Conduit choice for coronary artery bypass grafting after mediastinal radiation

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Objective: Patients who have undergone prior mediastinal radiation might require coronary artery bypass grafting. However, there is some concern regarding potential radiation damage to the internal thoracic artery. Our objective was to assess the late patency of the internal thoracic artery and venous grafts in patients with prior mediastinal radiation.

Methods: Patients undergoing coronary artery bypass grafting at our clinic after prior mediastinal radiation were identified, and medical records, including operative reports, clinical notes, and coronary angiography, were reviewed.

Results: Between 1985 and 2005, 138 patients had coronary artery bypass grafting after mediastinal radiation. Of these, 25 underwent clinically indicated postoperative angiography. The mean patient age was 56.1 ± 13.8 years, and 24% were female. All patients received between 3000 and 6000 rads in fractionated doses. Seventy-two percent of patients had 3-vessel coronary artery disease. At late angiography (mean, 2.2 years), 6 (32%) of 19 internal thoracic arteries and 13 (27%) of 48 venous or radial arterial conduits showed stenosis of 70% or greater ($P = .72$). Assessing only grafts that were anastomosed to the left anterior descending coronary artery, 35% (6 of 17) of internal thoracic artery grafts and 60% (3 of 5) of non-internal thoracic artery grafts showed narrowing of 70% or greater ($P = .61$). Among patients who received a graft to the left anterior descending coronary artery ($n = 113$), however, age-adjusted survival at 5 years was superior among those receiving an internal thoracic artery graft to the left anterior descending coronary artery.

Conclusions: Internal thoracic artery graft patency among patients with prior radiation was less than expected and similar to that for venous grafts, although the effect of conduit disease versus distal target vessel runoff is unknown. Despite this, late survival was superior among those receiving an internal thoracic artery graft to the left anterior descending coronary artery. These data support use of an internal thoracic artery graft to the left anterior descending coronary artery when it appears grossly to be an acceptable conduit.

Patients who have undergone prior mediastinal radiation are at risk for early development of coronary artery disease¹ and might require surgical revascularization. The preferred conduit for coronary artery bypass grafting (CABG), particularly to the left anterior descending coronary artery (LAD), is the internal thoracic artery (ITA); however, the effect of therapeutic doses of radiation on the integrity of the ITA itself is unknown. Studies regarding the late patency of irradiated ITAs are small and conflicting.²⁻¹³ We therefore retrospectively reviewed patients who had a history of mediastinal radiation and underwent CABG at our institution and subsequent graft angiography.

MATERIALS AND METHODS

Patients

Institutional review board approval was obtained. Patients who received large doses of radiation (3000–6000 rads) to the mediastinum before cardiac operation were identified from institutional databases. Patients who received only neck, spine, or tangential radiation for breast cancer were excluded. Be-

tween 1985 and 2005, 138 patients were identified with a history of previous mediastinal radiation and CABG. After review of clinical information from the medical record, 25 (18%) patients underwent follow-up angiography. In all cases angiography was performed for clinical indications, including chest pain or shortness of breath.

Surgical Approach

Although there is no policy at our institution regarding patients with mediastinal radiation therapy in general, the ITA is preferred as the conduit of choice to the LAD. After median sternotomy, ITAs were harvested by using a pedicled technique and grossly inspected for patency. If the ITA did not appear to have adequate blood flow or was fibrotic, the artery was ligated, and venous or radial arterial conduits were used as bypass conduits. It has not been the practice in our institution to assess the ITAs preoperatively for patency during coronary artery catheterization. Intraoperative graft flow measurements were not performed. At the time of the operation, concomitant procedures were performed as indicated.

Statistical Analysis

Continuous variables are expressed as means and standard deviations or medians and ranges. Groups were compared by using t tests or χ^2 tests, as appropriate. Vital status for all patients was attained through use of Accurint (www accurint.com) and the Social Security Death Index. Kaplan-Meier survival curves were created with SAS version 9.1 (SAS Institute, Inc, Cary, NC) and compared with a log-rank test.

