Purely internal thoracic artery grafts: outcomes

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Purely Internal Thoracic Artery Grafts: Outcomes

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Background. **Most of our patients with coronary artery disease have undergone bypass exclusively with purely internal thoracic artery grafts (PITA). Our goal has been to lengthen the time a patient benefits from coronary bypass operations. The present report describes an 8.5-year study of outcomes including mortality and the need for reintervention in patients who have undergone bypass with PITA.**

Methods. **We studied 897 patients who underwent PITA with a total of 3,784 internal thoracic artery (ITA) grafts (4.2 grafts per patient). Connecting ITA to ITA along with sequential anastomosis made the procedure possible.**

Results. **Early mortality for the group was 2.3%. Freedom from death was 86% and freedom from reintervention was 94% at 5 years after the operation.**

Conclusions. **The acceptable early and late mortality and the 94% freedom from reintervention as long as 8.5 years after operation in this group of patients inspire us to continue choosing PITA for patients with three-vessel coronary artery disease.**

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Outcomes after coronary artery bypass grafting (CABG) are affected by obstruction of the bypass conduit and new disease or progression of arteriosclerosis in the native coronary arteries. Failure of the graft can occur early after the operation from technical errors and spasm. Intimal hyperplasia produces closure usually within the first year. Arteriosclerosis begins to cause obstruction in the bypasses after several years. Choosing the conduit with the highest early and long-term patency for all of the diseased coronary arteries is one way the cardiac surgeon may improve outcomes of CABG procedures.

We began bypassing the left anterior descending coronary artery (LAD) with the left internal thoracic artery (LITA) in 1970 after observing intimal hyperplasia in saphenous vein grafts (SVGs) causing early graft closures [1]. After learning of its superior 10-year patency [2], we started bypassing as many coronary arteries as possible with bilateral ITAs (BITA) [3] and sequential anastomoses. Since 1990 [4] we began connecting the free right ITA (RITA) perpendicularly end to side (E-S) to the attached LITA as a T graft or end-to-end (E-E) as a tandem/sequential graft. These techniques locate the proximal RITA closer to the inferior and posterior coronary arteries of the heart. This method permitted us to achieve our optimal goal of conducting complete bypass on our patients who had three-vessel coronary artery disease or its equivalent entirely with the most ideal bypass graft, the ITA [5–8]. In some patients with dilated and enlarged left ventricles we were able to bypass all of the obstructed coronary arteries by using the tandem/sequential technique but not with the T graft attachment.

Outcomes of coronary revascularization procedures are the true predictors of their success. Early and late mortality and the reduced need for reintervention such as angioplasty, stenting, and reoperation are the most solid indicators of benefit from coronary artery bypass procedures. We report here on the outcomes of the first 897 patients who had three-vessel coronary artery disease or its equivalent and were completely revascularized with purely internal thoracic artery grafts (PITA) from September 1990 through February 1998.

Material and Methods

Patients

From September 1990 through February 1998, 897 patients with 70% or more narrowing in all of their coronary arteries determined by coronary angiography underwent total coronary artery revascularization using PITA grafts. Patients were not excluded for poor left ventricular function, diffuse disease, increased operative risk, female sex, or older age. One hundred nine (12.2%) patients were undergoing their first or second reoperation and 195 (22%) had greater than 50% left main coronary stenosis in addition to three-vessel coronary disease. A total of 3,784 ITA coronary anastomoses were fashioned for an average of 4.2 grafts per patient; 837 (93.3%) T grafts and 60 (6.7%) tandem/sequential grafts were constructed. No other types of arterial or venous conduits were used.

Most of the ITA grafts were harvested as a pedicle, although some were skeletonized. The pedicle technique includes dissection of the fat, muscle, and fascia down to the adventitia on the posterior surface of the ITA to

