

## Does Clinical Profile Preclude Use of Radial Artery as a Conduit in Coronary Artery Bypass Grafting?

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### Abstract

**Aims:** Use of radial artery in coronary artery bypass grafting has been supported by the results of several histopathology and angiographic studies that have shown excellent short, medium and long term results. However the effect of coronary risk factors on its results may be of concern. This study was undertaken to correlate the association of major clinical risk factors with intimal hyperplasia and atherosclerosis in radial artery using preoperative doppler studies, intraoperative morphometry and postoperative histopathology (HP) and morphometry.

**Methods and results:** This was a prospective study involving 100 patients undergoing coronary artery bypass grafting surgery in whom radial artery was used as a conduit. The radial artery was assessed using preoperative doppler ultrasound studies, intraoperative morphometry and postoperative histopathology (HP) and morphometry. In our series hypertension (69%), diabetes mellitus (54%), tobacco usage (33%) and dyslipidaemia (10%) were dominant coronary risk factors. A correlation was sought to be established between these risk factors and presence of radial artery disease. Presence of diabetes did not correlate with radial artery disease ( $p=0.487$ ). Although the prevalence of disease was higher in patients having hypertension, dyslipidaemia and history of smoking, the numbers were not statistically significant. ( $p=0.7085$  for hypertension,  $p=0.248$  for dyslipidaemia and  $p$  of 0.387 for smoking).

**Conclusions:** In view of the variable or no predictive value of these clinical risk factors, we conclude that radial artery should be used as a second arterial conduit after internal mammary artery in all patients undergoing coronary artery bypass grafting irrespective of clinical risk profile.

**Keywords:** Coronary artery bypass grafting; Radial artery; Coronary artery disease; Risk factors

contraindicate the use of RA as a conduit in CABG owing to significant disease in it.

### Introduction

Survival after coronary artery bypass graft (CABG) surgery is attendant to long term graft patency and arterial grafts score over the venous grafts in that respect. Among arterial grafts, radial artery (RA) is considered to be the best conduit after internal mammary artery (IMA). Use of RA has been supported by the results of several histopathology [1] and angiographic [2,3] studies that have shown excellent short, medium and long term results. However, the effect of coronary risk factors and the clinical profile of the patient like gender, age, diabetes mellitus (DM), smoking etc. on radial atherosclerosis is controversial with some studies showing that RA loses its survival benefit beyond the age of 70 [4] and others showing that one should be cautious using them in diabetics [5] and in those with peripheral vascular disease (PVD) [6]. This study was therefore undertaken to correlate the association of major demographic and clinical risk factors with intimal hyperplasia and atherosclerosis in radial artery using preoperative doppler studies, intraoperative morphometry and postoperative histopathology (HP) and morphometry. Primary outcome aimed at seeing if the presence of these risk factors would

