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Bypass Surgery

What Constitutes Optimal Surgical Revascularization?

Answers From the Bypass Angioplasty Revascularization Investigation (BARI)

Thomas J. Vander Salm, MD, FACC,* Kevin E. Kip, PHD,† Robert H. Jones, MD, FACC,‡ Hartzell V. Schaff, MD, FACC,§ Richard J. Shemin, MD, FACC,‖ Gabriel S. Aldea, MD, FACC,¶ Katherine M. Detre, MD, DRPH, FACC†

Worcester, Massachusetts; Pittsburgh, Pennsylvania; Durham, North Carolina; Rochester, Minnesota; Boston, Massachusetts; and Seattle, Washington

OBJECTIVES The study was done to derive the optimum definition of complete revascularization in coronary artery bypass surgery.

BACKGROUND "Complete revascularization" has been considered the goal of coronary artery bypass operations, but various definitions of completeness exist.

METHODS We evaluated the Bypass Angioplasty Revascularization Investigation (BARI) surgical results in the seven years after operation. Different definitions of completeness of revascularization were retrospectively applied to the 1,507 patients in the combined randomized/registry group to derive the definition of complete operative revascularization with the best discrimination in long-term results between those with and without complete revascularization as defined. Four definitions were evaluated: 1) traditional complete revascularization with one graft to each major diseased artery system; 2) functional complete revascularization with one graft to all diseased major or primary segmental vessels; 3) number of distal anastomoses greater than, equal to or less than the number of diseased coronary segments; and 4) number of distal anastomoses to the major coronary systems equal to 1 or greater than 1.

RESULTS No independent survival advantage existed for traditional or functional complete revascularization as compared with incomplete revascularization. No survival advantage existed for any of the three arms of definition 3. For definition 4, seven-year death/myocardial infarction was highest (32.9%) when more than one anastomosis was constructed to any non-left anterior descending coronary artery (LAD) system (relative risk 1.37, p = 0.03). No increased risk was associated with constructing more than one anastomosis into the LAD system.

CONCLUSIONS The construction of more than one graft to any system other than the LAD appears to confer no long-term advantage, and may actually be deleterious. (J Am Coll Cardiol 2002;39: 565–72) © 2002 by the American College of Cardiology

"Complete revascularization" has achieved the stature of a surgical mantra; its importance to superior long-term results after coronary artery bypass operations has become accepted as a truism. Indeed, numerous studies have demonstrated the dichotomy in both survival and function between patients receiving complete and incomplete revascularization (1–14). However, prior studies have used different definitions for complete or adequate revascularization. Thus, a surgeon, deciding on a strategy for an individual patient, has scant guidance from the literature as to which specific arteries should be bypassed in order to achieve complete revascularization. Unresolved are answers to such questions as: "are more grafts always better than fewer?" and "should each diseased branch of a major vessel be bypassed?" Therefore, in this study, we sought to derive the definition of optimal revascularization by starting with surgical results and retrospectively applying various definitions of revascularization completeness to an entire well-defined patient population. We hypothesize that the definition(s) most clearly separating patients with good long-term results from those with lesser results could be applied prospectively by surgeons contemplating the operative strategy to achieve optimal revascularization.

METHODS

The Bypass Angioplasty Revascularization Investigation (BARI) was designed as a multi-institutional study to compare, in patients with multivessel coronary artery disease, the outcomes of patients initially assigned to percutaneous transluminal coronary angioplasty (PTCA) versus coronary artery bypass graft (CABG) surgery (15). During a three-year span beginning in August 1988, a total of 1,829 patients were enrolled in the randomized clinical trial. During that same time, 2,010 patients who met all the BARI randomization criteria were enrolled in the BARI

From the *Division of Thoracic and Cardiac Surgery, University of Massachusetts Medical School, Worcester, Massachusetts; †Department of Epidemiology, University of Pittsburgh, Pittsburgh, Pennsylvania; ‡Duke University Medical Center, Durham, North Carolina; §Mayo Clinic, Rochester, Minnesota; ‖Division of Cardiothoracic Surgery, Boston University Medical Center, Boston, Massachusetts; and ¶Division of Cardiothoracic Surgery, University of Washington, Seattle, Washington. The Bypass Angioplasty Revascularization Investigation was sponsored by National Heart, Lung and Blood Institute grants HL38493, HL38504, HL38509, HL38512, HL38514-6, HL38518, HL38524-5, HL38529, HL38532, HL38556, HL38610, HL38642 and HL42145.

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Abbreviations and Acronyms

BARI = Bypass Angioplasty Revascularization Investigation
CABG = coronary artery bypass graft
CASS = Coronary Artery Surgery Study
CHF = congestive heart failure
ECG = electrocardiogram
IMA = internal mammary artery
LAD = left anterior descending coronary artery
LCx = left circumflex coronary artery
MI = myocardial infarction
PTCA = percutaneous transluminal coronary angioplasty
Ramus = ramus intermedius artery
RCA = right coronary artery
RR = relative risk

registry because either they or their referring physicians elected not to participate in the randomized trial. From these patients, 901 patients in the randomized arm and 625 in the registry arm (total 1,526) received CABG surgery. The BARI results at five and seven years have been analyzed and reported, and further follow-up studies continue (16–23).