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increase its length. This method is preferred because fewer hemorrhages occur in the wall of the artery that could lead to late scarring and obstruction. Intraluminal infusion with a saline or blood papaverine solution puts the drug in contact with the receptors that are located in the media of the ITA, producing maximal dilatation and flow in the vessel. It is unusual for the ITA to be injured during harvesting, but when it does occur the damaged area can be excised and the ends reapproximated. Constructing the T graft before placing the patient on cardiopulmonary bypass not only reduces time on the pump but also allows for measuring of the flow in the limbs of the graft. If the flow is insufficient, the anastomosis is redone, which corrects the problem. When the heart is severely enlarged, it may be necessary to use the tandem/sequential technique instead of the T graft to reach all of the obstructed coronary arteries. The T graft is easily placed on the heart without kinking or twisting. It provides the shortest route to the first lateral coronary branch to be bypassed. In addition to the LAD and circumflex, the right coronary artery was always bypassed unless it was nondominant and small. The posterior descending branch of the right or circumflex coronary arteries was bypassed in 733 (81.7%) of the patients and the distal right or the posterior marginal branch of the dominant circumflex in the remaining patients. All distal bypasses were performed with cardiopulmonary bypass, aortic cross-clamping, and cold and warm antegrade and retrograde blood cardioplegia. The alignment of the limbs of the T graft to the obstructed coronary arteries is maintained in a straight line and the ITA is kept loose between the anastomoses. Parallel and perpendicular anastomoses are used, but parallel anastomoses are preferred because narrowing at the anastomotic site is less likely. Only patients whose ITAs were not used in their original operation were included among the 109 patients who had their first or second reoperation. Old SVGs were ligated in some of these patients to prevent competition of flow or embolization of atherosclerotic debris. The patients were advised to take one 325-mg aspirin tablet daily. Calcium-channel blockers or nitrates for prevention of spasm were not given. Patients with elevated cholesterol or low-density lipoprotein levels were encouraged to take cholesterol-lowering drugs. The T graft procedure has been used in some of our off-pump coronary bypass patients, but none of these people is included in this series. A more comprehensive description of the technical details of the procedure has been described previously [4, 9]

The group included 189 women and 708 men whose ages ranged from 30 to 88 years (mean 64.8 years). Ejection fractions (EF) were measured preoperatively in 578 patients: 221 (38.2%) were normal, 137 (23.7%) had mild dysfunction (EF 0.45 to 0.54), 151 (26.1%) had moderate dysfunction (EF 0.35 to 0.44), and 69 (11.9%) had severe dysfunction (EF less than 0.35). Patient risk factors included hypertension (56.2%), smoking (55.6%), preoperative myocardial infarction (33.7%), diabetes (26.5%), peripheral vascular disease (10%), previous cerebrovascular accident (5.9%), chronic obstructive lung disease (5.8%), atrial fibrillation (4.8%), chronic renal failure (2.5%), and acute renal failure (1.7%). Patient follow-up ranged from 1 to 102 months and was obtained from questionnaires, recent office visits, and telephone survey. All operations were performed by the first author (A.J.T.). The same person conducted all telephone surveys. This information was added to the Midwest Heart Surgery Institute database containing all preoperative and perioperative patient information.

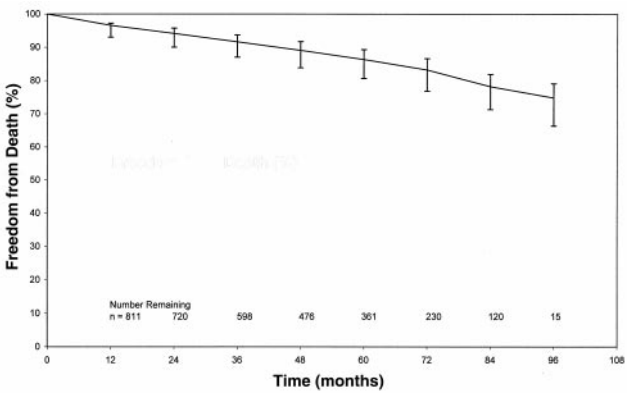

Fig 1. Kaplan–Meier plots for freedom from death.

Statistical Methods

Operative deaths were analyzed with logistic regression. For each significant factor in the model, the odds ratio was reported along with a 95% confidence interval.

All early events were estimated using simple percentages. Late deaths and time to reintervention were analyzed with a Cox [10] proportional hazards regression models. Risk ratios are reported for each significant factor, along with a 95% confidence interval. All factors were examined for time dependency, and no corrections were necessary. Five-year survival probabilities are calculated using the Kaplan–Meier method for each of the significant variables in the regression model. The log-transform method was used for the confidence intervals on the survival probabilities. Freedom from death and freedom from reintervention plots showed the estimated survival probability at 12-month intervals by the Kaplan–Meier method, with log-transformed 95% point-wise confidence intervals.

