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Radial Artery as a Coronary Artery Bypass Conduit

20-Year Results

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ABSTRACT

BACKGROUND There is a lack of evidence for the choice of the second conduit in coronary surgery. The radial artery (RA) is a possible option, but few data on very-long-term outcomes exist.

OBJECTIVES This study describes 20-year results of RA grafts used for coronary artery bypass grafting and the effects of RA removal on forearm circulation.

METHODS We report the results of the prospective 20-year follow-up of the first 100 consecutive patients who received the RA as a coronary bypass conduit at our institution.

RESULTS Follow-up was 100% complete. There were 64 deaths, 23 (35.9%) from cardiovascular causes. Kaplan-Meier 20-year survival was 31%. Of the 36 survivors, 33 (91.6%) underwent RA graft control at a mean of 19.0 ± 2.5 years after surgery. The RA was found to be patent in 24 cases (84.8% patency). In the overall population, probability of graft failure at 20 years was 19.0 ± 0.2% for the left internal thoracic artery (ITA), 25.0 ± 0.2% for the RA, and 55.0 ± 0.2% for the saphenous vein ($p = 0.002$ for RA vs. saphenous vein, 0.11 for RA vs. ITA, and $p < 0.001$ for ITA vs. saphenous vein). Target vessel stenosis >90%, but not location of distal anastomosis, significantly influenced long-term RA graft patency. No patients reported hand or forearm symptoms. The ulnar artery diameter was increased in the operated arm (2.44 ± 0.43 mm vs. 2.01 ± 0.47 mm; $p < 0.05$) and correlated with the peak systolic velocity of the second palmar digital artery (Pearson coefficient: 0.621; $p < 0.05$).

CONCLUSIONS The 20-year patency rate of RA grafts is good, and not inferior to the ITA, especially when the conduit is used to graft a vessel with >90% stenosis. RA harvesting does not lead to hand or forearm symptoms, even at a very-long-term follow-up. (J Am Coll Cardiol 2016;68:603–10) © 2016 by the American College of Cardiology Foundation.

The radial artery (RA) is the conduit most recently introduced in coronary artery bypass graft (CABG) surgery, after the great saphenous vein (SV) and the internal thoracic artery (ITA) (1). To date, there is evidence that the conduit has a post-operative patency rate higher than the SV and equivalent to the right ITA, and its use can lead to substantial clinical advantages in selected groups of patients (2). However, the RA is relatively underused. In a recent report from the Society of Thoracic Surgery Adult Cardiac Surgery Database, the RA was used in <6% of all primary isolated CABGs in the United States in the 2000 to 2009 period (3).

One of the reasons for its limited adoption is probably the fact that, up to now, only limited information exists on very-long-term results of using the RA, with most studies reporting a mean follow-up of <10 years. In addition, previous reports

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ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass graft

ITA = internal thoracic artery

RA = radial artery

SV = saphenous vein

(including ours) have expressed concerns about possible harm to the forearm circulation after RA harvesting (4). This has possibly further limited adoption of this conduit by the surgical community.

To contribute to the diffusion of use of the RA as a coronary artery bypass conduit, we herein describe the results of the 20-year prospective follow-up of our initial cohort of 100 patients who received an RA graft for myocardial revascularization.

METHODS

The use of the RA as a coronary artery bypass conduit was started prospectively at the Catholic University of Rome in January 1993, on approval by the local Ethics Committee (5). For the first 100 consecutive patients, we adopted a very strict follow-up protocol that included the following:

- yearly clinical examination
- yearly stress test or stress myocardial scintigraphy
- 1-, 5-, and 10-year angiographic control studies
- 1-, 5-, and 10-year echo Doppler evaluation of forearm circulation

Results of the 1-, 5-, and 10-year clinical and angiographic follow-ups, and detailed descriptions of the modifications of the forearm circulation after RA removal, and of the effects of the calcium-channel blocker therapy and morphofunctional remodeling of the artery after implantation in the coronary circulation were previously published (4–10). In this report, we describe the 20-year clinical, angiographic, and echo Doppler results for this cohort of patients.

