft attachment were recorded. In a few cases, available records did not indicate the presence of non-LAD lesions of 50% or more, and in 3 cases (1.5%), data entry was erroneous.

Correlates of incomplete revascularization included men, old age, greater left ventricular dysfunction, previous myocardial infarction, a left dominant coronary circulation, diabetes, higher cholesterol level, peripheral vascular disease, and earlier date of operation (Table III).

Survival. Risk-unadjusted survival was 99.1%, 96%, 88%, 76%, 62%, and 48% at 1, 5, 10, 15, 20, and 25 years after LITA-LAD grafting, respectively (Fig 2). The instantaneous risk of death was highest immediately after operation, fell to a low level, and then began to rise steadily about 6 months after the operation (Fig

*Available by anonymous ftp from <ftp://uabcvsr.cvsr.uab.edu>

Fig 1. Prevalence of incomplete revascularization across calendar date. The *filled circles* represent the proportion of each calendar year's LITA-LAD grafting cases with incomplete revascularization, defined as 50% or greater obstructions in the RCA or LCx coronary systems. The *solid line* is a Lowes approximation to the distribution of this prevalence, performed in S-Plus with the use of default options.²⁸

Table II. Recorded reasons for incomplete revascularization

Reason	n	% of 206
Small and/or severely diseased artery	92	45
No reason recorded	67	33
CABG not justified (operative note)	10	4.9
Nondominant diseased RCA	5	2.4
No suitable conduit (eg, vein graft) available	4	1.9
Intramyocardial vessel could not be found	2	1.0
Posterior coronary artery inaccessible	2	1.0
Infarcted area	1	0.5
Not a vessel normally bypassed	1	0.5
Inadequate data	3	1.5
LITA-LAD grafting incorrectly coded (and subsequently removed)	3	1.5
No non-LAD disease $\geq 50\%$ on review of available records	13	6.3
Total	206	100

CABG, Coronary artery bypass grafting; LAD, left anterior descending coronary artery; LITA, left internal thoracic artery; RCA, right coronary artery.

2, B). By way of orientation, this hazard function was similar to that predicted for the age-sex-matched US population after about 8 years. The hazard function consisted of a brief early phase, a small constant hazard phase, and a late rising hazard phase. The early hazard phase accounted for only 9 deaths, the constant hazard phase for 111, and the late hazard phase for 453. Thus, in the nonproportional hazards multivariable models, a risk factor in the late hazard phase of similar magnitude to one in the constant hazard phase will have many times larger impact on survival.

Table III. Correlates of incomplete revascularization (unbypassed stenoses $\geq 50\%$ in LCx or RCA systems)

Correlate	Logistic coefficient $\pm$ SD	Direction of influence	P value
Demography			
Men	0.56 ± 0.138	$\uparrow$	<.0001
Age*	0.96 ± 0.140	$\uparrow$	<.0001
LV function			
LV dysfunction†	1.27 ± 0.133	$\uparrow$	<.0001
Previous MI	0.78 ± 0.137	$\uparrow$	<.0001
Left dominant coronary circulation	0.62 ± 0.138	$\uparrow$	<.0001
Noncardiac comorbidity			
Diabetes	0.54 ± 0.20	$\uparrow$	.007
Cholesterol level‡	1.49 ± 0.27	$\uparrow$	<.0001
PVD	0.81 ± 0.22	$\uparrow$	.0002
Date of operation§	-0.87 ± 0.075	$\downarrow$	<.0001
Intercept	-9.3		

LV, Left ventricular; MI, myocardial infarction; PVD, peripheral vascular disease; SD, standard deviation.

*[age/50]² squared transformation.

†ln[LV dysfunction grade] logarithmic transformation.

‡ln[cholesterol level, mg/dL] logarithmic transformation.

§ln[years since 1/1/1971] logarithmic transformation.