The current investigation focuses only on these surgical patients. Of these patients, 1,507 were evaluable; 19 were excluded because of incomplete baseline angiographic or initial surgical procedure data.

The BARI patient characteristics have been described (15,24,25). Patients had multivessel coronary artery disease, clinically severe angina or objective evidence of ischemia, a need for revascularization, no prior coronary revascularization and were suitable candidates for both PTCA and CABG. Excluded were patients with left main stenosis ≥50% or primary coronary spasm.

Data collection. Baseline data collection included a demographic, clinical and angiographic profile, previous angina history, electrocardiogram (ECG), medication use, functional status and quality-of-life measures. Intraoperative data collected included vessels bypassed, conduits used and their configuration, adequacy of graft flow, distal vessel size, reasons for intended vessels not bypassed, myocardial protection and anesthetic techniques and cardiopulmonary bypass and cross-clamp times. Initial postsurgical data collection included postoperative (after hospital discharge) death, myocardial infarction (MI), congestive heart failure (CHF), hemorrhage, hypotension and cerebrovascular accident.

Throughout patient follow-up (mean 7.1 years), all hospitalizations for intercurrent cardiovascular events were carefully documented (including exact date) by use of standard data collection forms and routine annual patient contact. The ECGs were routinely collected throughout follow-up and for all suspected MI events. A central ECG laboratory coded all Q-wave events.

Angiographic definitions. The angiographic definitions used in BARI have been described (26). Briefly, a significant lesion was defined as a stenosis ≥50% diameter severity by caliper measurement in a vessel with a reference diameter ≥1.5 mm. The vast majority of significant lesions identified in BARI patients were in the proximal and mid-portions of the major coronary arteries. In this report, we evaluated surgical strategy using a four-vessel system consisting of the right coronary artery (RCA), left anterior descending coronary artery (LAD), left circumflex coronary artery (LCx) and, if present, the ramus intermedius artery (Ramus). A central radiologic laboratory interpreted angiograms from patients in the randomized trial but not from those in the observational registry. Therefore, clinical site readings were used for all patients.

Definitions of completeness of revascularization. After the surgical revascularization, different definitions of revascularization completeness were individually applied to each patient. By each of the definitions, patients were placed into an analysis group of either complete or incomplete revascularization. In essence, four new variables were created for each patient. We considered four primary definitions of complete revascularization (Table 1). *Definition 1*: "Traditional" complete revascularization was defined as all diseased arterial systems (stenosis ≥50%) receiving at least one graft insertion (83% of study population). *Definition 2*: "Functional" complete revascularization was defined as bypassing all diseased "primary" (Table 2) coronary segments (74% of study population). *Definition 3*: Patients were grouped by whether the number of distal anastomoses was less than

Table 1. Definitions of Extent of Revascularization

No.	Definition	Patient Subgroups	n (%)
1	Traditional: all coronary arteries with at least one significant lesion receive a graft	Complete revascularization	1,253 (83)
		Incomplete revascularization	254 (17)
2	Functional: all diseased "primary" coronary segments are bypassed*	Complete revascularization	1,114 (74)
		Incomplete revascularization	393 (26)
3	Number of distal anastomoses are either less than, equal to or greater than the number of diseased coronary segments	Distal sites < number of diseased segments	446 (30)
		Distal sites = number of diseased segments	518 (34)
		Distal sites > number of diseased segments	543 (36)
4	Number of distal anastomoses to the LAD or other coronary arteries	≥2 distal sites to LAD and to another artery	115 (8)
		≥2 distal sites to LAD	426 (28)
		≥2 distal sites to an artery other than LAD	216 (14)
		<2 distal sites to all arteries	750 (50)

*See Table 2 for explanation.
LAD = left anterior descending coronary artery.

Table 2. Algorithm for "Functional" Revascularization (Strategy 2) (Refer to Fig. 1)

Arterial System	Diseased Coronary Segment(s)	No. of Distal Insertions Required
RCA	1 only, 2 only, 3 only, 4 only, 5 only	1
RCA	1 and 2, 1 and 3, 2 and 3	1
RCA	1 and 4 or 5	2
RCA	2 and 4 or 5	2
RCA	3 and 4 or 5	2
RCA	6 or 7 or 8 or 9 or 10	0
LAD	12 only, 13 only, 14 only, 15 only, 16 only, 29 only	1
LAD	12 and 13, or 12 and 14, or 13 and 14	1
LAD	12 and 15 or 16 or 29	2
LAD	13 and 15 or 16 or 29	2
LAD	14 and 15 or 16 or 29	2
LAD	15a or 16a or 29a	0
LCx	18 only, 19 only, 19a only, 20 only, 21 only, 22 only	1
LCx	23 only (if left dominant)	1
LCx	18 and 19, or 18 and 19a, or 18 and 23	1
LCx	19 and 19a, or 19 and 23, or 19a and 23	1
LCx	18 and 20, 21, or 22	2
LCx	19 and 20, 21, or 22	2
LCx	19a and 20, 21, or 22	2
LCx	23 and 20, 21, or 22	2
LCx	20a or 21a or 22a or 24 or 25 or 26 or 27	0
Ramus	28	1
Ramus	28a	0

LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; Ramus = ramus intermedius artery; RCA = right coronary artery.