PATIENT POPULATION AND SURGICAL TECHNIQUE. Preoperative clinical details are summarized in Table 1. Details of our surgical technique have been published (5). Briefly, the same surgical team performed all operations, using cardiopulmonary bypass and cardioplegic arrest. The left ITA was usually used to graft the left anterior descending artery, whereas the RA was grafted to the second target vessel. The RA target vessel was a branch of the circumflex artery in 53 cases, a branch of the right coronary artery in 36 cases, and a diagonal in 11 cases. SV grafts usually completed the revascularization, whereas the right ITA and the gastroepiploic artery were used in a minority of cases. The RA was anastomosed to the ascending aorta in 85 patients, and to the left ITA in the remaining patients.

TABLE 1 Pre-Operative and Intraoperative Characteristics

Male/female ratio	72/28
Mean age, yrs	63.7 ± 6.6
Cardiovascular risk factors	
Diabetes	20
Smoking	56
Dyslipidemia	51
Hypertension	44
Previous myocardial infarction	60
Number of diseased vessels	2.8 ± 0.4
Mean ejection fraction	0.62 ± 0.15
Number of anastomoses per patient	2.9 ± 0.1

Values are n or mean ± SD.

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Since the beginning of our study, we adopted systematic Doppler or echo Doppler assessment of the adequacy of collateral ulnar circulation before RA removal, according to a published method (10). The RA was always harvested from the nondominant arm, and bilateral RA harvesting was never performed.

Long-term calcium-channel blocker therapy (diltiazem, 120 mg/day) was prescribed for all patients for the first post-operative year. After the results of 2 prospective randomized trials by our group (8,9), calcium-channel blocker therapy was abandoned, and is not currently part of our routine.

FOLLOW-UP. Each patient was followed up regularly at our institution 6 months after surgery and every year thereafter. At each time interval, clinical examination and echo Doppler evaluation of the forearm were performed, and the results of surface electrocardiography, stress myocardial scintigraphy, 24-h Holter monitoring, and transthoracic echocardiography were reviewed. In the case of death during the follow-up period, all medical and autopsy reports were reviewed for attribution of the cause. For out-of-hospital fatalities, the death certificate was requested and reviewed. Death was considered cardiac in origin when it was preceded by evidence of myocardial ischemia, heart failure, or arrhythmia.

Angiographic control or (in recent years) computed tomography–angiographic assessment was proposed to all patients at the early (1-year), midterm (5-year), long-term (10-year), and very-long-term (20-year) follow-up visits, and at any time when there was instrumental evidence of inducible ischemia.

Two experienced observers independently graded angiographies using a previously described 4-grade angiographic scale (perfectly patent, patent with irregularities, stringed, occluded) (6).

STATISTICAL ANALYSES. Data are expressed as mean ± SD. Statistical analysis was performed with an unpaired, 2-tailed Student *t* test for means or the chi-square test for categorical variables. Competing risks

TABLE 2 Causes of Follow-Up Deaths

	First Decade of Follow-Up	Second Decade of Follow-Up
Cardiac deaths	2	21
MI	1	5
CHF	1	11
Arrhythmia	0	4
Re-CABG	0	1
Noncardiac deaths	4	37
Cancer	4	11
Stroke	0	10
Accident	0	4
Suicide	0	1
Aortic aneurysm	0	5
Respiratory failure	0	4
Pulmonary embolism	0	2

Values are n.
CHF = congestive heart failure; MI = myocardial infarction; Re-CABG = reoperative coronary artery bypass grafting.

analysis was used to estimate the cumulative incidence function for late graft occlusion for the 3 different conduits (10). In this analysis, patients who died from causes that could possibly be related to acute graft occlusion (myocardial infarction, arrhythmias) without perimortem angiographic verification of graft patency were considered as having all grafts occluded. Subgroup analysis was conducted according to the RA target (circumflex or right coronary artery) and the RA target stenosis degree (≥90% vs. <90%).