Incremental risk factors for death included older age, left ventricular dysfunction, and a history of previous myocardial infarction, peripheral vascular disease, and diabetes (Table IV). In addition, survival was less in patients with left main trunk stenosis of any degree, with incomplete revascularization ($\geq 50\%$) of the LCx and RCA, with high-grade ($\geq 70\%$) stenosis in the LCx system, and with high-grade proximal RCA stenosis.

Fig 2. Survival after LITA-LAD conventional coronary artery bypass grafting (CABG). **A**, Survival. The nonparametric (*small dots*) and parametric (*smooth curves*) estimates are presented as described in the “Methods” section. The *dash-dot-dash line* is an age-sex-matched US population life table estimate for these same patients. **B**, Hazard function.

Left main trunk disease. Lesions in the left main trunk at the time of LITA-LAD grafting were recognized in 165 patients. Stenosis of any degree in the left main trunk was a risk factor for late death (Table IV). To illustrate the impact of left main trunk disease on survival using raw data, Fig 3 compares patients with left main lesions of any degree (unadjusted for other lesions and patient characteristics) with the subgroup patients having no recognized obstructions other than that in the LAD system. At 20 years, survival was 44% (CL 39%-49%) for patients with any degree of left main disease (Table V) compared with 75% (CL 72%-77%).

Correlates of unbypassed left main trunk disease of any degree included men, older age, greater left ventricular dysfunction, peripheral vascular disease, and earlier date of operation (Table VI).

LCx coronary system disease. High-grade ($\geq 70\%$) LCx system disease was present preoperatively in 301 patients (Table V). At 20 years, survival among these patients was 44% (CL 41%-47%) (Fig 5). Those with disease in the lateral LCx branches fared somewhat worse (Fig 5, Table V); their increased risk occurred somewhat earlier than it did with other LCx system lesions (constant hazard phase, Table IV).

RCA system disease. Patients with high-grade proximal RCA lesions, present in 228, had a 42% (CL 38%-46%) 20-year survival (Table V). Their survival was worse compared with a group of patients with RCA system disease ($\geq 50\%$), including those with proximal RCA disease between 50% and 70%, but without left main or LCx disease of any degree (Fig 6). Survival of both these groups, however, was worse than that for the

Table IV. Incremental risk factors for death after LITA-LAD grafting

Incremental risk factor	Coefficient $\pm$ SD	Direction of influence	P value
Early hazard phase			
None	—		—
Constant hazard phase			
Left main trunk stenosis of any degree	1.04 $\pm$ 0.24	↑	<.0001
Incomplete revascularization of LCx or RCA*	0.59 $\pm$ 0.25	↑	.02
LCx lateral branch disease $\geq$ 70%	0.73 $\pm$ 0.30	↑	.01
Increasing grade of LV dysfunction	0.50 $\pm$ 0.122	↑	<.0001
History of previous MI	0.65 $\pm$ 0.28	↑	.02
Late hazard phase			
LCx system disease (any location) $\geq$ 70%	0.36 $\pm$ 0.149	↑	.02
RCA proximal disease $\geq$ 70%	0.42 $\pm$ 0.165	↑	.01
Older age	0.092 $\pm$ 0.0100	↑	<.0001
PVD	0.69 $\pm$ 0.20	↑	.0004
Diabetes, pharmacologically treated	0.75 $\pm$ 0.184	↑	<.0001

LCx, Left circumflex; LITA-LAD, left internal thoracic artery–left anterior descending coronary artery; LV, left ventricular; MI, myocardial infarction; PVD, peripheral vascular disease; RCA, right coronary artery; SD, standard deviation.

*Unbypassed stenoses $>$ 50%.