(30% of study population), equal to (34%) or greater than (36%) the number of diseased coronary segments. *Definition 4*: Patients were grouped by whether they had ≥2 distal site insertions to both the LAD and to a non-LAD arterial system (8% of study population), ≥2 distal sites to the LAD (28%), ≥2 distal site insertions to a non-LAD arterial system (14%) or by whether no arterial system had multiple distal site insertions (50%).

We attempted to explore a fifth definition based on specific segmental lesions compared to coronary grafts to those specific segments. However, this proved not to be feasible due to differential interpretation (misclassification) of the boundaries of the 37 defined coronary segments between the angiographers and the surgeons.

EXPLANATION OF TERMS IN PRECEDING DEFINITIONS. *Arterial system:* Any of the four major arterial systems consisting of LAD (including the diagonal), LCx, RCA and Ramus. *Segment:* Any of the 29 segments of coronary arteries as defined in the BARI study, and as shown in Figure 1. *Primary segment*: Any of the following vessels: RCA or its major branches of posterior descending coronary artery and posterior atrioventricular segment; LAD or its major diagonal branches; LCx or its major obtuse marginal branches; and the Ramus. *Diseased artery:* Any artery of ≥1.5 mm with a diameter reduction of ≥50%.

Statistical analysis. For dichotomous definitions of the extent of revascularization (definitions 1 and 2 in the previous text), chi-square and the Student *t* tests were used to compare differences in baseline angiographic characteristics and initial in-hospital outcomes between patients with and without complete revascularization; for initial in-hospital outcomes between patients with and without complete revascularization; for polychotomous definitions (definitions 3 and 4), chi-square tests and general linear models were fit using a single between-group F test. The Kaplan-Meier method (27) was used to calculate clinical event rates over seven years of follow-up. Patients with incomplete follow-up were censored at the last known date of follow-up. The log-rank test (chi-square statistic) was used to compare event-free survival curves over seven years between subgroups of patients within each definition of revascularization extent; a single main-effects test was used for each definition. Seven-year clinical event rates were calculated among all patients, and also *after excluding* the 23 operative deaths from the analysis in order to assess the revascularization strategy effect on late outcomes.

Clinical outcomes evaluated included death, cardiac death, MI, need for repeat revascularization, angina pectoris and the composite outcomes of death/MI and cardiac death/MI. Separate Cox regression models (28) were fit to assess the independent effect of each definition of revascularization extent on clinical outcomes over seven-years of follow-up, using a multistage stepwise algorithm. In the first stage, the variables age, gender, race, number of significant lesions, number of diffuse lesions and the use of an internal mammary artery (IMA) graft were included (forced) as a block in each model. In the second stage, 11 additional baseline factors (history of CHF, MI, hypertension, treated diabetes and renal dysfunction; current or past smoker; unstable angina; number of class C lesions; peripheral vascular disease; and left dominance) were allowed to "step" into each model using a p value entry criterion of <0.10. In the third stage, each one of the four revascularization definitions was separately added to the model with the variables from stages 1 and 2. Across all outcomes, the maximum number of variables included in a model was 15, and the minimum number of events (for cardiac death) was 70. All p values presented are two-sided.

RESULTS

Patient population. The mean age of the 1,507 patients at study entry was 62 ± 9 years; 26% were women and 92% were white. In addition, 53% of the study population had a prior history of MI, 65% presented with unstable angina, 19% had a history of treated diabetes and 8% had a history of CHF. The mean ejection fraction was 61 ± 13%.

Angiographic and procedural characteristics. Across the first three definitions of the extent of revascularization, patients who were incompletely revascularized had, on average, more significant lesions than completely revascularized patients (range 3.8 to 4.3 vs. 2.7 to 3.3), a higher prevalence of three- or four-vessel disease (range 64% to