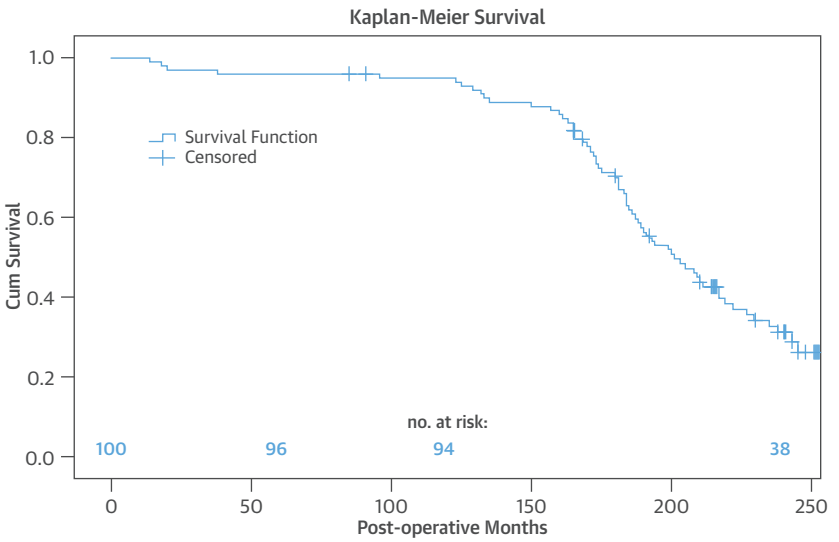
Adjustment for baseline characteristics was not required, because each of the 3 conduits analyzed was used in all patients, except for 9 subjects who did not receive SV grafts. All analyses were conducted with R (11). Spearman coefficient correlation was used to explore the association between morphological and hemodynamic measures at echo Doppler evaluation.

RESULTS

CLINICAL RESULTS. Follow-up was 100% complete, and the mean follow-up time was 20.8 ± 1.5 years. During this period, 64 of 100 patients died (64%). The cause of death was noncardiac in 41 cases and cardiac in 23 (35.9%). The causes of cardiac and noncardiac death are summarized in Table 2. The Kaplan-Meier 20-year survival curve is shown in Figure 1. During the follow-up, clinical or instrumental evidence of myocardial ischemia occurred in 79 patients; thus, the 20-year ischemia-free survival was 21%.

20-YEAR RESULTS. Thirty-three of the 36 survivors (91.6%) underwent angiographic (n = 30) or

FIGURE 1 Clinical Follow-Up: Long-Term Survival Curve Using the Kaplan-Meier Method



	12 Months (95% CI)	60 Months (95% CI)	120 Months (95% CI)	240 Months (95% CI)
Survival	100%	96.0% (92.1-99.9%)	94.0% (89.3-98.7%)	43.8% (33.6-54.0%)

Follow-up was 100% complete, and the mean follow-up time was 20.8 ± 1.5 years. During follow-up, 64 patients died, mostly from noncardiac causes. Estimated 10- and 20-year survival were 94% and 43.8%, respectively. CI = confidence interval.

TABLE 3 20-Year Angiographic Results*

	LITA (n = 33)	RA (n = 33)	RITA (n = 4)	RGEA (n = 8)	GSV (n = 31)
Perfectly patent	31	24	3	5	8
Patent with irregularities	0	4	0	0	6
String	0	1	0	1	0
Occluded	2	4	1	2	17
Patency rate, %	93.9	84.8			45.1
Perfect patency rate, %	93.9	72.7			25.8

Values are n or %. *19.0 ± 2.5 years. p = 0.23 for comparison between RA and ITA, and p < 0.0001 for comparisons between ITA and GSV and between RA and GSV.

GSV = great saphenous vein; LITA = left internal thoracic artery; RA = radial artery; RGEA = right gastroepiploic artery; RITA = right internal thoracic artery.

