

# Atherosclerosis of Radial and Internal Thoracic Arteries Used in Coronary Bypass: Atherosclerosis in Arterial Grafts

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**ABSTRACT** *Background:* This study aimed to evaluate the degree and incidence of atherosclerosis in internal thoracic (ITA) and radial arteries (RA) harvested for coronary bypass grafting. *Materials and Methods:* The association of major clinical events and etiological factors for atherosclerosis was investigated in 770 arterial segments obtained prospectively from 480 patients. Potential risk factors for atherosclerosis were age, gender, smoking, diabetes mellitus, peripheral vascular disease, cerebrovascular disease, chronic renal failure, hypercholesterolemia, obesity, hypertension, and a positive family history. *Results:* Six types of histological lesions have been defined; grade III or more was present in the RA in 47 (16%) patients and in the ITA in 30 (7%). The mean grade was  $1.6 \pm 0.6$  in the ITA and  $2.1 \pm 0.9$  in the RA ( $p < 0.001$ ). *Conclusion:* RA had a significantly greater prevalence of atherosclerosis than the same patients' ITA. There was a strong correlation between ITA atherosclerosis and age. The presence of calcification may lead surgeons to avoid an extra incision according to risk factors, although most of these are not predictive. doi: 10.1111/j.1540-8191.2007.00431.x (*J Card Surg* 2007;22:385-389)

Alternative arterial conduits for myocardial revascularization have been sought since the early 1970s. The radial artery (RA) was proposed but soon abandoned because of a high failure rate, until it was shown by Acar and colleagues<sup>1</sup> that RA grafts were free from atherosclerosis and functioning after 15 years. Several investigations confirmed that the patency of RA was higher than 90% at 12 months.<sup>2-4</sup> This improvement has been attributed to better harvesting and preparation techniques and the use of calcium-channel blockers. The patency rate of RA grafts at 5.6 years was reported to be 85%.<sup>4</sup> The internal thoracic artery (ITA) is the first choice of graft because of its excellent late patency rate. As late patency results of the RA resemble those of the ITA, use of the RA as a conduit for coronary artery bypass grafting (CABG) has increased, but the incidence of atherosclerosis in the RA has not been widely investigated. This study was conceived to evaluate the degree and incidence of atherosclerosis in segments of the RA and ITA in a group of patients in whom both arteries were harvested for CABG. These findings were also compared to the association of major clinical events and etiological factors for atherosclerosis.

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## MATERIALS AND METHODS

Between January 2002 and February 2004, 770 segments of RA and ITA were obtained from 480 patients who underwent CABG. Comorbidity that might affect the progression of atherosclerosis was recorded prospectively. The potential risk factors considered for atherosclerosis were age, gender, smoking, diabetes mellitus, peripheral vascular disease, cerebrovascular disease, chronic renal failure, hypercholesterolemia, obesity, hypertension, and a positive family history.

B-mode and duplex ultrasonography are not as precise as angiography in detecting the extent of lesions, and we did not perform an ultrasonographic study. Angiography does not detect early lesions. Morphometric analysis was not performed because a histopathologic study was thought to be the most sensitive technique, as reported by the American Heart Association Committee on Vascular Lesions.<sup>5</sup> Six types of histological lesion have been defined.<sup>5</sup> Type I (initial) lesions contain scattered macrophage foam cells. Type II lesions consist of macrophages and smooth muscle cells forming grossly fatty streaks. Type III is intermediate between type II and IV and contains small extracellular lipid droplets. Type IV (atheroma) is a potentially symptom-producing lesion that contains a large confluent and more disruptive core of extracellular lipid; it usually forms an eccentric lesion. A type V lesion

contains thick layers of fibrous connective tissue. If there is a fissure with thrombus invasion, the lesion is type VI. Some type V lesions contain calcifications (type Vb), and some consist mainly of fibrous connective tissue with little or no calcium or lipid (type Vc). At least two sections per segment of artery were collected from each patient, fixed in 10% formalin, and embedded in paraffin blocks for histopathology. Several 4- $\mu$ m sections were obtained from each paraffin block, processed routinely, and stained with hematoxylin and eosin, elastic stain, and Mason's trichrome. Histological diagnosis of atherosclerosis was evaluated and typed according to the classification described above. An independent pathologist evaluated all biopsies in a blinded fashion.