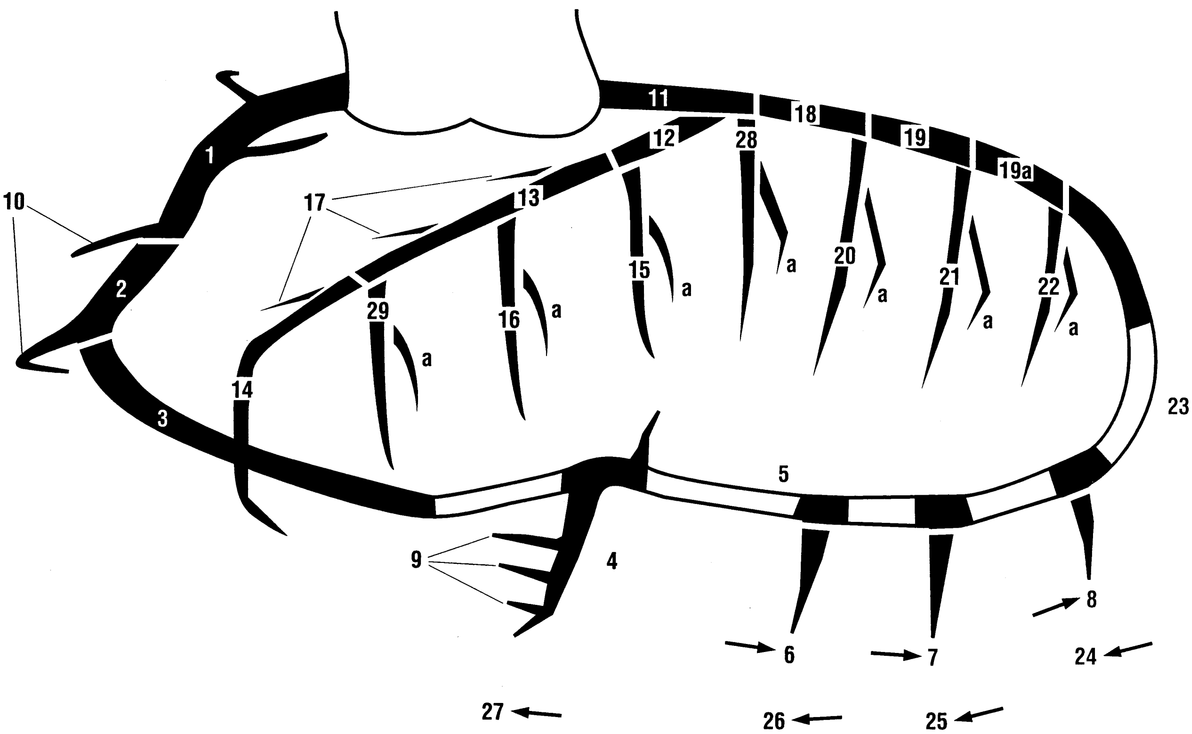

Figure 1. The Bypass Angioplasty Revascularization Investigation coronary artery map. Right coronary artery: **1** = proximal; **2** = middle; **3** = distal; **4** = posterior descending; **5** = right posteroatrioventricular; **6** = first posterolateral; **7** = second posterolateral; **8** = third posterolateral; **9** = inferior septal artery; **10** = acute marginal artery. Left coronary artery: **11** = left main; **12** = proximal left anterior descending; **13** = middle left anterior descending; **14** = distal left anterior descending; **15** = first diagonal; **15a** = first diagonal branch; **16** = second diagonal; **16a** = second diagonal branch; **17** = anterior septals; **18** = proximal circumflex; **19** = middle circumflex; **19a** = distal circumflex; **20, 21, 22** = first, second and third obtuse marginal; **20a, 21a, 22a** = first, second and third obtuse marginal branches; **23** = left atrioventricular; **24, 25, 26** = first, second and third posterolaterals; **27** = left posterior descending; **28** = Ramus; **28a** = Ramus branch; **29** = third diagonal; **29a** = third diagonal branch.

76% vs. 19% to 34%), fewer grafts placed (range 2.7 to 2.8 vs. 2.9 to 3.2) and fewer distal site insertions (range 2.9 to 3.1 vs. 3.3 to 3.6). For definition 4, patients with no more than one distal site insertion to any vessel had, on average, fewer significant lesions and a lower prevalence of three- or four-vessel disease than patients with multiple distal site insertions to a vessel.

In-hospital complications. Comparing subgroups of patients classified by the four definitions of the extent of revascularization, the incidence of in-hospital complications was similar among all subgroups (death: range 0.9% to 2.8%; Q-wave MI: range 3.6% to 6.1%; death/Q-wave MI: range 4.7% to 8.0%; CHF or pulmonary edema: range 1.6% to 5.1%).

Long-term outcome. DEFINITION 1. The incidence and adjusted relative risks of all clinical outcomes over seven-years of follow-up were similar between completely revascularized and incompletely revascularized patients, although the risk estimates were generally in the direction that favored complete revascularization (Table 3).

DEFINITION 2. The incidence of mortality over seven-years of follow-up was lower in patients with complete revascularization than in those without (13.6% vs. 18.9%, Table 4); this lower occurrence persisted after excluding the 23 patients who died in-hospital (12.5% vs. 16.8%). After statistical adjustment, the lower risk of long-term mortality associated with complete revascularization was attenuated and no longer statistically significant, but it remained in the direction of being protective.

DEFINITION 3. Both the incidence and the adjusted risk of all clinical outcomes were similar among the three groups of patients defined by the number of distal sites less than, equal to or greater than the number of diseased segments (data not shown). However, there was a nonsignificant suggestion that patients with the number of distal sites equal to the number of diseased segments had the most favorable long-term outcome.

DEFINITION 4. The incidence of death, cardiac death and MI over seven years was nonsignificantly higher in the two subgroups of patients with multiple distal site insertions to a non-LAD vessel (e.g., irrespective of whether there were multiple LAD insertions) (Table 5). This trend of lower long-term survival among patients with multiple distal site insertions to a non-LAD vessel persisted after excluding the 23 patients who died in-hospital. When the combined death/MI outcome was evaluated, the unadjusted and adjusted risks were significantly higher in the subgroup of patients with multiple distal site insertions to a non-LAD vessel and no more than one LAD graft insertion (Table 5).