TABLE 5 Comparison of Radial Artery Graft Status Between the 10- and 20-Year Angiographic Controls in the 30 Patients Who Underwent Both Studies

	10-Year Angiographic Control		20-Year Angiographic Control
Perfectly patent	26	2	22
Patent with irregularities	2	2	4
String	1		1
Occluded	1		3
Patency rate	93.3		86.6
Perfect patency rate	86.6		73.3

Values are n or %.

angiographic-computed tomography (3 cases) control studies at a mean of 19.0 ± 2.5 years after surgery. The main angiographic results are reported in Table 3.

In these 33 patients, the very-long-term patency and perfect patency rates were, respectively, 93.9% and 93.9% for the left ITA, 84.8% and 72.7% for the RA, and 45.1% and 25.8% for the SV (p = 0.23 for the left ITA vs. RA comparison and p < 0.001 for both the ITA vs. SV and RA vs. SV comparisons).

Most (4 of 5 = 80%) of the cases of RA occlusion or string sign occurred in patients in whom the artery was anastomosed to coronary arteries with stenosis ≤90%. No correlation was found between the location of the distal anastomosis (circumflex or right coronary artery) and the very-long-term angiographic status (Table 4).

Table 5 compares the 10- and 20-year angiographic studies in the 30 patients who underwent both angiographies. Two RA grafts that were perfectly patent at 10 years were occluded at 20 years, and 2 others developed some irregularity between the 2 controls, leading to a drop in the patency and perfect patency rates, from 93.3% and 86.6% at 10 years to 86.6% and 73.3%, respectively, at 20 years.

OVERALL EXPERIENCE. During the 20 years of follow-up, 98 of the 100 patients underwent at least 1 angiographic control study: 9 patients underwent 1, 49 patients underwent 2, and the remaining 40 patients underwent more than 2. The cumulative incidence of graft occlusion at 20 years was 19.0 ± 0.2% for the left ITA, 25.0 ± 0.2% for the RA, and 55.0 ± 0.2% for the SV (p = 0.001 for RA vs. SV, 0.11 for RA vs. ITA, and p < 0.001 for ITA vs. SV) (Central Illustration).

As detailed in the Methods section, in this analysis, patients who died from causes that may have been related to acute graft occlusion were considered as having all grafts occluded even in the absence of perimortem angiography. Graft occlusion was verified angiographically in 18 patients, and inferred from the clinical course in 8 cases.

The severity of target vessel stenosis had a major influence on graft patency. When the target vessel stenosis was ≥90%, the patency of the RA was similar to that of the left ITA, whereas for less severe stenosis, the angiographic outcome was more similar to that of the SV (Figure 2). The location of the distal anastomosis on the circumflex or right coronary system did not influence RA patency (Figure 3).