RESULTS

Of the 138 patients undergoing CABG after mediastinal radiation, 51% were female, and the mean age was 63 ± 13

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting

ITA = internal thoracic artery

LAD = left anterior descending coronary artery

years. The most common reasons for mediastinal radiation included breast cancer (40%), lymphomas (including Hodgkin's and non-Hodgkin's lymphoma: 34%), germ cell tumors (9%), lung cancers (8%), and others (thymic, esophageal, and laryngeal: 9%).

Patients With Follow-up Angiography

Of the 25 patients who had follow-up angiography, a lower percentage were female (24%), and the patients were younger when compared with the entire cohort (Table 1). The most common reasons for radiation therapy were similar (52% lymphoma, 24% germ cell cancer, and 20% breast cancer). The median time from radiation exposure to CABG was 23.1 years (range, 2.1–40.3 years) for the angiography group. Fifteen patients had a history of hypertension, 17 patients had hyperlipidemia, 12 patients were previous or current smokers, and 4 patients had diabetes (Table 2). Twenty-one (84%) of the patients were in New York Heart Association class III or IV, and the mean ejection fraction was $56\% \pm 12\%$.

Among those patients undergoing postoperative angiography, the majority (72%) had 3-vessel disease, and the average number of distal anastomoses per patient was 2.6 versus 2.4 ($P = .33$) in those patients who did not have follow-up angiography. Conduit selection was similar between the angiography group and the whole group. Among the angiography group ($n = 25$), there were 19 ITAs used (16 left and 3 right), 2 radial arteries, and 46 vein grafts. Sixteen ITA grafts and 5 vein grafts were anastomosed to the LAD. Concomitant procedures were performed in 9 patients, including aortic valve replacement ($n = 6$), mitral valve replacement ($n = 1$), mitral valve repair ($n = 1$), pericardiectomy ($n = 1$), and septal myectomy ($n = 1$).

The median time from operation to angiography was 2.2 years (range, 0.5–10.3 years). Angiograms were performed for clinical indications, including symptoms or positive non-invasive test results. In the ITA grafts, 4 were completely occluded, leaving 15 (79%) of 19 patent. Of these, 9 ITA grafts were perfectly patent, 4 had narrowing of less than 70%, and 2 were narrowed by 70% or more. Analysis of other conduits, both radial arteries and vein grafts, revealed that 13 grafts were completely occluded, resulting in 36 (73%) of 48 patent grafts. This included 12 that were perfectly patent, 19 that showed less than 70% stenosis, and 5 that showed 70% or greater stenosis. Late patency on angiography was not significantly different between ITA grafts and venous

TABLE 1. Preoperative and operative characteristics of the entire cohort of patients with prior mediastinal radiation

Patient characteristics	Patients with follow-up angiography (n = 25)	Patients without follow-up angiography (n = 113)	P value
Mean age (y)	56 $\pm$ 13	64 $\pm$ 13	.007
Female sex (%)	6 (24)	65 (58)	.002
History of smoking (%)	12 (48)	61 (54)	.588
History of diabetes (%)	4 (16)	24 (21)	.556
History of hypercholesterolemia (%)	17 (68)	74 (65)	.810
History of hypertension	15 (52)	63 (58)	.698
New York Heart Association class III/IV (%)	21 (84)	88 (78)	.288
Mean ejection fraction (%)	56 $\pm$ 12	57 $\pm$ 13	.212
Isolated bypass procedure (%)	17 (68)	63 (56)	.262
Mean no. of distal anastomoses	2.6 $\pm$ 1.2	2.4 $\pm$ 1.0	.333
ITA use (no. of patients, %)	18 (72)	65 (58)	
Left ITA	15	59	.731
Right ITA	2	4	.298
Bilateral ITA	1	2	.454
Radial artery use (no. of patients, %)	2 (8)	4 (4)	.298
Venous distal anastomoses			
1	4	27	.392
2	9	44	.237
3	8	26	.345
4	0	1	1.000

ITA, Internal thoracic artery.

grafts ($P = .44$). Assessing only grafts that were anastomosed to the LAD, 32% of ITA grafts and 60% of the non-ITA grafts showed stenosis of 70% or greater ($P = .61$).