Table 3. Evaluation of Definition 1: Traditional Complete Revascularization

Seven-Year Clinical Outcome†	Patient Group	All Patients (n = 1,507) Incidence	Adjusted RR‡	95% CI	p	Patients Without In-Hospital Death (n = 1,484) Incidence	Adjusted RR‡	95% CI	p
Death	Incomplete	17.3	1.0	—	—	15.0	1.0	—	—
	Complete	14.5	0.78	0.55, 1.11	0.17	13.4	0.84	0.58, 1.23	0.37
Cardiac death	Incomplete	8.0	1.0	—	—	5.8	1.0	—	—
	Complete	5.8	0.69	0.40, 1.17	0.17	4.9	0.84	0.45, 1.58	0.58
MI§	Incomplete	14.1	1.0	—	—	13.8	1.0	—	—
	Complete	14.4	0.97	0.66, 1.42	0.86	14.4	0.99	0.67, 1.46	0.96
Death/MI	Incomplete	25.8	1.0	—	—	23.7	1.0	—	—
	Complete	25.8	0.92	0.69, 1.22	0.55	24.8	0.97	0.72, 1.30	0.83
Cardiac death/MI	Incomplete	18.2	1.0	—	—	16.2	1.0	—	—
	Complete	18.4	0.94	0.67, 1.32	0.73	17.6	1.03	0.72, 1.48	0.87
Repeat revascularization	Incomplete	10.8	1.0	—	—	10.5	1.0	—	—
	Complete	12.9	1.14	0.73, 1.78	0.55	12.9	1.19	0.76, 1.87	0.45
Angina during follow-up‖	Incomplete	40.8	1.0	—	—	42.0	1.0	—	—
	Complete	39.1	0.92	0.68, 1.24	0.58	39.6	0.89	0.66, 1.20	0.45

†In the Kaplan-Meier and Cox regression analyses, patients with incomplete follow-up were censored at the last known date of follow-up; censored patients do not contribute to the estimation of clinical outcomes at seven years. ‡Per description in methods; owing to missing covariate data, as many as 22 cases were missing in the analysis. §Includes both Q-wave and non–Q-wave infarctions. ‖Excludes 51 surviving patients without reported angina status on at least 80% of the routinely scheduled follow-up forms.
CI = confidence interval; MI = myocardial infarction; RR = relative risk.

Similar nonsignificant results were observed for the subgroup of patients with multiple distal site insertions to both the LAD and a non-LAD vessel. Overall, the adjusted risks (death/MI, cardiac death/MI) associated with having multiple distal site insertions to a non-LAD vessel were on the order of approximately 35% higher risk.

Thus, across the four definitions of the extent of revascularization, the most evident finding was an apparent worse long-term outcome associated with multiple distal site insertions to a non-LAD vessel (definition 4).

Further investigation of patients with multiple anastomoses to a non-LAD system (definition 4). Among all 1,507 patients, a subgroup of 1,003 patients (67%) had no more than one significant lesion (by the BARI definition) in the LCx, RCA and Ramus systems. Unexpectedly, the apparent lower survival associated with multiple distal anastomoses to a non-LAD system was restricted to this subgroup, as described in the following text.

The unadjusted survival rate over seven years was 81% for the 148 patients who had multiple distal anastomoses to a non-LAD system compared to 88% for the 855 patients with no more than one graft insertion to a non-LAD system ($p = 0.04$). Freedom from death/MI over seven years in the same subgroups was 68% and 77%, respectively ($p = 0.02$). Among the 148 patients with multiple distal anastomoses to a non-LAD system (and overall poorer clinical outcome), 42% possessed one significant lesion and at least one nonsignificant lesion in the non-LAD system that was bypassed. An additional 46% of these 148 patients had only one significant lesion and no recorded nonsignificant lesions

Table 4. Evaluation of Definition 2: Functional Complete Revascularization

Seven-Year Clinical Outcome†	Patient Group	All Patients (n = 1,507) Incidence	Adjusted RR‡	95% CI	p	Patients Without In-Hospital Death (n = 1,484) Incidence	Adjusted RR‡	95% CI	p
Death	Incomplete	18.9	1.0	—	—	16.8	1.0	—	—
	Complete	13.6**	0.77	0.57, 1.05	0.10	12.5*	0.82	0.59, 1.14	0.24
Cardiac death	Incomplete	7.6	1.0	—	—	5.7	1.0	—	—
	Complete	5.7	0.81	0.49, 1.33	0.41	4.8	0.97	0.55, 1.71	0.91
MI§	Incomplete	14.2	1.0	—	—	14.1	1.0	—	—
	Complete	14.4	1.06	0.75, 1.49	0.75	14.3	1.07	0.76, 1.51	0.70
Death/MI	Incomplete	28.0	1.0	—	—	26.1	1.0	—	—
	Complete	25.0	0.92	0.72, 1.17	0.50	24.1	0.96	0.74, 1.24	0.76
Cardiac death/MI	Incomplete	18.7	1.0	—	—	17.0	1.0	—	—
	Complete	18.3	1.01	0.74, 1.36	0.98	17.5	1.08	0.79, 1.47	0.65
Repeat revascularization	Incomplete	13.1	1.0	—	—	12.8	1.0	—	—
	Complete	12.4	0.92	0.63, 1.35	0.66	12.3	0.95	0.64, 1.39	0.78
Angina during follow-up‖	Incomplete	38.1	1.0	—	—	39.1	1.0	—	—
	Complete	39.8	1.06	0.81, 1.39	0.65	40.3	1.03	0.79, 1.36	0.81

†‡§‖See footnotes in Table 3. **$p < 0.01$; *$p < 0.05$.
Abbreviations as in Table 3.