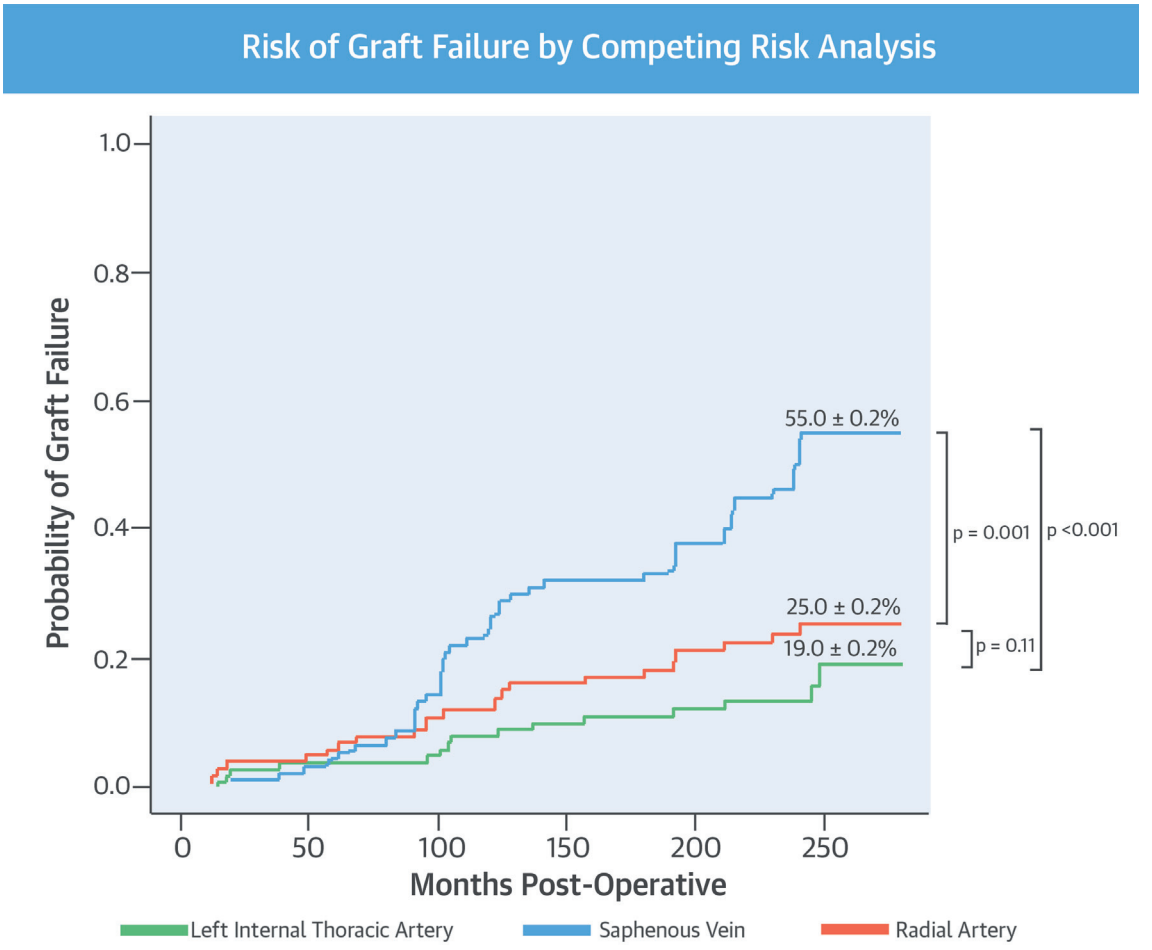
EVALUATION OF FOREARM CIRCULATION. None of the patients had signs of symptoms of hand ischemia during the post-operative follow-up. Twenty-five patients underwent echo Doppler evaluation of the forearm circulation at a mean interval of 17.6 ± 2.1 years from surgery. In the operated forearm, there was a significant increase in the diameter of the ulnar artery (2.44 ± 0.43 mm vs. 2.01 ± 0.47 mm; p < 0.05). All other flow parameters were similar between the operated and control arms (Table 6). In the operated arm, there was a significant correlation between the diameter of the ulnar artery and the peak systolic velocity of the second proper palmar digital artery (Spearman coefficient: 0.621; p = 0.41) (Figure 4A).

TABLE 4 Long-Term Radial Artery Angiographic Results in Relation to the Location of Target Vessel

	Patent	Occluded
Left anterior descending	0	0
Diagonal	4	0
Circumflex	16 (84.2)	3
Right coronary artery	8 (80.0)	2

Values are n or n (%).

CENTRAL ILLUSTRATION **Radial Artery as a Coronary Artery Bypass Conduit**



Gaudino, M. et al. J Am Coll Cardiol. 2016;68(6):603-10.

Risk of graft failure by competing risk analysis for the radial artery, the left internal thoracic artery, and the saphenous vein. In the very long term, the angiographic outcome of radial artery grafts is similar to that of internal thoracic artery grafts.