Patients With Grafts to the LAD

We selected all patients who had a graft to the LAD ($n = 113$, 82%). Patients did not receive an ITA graft to the LAD ($n = 34$) for several reasons: 10 were fibrotic or scarred, 4 were not used because the patient's condition was unstable, 2 had prior injury to the ITA, 2 had a known ITA stenosis on angiography, 1 had poor pulsations, 1 was of inadequate length, and 1 had tumor-positive tissue around the ITA. In 13 patients there was inadequate documentation to determine the reason why the ITA was not used.

Late survival was compared between patients who had an ITA graft ($n = 79$) and those who had a venous graft ($n = 34$) to the LAD. At 1 and 5 years, the age-adjusted survivals of patients with an ITA graft to the LAD were 89% and 67% compared with 80% and 51% in patients with a venous graft to the LAD, respectively ($P = .16$, Figure 1). When all patients who received a graft to the LAD ($n = 113$) were compared with an age- and sex-matched population, the overall survival was decreased ($P < .001$, Figure 2).

TABLE 2. Characteristics of patients who had follow-up angiography available

Patient no.	Age at operation (y)	M/F	Year of radiation	Cancer type	↑ BP	Smoking Hx	DM	↑ Lipids	NYHA class
1	57	M	1968	Sarcoma	No	No	No	No	2
2	62	M	1986	Hodgkin's	No	Yes	No	No	3
3	61	M	1986	Hodgkin's	No	No	Yes	No	3
4	39	M	1980	Non-Hodgkin's	Yes	No	No	No	3
5	71	F	1955	Breast (L)	Yes	No	No	No	3
6	76	F	1984	Breast (L)	No	No	No	Yes	4
7	39	M	1969	Hodgkin's	No	No	No	Yes	3
8	45	M	1976	Hodgkin's	No	No	No	No	2
9	48	M	1964	Hodgkin's	Yes	Yes	Yes	Yes	2
10	49	M	1976	Germ cell	Yes	Yes	No	Yes	4
11	39	M	1974	Hodgkin's	Yes	No	No	No	4
12	46	M	1967	Hodgkin's	No	Yes	No	Yes	3
13	57	M	1986	Germ cell	No	Yes	No	Yes	3
14	47	M	1970	Hodgkin's	No	Yes	No	Yes	4
15	67	F	1969	Breast (R)	Yes	No	Yes	Yes	3
16	37	M	1976	Hodgkin's	Yes	Yes	No	Yes	3
17	58	M	1975	Germ cell	Yes	No	No	Yes	4
18	64	M	1967	Hodgkin's	Yes	Yes	No	Yes	2
19	60	F	1960	Germ Cell	Yes	Yes	No	Mo	4
20	46	M	1970	Non-Hodgkin's	No	No	No	Yes	4
21	89	F	1992	Breast (R)	No	No	No	Yes	3
22	53	M	1965	Non-Hodgkin's	No	Yes	No	Yes	3
23	63	M	1963	Seminoma	Yes	No	No	Yes	4
24	76	F	2002	Breast (L)	Yes	Yes	Yes	Yes	4
25	62	M	1980	Seminoma	Yes	Yes	No	Yes	4

M, Male; F, female; BP, blood pressure; Hx, history; DM, diabetes mellitus; NYHA, New York Heart Association; L, left; R, right.

DISCUSSION

Patients with prior mediastinal radiation can present with myocardial, pericardial, valvular, and coronary artery disease. Radiation can cause damage to the vasculature through direct damage to the endothelial cells.¹ Fibrous proliferation can then occur, resulting in a loss of parenchymal cells.² In patients who have medical conditions that also affect the

vascular system, such as hypertension or diabetes, radiation damage to vessels can be greater in severity.² When CABG surgery is required, the choice of bypass conduit presents an additional challenge. The ITA is the preferred conduit in most circumstances, with 5-year patency rates in contemporary series for nonirradiated ITA grafts as high as 96% to 98% in comparison with venous grafts as low as 83% to

FIGURE 1. Age-adjusted survival compared between patients with prior mediastinal radiation therapy who received an internal thoracic artery (ITA) graft compared with a venous graft to the left anterior artery. This age-adjusted comparison demonstrates superior survival in patients who received an internal thoracic artery graft, but overall, it was not statistically significant.