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Table 5. Evaluation of Definition 4: Number of Distal Sites to Different Vessels

Seven-Year Clinical Outcome†	Patient Group	All Patients (n = 1,507) Incidence	Adjusted RR‡	95% CI	p	Patients Without In-Hospital Death (n = 1,484) Incidence	Adjusted RR‡	95% CI	p
Death	<2 sites to each vessel	14.4	1.0	—	—	13.4	1.0	—	—
	≥2 sites to LAD and other vessel	14.2	1.13	0.65, 1.96	0.66	13.5	1.15	0.65, 2.03	0.64
	≥2 sites to LAD, <2 to others	13.5	1.07	0.76, 1.49	0.70	11.4	0.95	0.66, 1.36	0.76
	≥2 sites to non-LAD, <2 to LAD	20.3	1.26	0.87, 1.82	0.21	18.8	1.23	0.84, 1.80	0.30
Cardiac death	<2 sites to each vessel	5.8	1.0	—	—	5.0	1.0	—	—
	≥2 sites to LAD and other vessel	8.3	1.70	0.80, 3.64	0.17	8.3	2.17	0.99, 4.78	0.05
	≥2 sites to LAD, <2 to others	5.7	1.18	0.70, 2.01	0.53	4.1	1.02	0.55, 1.89	0.94
	≥2 sites to non-LAD, <2 to LAD	7.0	1.12	0.60, 2.08	0.71	5.3	0.95	0.46, 1.95	0.89
MI§	<2 sites to each vessel	13.2	1.0	—	—	13.3	1.0	—	—
	≥2 sites to LAD and other vessel	15.2	1.29	0.75, 2.19	0.35	15.3	1.29	0.76, 2.21	0.34
	≥2 sites to LAD, <2 to others	13.4	1.06	0.75, 1.50	0.75	13.3	1.04	0.74, 1.48	0.81
	≥2 sites to non-LAD, <2 to LAD	19.7	1.44	0.99, 2.10	0.06	19.4	1.41	0.96, 2.06	0.08
Death/MI	<2 sites to each vessel	24.3	1.0	—	—	23.4	1.0	—	—
	≥2 sites to LAD and other vessel	26.4	1.27	0.84, 1.91	0.26	25.8	1.27	0.84, 1.91	0.26
	≥2 sites to LAD, <2 to others	24.0	1.04	0.80, 1.35	0.78	22.2	1.04	0.80, 1.35	0.78
	≥2 sites to non-LAD, <2 to LAD	34.2*	1.37	1.03, 1.83	0.03	32.9*	1.37	1.03, 1.83	0.03
Cardiac death/MI	<2 sites to each vessel	17.1	1.0	—	—	16.3	1.0	—	—
	≥2 sites to LAD and other vessel	20.7	1.37	0.86, 2.18	0.18	20.7	1.49	0.93, 2.38	0.09
	≥2 sites to LAD, <2 to others	17.1	1.10	0.81, 1.49	0.54	15.7	1.05	0.77, 1.45	0.74
	≥2 sites to non-LAD, <2 to LAD	24.2	1.39	0.99, 1.94	0.06	22.8	1.36	0.96, 1.93	0.08
Repeat revascularization	<2 sites to each vessel	14.0	1.0	—	—	14.0	1.0	—	—
	≥2 sites to LAD and other vessel	6.4	0.52	0.24, 1.15	0.11	6.4	0.52	0.24, 1.14	0.10
	≥2 sites to LAD, <2 to others	10.7	0.82	0.56, 1.21	0.32	10.4	0.80	0.54, 1.18	0.25
	≥2 sites to non-LAD, <2 to LAD	15.0	1.09	0.70, 1.69	0.71	14.6	1.04	0.66, 1.62	0.87
Angina during follow-up‖	<2 sites to each vessel	40.9	1.0	—	—	41.3	1.0	—	—
	≥2 sites to LAD and other vessel	39.8	1.09	0.71, 1.68	0.69	40.2	1.11	0.72, 1.71	0.64
	≥2 sites to LAD, <2 to others	34.4	0.85	0.65, 1.11	0.23	35.3	0.87	0.67, 1.14	0.33
	≥2 sites to non-LAD, <2 to LAD	43.4	1.11	0.80, 1.54	0.53	44.2	1.12	0.81, 1.56	0.49

†‡§‖See footnotes in Table 3. *$p < 0.05$ for single comparison among all four groups.
LAD = left anterior descending coronary artery, other abbreviations as in Table 3.

(<50% stenosis) in the non-LAD system that received multiple anastomoses. Finally, the remaining 12% of patients had nonsignificant disease only (no lesions ≥50% stenosis) in the non-LAD system that received multiple distal anastomoses.

DISCUSSION

No independent advantage existed from complete revascularization by either the traditional (no. 1) or functional (no. 2) definitions, although the risk estimates were in the direction that favored complete revascularization.

Contrary to our expectations, and perhaps to accepted tenets of surgical coronary artery revascularization, we found that increasing the number of anastomoses beyond one to non-LAD arteries (definition 4) yielded apparently worse rather than better long-term results. Two or more anastomoses into the RCA, circumflex or Ramus systems increased the risk of death/MI over seven years in both the entire patient population and among operative survivors, and nonsignificantly increased the risk of MI and cardiac death/MI. When the groups were subdivided by the number of distal stenoses in the arterial systems, the apparent deleterious effect of more than one anastomosis into a non-LAD arterial system was limited to patients with fewer than two lesions (by the BARI definition) in each of these systems.