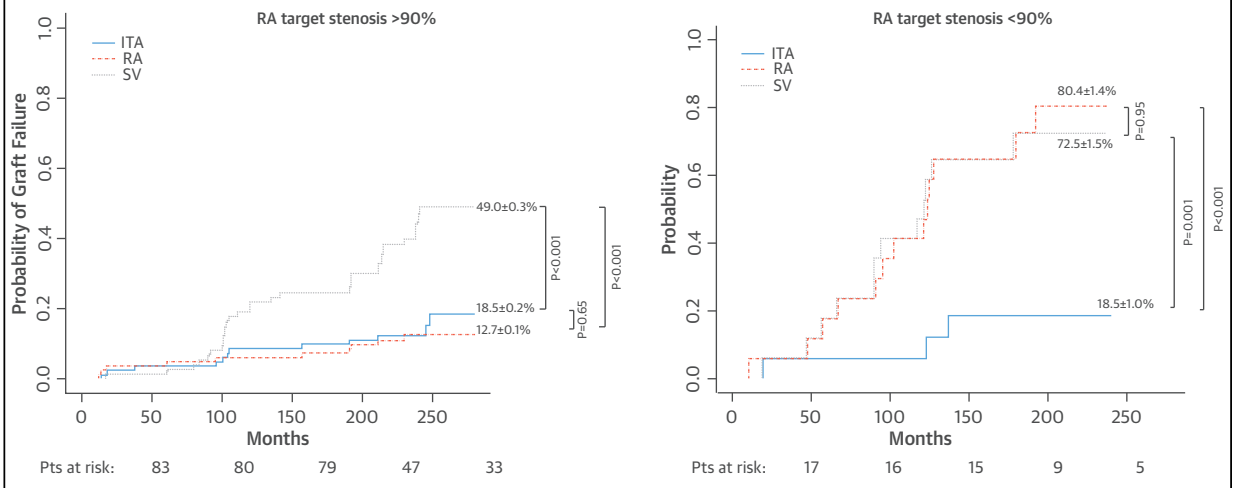
This correlation was absent in the control arm (**Figure 4B**).

DISCUSSION

Since the reintroduction of the RA as a conduit in coronary surgery in the early 1990s (1), its morpho-functional features, biological properties, and vaso-reactive profile of RA grafts have been mostly elucidated (11). The early and intermediate angiographic patency rates have been published (2), and the Radial Artery Patency and Clinical Outcome trial should be reporting its 10-year angiographic and clinical results this year. There is growing evidence that the patency rate of the RA is better than that of the SV (2). The RA contends with the right ITA for the role of the second artery for CABG, and is probably a better choice in patients at high risk of sternal complications (2,12).

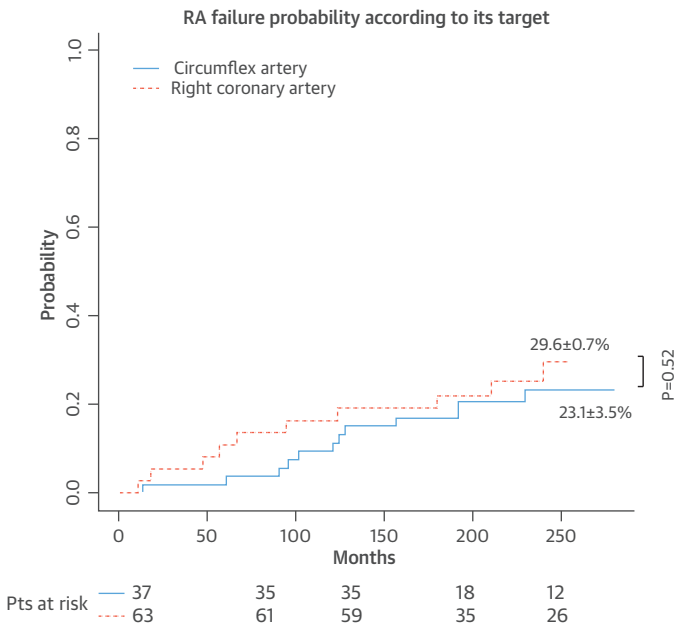
Despite that, the RA is markedly underused. In a recent report from the Society of Thoracic Surgeons Adult Cardiac Surgery Database, this conduit was used in slightly more than 5% of all primary isolated CABG procedures performed in the United States from 2000 to 2009 (3). Possible reasons for this underuse are the lack of very-long-term data and concerns regarding accelerated atherosclerosis of the ulnar artery after RA removal (4).