Table V. Survival after LITA-LAD grafting, overall and in subgroups

Group	One year			Five years			Ten years			Twenty years			
	n	%	CL (%)	n*	%	CL (%)	n*	%	CL (%)	n*	%	CL (%)	n*
Overall	2067	99.1	98.9-99.3	2003	95.7	95.2-96.1	1802	88	87-88	1380	62	61-63	520
Complete revascularization†	1276	99.4	99.2-99.6	1244	97.3	96.7-97.7	1127	91.1	90.1-91.9	893	70	68-71	286
Incomplete revascularization‡	791	98.3	97.8-98.7	758	93.1	92.1-93.9	665	81	80-83	502	53	51-55	218
No non-LAD disease§	682	99.6	99.4-99.8	664	97.8	97.1-98.3	600	93.6	92.6-94.5	455	75	72-77	150
Any left main trunk disease	165	97.0	95.3-98.0	159	90	87-92	136	71	67-75	86	44	39-49	32
>70% LCx system disease	301	98.6	97.8-99.2	291	90	89-92	247	73	70-76	173	44	41-47	74
>70% LCx-lateral disease	89	98.9	97.0-99.6	87	84	80-88	67	67	61-72	46	41	35-48	13
>70% proximal RCA disease	228	98.2	97.1-98.9	220	91	89-93	188	76	73-79	133	42	38-46	34

CL, 70% confidence limits; LAD, left anterior descending; LCx, left circumflex; LITA-LAD, left internal thoracic artery–left anterior descending coronary artery; RCA, right coronary artery.

*Number of patients alive and traced after this time interval.

†<50% stenosis in RCA or LCx systems.

‡ $\geq$ 50% stenosis in RCA or LCx systems.

§No disease of any degree recorded in left main, LCx, or RCA systems.

cohort of patients with no disease appreciated outside the LAD.

Reintervention. Freedom from reintervention by PTCA or reoperation was 89% and 65% at 10 and 20 years postoperatively (Fig 7). Risk factors for reintervention included earlier date of operation, paralleling the higher prevalence of incomplete revascularization in the early time period (see Fig 1), but were further complicated by the introduction of percutaneous methods in the 1980s (Table VII). Importantly, disease in the mid and distal RCA were risk factors for reintervention, in contrast to the association of proximal RCA disease and death in the dominating late phase of hazard. LCx disease was associated with a reduced rate of reintervention, even though it increased the risk of death. The small number of patients with high-grade ($\geq$ 70%) left main trunk disease

came rapidly to reintervention, but not those with less severe grades of stenosis.

Discussion

Principal findings. The clearest lesson from this study is that, by itself, the LITA-LAD graft does not fully compensate for the presence of disease in other coronary systems. Certainly, the LITA-LAD graft is the most important part of the bypass operation for most patients. The long-term patency of LITA-LAD grafts is the best of any grafting strategy, and clinical studies have shown that the LITA-LAD graft leads to improved late survival and decreased late cardiac events after operations for either single or multivessel disease.^{8,14-19} However, in this study the patients with unbypassed lesions in the proximal RCA or in the

Fig 3. Survival impact of incomplete revascularization. Survival, depicted as in Fig 1, is shown for LITA-LAD grafting patients stratified according to the presence (incomplete revascularization, *open circles*) or absence (complete revascularization, *filled circles*) of important (50% or more diameter obstruction) lesions in non-LAD systems.

Fig 4. Effect of left main disease on survival. Patients with any left main disease at the time of isolated LITA-LAD grafting are shown by the *open circles* and *parametric curves*. The *upper parametric curves* represent a risk-unadjusted depiction of all patients with absence of lesions in the left main trunk or RCA or LCx systems (no non-LAD disease).

LCx coronary artery, or any lesion (regardless of severity) in the left main coronary artery, had importantly worse survival than patients without those lesions. The magnitude of the difference between completely and incompletely revascularized patients was substantial and became particularly striking in the second decade after operation.