These results raise two questions: First, are these findings discrepant with published results of the benefits of complete revascularization; and second, how can our results be explained?

Comparison with other studies. Numerous studies attest to the value of complete revascularization, yet our study shows no independent advantage to classically defined complete revascularization as exemplified by definitions 1 and 2.

Studies by Bell in the Coronary Artery Surgery Study (CASS), Bertelsen, Cukingnan, Tyras, Jones, Schaff, Cosgrove, and Laurie all documented reduced long-term mortality by the use of complete surgical revascularization (1,2,4,5,11–14). Although these eight studies attest to the advantage of complete revascularization, they all appear to define that state as the revascularization of one vessel in each of the three major coronary artery systems diseased, and they do not necessarily advocate bypassing every stenotic vessel, regardless of the number involved. Thus, there may not be any functional difference between the strategy suggested by these results and that suggested by the current study.

Interpretation of the results. We found no independent survival advantage or disadvantage to what we defined as "traditional" complete revascularization in which every arterial *system* containing a stenosis was bypassed. In fact, these data suggest an apparent survival *disadvantage* of placing more than one graft in any system other than the LAD. Based on studies such as those cited in the previous text, we believe that surgeons have almost universally, and perhaps even logically, concluded that no stenoses in vessels of bypassable size should be left un-bypassed. We also realize that advice to the contrary may be viewed as heretical. But in retrospect, the studies cited above appear to advocate a strategy that may be no different from the one suggested by our data, although none of them specifically examined the possible disadvantage of adding extra grafts as we did.

Because we found that the apparent disadvantage of multiple grafts into any non-LAD system was confined to those patients with $<$2 diseased segmental branches in each of those systems, the obvious and immediate question to be asked is: "why would any surgeon choose to graft nondiseased vessels?" In the present study, about 15% of patients in whom multiple grafts were performed into a non-LAD system fell into that category. The primary explanation for what might seem to be illogical surgical judgment is that the vessel disease severity analysis was performed by the catheterization laboratory personnel at each site, not by the surgeons. A vessel was considered nondiseased if it was $<$1.5 mm in diameter by caliper measurement regardless of the degree of stenosis, or with a stenosis of $<$50%. As previously mentioned, 42% of these patients had, by angiographic assessment, one significant and one nonsignificant lesion in the non-LAD system bypassed, 46% had only one lesion, and 12% had no significant lesions. But many of these same vessels were thought to have sufficient disease and to be of sufficient size by the surgeons to warrant multiple graft insertions. Vessels with no disease were not bypassed.

The finding that more than one graft to a non-LAD system was associated with higher seven-year death/MI could be explained with the criticism that the additional grafts did not cause the worse results, but instead were a marker for more extensive disease that contributed to the increased late mortality. However, the number of significant lesions and the number of diffuse lesions were included as covariates in the multivariable models and individually were not associated with seven-year mortality (relative risk [RR] = 1.08, p = 0.14; RR = 1.04, p = 0.56, respectively). Furthermore, the finding of higher death/MI with multiple grafts to a non-LAD system was present after statistical adjustment for prognostic baseline variables and use of an IMA graft. Thus, our data indicate a possible independent adverse effect associated with inserting multiple grafts to a non-LAD system and, almost certainly, no advantage associated with such a strategy.

Study limitations. Our results and conclusions are based on BARI patients, all of whom had multivessel disease. However, because all BARI patients were required to be clinically suitable for PTCA, patients with the most severe and extensive disease were deemed ineligible for study inclusion. Hence, our study probably included fewer patients with complex and severe coronary stenoses than were present in other medical/surgical studies such as CASS. A second criticism, and one difficult to gainsay, is that those patients who had more than one graft insertion to a non-LAD system possibly had grafts constructed to vessels of size sufficiently small to predispose to a higher graft occlusion rate. Because late follow-up angiography was not routinely performed in BARI, we were unable to investigate the plausibility of this criticism. Finally, there may be some unmeasured confounding variables that could contribute to the apparent worse outcomes associated with multiple grafts to a non-LAD system.

Conclusions. We conclude that, in the population studied, regardless of the extent of distal disease, inserting more than one graft into the RCA, LCx or Ramus systems may not be warranted and may, in fact, increase the long-term risk of death/MI as compared with inserting no more than one graft to each of these vessels. In contrast, placement of more than one graft in the LAD system, when indicated by disease in more than one segmental branch, does not adversely influence long-term patient prognosis.

In summary, we recommend considering that no more than one graft need be performed into a non-LAD system, regardless of the number of diseased vessel segments, with the consequence of the contrary strategy being results that are no better, and perhaps worse. Conversely, two or more grafts may be considered in the LAD under appropriate anatomical circumstances, such as when more than two large branches are stenotic.

Reprint requests and correspondence: Dr. Thomas J. Vander Salm, Division of Cardiothoracic Surgery, University of Massachusetts Medical School, 55 Lake Avenue, North, Worcester, Massachusetts 01655-3304. E-mail: vanderst@ummhc.org.