FIGURE 2 RA Status in Relation to Target Vessel Stenosis



Risk of graft failure by competing risk analysis for RA grafts anastomosed to target vessels with >90% and <90% stenosis. The severity of target vessel stenosis has a major impact on RA graft status. For target vessel stenosis >90%, the patency of the RA was similar to that of the ITA, whereas for <90% stenosis, the angiographic outcome was more similar to that of the SV (modified chi-square test). ITA = internal thoracic artery; RA = radial artery; SV = saphenous vein.

FIGURE 3 RA Patency Rate, According to Location of the Distal Anastomosis



Risk of graft failure by competing risk analysis for RA grafts anastomosed to the circumflex system or to the right coronary artery. The location of the distal anastomosis did not influence the long-term angiographic outcome (modified chi-square test). RA grafts anastomosed to the circumflex or right coronary artery had similar patency rates. Abbreviation as in Figure 2.

To date, only 1 group has reported a RA follow-up of >10 years. Acar's group (1) (who rediscovered the RA in the 1990s) reported their 20-year experience in a cohort of 563 patients. At a 9.2-year mean follow-up, freedom from overall and cardiovascular death was 80.3% and 92.7%, respectively. Angiographic follow-up was obtained in 351 patients at a mean interval of 7.0 years from surgery, and the RA patency rate was 87.9%. In patients with the longest follow-up interval, the RA patency rate was 81.4% at 13.1 years (13).

In our series, the RA patency rate in the group of patients who reached the 20-year follow-up was

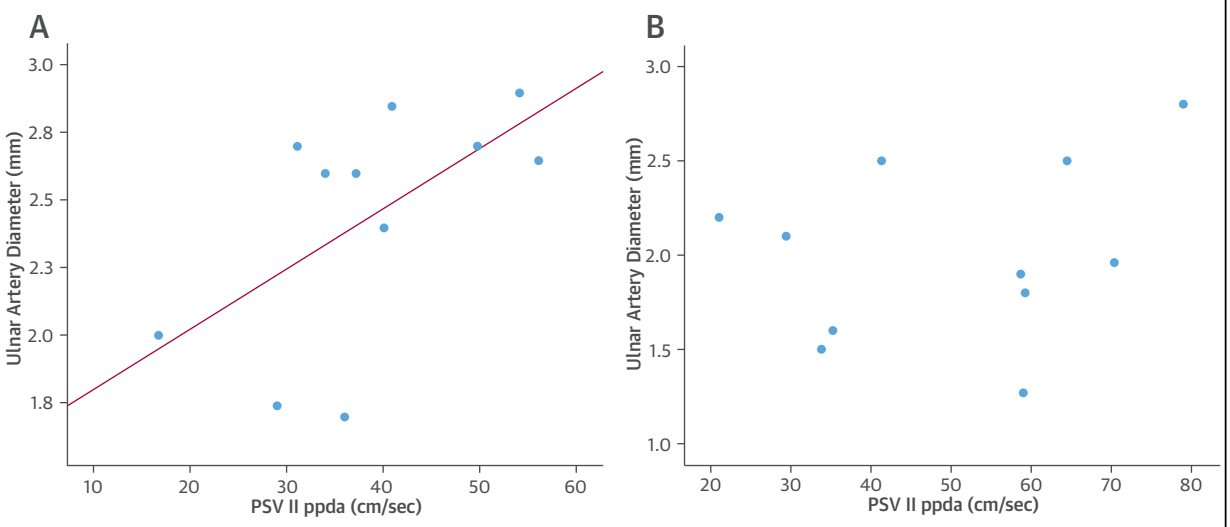
TABLE 6 Echo Doppler Comparison of the Operated and Control Arms