Results

Follow-up was obtained in 894 of the 897 patients (99.7%). The median follow-up was 4.2 years (range 30 days to 8.5 years). There were 21 early deaths (2.3%) and 118 late deaths (13.2%). Early deaths occurred while the patient was in the hospital or within 30 days of the operation; late deaths included all deaths after that period. Survival probability was 86% at 5 years and 75% at 8 years (Fig 1, Table 1). Sixty of the 118 (50.8%) late deaths were cardiac related, 53 (44.9%) deaths were noncardiac related, and 5 (4.2%) were unknown. Older age, previous CABG, chronic renal failure, and hypothyroidism were signifi-

Table 1. Freedom From Death: Survival Probabilities

Time		Survival	95% Confidence Interval		Number of Failures	
Days	Months	Probability	Lower	Upper	Number Failed	Number Left
0	0	1.0000	N/A	N/A	0	
365	12	0.9655	0.9251	0.9843	30	811
730	24	0.9416	0.8953	0.9678	49	720
1,095	36	0.9164	0.8649	0.9489	67	598
1,460	48	0.8909	0.8338	0.9292	82	476
1,825	60	0.8635	0.8007	0.9076	95	361
2,190	72	0.8323	0.7618	0.8835	106	230
2,555	84	0.7823	0.6959	0.8468	117	120
2,920	96	0.7483	0.5879	0.8536	118	15

N/A = not applicable.

cant risk factors for operative death. Those patients with tandem sequential grafts were no more likely to experience operative death than those with T grafts ($p = 0.992$). The odds ratio and p value for each of these risks is shown in Table 2. For all the variables analyzed (see Table 3), age, severely decreased ejection fraction, acute renal failure, chronic renal failure, carotid disease, deep vein thrombosis and pulmonary embolism, hypertension, and smoking were all significant risk factors for late deaths (Table 4). The patients were separated into four age groups (30 to 54 years, n = 150 patients; 55 to 64 years, n = 225 patients; 65 to 74 years, n = 375 patients; and 75 to 88 years, n = 147 patients) to determine the influence of age on early and late mortality and outcomes in patients with PITA grafts (Table 5).

Analysis of the group based on sex, diabetes, reoperations, and postoperative infection was performed. Separating the group by sex demonstrated that mortality in women was 2.6% early and 13.8% late and in men it was 2.3% early and 13.0% late, $p = 0.6757$ and $p = 0.8490$, respectively. All patients were diagnosed with diabetes before their operation by their referring doctors or their consultants. When comparing diabetic with nondiabetic patients, 6 of 238 (2.5%) diabetic patients died early compared with 15 (2.3%) of the 659 nondiabetics, $p = 0.6110$; also 39 (16.4%) of the diabetics died late compared with 79 (12%) of the nondiabetics, $p = 0.6893$, both statistically nonsignificant. Five (4.8%) of the patients who had PITA as a reoperation died early, which was statistically significant. Sixteen (14.7%) died late, a statistically nonsignificant difference. Sternal infections involving the bone occurred in 30 patients (3%) from the group. No patient died because of a sternal infection. Forty-three patients (4.8%) had a stroke, and 14 needed an intraaortic balloon pump.

Among the surviving patients, 6 of the 876 (0.7%)

Table 2. Risk Factors for Operative Deaths

	Odds Ratio (95% Confidence Interval)	p
Age: 65–74 years	5.81 (1.27–26.5)	0.023
Age: 74–88 years	9.06 (1.81–45.3)	0.007
Previous coronary artery bypass graft	3.17 (1.08–9.32)	0.035
Chronic renal failure	7.41 (1.88–29.1)	0.004
Hypothyroidism	4.07 (1.08–15.3)	0.038

Table 3. Variables Analyzed for Risk Factors

Age range
30–54 years
55–64 years
65–74 years
75–88 years
Acute renal failure
Chronic renal failure
Carotid disease
Deep vein thrombosis & pulmonary embolism
Ejection fraction
Hypertension
Smoking
Abdominal aortic aneurysm
Atrial fibrillation
Previous CABG
Cerebral vascular accident/TIA
Diabetes
Family history
Hyperlipidemia
Hypothyroidism
Myocardial infarction: previous
New York Heart Association class
Obesity
Peptic ulcer disease
Peripheral vascular disease
Sex
Graft type: tandem versus T graft
Ventricular fibrillation

CABG = coronary artery bypass grafting; TIA = transient ischemic attack.