The mechanism for these findings is not clear. Was the increased rate of late death related to the ischemic burden existing at the time of operation, or were these

unbypassed lesions markers of a more severe atherogenic diathesis that produced more aggressive progression of native vessel disease during the follow-up period? Our data do not allow us to say. We sought to gain some insight by examining the reasons for incomplete revascularization. Incomplete revascularization was more common in the early years of the coronary bypass era and was usually based on the thought that the unbypassed arteries were not important because of small size or infarction in their distribution. However,

Fig 5. Impact of LCx system disease on survival. Survival is depicted as in Fig 4, where the *circles* and *lighter parametric curves* represent patients with high-grade (70% or more) lesions in any portion of the LCx system and the *squares* and *heavy parametric curves* represent a subset of these patients with high-grade lesions in the lateral branches of the LCx system.

Table VI. Correlates of left main trunk disease of any degree

Correlate	Logistic coefficient ± SD	Direction of influence	P value
Demography			
Men	0.48 ± 0.23	↑	.04
Age	0.049 ± 0.0097	↑	<.0001
LV dysfunction	0.35 ± 0.099	↑	.0004
PVD	1.16 ± 0.25	↑	<.0001
Date of operation*	0.70 ± 0.31	↓	.02
Intercept	-6.3		

LV, Left ventricular; PVD, peripheral vascular disease; SD, standard deviation.
*1/[years since 1/1/1971] inverse transformation.

they may have been more important than originally recognized.

A second important observation is that left main stenosis of any degree predicted decreased late survival. Again, the question arises whether the negative impact of seemingly “nonsignificant” left main stenoses was related to an underestimation of those stenoses at the time of operation or the rate of subsequent disease progression. Angiographic evaluation of left main coronary lesions can be difficult, and considerable interobserver and intraobserver variability has been noted.^{20,21} Intravascular ultrasound has documented the presence of important disease in patients for whom angiograms did not clearly document left main stenosis and may provide a more accu-

rate means for assessing the left main coronary artery in the future.²²

A third lesson from the study is that the likelihood of reintervention may be associated with variables that are not associated with the risk of death, for example, ungrafted distal RCA stenoses. Sergeant, Blackstone, and Meyns²³ have made that observation in the assessment of large numbers of patients with multivessel disease as well.

Importance of incomplete revascularization. The advent of percutaneous and less invasive surgical approaches to myocardial revascularization has raised the issue of the importance of complete revascularization, because those strategies are less consistently able to achieve complete revascularization than standard surgical methods.^{24,25} The concept of “functionally adequate revascularization”—restoration of perfusion to vessels judged bypassable that supply normal myocardium—has arisen from the interventional cardiology literature.²⁶ Some studies of small numbers of patients with multivessel disease undergoing PTCA have not demonstrated a significant difference in 1-year survival when comparing patients receiving “functionally adequate” versus “complete” revascularization.²⁶ However, those observations are not clearly applicable to the surgical situation. First, patients undergoing multiple PTCAs during the time period when these studies were conducted tended to be patients who were not at a high risk of short-term death regardless of treatment success.²⁴⁻²⁶ Second, the follow-up interval of 1 year has little relationship to long-

Fig 6. Impact of RCA system disease on survival. The depiction is as in Fig 4. The *circles* represent patients with high-grade (70% or more) lesions in the proximal RCA. In contrast, patients with RCA system disease of 50% or more and without left main or LCx disease (with or without other disease in the LCx system) are shown by the *squares*. These latter patients were not shown by multivariable analysis to be at increased risk of late mortality (Table IV).

Table VII. Incremental risk factors for reintervention after LITA-LAD grafting

Incremental risk factor	Coefficient $\pm$ SD	Direction of influence	P value
Early hazard phase			
Date of operation	0.152 $\pm$ 0.044	$\uparrow$	.0006
Late hazard phase			
Left main trunk disease $\geq$ 70%	2.2 $\pm$ 0.49	$\uparrow$	<.0001
LCx proximal disease $\geq$ 50%	-1.08 $\pm$ 0.43	$\downarrow$	.01
LCx lateral disease $\geq$ 70%	-1.30 $\pm$ 0.50	$\downarrow$	.01
RCA mid disease of any degree	0.37 $\pm$ 0.116	$\uparrow$	.001
RCA distal disease of any degree	0.40 $\pm$ 0.155	$\uparrow$	.01
Age*	-4.2 $\pm$ 1.60	$\downarrow$	.009
Date of operation†	0.104 $\pm$ 0.043	$\downarrow$	.02

LCx, Left circumflex; LITA-LAD, left internal thoracic artery–left anterior descending coronary artery; RCA, right coronary artery; SD, standard deviation.