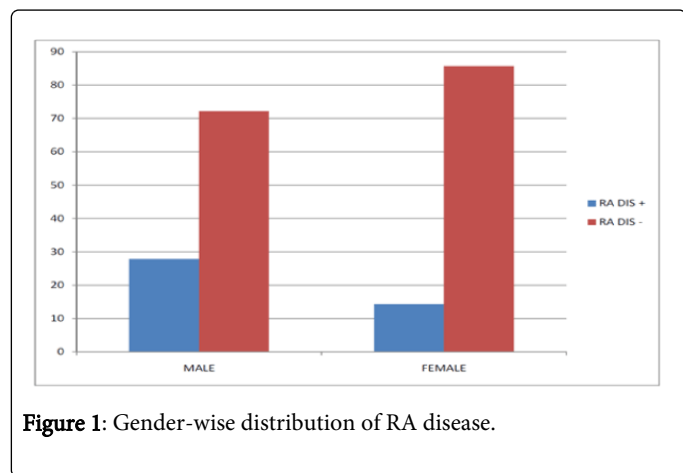
### Patients and methods

This prospective study included 100 patients of coronary artery disease (CAD) with the mean age of 61.45 years (range 44 to 80 years). There were 79 males and 21 females. The suitability of RA for use as a conduit was assessed by modified Allen's test in the non-dominant arm at the bedside using pulse oximeter. All the patients who had a negative modified Allen's test, which signified a complete palmar arch, were subjected to doppler ultrasonography (USG), which was performed by a single experienced observer, using PHILIPS-IE-33 machine with 7.5 MHz phased array rectangular vascular probe. Thorough and complete scanning of the RA was done starting just after ulnar artery branching (proximally) up to the wrist (distally). Along with other parameters the scanning evaluation included (i) luminal diameter (ii) measurements of intimal and medial thickness and (iii) measurements of intima-media thickness ratio.

Patient data was recorded which included gender, age, body surface area, presence of coronary risk factors like hypertension, DM, tobacco intake, dyslipidemia, PVD and stroke. Dyslipidemia was defined by the presence of any one of triglyceride >150 mg/dl, LDL cholesterol

>100 mg/dl, HDL cholesterol <50 mg/dl (male), and <40 mg/dl (females) and total cholesterol >200 mg/dl [7].

All surgeries were performed electively and without use of cardiopulmonary bypass. Left internal mammary artery (LIMA) was grafted to the left anterior descending (LAD) artery in all patients and the second most important target vessel, which in the majority was the marginal branch of the left circumflex artery, was grafted using the RA.



**Figure 1:** Gender-wise distribution of RA disease.

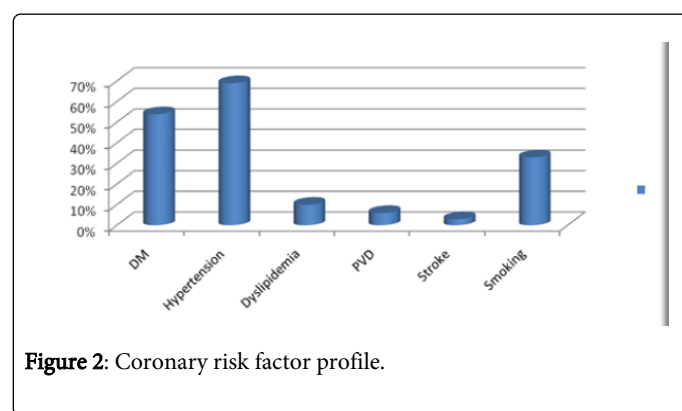
RA was harvested concomitantly with sternotomy and harvesting of other conduits using a no-touch technique. Visual assessment for any gross abnormality was made along with diameter of the vessel. RA was palpated for assessment of wall thickness. Any abnormality disqualified the RA for its use and hence the patient was excluded from the study. After the RA was harvested, sections of 1cm length from both ends were cut with fine scissors before hydrostatic dilatation. The luminal diameter and thickness of arterial wall were measured using vernier calipers. After intra operative morphometry measurements, specimens which constituted both the proximal and distal ends of RA were preserved in 5% formaldehyde solution and sent for HP study. 5-20 sections were analysed per segment of artery submitted for evaluation. These were cross sectioned at 5 micrometer and stained with hematoxylin eosin, verhoff von gieson's elastic stain and masson's trichrome stain. Histopathological assessments were followed by evaluation of the slides by a pathologist having expertise in morphometric measurements, who was blinded to the previous findings. The specimens were analyzed with a color image analysis system. The morphometric measurements included (i) luminal diameter (ii) intimal and medial thickness and (iii) intima-media thickness ratio.

Three criteria from the characteristics defined by pre-operative doppler and post-operative histopathology and morphometry studies were taken into consideration. These were abnormal intimal thickening, atherosclerosis and medial calcification. If any two of them were present, radial artery was considered to be diseased.