Table 4. Risk Factors for Late Deaths

	Risk Ratio (95% Confidence Interval)	p
Age		
55–64 years	2.60 (1.05–6.40)	0.038
65–74 years	3.76 (1.60–8.85)	0.002
75–84 years	7.18 (2.97–17.3)	0.000
Ejection fraction—severe dysfunction	3.30 (2.01–5.40)	0.000
Acute renal failure	4.80 (1.89–12.2)	0.001
Chronic renal failure	3.05 (1.50–6.17)	0.002
Carotid disease	1.95 (1.04–3.65)	0.037
Deep vein thrombosis & pulmonary embolism	2.66 (1.26–5.61)	0.010
Hypertension	1.65 (1.12–2.43)	0.011
Smoking	1.71 (1.16–2.54)	0.007

Table 5. Etiology of Deaths

	30–54 Years	55–64 Years	65–74 Years	75–88 Years	Overall
Early deaths (w/in 30 days)	0	2 (0.9%)	12 (3.2%)	7 (4.8%)	21 (2.3%)
Late deaths	6 (4%)	24 (10.7%)	52 (13.9%)	36 (24.5%)	118 (13.2%)
Cardiac	6 (100%)	12 (50%)	22 (42.3%)	20 (55.6%)	60 (50.8%)
Noncardiac	0	10 (41.7%)	28 (53.8%)	15 (41.7%)	53 (44.9%)
Unknown	0	2 (8.3%)	2 (3.8%)	1 (2.8%)	5 (4.2%)

Number and percent of early versus late mortality and late death by etiology (by age group).

required CABG reoperation. One patient was found to have all grafts occluded, including his LITA, and was reoperated on within 9 months. Two patients had RITA obstruction, 2 had new disease with patent ITAs, and 1 patient who had poor left ventricular function preoperatively and postoperatively required cardiac transplantation. Two of the patients were reoperated on within 1 year and the others were reoperated on from 15 to 53 months after their first operation. Thirty-seven patients (4.2%) had reintervention with percutaneous transluminal angioplasty or stenting, 7 of whom were treated for LITA failure from 20 to 68 months postoperatively. Eighteen of the group had RITA obstruction and 12 had new coronary artery disease. Six of the 37 patients required the procedure within the first year and the remaining 31 patients between 13 and 88 months postoperatively. Freedom from reintervention was 94% at 5 years and 92% at 8 years (Fig 2, Table 6). Risk for reintervention was the same in all age groups (Table 7). It should be noted that the youngest age category did not have a high enough incidence of reintervention to make a valid estimate. Chronic obstructed pulmonary disease and New York Heart Association classes III to IV were significant risk factors for reintervention (Table 8).

Fourteen patients (1.6%) had a documented postoperative myocardial infarction. Fifty-two (5.9%) reported on the questionnaire or during the telephone interview that they had angina postoperatively. Return of angina was more frequent in the 30-to-54 age group (12%) and was evenly distributed in the other groups at 4.5%, 5.2%, and 3.6%. The occurrence of postoperative myocardial infarcts was distributed equally in all the age groups.

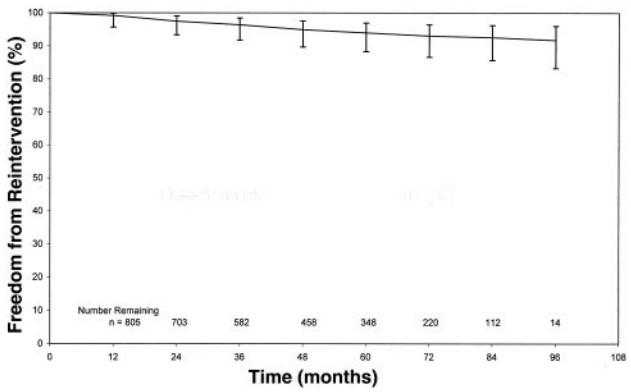

Fig 2. Kaplan–Meier plots for freedom from reintervention.