REFERENCES

1. Bell MR, Gersh BJ, Schaff HV, et al. Effect of completeness of revascularization on long-term outcome of patients with three-vessel disease undergoing coronary artery bypass surgery: a report from the Coronary Artery Surgery Study (CASS) registry. Circulation 1992;86: 446–57.
2. Bertelsen CA, Kjoller M, Hoier-Madsen K, Folke K, Fritz-Hansen P. Influence of complete revascularization on long-term survival after coronary artery bypass surgery. Scand Cardiovasc J 1997;31:271–4.
3. Lavee J, Rath S, Tran-Quang-Hoa, et al. Does complete revascularization by the conventional method truly provide the best possible results? Analysis of results and comparison with revascularization of infarct-prone segments (systematic segmental myocardial revascularization): the Sheba Study. J Thorac Cardiovasc Surg 1986;92:279–90.
4. Cukingnan RA, Carey JS, Wittig JH, Brown BG. Influence of complete coronary revascularization on relief of angina. J Thorac Cardiovasc Surg 1980;79:188–93.
5. Tyras DH, Barner HB, Kaiser GC et al. Long-term results of myocardial revascularization. Am J Cardiol 1979;44:1290–6.

6. Lawrie GM, Morris GC, Jr. Factors influencing late survival after coronary bypass surgery. Ann Surg 1978;187:665–76.
7. Frick MH, Harjola P-T, Valle M. Persistent improvement after coronary bypass surgery: ergometric and angiographic correlations at 5 years. Circulation 1983;67:491–6.
8. Assad-Morell JL, Frye RL, Connolly DC, et al. Aorta-coronary artery saphenous vein bypass surgery: clinical and angiographic results. Mayo Clinic Proc 1975;50:379–86.
9. Lawrie GM, Morris GC, Jr., Silvers A, et al. The influence of residual disease after coronary bypass on the 5-year survival rate of 1274 men with coronary artery disease. Circulation 1982;66:717–23.
10. Gohlke H, Gohlke-Barwolf C, Samek L, Sturzenofecker P, Schmuziger M, Roskamm H. Serial exercise testing up to 6 years after coronary bypass surgery: behavior of exercise parameters in groups with different degrees of revascularization determined by postoperative angiography. Am J Cardiol 1983;51:1301–6.
11. Jones EL, Weintraub WS. Surgery for acquired heart disease: the importance of completeness of revascularization during long-term follow-up after coronary artery operations. J Thorac Cardiovasc Surg 1996;112:227–37.
12. Schaff HV, Gersh BJ, Pluth JR, et al. Survival and functional status after coronary artery bypass grafting: results 10 to 12 years after surgery in 500 patients. Circulation 1983;68:II200–4.
13. Cosgrove DM, Loop FD, Lytle BW, et al. Determinants of 10-year survival after primary myocardial revascularization. Ann Surg 1985; 202:480–90.
14. Lawrie GM, Morris GC Jr. Long-term results of coronary bypass surgery. Ann Surg 1991;213:377–87.
15. Bourassa MG, Roubin GS, Detre KM, et al. Bypass Angioplasty Revascularization Investigation: Patient screening, selection and recruitment. Am J Cardiol 1995;75:3C–8C.
16. Writing Group for the Bypass Angioplasty Revascularization Investigation (BARI) Investigators. Five-year clinical and functional outcome comparing bypass surgery and angioplasty in patients with multivessel coronary disease. JAMA 1997;277:715–21.
17. Chaitman BR, Rosen AD, Williams DO, et al. Myocardial infarction and cardiac mortality in the Bypass Angioplasty Revascularization Investigation (BARI) randomized trial. Circulation 1997;96:2161–70.
18. BARI investigators. Influence of diabetes on 5-year mortality and morbidity in a randomized trial comparing CABG and PTCA in patients with multivessel disease. The Bypass Angioplasty Revascularization Investigation (BARI). Circulation 1997;96:1761–9.
19. Bourassa MG, Kip KE, Jacobs AK, et al. Is a strategy of intended incomplete percutaneous transluminal coronary angioplasty revascularization acceptable in non-diabetic patients who are candidates for coronary artery bypass graft surgery? The Bypass Angioplasty Revascularization Investigation (BARI). J Am Coll Cardiol 1999;33:1627–36.
20. Whitlow PL, Dimas AP, Bashore TM, et al. Relationship of extent of revascularization with angina at one year in the Bypass Angioplasty Revascularization Investigation (BARI). J Am Coll Cardiol 1999;34: 1750–9.
21. Detre KM, Guo P, Holubkov R, et al. Coronary revascularization in diabetic patients: a comparison of the randomized and observational components of the Bypass Angioplasty Revascularization Investigation (BARI). Circulation 1999;99:633–40.
22. Bypass Angioplasty Revascularization Investigation (BARI) investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. N Engl J Med 1996;335:217–25.
23. The BARI investigators. Seven-year outcome in the Bypass Angioplasty Revascularization Investigation (BARI) by treatment and diabetic status. J Am Coll Cardiol 2000;35:1122–9.
24. BARI investigators. Protocol for the Bypass Angioplasty Revascularization Investigation. Circulation 1991;84:V1–V27.
25. Rogers WJ, Alderman EL, Chaitman BR, et al. Bypass Angioplasty Revascularization Investigation (BARI): baseline clinical and angiographic data. Am J Cardiol 1995;75:9C–17C.
26. Alderman EL, Stadius ML. The angiographic definitions of the Bypass Angioplasty Revascularization Investigation. Coron Artery Dis 1992;3:1189–207.
27. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457–81.
28. Cox DR. Regression models and life tables. J R Stat Soc (B) 1972;34:187–220.