<b>Total number</b>	<b>100</b>
Males:Females	79:21
Mean age (years)	61.45
Mean body surface area (sq. m)	1.74
Mean left ventricular ejection fraction (%)	51.57

Double vessel disease	17
Triple vessel disease	83
Diabetes mellitus	54
Hypertension	69
Dyslipidemia	10
Smoking	33
Peripheral vascular disease	6
Stroke	3

**Table 1:** Patient demographics.



**Figure 2:** Coronary risk factor profile.

### Statistical analysis

Data was assessed and represented in mean values and association in categorical variables was evaluated by fisher's exact/chi-square test. In case of continuous variables, two groups were compared by using t-test. Intra class correlation, sensitivity and specificity and diagnostic accuracy were calculated with 95% confidence interval.

### Observations and results

There were 79 males and 21 females (Figure 1) with a gender bias of RA disease being more in the males as compared to the females (p value 0.01). The minimum age of the patients was 44 years and the maximum was 80 years, the mean being 61.45 years (Table 1). In our series hypertension (69%), diabetes mellitus (54%), tobacco usage (33%) and dyslipidaemia (10%) were the dominant clinical risk factors for CAD (Figure 2). These risk factors along with PVD and strokes were compared to presence of RA disease. Presence of DM did not correlate with RA disease (p=0.487).

Although the prevalence of RA disease was more in patients having hypertension, dyslipidaemia and history of smoking, the numbers were not statistically significant. (p=0.7085 for hypertension, p=0.248 for dyslipidaemia and p of 0.387 for smoking). Presence of PVD too did not correlate with RA disease. Out of six patients with PVD, none had RA disease, though out of 94 patients free of PVD, 92.55% (n=87) were free of RA disease and 7.45% (n=7) showed diseased RA. Three patients with history of strokes did not reveal any disease in their RA (Table 2).

S. No.	Risk factor	RA Disease (+)	RA Disease (-)	P value
1	DM+ (n=54)	3.70% (n=2)	96.30% (n=52)	0.487
2	DM- (n=46)	10.87% (n=5)	89.13% (n=41)	-
3	HTN+ (n=69)	8.70% (n=6)	91.3% (n=63)	0.7085
4	HTN- (n=31)	3.23% (n=1)	96.77% (n=30)	-
5	DISLIP+ (n=10)	10% (n=1)	90% (n=9)	0.248
6	DISLIP- (n=90)	6.6% (n=6)	93.33% (n=84)	-
7	Smoking+ (n=33)	12.2% (n=4)	87.88% (n=29)	0.387
8	Smoking- (n=67)	4.48% (n=3)	95.52% (n=64)	-
9	PVD+ (n=6)	0% (n=0)	100% (n=100)	-
10	PVD- (n=94)	7.45% (n=7)	92.55% (n=87)	-
11	Stroke+ (n=3)	0% (n=0)	100% (n=3)	-
12	Stroke- (n=97)	7.22% (n=7)	92.78% (n=90)	-

**Table 2:** Distribution of RA disease with respect to clinical risk factors.

Risk factor	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Diabetes	3.5	89.1	28.6	44.1
Hypertension	8.7	96.8	85.7	32.3
Dyslipidemia	10	93.3	14.3	90.3
Smoking	12.1	95.5	57.1	68.8
Peripheral vascular disease	No true positives	92.5	No true positive	46.5
Stroke	No true positives	92.8	No true positives	96.8

**Table 3:** Sensitivity, specificity and predictive values of clinical risk factors for RA disease.

In our series no risk factor was associated with a higher incidence of RA disease as evidenced by the low sensitivity and positive predictive values (Table 3). The sensitivity of diabetes mellitus and hypertension for the presence of RA disease was low, 3.5% and 8.7% respectively, with a positive predictive value (PPV) of 28.6% and 85.7% respectively. Even the presence of dyslipidemia had a low sensitivity of 10% and PPV of 14.3%.