The decision to harvest RA was made according to the Allen test results.<sup>6</sup> It was performed in the classic way and as a modified Allen test by means of ultrasonography.<sup>7</sup> The patients were also tested in the operating room by pulse oximetry just before the operation, and by observing the backflow of blood from distal RA intraoperatively. Unless backflow pressure was zero or the trace was asystolic, the RA was harvested. During harvesting, specimens were obtained from the distal end of the ITA before its bifurcation and the proximal and distal ends of the RA before the application of mechanical or pharmacological dilators.

Data were analyzed using SPSS for Windows, Version 11.0 (SPSS, Inc., Chicago, IL, USA) and presented as mean  $\pm$  standard deviation. Comparisons between groups were performed by the chi-squared test. Statistical significance was established at  $p < 0.05$ . Logistic regression was used for the clinical risk factors and grade III or more atherosclerosis for all patients to reflect the overall atherosclerosis in the study population. This was also performed for RA and ITA grafted patients either both or separately.

## RESULTS

Among the 770 segments of RA and ITA, there were 166 isolated ITA specimens and 22 isolated RA specimens. Paired segments of RA and ITA were obtained from 292 patients. The total number of ITA specimens was 458, and the total number of RA specimens was 312. There were 377 (79%) men and 103 (21%) women. Their ages ranged from 27 to 82 years (mean, 60 years). Overall hospital mortality was 11 (2.3%) patients. Table 1 summarizes the clinical features selected as potential risk factors for atherosclerosis within our population. Smoking, hypertension, male gender, and a positive family history were predominant.

The ITA and RA samples were graded histopathologically as shown in Table 2. No stenosis was detected, and no grade VI atherosclerosis was encountered. Grade III or more atherosclerosis was found in 47 (15%) RA samples and in 30 (7%) ITA samples. When comparing an RA specimen with the corresponding ITA specimen from the same patient, the mean ITA grade was  $1.6 \pm 0.6$  and the mean RA grade was  $2.1 \pm 0.9$  ( $p < 0.001$ ). The pre-atheroma and atheromas (grade IV/V) both in RA and ITA samples were detected in

**TABLE 1**  
**Clinical Characteristics of 480 Patients Undergoing**  
**Coronary Bypass Grafting**

Variable	No. of Patients	%
Age (years) [range]	60.1 $\pm$ 10	[27-82]
Gender		
Male	377	79
Female	103	21
Diabetes mellitus	177	36
Hypertension	302	62
Smoking	302	62
Peripheral vascular disease	56	11
Cerebrovascular disease	27	5
Chronic renal failure	36	7
Hypercholesterolemia	227	47
Obesity	152	31
Family history	261	54

17 patients (3%). The results of stepwise regression analysis on risk factors for grade III or more (atheroma subgroup) and less than grade III (intimal hyperplasia) for both ITA and RA are shown in Table 3. The analyses demonstrated a weak positive correlation between age and the degree of atherosclerosis in both the ITA and RA, but it was not statistically significant. Smoking possibly affected the risk. Table 4 shows a strong correlation between ITA atherosclerosis and age. Smoking had a tendency to increase the risk of ITA atherosclerosis, but there was no correlation with other risk factors. Table 5 shows a weak correlation between positive family history and RA atherosclerosis; age was not a significant predictor, and none of the other clinical risk factors was statistically important.

## DISCUSSION

The ITA graft has the best long-term patency rates of all conduits currently used for CABG, because of its resistance to atherosclerosis.<sup>8,9</sup> This may be due to some morphologic differences, such as blood supply from the vasa vasorum, the components of the medial layer, and innervation. Biochemical factors may also differ, such as the supply of nutrients to the wall of the conduit, effects of produced vasoactive substances, and the removal of metabolites. A 20-year follow-up study with angiographic confirmation in 90% of survivors demonstrated 89% patency in ITA grafts.<sup>10</sup> Histological

**TABLE 2**  
**Specimens Graded by Degree of Atherosclerosis**

Grade	RA	ITA
I	49	217
II	216	211
III	16	26
IV	7	2
V	24	2
VI	0	0
Mean grade	1.41 $\pm$ 1.3	1.53 $\pm$ 0.7
Total no. of specimens	312	458

ITA = internal thoracic artery; RA = radial artery.