*[age/50]² squared transformation, supplemented by a slight shaping of untransformed age (coefficient 0.146 $\pm$ 0.066, P = .03).

†[1/number of years since 1/1/1971]² squared inverse transformed shape prolonged by untransformed date of operation (coefficient 0.066 $\pm$ 0.0130, P < .0001).

term survival considerations. Third, patients undergoing PTCA are at a relatively high risk of failure of treatment (restenosis) even in those vessels that are treated, making differences between complete and incomplete treatment relatively smaller. Fourth, patients with incomplete revascularization after PTCA are more apt to come to surgical revascularization that may improve their survival. It is of interest that the characteristics of PTCA patients receiving “functionally adequate revascularization” appear to be similar to our patients who received “incomplete revascularization,” a group who had inferior long-term outcomes despite LITA-LAD grafting.

Limitations. This study has obvious limitations. It is an observational clinical study. We did not have data regarding myocardial viability or serial angiographic data related to disease progression. The ideal control group, patients with similar multivessel lesions who did not receive bypass grafts, does not exist. Although we infer that complete revascularization might improve outcomes, the evidence for that is indirect and untested.

However, these data do provide some insight into complete revascularization and late outcome. Previous studies of complete versus incomplete revascularization have involved groups of patients with multivessel

Fig 7. Freedom from reintervention (either PTCA or reoperation). The depiction is as in Fig 2.

disease, few of whom received internal thoracic artery grafts. Today, it might be argued that, so long as LAD revascularization is secure with a LITA-LAD graft, revascularization of the other coronary systems does not influence survival and can be either ignored or approached with techniques less likely to lead to long-term patency. The data in this study argue against that concept. Over a 20-year follow-up, the LAD revascularization, while important, is not all-important.

Clinical inferences. As we move into a differently invasive era, techniques of revascularization and combinations of techniques of revascularization will be developed that are appropriate for different situations. Complete revascularization is not the only thing that is important about revascularization strategies, and considerations of periprocedure morbidity always must be strongly considered. However, over the long term, the status of the LAD coronary artery is not the only thing that influences survival.

We thank Penny Houghtaling, MS, for her biostatistical expertise; Colleen Vahcic, Karen Mrazek, William Blackstone, and DeDe Orraca-Tetteh for data collection and patient follow-up; and Lucinda Mitchin for manuscript preparation.

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Appendix Table I. *Potential risk factors examined in multivariable analysis*

Patient	Patient—cont'd
Demographic variables	LCx system disease (maximum percent, $\geq 50\%$, $\geq 70\%$, any LCx disease) in general and in:
Female sex	Proximal LCx
Age	LCx lateral branches
Height	Obtuse marginal (ramus intermedius), if not arising from LAD
Weight	Posterior descending, if arising from the LCx
Weight/height ratio	RCA system disease (maximum percent, $\geq 50\%$, $\geq 70\%$, any RCA disease) in general and in:
Body surface area	Proximal, mid, and distal RCA
Body mass index	Marginals
Symptoms of reversible ischemia	Posterior descending, if not arising from LCx
Angina class	Noncardiac comorbidity
Emergency surgery	Previous or current smoker
Ventricular function	Cholesterol level
Left ventricular dysfunction grade (none, mild, moderate, or severe impairment)	Triglyceride level
Electrocardiographic evidence of previous myocardial infarction	Presence of peripheral vascular disease
History of previous myocardial infarction	Chronic obstructive pulmonary disease
Cardiac comorbidity	Pharmacologically treated diabetes
Family history of coronary artery disease	Procedure
Rhythm disturbance on electrocardiogram	Incomplete revascularization of non-LAD territories (50% or greater lesion in RCA or LCx systems)
Preoperative atrial fibrillation	Experience
Coronary arterial disease	Date of operation
Coronary dominance (right, left, codominant)	
Left main disease (maximum percent, $\geq 50\%$, $\geq 70\%$, any left main disease)	
LAD coronary system disease (maximum percent, $\geq 50\%$, $\geq 70\%$, any LAD disease) in general and in:	
Proximal, mid, and distal LAD	
Diagonal	
Major septal perforators	