FIGURE 2. Survival of patients who had prior mediastinal radiation therapy and had either an internal thoracic artery or vein grafted to the left anterior descending coronary artery (LAD; n = 113). When compared with an age- and sex-matched Minnesota population, patients who had prior mediastinal radiation therapy had a significantly reduced late survival.

95%.^{14,15} The effect of radiation vasculopathy on the ITA, however, is uncertain.

Prior literature on the subject is divided. A study from Nasso and colleagues³ suggested that irradiated skeletonized ITAs have equal patency as saphenous veins and other arterial conduits. Other authors have also supported the use of the ITA in these patients with prior mediastinal radiation exposure⁴⁻⁹; however, others have suggested that mediastinal radiation might damage the ITA, causing either fragility or leading to early graft failure if it is used as a conduit.¹⁰⁻¹³ Several of these studies¹⁰⁻¹² are case reports, but in the study by Hicks,¹³ the ITA was only usable as a graft in 3 of 14 patients with previous mediastinal radiation exposure because of friability and fibrosis.

A previous study from our institution¹⁶ suggested that because of the unknown quality of the ITA graft and the increased risk of mediastinal wound complications in patients with previous mediastinal radiation therapy, alternative conduits should be considered. Despite these concerns, because of the well-documented effect of an ITA graft to the LAD on late survival,¹⁷ it has been our strong institutional bias to use the ITA conduit when possible. Indeed, in this series 79 (70%) of 113 patients with significant LAD disease received an ITA graft. The argument to use the ITA is particularly compelling because these patients are often young. Furthermore, with concerns about small-vessel disease and the adequacy of distal runoff, the ITA is an appealing conduit. This provided us with a sizeable population from which to draw survival data. Unfortunately, only a small minority underwent postoperative coronary angiography.

Preoperative assessment of the ITA might be a consideration, although it has not been our practice up to now. Van Son and coworkers⁴ and others^{6,7} suggest that if the patency is ascertained preoperatively, the ITA can be safely used. In general, patients in this study did not have examination of the ITA on angiography before surgical revascularization unless subclavian steal was suspected. All ITA grafts were grossly inspected at time of surgical intervention for patency.

In this study, graft patency after CABG in patients with prior mediastinal radiation therapy was lower than anticipated for patients without radiation therapy. Explanations might include greater severity of native coronary artery disease and poor distal arterial run-off caused by radiation damage. Radiation might also cause intimal injury to the ITA, although in a recent report irradiated ITAs had similar amounts of fibrosis on histomorphologic examination when compared with nonirradiated ITAs.⁹ Another important factor in understanding overall graft patency is that patients underwent symptom-directed angiography rather than routine catheterization. Buxton and associates¹⁸ have previously shown that symptom-directed graft failure rates might be as much as double those of an asymptomatic group (17% vs 9% in the ITA at 5 years, $P = .002$). There are few data

published on graft patency in patients with prior mediastinal radiation because prior studies used both clinical and noninvasive follow-up.^{3,4}

Age-adjusted survival was superior among patients who had an ITA graft to the LAD when compared with those who had a venous graft, although this was not statistically significant. This is likely highly susceptible to selection bias because in most cases the ITA was considered for use unless it appeared fibrotic or had poor flow. In addition, it is also possible that surgeons have a preference for placing ITA grafts in healthier patients. Our study reports a somewhat lower survival than our previously reported 5-year survival of 73% for patients undergoing CABG after previous mediastinal radiation.¹⁶ In the current series, however, we included patients who had concomitant valvular heart disease that might indicate a poorer prognosis.¹⁹

Finally, it must be acknowledged that our study might simply be underpowered to detect a difference between the patency of an ITA or venous conduit. In addition, we did not have adequate patient numbers to assess the effect of the radial artery in this cohort.

CONCLUSION

Irradiated ITA grafts had similar patency rates to venous or radial arterial conduits. Either ITA grafts or venous conduits can be used in patients who have received previous mediastinal radiation. However, when patent, these data suggest the ITA graft remains the conduit choice for grafting to the LAD in patients with prior mediastinal radiation therapy.

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