**TABLE 3**  
**Risk Factors for the Patients Who had Both RA and ITA Grafting**

Variable	Beta	Odds Ratio	95% CI	p Value
Age	0.044	1.04	1-1.1	0.11
Gender	0.161	1.17	0.3-3.7	0.78
Smoking	0.883	2.41	0.7-7.8	0.14
Family history	0.468	1.59	0.5-4.4	0.37
Hypercholesterolemia	-0.909	0.4	0.1-1.2	0.10
Obesity	0.357	1.42	0.5-4.1	0.50
Diabetes mellitus	-0.387	0.67	0.2-2.0	0.49
Hypertension	-0.139	0.87	0.3-2.4	0.75
Cerebrovascular disease	-5.947	0	0-13	0.79
Chronic renal failure	-0.184	0.83	0.1-6.8	0.80
Peripheral vascular disease	-0.210	0.81	0.1-5.3	0.76

CI = confidence interval.

specifications, arterial wall metabolism, and arterial tone regulation capability give rise to high resistance to atherosclerosis of the ITA. Although the RA is generally successful as a graft, significant differences between the RA and the ITA have been noted in vasoreactivity and anatomy, which may explain the higher degree of atherosclerosis of the RA.<sup>11-13</sup>

Total arterial coronary revascularization strategies were adapted to overcome the problems of late vein graft atherosclerosis and occlusion. RA use has increased up to 75% in all myocardial revascularization procedures, and bilateral RA use is approximately 20%. In reoperations, RA is often the first alternative graft to ITA for left anterior descending coronary artery revascularization. Therefore, atherosclerotic change in the RA has become crucial. Tatoulis and colleagues<sup>14</sup> stressed the importance of the RA for total arterial coronary revascularization, using Y- and T-grafting methods in 3220 patients; overcoming RA spasm and probable etiologic factors for string sign were discussed, but preoperative RA atherosclerosis and postoperative patency were not mentioned. We believe that this could be a reason for the lower early rate of RA patency. It is important that vasospasm is resolved, but existing atherosclerosis cannot be evaluated after grafting.

Histopathological comparison of the RA and ITA has indicated a higher incidence of atherosclerotic changes in the RA.<sup>15</sup> The degree of pathological change in the

RA was related to age, gender, diabetes, and peripheral vascular disease, but none of these risk factors correlated with ITA atherosclerosis. Ruengsakulrach and colleagues<sup>16</sup> found the incidence of medial calcification (Monckeberg's sclerosis) in the RA was 13.3% but this was independent of the presence of atherosclerosis; they also found age, smoking, diabetes, and peripheral vascular disease were significant risk factors for atherosclerosis. Our findings show that although age was a risk factor for ITA atherosclerosis, smoking and family history did not reach statistical significance. This conclusion agrees with the results of Ruengsakulrach and colleagues,<sup>16</sup> yet contrasts with the report of Kaufer and colleagues.<sup>15</sup> Although 36% of patients had diabetes, it was not a predictor of RA and ITA atherosclerosis in our study, unlike the findings of Nicolosi and colleagues;<sup>17</sup> however, they did not examine histological data.

In our study, it was surprising that diabetes, peripheral or cerebral vascular disease, chronic renal failure, hypercholesterolemia, and gender were not related to pathology, although smoking, positive family history, and age were important risk factors. RA atherosclerosis was predominant, as found in previous studies.<sup>15-17</sup> When comparing RA specimens with the corresponding ITA specimen from the same patient, the mean grade of atherosclerosis was markedly different, showing that it is important to compare atherosclerosis in