Discussion

Dr Antonio Maria Calafiore (*Cheiti, Italy*). This paper underlines some important points in the strategy of myocardial revascularization. First, the presence of a severe lesion of 70% or greater in the LCx territory is a crucial factor for the survival of patients. This aspect emphasizes the necessity to graft, when possible, this territory with a second thoracic artery. Strangely, the same factor was not predictive of late intervention.

Second, this same pattern is shown by any proximal lesion of the RCA of 70% or greater: negative influence on survival and no influence on late reintervention rate. However, any RCA lesion in the mid or distal portion, of any degree, had a significant impact on the reintervention rate.

Third, any residual lesion of less than 70% on the LCx or RCA territories did not affect survival. These conclusions allow us to draw some considerations.

The concept of complete revascularization has to be revisited in favor of the concept of adequate revascularization. This means that myocardial revascularization has to be guided by the demonstration of ischemia in the target territory when the lesion is not critical. The necessity to graft lesions if less than 70% becomes, after this presentation, less evident.

I have a comment and a few questions for Dr Scott. You demonstrated that the late negative impact of an ungrafted lesion of 70% or greater in the LCx territory or in the proximal RCA is so important that any such lesion is to be grafted during the first operation. I do not think that there is a surgeon in this room who can deny this evident truth. The purpose of minimally invasive coronary surgery is to do the same operation in a different way, not to question whether a severe non-LAD lesion has to be grafted or not.

Furthermore, the natural history of a single-vessel non-LAD disease is favorable. Since medical treatment in the United States had some practical limitation compared with Europe in the past, such as lack of availability of calcium channel blockers, and the modern interventional treatment is

relatively recent, do you not think that today the data you showed are, in some way, too old?

Finally, I noticed that, for practical reasons, only 13% of the angiograms were reviewed. Eighteen percent of them showed some mistake, and often a lesion was downgraded to less than 50%. No angiogram with non-LAD coronary arteries normal or with a lesion lower than 50% was examined. Do you not think that the possibility of mistake, 18%, is too high and that all the angiograms need to be carefully checked before giving definite results?

Dr Scott. Thank you, Dr Calafiore, for your remarks. We would certainly agree that most surgeons in this country attempt to bypass coronary arteries with greater than 70% stenoses.

The late postoperative management of patients undergoing coronary bypass surgery has improved over time. Today more patients are treated with platelet inhibitors, and the current availability of multiple medications for altering the patient's lipid profiles is likely to improve long-term outcomes. We believe these factors are important and can diminish the progression of disease. However, incomplete revascularization is still incomplete revascularization. The main lesson of this study is that over a long period of follow-up the status of the LCx and RCA systems can influence the survival despite effective revascularization of the LAD. The LAD is not the only vessel that influences long-term survival.

In regard to your question about the angiographic accuracy of the information that we presented, we do know that the review of angiograms by multiple readers does show variability, especially in the case of left main disease. Intravascular ultrasound studies of left main disease have shown us that angiographic studies are not perfectly accurate. However, the message of this paper is not going to be changed by some variability in reading angiograms. The important message here is that as surgery evolves and as new techniques and combinations of techniques become possible, we must always remember that optimal complete revascularization is important in achieving long-term survival.

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