### Radial artery measurements

The mean luminal diameter on preoperative doppler evaluation was 2.342 mm proximally and decreased distally with a reciprocal increase

in intimal thickness, as we moved down towards the wrist. The IMT ratios in the proximal, mid and distal segments were 0.530, 0.584 and 0.501 respectively (Table 4). Abnormal intimal thickening was found in 10 patients. On intraoperative assessment (Table 5) abnormal thickness to palpation was detected in 6 patients. The findings of post-operative morphometry studies showed similar trends as pre-operative morphometry (Table 6).

S. No.	Findings	Mean value in mm (S.Nos. 1-9)
1	Lum Dia (P)	2.342
2	Lum Dia (M)	2.264
3	Lum Dia (D)	2.164
4	IT (P)	0.064
5	IT (M)	0.075
6	IT (D)	0.1
7	MT (P)	0.137
8	MT (M)	0.174
9	MT (D)	0.211
10	IMTR (P)	0.53
11	IMTR (M)	0.584
12	IMTR (D)	0.501

**Table 4:** Preoperative doppler measurements.

S. No.	Findings (Mean)	Proximal	Distal
1	Wall thickness (mm)	0.5023	0.5483
2	Diameter (mm)	2.306	2.182

**Table 5:** Intraoperative morphometry measurements.

S. No.	Findings (Mean) in mm (S.No. 1, 2 and 4)	Proximal	Distal
1	Intimal thickness	0.065	0.105
2	Medial thickness	0.142	0.213
3	Intima-media thickness ratio	0.534	0.501
4	Luminal diameter	2.351	2.165

**Table 6:** Postoperative morphometry.

### Discussion

Ever since the resurgence of the RAs in early 90's, it has become the preferred alternative conduit, next only to IMAs. After an initial period of debate and controversy regarding superiority of RA over saphenous vein, especially after the assertion of Buxton et al. [8] that the RA grafts may not be superior to saphenous vein in patients younger than 70 years of age, it has found its rightful place in the armamentarium of a coronary surgeon, more so after the publication of the RAPCOS [9] and RAPS [10] Studies. Also now we are more

clear that these grafts should be used only in patients with more than 70%, [2,3,11] and preferably more than 90%, stenosis of the target vessel, as was shown by Desai et al. [12] Kane-Todd Hall et al. [13] comparing RA, IMA and LSV grafts found increased prevalence of intimal thickening, medial sclerosis and medial calcification in the RAs compared to other conduits, but in the vast majority of specimens, this was mild. The conclusion was that mild pre-existing disease in the RA is probably of little relevance to long term patency. In fact Caputo et al. [14] demonstrated better survival and clinical outcomes with RA as a second conduit as opposed to RIMA. However, advanced atherosclerotic changes may limit its use. But to date it is not conclusively demonstrated if demographic profile like age and sex and clinical risk profiles of coronary risk factors like hypertension, diabetes, tobacco intake, dyslipidaemia and involvement of other arterial beds like PVD and CVD, preclude the use of RA for CABG.

Prospective studies have demonstrated that different arterial beds have different risk factors for the development of atherosclerosis. Hypertension, diabetes, dyslipidaemia and tobacco are common risk factors for CAD, cerebral vascular disease (CVD) and PVD, but these factors appear to have different effects on arteries in different locations of the body [15]. Kay et al. [16] demonstrated that intimal thickening of IMA correlated with age, hypertension, diabetes and PVD. However, an autopsy series from Sisto and Isola [17] showed that only hypertension correlated with intimal thickness in IMAs and age, tobacco, body mass index and diabetes were not associated with atherosclerosis. Even in experience of Singh et al. [18] (an angiographic study), the incidence of atherosclerosis in IMA was not influenced by either age or PVD. But a contrarian view point was expressed by Sons et al. [19] who in an angiographic study showed that presence of PVD and hyperlipidaemia increased the relative risk of atherosclerosis in the IMA.