	Operated Arm	Control Arm	p Value
UA diameter, mm	2.44 ± 0.43	2.01 ± 0.47	<0.05
UA IMT, mm	0.47 ± 0.19	0.40 ± 0.16	0.42
UA PSV, cm/s	92.6 ± 27.9	86.0 ± 28.0	0.58
UA resistance index	0.87 ± 0.1	0.92 ± 0.08	0.19
UA pulsatility index	8.07 ± 10.11	6.31 ± 5.40	0.61
Second PPDA PSV, cm/s	38.56 ± 11.53	50.13 ± 18.79	0.09
Fourth PPDA PSV, cm/s	38.90 ± 18.09	36.82 ± 21.83	0.81
UA atherosclerosis	3	1	0.53

Values are mean ± SD or n.

IMT = intima-media thickness; PPDA = proper palmar digital arteries; PSV = peaks systolic velocity; UA = ulnar artery.

FIGURE 4 Long-Term Effect of RA Removal on the Forearm Circulation



Correlation between ulnar artery diameter and PSV of the II PPDA in the operated **(A)** and control **(B)** forearms. In the long term, after harvesting of the RA, the ulnar collateral circulation provides collateral flow to the arm. In the operated arm (but not in the control arm), there is a significant correlation between the ulnar artery diameter and the PSV of the II PPDA (Spearman coefficient: 0.621; p = 0.41). II PPDA = second proper palmar digital artery; PSV = peak systolic velocity; other abbreviation as in Figure 2.

84.8%, with a perfect patency rate of 72.7%. The status of the graft remained substantially stable in the very long term, with only 2 occlusions occurring between the 10- and 20-year control studies in the group of patients who underwent both (Table 5). Overall, the long-term patency rate of the RA was not statistically different than that of the gold standard ITA.

Confirming previous observations (14,15), we found a strong correlation between the severity of the target vessel stenosis and the RA patency. When the RA was used to revascularize target vessels with ≥90% stenosis, the patency rate of the conduit was similar to that of the left ITA, whereas for a lower degree of coronary stenosis, the angiographic outcome was more similar to that of the SV (Figure 2).

As in our previous reports (2,6), the location of the target vessel did not influence the graft outcome. In fact, the circumflex and right coronary artery distributions had similar RA graft patency rates (Figure 3).

The echo Doppler evaluation of the forearm circulation testified to the development of an adequate ulnar collateral circulation several years after surgery. Most flow parameters were similar between the 2 forearms, and there was a clear correlation between the diameter of the ulnar artery and the peak systolic velocity of the second proper palmar digital artery in the operated site. Most importantly, no patient had signs or symptoms of hand ischemia during the 20-year follow-up (and this is common to our overall experience in more than 1,600 RA cases). The small echo Doppler differences reported between the operated and control arms did not have a clinical correlate and, at this point of the follow-up, are unlikely to ever have any.

STUDY LIMITATIONS. On this basis, previous concerns about possible accelerated atherosclerosis in the ulnar artery of the operated forearm (4) seem unsubstantiated. This is an observational prospective study, and has obvious limitations related to the sample size and lack of a control group. However, the main strength of this study is the 100% complete prospective 20-year clinical and serial angiographic follow-up.

CONCLUSIONS

The 20-year angiographic outcome of RA conduits used for CABG is not inferior to that of the gold standard left ITA. The status of the artery remains stable during the very-long-term follow-up. The location of the target vessel does not influence graft status, whereas the severity of the coronary stenosis

is a major determinant of patency. Finally, after harvesting of the RA, the ulnar collateral circulation provides sufficient flow to the arm and clinically evident forearm or hand ischemia never occurs, even at extended follow-up.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: The use of the RA during coronary artery bypass operations is associated with patency rates better than the SV and similar to the ITA in patients with occlusive or subocclusive target vessel lesions.

TRANSLATIONAL OUTLOOK: Randomized trials are needed to compare short- and long-term outcomes of revascularization using the RA with alternative vascular conduits in patients with less severe stenosis undergoing coronary artery bypass surgery.

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KEY WORDS angiography, follow-up studies, internal thoracic artery, prospective studies, saphenous vein