There was one early death (1.7%) and 9 late deaths (15%) in the 60 patients who had tandem/sequential grafts. One of these patients had a postoperative myocardial infarct (1.7%), 4 patients had angina after their operation (6.7%), and none of the group required reintervention.

Comment

Failure of CABG procedures is most often the result of bypass graft obstruction, new narrowing in the coronary arteries, or a combination of the two. Connecting the RITA E-S to the LITA as a T graft or E-E as a tandem/sequential graft locates the RITA 10 or more cm closer to the coronary arteries on the inferior and posterior surface of the heart. Combining the T graft or tandem/sequential graft with sequential grafting makes it possible for most patients to undergo bypass with PITA grafts. The coronary arteries on the anterior surface of the heart are bypassed with the LITA and the arteries on the posterior and inferior areas are grafted with the RITA. The most important coronary artery in nearly all patients, the LAD, is always bypassed with the graft having the greatest proved patency, that is, the attached LITA. A separate harvesting incision and an aortic anastomosis are not needed. In addition, the bypass conduits are placed out of the way of reentry and are well protected from injury in case the patient needs a repeat sternal incision. Atherosclerotic embolization from old patent ITA grafts during reoperations has not been reported.

Table 6. Freedom From Reintervention: Survival Probabilities

Time		Survival	95% Confidence Interval		Number of Failures	
Days	Months	Probability	Lower	Upper	Number Failed	Number Left
0	0	1.0000	N/A	N/A	0	. . .
365	12	0.9918	0.9564	0.9985	7	805
730	24	0.9747	0.9335	0.9905	20	703
1,095	36	0.9636	0.9175	0.9842	27	582
1,460	48	0.9492	0.8968	0.9754	35	458
1,825	60	0.940	0.8830	0.9697	39	348
2,190	72	0.9333	0.8679	0.9669	41	221
2,555	84	0.9285	0.8581	0.9647	42	113
2,920	96	0.9203	0.8339	0.9627	43	14

N/A = not applicable.

Table 7. Reintervention by Age (% of Age Group)

	30–54 Years	55–64 Years	65–74 Years	75–88 Years	Overall
Reoperation	0.7%	0.9%	0.8%	0%	0.7%
Percutaneous transluminal angioplasty/stents	2.0%	6.7%	4.1%	2.6%	4.2%

A major concern of the PITA operation is the chance of the single attached LITA not being able to supply enough blood to the revascularized myocardium [11]. Early hypoperfusion has been rare and can usually be detected before the patient comes off cardiopulmonary bypass. Technical errors with the anastomosis or pedicle attachment to the myocardium are the usual cause. Late hypoperfusion is the result of significant left subclavian artery obstruction from arteriosclerosis. When this phenomenon has occurred in patients with a single LITA-LAD graft, it has been corrected with left subclavian angioplasty or left carotid subclavian bypass [12]. Left carotid subclavian bypass relieved recurrent angina in 1 of the patients in this group who developed left subclavian artery stenosis several years after her T graft procedure. Carotid subclavian bypass and left subclavian angioplasty are much smaller procedures than the reoperation coronary artery bypass that would be required if the bypass grafts were detached and anastomosed to the ascending aorta for their source of blood. If left subclavian artery stenosis is present at the operation, the T graft or tandem/sequential graft can be reversed by connecting the detached LITA to the attached RITA. The good survival and rarity of hypoperfusion in this group of patients suggests that the single source inflow of the attached ITA is sufficient to perfuse the revascularized myocardium. Further evidence supporting the adequacy of inflow in the attached LITA has been reported by Wendler and associates [13]. They measured base line flow and maximum flow after stimulation with adenosine with a Doppler guidewire. They then calculated critical flow reserve in patients who had total revascularization with T grafts at 1 week and 6 months after their operation. When compared, base line flow measurements were higher in patients with T grafts than those with a single LITA. Maximum flow and critical flow reserve at 6 months were reported to be significantly elevated from similar measurements at 1 week after the operation.

The main limitation of this study is the lack of a significant number of postoperative graft visualization studies. Early in our experience, postoperative angiograms in 26 patients had been reviewed. All 26 LITA grafts to the LAD and diagonal were patent and 62 of the 68 (91%) RITA anastomoses were open [4]. This finding combined with the fact that less than 1% of the LITA grafts in this series required any form of reintervention within 8.5 years minimizes the concern that T-graft procedures will reduce the high LITA-LAD patency experienced with single LITA grafting.

