Editorial
Can a muscular artery be used as a coronary artery bypass conduit? Lessons learned from the mid-term control of radial artery grafts

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(Ital Heart J 2000; 1 (9): 581-584)

Received July 5, 2000;
accepted July 12, 2000.

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Introduction

After the first disappointing experience of more than two decades ago, the radial artery (RA) was reintroduced in coronary artery bypass surgery in the early 1990s and, due to its favorable anatomical position, caliber and length, soon gained good popularity.

However, since the early days of its reproposal, the peculiar morpho-functional features of this conduit elicited major theoretical doubts on its adequacy in being used as a coronary artery bypass graft. The early reports of cases of RA spasm during postoperative control angiography created concerns about the hyperspastic attitude of this conduit, and data derived from the microscopic analysis of the artery *in situ* coupled with the historic finding of an alarming high incidence of intimal hyperplasia in RA grafts further fueled the debate about this alternative arterial conduit[1,2].

For these reasons the prescription of a chronic antispastic therapy (usually using oral calcium channel blockers for an indefinite period of time) was considered mandatory for patients receiving RA grafts. Moreover, some authors even suggested to proximally connect the RA to a vascular district with a $\Delta P/\Delta T$ smoother than that registered in the ascending aorta (such as an *in situ* mammary artery graft), in order to minimize the hemodynamic stress on the hyperreactive RA wall and to reduce the incidence of spasm and intimal hyperplasia[3].

Theoretical basis for the concerns about radial artery grafts

From a histological point of view the RA is a thick walled muscular artery, whose vascular wall is irrorated at least in part by vasa-vasorum and characterized by a high number of discontinuities of the internal elastic lamina (IEL)[1]. This histological architecture is strikingly different from that of the elasto-muscular, endoluminally-nourished, IEL-fenestration-free internal thoracic artery (ITA) (usually considered as the gold standard coronary artery bypass conduit).

The abundant muscular component of the RA is the anatomical background of the hyperspastic attitude of the artery; indeed it is known that, despite similar endothelial function, the RA can develop a significantly higher contractile force in response to vasoconstricting or depolarizing agents compared, for example, with the ITA[4,5].

Moreover, as smooth muscle cells have a higher metabolic demand than elastin, it has been proposed that the muscular RA wall can be subjected to a greater degree of ischemia when used as a free graft (with consequent deprivation of vasa-vasorum perfusion) in comparison to elastic arteries constituted mainly by the bradytrophic and inert elastic tissue[1]. These considerations, coupled with the high number of RA IEL discontinuities (significantly superior to those observed in the ITA and proposed as a risk factor for the migration of smooth muscle cells in the intima) has led several authors to consider the RA a conduit at high risk of fibrous intimal

hyperplasia[1]. On the other hand, basic research data on the biology of the RA have reported conflicting results: in a classic organ-bath study published soon after its re-introduction in clinical practice, Chardigny et al.[2] reported that the contractile response elicited on RA rings by a variety of vasoconstricting stimuli is markedly superior to that exhibited by both the ITA and the gastroepiploic artery, further increasing the early concerns about RA hyperreactivity.

However, other studies have demonstrated that, like the ITA, the *in situ* RA has a high basal and stimulated release of nitric oxide and one study in particular testified how both endothelium-dependent and independent vasodilation are similar between the two arteries[5,6].

As a final point, surgical removal of the RA halves the blood supply to the hand and forearm circulation and several authors have expressed concerns about the possible ischemic consequences of this deprivation[1,2].

Table I. Comparison between early and mid-term serotonin infusion.

	RA	ITA
Early angiography		
Baseline diameter (mm)	2.11 ± 0.10	2.42 ± 0.05
Serotonin	1.70 ± 0.37	2.41 ± 0.17
Constriction (%)	18.91 ± 8.40*	0.41 ± 0.22**
Mid-term angiography		
Baseline diameter (mm)	2.58 ± 0.37	2.53 ± 0.17
Serotonin	2.48 ± 0.72	2.45 ± 0.14
Constriction (%)	3.94 ± 1.92***§	3.21 ± 0.84§§

ITA = internal thoracic artery; RA = radial artery. * $p < 0.01$ compared with baseline and with ITA constriction at the same time; ** p = NS compared with baseline; *** p = NS compared with baseline and with ITA constriction at the same time; § $p < 0.01$ compared with RA constriction at early angiography; §§ p = NS compared with baseline and with ITA constriction at early angiography.

Our experience with the use of radial artery grafts

Our experience with the use of the RA began in January 1993, immediately after its re-introduction into clinical practice. From this date, a study on this conduit was prospectively started; the three main objectives of the study were to establish: 1) the mid- and long-term clinical and angiographic results of RA grafts, 2) the chronic effect of RA removal on the forearm blood supply, and 3) the vasoreactive profile of RA grafts and their evolution over time[7-11].

The early results were extremely favorable, with a 1-year angiographic patency rate of 88.8%, slightly inferior to that of the ITA, but clearly superior to that of the saphenous vein[7].

During the first postoperative year all patients were maintained on chronic calcium channel blocker therapy (diltiazem 120 mg/daily). Thereafter, in order to objectivate the effective benefits of the antispastic therapy (who has always been based only on theoretical presumptions and never supported by objective data) we decided to randomize the first 120 patients that at 1-year follow-up had angiographic evidence of functioning RA graft and/or scintigraphic demonstration of the absence of inducible ischemia in the RA territory, to continue or suspend the calcium channel blockers and to closely follow-up the two groups.

Moreover, an endovascular infusion of a powerful vasoconstricting stimulus (serotonin hydrochloride) was administered to a small cohort of patients undergoing early angiographic control to evaluate the spastic attitude of the RA (which in the early postoperative period was confirmed to be significantly superior to that of the ITA) (Table I).