In our experience, none of the clinical risk factors studied had any statistically significant correlation to RA disease. Indeed, the sensitivity for these risk factors for the presence of radial artery disease (as per the measurements we carried out) was found to be very low. Zou et al. [5] taking presence of cellular or stromal tissue between the endothelium and the internal elastic lamina as the sign of disease found RA to be normal in only 26.7% of diabetic patients as against 76.7% of the non-diabetic patients undergoing CABG ( $p=0.0002$ ). Our series on the other hand found 96.3% of normal radial arteries in diabetics. Their study showed that intimal thickness index ( $p<0.05$ ) and intima: media ratio ( $p<0.05$ ) were higher in diabetics than in non-diabetics. However, there was no significant difference in luminal narrowing ( $p>0.05$ ). They thus opined that the quality of the RA in patients with diabetes was inferior to that in non-diabetic patients. They further corroborated their view with electron microscopic scores and molecular biology parameters of endothelial nitric oxide synthase (eNOS) protein expression and optical density scores which were higher in non-diabetics ( $p<0.001$ ). Even von willebrand factor and endothelin-1 messenger RNA (mRNA) levels were higher in the diabetic patients ( $p<0.001$ ) [5]. They thus found diabetes to be having negative effects on RA endothelial function. Unfortunately however, our study did not explore this molecular aspect of RA function. Even Kaufer et al. [6] found DM to be an incriminating risk factor for radial atherosclerosis. However Wildhirt [20] and Kohonen [21] found no such correlation, much like our study. One of the reasons for this discrepancy has been conjectured by Wildhirt et al. [20] that the RAs not found suitable by doppler and allen test were not harvested and also those vessels which were found intra operatively to be significantly diseased or calcified, were not used as a graft and were

excluded from the study and this could have influenced the results and caused this discrepancy. We acknowledge that this could have led to the very low sensitivity values of the clinical risk factors for the presence of RA disease in our study.

We found that the prevalence of RA disease was higher in patients having hypertension, dyslipidaemia and history of tobacco intake, but this tendency did not achieve statistical significance. However, Kaufer et al. [6] found that the degree of disease in the RA was related to sex, age, diabetes and PVD (aorto-iliac and femoro-popliteal atherosclerosis). Ruengsakulrach et al. [22] demonstrated strong predictive value of intimal hyperplasia in the RA of tobacco intake. In Ruengsakulrach's experience, there was differential predictive value of various parameters. For example, when they used percentage of luminal narrowing as the dependant variable, they found PVD and cigarette smoking as the dominant predictors. But when intimal thickness was used as the dependent variable, age and diabetes were the most important factors, and when IMR was used, the strongest predictor was only age. They thus concluded that the predictive variables cannot precisely indicate the risk of intimal hyperplasia and atherosclerosis and there was considerable unexplained variation in these predictive variables.

Ruengsakulrach et al. [23] found an overall prevalence of atherosclerosis of 31.5% in the RAs with 24.6% being affected with calcification and 6.8% with plaques. Our arteries showed atherosclerosis in 42%. Age, male sex and carotid artery disease predicted RA calcification and the radial artery plaque was best predicted by carotid disease and PVD. However, Kohonen [21] found no relationship of age, smoking and diabetes with atherosclerosis in the forearm arteries. We also found no such predilection. The author conjectured that the genetic predisposition for the atherosclerotic disease is so dominant that other acquired factors play a minor role and are in fact, overruled by hereditary factors.

The relation of atherosclerosis in the RAs to carotid artery atherosclerosis has been unclear. Opposite relation was found by Ruengsakulrach [22] while Kohonen [21] found atherosclerosis of the forearm arteries to be related to carotid artery disease. In fact Kohonen [21] suggests that if RAs on sonography are found to have atherosclerotic changes, then screening of the carotid arteries should always be performed.

## Conclusion

In view of the variable or no predictive value of these clinical risk factors, we propose that RA should be used as a second arterial conduit to IMA in all patients irrespective of gender or clinical risk profile. However the major limitations of this study are the low numbers of diseased radial arteries and the exclusion of molecular and biochemical studies of endothelial function.

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