Table 8. Risk Factors for Reintervention

	Risk Ratio (95% Confidence Interval)	*p*
Chronic obstructive pulmonary disease	2.92 (1.22–7.01)	0.016
New York Heart Association class III–IV	3.10 (1.46–6.59)	0.003

Single ITAs (SITA) grafted to the LAD produce a distinct improvement in outcomes when compared with SVGs [14]. Several studies [15–18] compared survival of BITA grafting with SITA and did not show a statistical difference between the two. Galbut and colleagues [19] found increased 8-year survival with BITA rather than SITA and SVGs in patients older than 65 years. Lytle and coworkers [20] reported better survival and outcomes in BITA patients at 5, 10, and 15 years when compared with SITA patients. Our midterm results with PITA in this group of patients demonstrate acceptable mortality and a low incidence of reintervention. Because only patients with three-vessel disease were included in this group, it is difficult to find a similar group of patients for comparison. An accurate evaluation of PITA on long-term survival will require a longer period of observation.

In conclusion, this follow-up of 99.7% of the 897 patients with three-vessel coronary artery disease or its equivalent who underwent PITA grafting demonstrated a 92% freedom from reintervention up to 8.5 years. The incidence of postoperative events was low after CABG operation combined with a low early and late mortality. Of the 118 late deaths, 45% were not caused by the patients' heart disease. The results in women are convincing, as they equaled those in men. Outcomes in diabetic patients were similar to those in nondiabetic patients. These encouraging midterm findings inspire us to continue to select PITA for our coronary artery bypass patients. Given these results this may be the only invasive procedure many of the patients with coronary artery disease will need for their entire life.

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INVITED COMMENTARY

A mountain of evidence indicates that the left internal thoracic artery (LITA) to left anterior descending graft improves early and late outcomes for a wide spectrum of patients having coronary bypass surgery. A lesser amount of evidence indicates that two ITA grafts may provide incremental clinical benefit when compared to the strategy of single ITA grafting. In this article Tector and colleagues examine midterm outcomes for patients with triple vessel disease where arterial revascularization is taken a step further, total arterial revascularization with only ITA grafts. To accomplish the average of 4.2 grafts per patient that were constructed, the ITAs were used as composite grafts, either "T" grafts (most often) or tandem grafts. Sequential ITA anastomoses were often employed.

There is no control group for this study and the patient population was heterogeneous. The outcomes are not dramatically different than one would expect from the use of more standard techniques although the incidence of reoperation was quite low. The mean postoperative follow-up interval was only 4.2 years and we would not expect to see an obvious difference in outcomes since most of the benefits of complex ITA grafting accrue with longer time intervals. Thus, this observational study does not yet demonstrate that total ITA revascularization is a superior strategy.

However, this study does show that complex ITA revascularization strategies are safe over the shortterm and midterm in the hands of an experienced and committed surgeon. This is an important observation. Total ITA revascularization offers the opportunity to achieve revascularization with those conduits known to have the most favorable late patency rates and to avoid the complications of vein graft atherosclerosis. The "T-graft" strategy avoids an ITA to aorta anastomosis and does not leave the patient with a critical graft crossing the sternal midline to increase the risk of reoperations. (Although the risk of reoperation after extensive ITA grafting is low, patients can develop aortic stenosis.) On the other side of the coin is the issue of potential hypoperfusion in a situation where the entire myocardium is dependent upon a single internal thoracic artery and the technical difficulty of the T anastomosis and multiple sequential ITA grafts. Hypoperfusion and clinical graft failure were both uncommon in this series indicating that these operations can be done safely. They are, however, technically difficult operations and, in this series, were all performed with the use of cardiopulmonary bypass.

There are other concepts of "total arterial revascularization" including the use of the radial artery or the gastroepiploic artery, along with the internal thoracic arteries. All have some appealing features. Vein graft atherosclerosis is the factor that most compromises the long term success of bypass surgery and arterial revascularization is the most obvious way to avoid this problem. The relative merits of different concepts of total arterial revascularization will take a long time to resolve, but extensive or total ITA revascularization is likely to be best for some patient subsets. Doctor Tector and his colleagues have shown that in experienced hands it is safe.

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