At 5-year follow-up we re-examined all patients by myocardial scintigraphy and/or angiography and testified optimal mid-term results and, most of all, excellent angiographic patency and perfect patency rates of RA grafts (92 and 87% respectively)[9].

More interestingly, in the cohort of patients who had undergone both the early and mid-term angiographic controls the comparison of the 1- and 5-year results demonstrated an evident increase in the perfect patency rate, due to the disappearance of parietal irregularities of the proximal part of the graft in some cases and to the finding of a perfectly patent RA in one case in whom the graft was considered occluded at early angiography (Table II).

This surprising increase is concordant with the marked reduction in the cases of catheter-induced RA spasm noticed between the early and mid-term controls.

In accordance with these findings is the observation that in patients who were given early serotonin infusion and in whom this vasoconstricting challenge was repeated at 5 years, the marked hyperreactivity of RA grafts was found to have almost totally disappeared at mid-term follow-up, and the vasoconstricting attitude of the artery became similar to that of the gold reference ITA (Table I).

The hypothesis of a progressive reduction of RA hyperreactivity is further supported by the fact that 5 years after surgery no differences in either the clinical and scintigraphic results or the RA angiographic status were

Table II. Comparison between early and mid-term radial artery angiographic status in a cohort of 48 patients who underwent both 1- and 5-year angiography.

	Early angiography	Mid-term angiography
Perfectly patent	33 (67.3%)	41 (83.6%)
Patent with irregularities	8 (16.3%)	1 (2.0%)
String sign	2 (4.0%)	2 (4.0%)
Occluded	6 (12.2%)	5 (10.2%)

found between patients who continued or suspended the calcium channel blocker therapy (Table III).

Moreover, in order to investigate the presumed tendency of RA grafts directly anastomosed to the ascending aorta to the progressive development of fibrous intimal hyperplasia, the first 20 cases in whom the RA was found perfectly patent at 1-year angiography underwent quantitative angiographic measurement of the RA graft and the corresponding grafted coronary arteries at 1- and 5-year controls and 11 patients with perfect RA at mid-term angiography were also given endovascular infusion of acetylcholine (in order to evaluate the capacity of endothelium-dependent vasodilation of RA grafts 5 years after surgery)[11].

This study showed how the diameter of the RA significantly increased over time, and that 5 years after surgery RA grafts maintained an appreciable endothelium-dependent vasodilating capacity (not inferior to that of the gold standard ITA) (Tables IV and V).

Although in the absence of histologic data or endovascular echographic imaging of the graft wall the development of intimal disease cannot be definitely excluded, these observations strongly argue against the presence of a hyperplastic regenerated endothelium and seem to put into perspective the expressed concerns on the tendency of the RA to develop fibrous intimal hyperplasia.

On the other hand, the low propensity of the RA to develop flow-induced intimal hyperplasia is further testified by the finding that this artery *in situ* reacts with a progressive remodeling of its structural architecture (characterized by a striking increase in internal diameter without vessel wall hypertrophy, with unchanged intima-media thickening and no luminal narrowing) when exposed to a major increase in flow (as occurs after creation of an artero-venous fistula in patients with dialysis-dependent renal failure)[12].

Finally, repeated echo-Doppler studies of the hand and forearm circulation after RA removal have demonstrated how, in selected patients, the ulnar artery is able to compensate for the loss of RA contribution to the forearm and hand blood supply at rest[8,9]; even in experimental stress conditions only instrumental, but not clinically evident, ischemia could be elicited[10].

Table III. Comparison of mid-term clinical, scintigraphic and angiographic results between patients who continued or suspended the chronic calcium channel blocker therapy after the first postoperative year.

Event	Suspended group	Continued group	p
Cardiac death	1	0	0.96
Angina recurrence	6	7	0.81
RA-related ischemia	2	3	0.88
Perfect RA	40	42	0.93
Stringed RA	1	1	0.50
Irregular RA	0	1	0.96
Occluded RA	1	1	0.50

RA = radial artery.

Table IV. Mid-term radial artery (RA) and internal thoracic artery (ITA) diameter change after acetylcholine infusion.

	RA	ITA
Baseline diameter (mm)	2.61 ± 0.39	2.68 ± 0.21
Acetylcholine infusion	2.90 ± 0.34*	2.93 ± 0.27*

* p = 0.01 compared with baseline.

Table V. Quantitative angiographic measurement of radial artery (RA) and grafted coronary artery (GCA) diameters at 1- and 5-year controls.

	RA	GCA
1-year diameter (mm)	2.08 ± 0.45	1.92 ± 0.47
5-year diameter (mm)	2.54 ± 0.53*	2.18 ± 0.41*

* p = 0.01 compared with baseline.

Conclusions

In conclusion, good evidence now exists that in the postoperative years RA grafts undergo a progressive morpho-functional remodeling, characterized by a marked reduction in the hyperspastic attitude and an increase in luminal diameter, while maintaining a good capacity of endothelium-dependent vasodilation. This remodeling seems to be the expression of a progressive adaptation of the artery to the new hemodynamic situation and has obvious favorable implications for its use as a coronary artery bypass conduit.

These observations seem to minimize the theoretical concerns expressed by some authors on the adequacy of this artery for surgical myocardial revascularization, and further support its continuous and widespread use.

As a practical note, these findings imply also that the chronic calcium channel blocker therapy (traditionally considered mandatory for patients with an RA graft) is useful only in the first year after surgery (when the RA is still a highly reactive conduit) and can be safely suspended after the first postoperative year.

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