**TABLE 4**  
**Risk Factors for the Patients Who had Only ITA Grafting**

Variable	Beta	Odds Ratio	95% CI	p Value
Age	0.070	1.07	1-1.12	0.002
Gender	0.237	1.26	0.5-3	0.59
Smoking	0.701	2.01	0.8-4.6	0.10
Family history	0.202	1.22	0.5-2.6	0.61
Hypercholesterolemia	-0.539	0.58	0.2-1.3	0.19
Obesity	0.282	1.32	0.5-2.9	0.50
Diabetes mellitus	-0.122	0.88	0.4-2	0.76
Hypertension	0.177	1.19	0.5-2.7	0.66
Cerebrovascular disease	-6.764	0	0-13	0.71
Chronic renal failure	-0.994	0.37	0.4-2.9	0.34
Peripheral vascular disease	-0.880	0.41	0.5-2.8	0.47

CI = confidence interval.

**TABLE 5**  
**Risk Factors for the Patients Who had Only RA Grafting**

Variable	Beta	Odds Ratio	95% CI	p Value
Age	0.016	1.01	0.98-1.05	0.34
Gender	0.316	1.37	0.6-2.7	0.38
Smoking	0.216	1.24	0.6-2.4	0.52
Family history	0.618	1.85	0.9-3.5	0.06
Hypercholesterolemia	-0.045	0.95	0.5-1.7	0.88
Obesity	0.376	1.45	0.7-2.7	0.25
Diabetes mellitus	-0.367	0.69	0.3-1.3	0.28
Hypertension	-0.046	0.95	0.5-1.8	0.88
Cerebrovascular disease	0.138	1.14	0.3-4	0.83
Chronic renal failure	-0.508	0.6	0.1-2.6	0.50
Peripheral vascular disease	-0.410	0.54	0.1-2.9	0.54

CI = confidence interval.

samples from the same patient. This study also revealed that well-known risk factors for coronary artery disease may be different from those implicated in peripheral vascular disease and graft atherosclerosis. He<sup>18</sup> published an impressive review of the choice of graft in different conditions, based on biological characteristics and functional classification of arterial grafts. Although anatomical differences, contractility, and vasospasm have been widely evaluated, the incidence of atherosclerosis in the RA was mentioned as unknown. Dystrophic calcification of RA was mentioned as intimal or medial calcification by Ruengsakulrach and colleagues<sup>16</sup> and Deshpande and colleagues.<sup>19</sup> Chronic renal failure and dystrophic calcification are well-known clinical entities that we also investigated but could not find a relationship with atherosclerosis in the RA.

A limitation of this study is the lack of morphometric data that might have made the results more precise. Postoperative angiography might be more definitive in determining the clinical results and existence of atherosclerotic pathology in the grafts. Further studies are planned to determine the long-term patency of the grafts used for coronary revascularization in this group of patients on whom pathological classification was carried out. This study may be repeated with other types of arterial conduits in the future. Moreover, it is not known if the histopathologic study of medial segments for both grafts can affect the results. Post-mortem studies could be the gold standard for such human researches. Even considering the probability of the different degrees of atherosclerosis in proximal and distal segments of RA, studying all segments of grafts for pathology could show us different aspects of disease and variability in etiology and localization. This is also a limitation of the study.

Ultrasonography was performed for modified Allen tests, but not for pathologic investigations. We believed that tissue sampling of the grafts would eliminate the need for an ultrasonographic study, as mentioned previously.<sup>20</sup> Most surgeons decide to use the RA according to its macroscopic appearance, and avoid vessels that appear to have severe atherosclerosis. It may be difficult to reach such an exact decision when there are borderline grossly atherosclerotic grafts, especially in

patients who need full arterial revascularization. In such cases, a quick histopathologic study may be very helpful. Our results are different from previous studies. This may be because of the different study groups, but it is possible that previous risk factors for graft atherosclerosis might have been exaggerated.

It was concluded from our findings that age correlated with pathology, but the RA and ITA are pathologically different arteries. In the same patient, the RA has a significantly greater prevalence of atherosclerosis, and the degree of pathology in the RA was higher. Thus, pathological changes in the RA do not reflect ITA pathology. The presence of calcification may lead surgeons to avoid an extra incision according to risk factors, although most of these are not predictive.

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