The fate of the radial artery conduit in coronary artery bypass grafting surgery

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Summary

Coronary artery bypass grafting (CABG) is the standard surgical procedure for the treatment of advanced coronary artery disease. CABG surgery has been demonstrated to improve symptoms and, in specific subgroups of patients, to prolong life. Despite its success, the long-term outcome of coronary bypass surgery is strongly influenced by the fate of the vascular conduits used. Impressive long-term disease-free patency rate of the left internal thoracic artery—left anterior descending coronary artery (LITA—LAD) graft, coupled with proven long-term survival benefits, has led to its becoming a 'golden standard' of CABG. Previous long-term studies have also shown unsatisfactory patency of saphenous vein grafts used for myocardial revascularization, compared with internal thoracic artery grafts. Thus, the use of arterial conduits has expanded beyond the internal thoracic arteries (ITAs) to include the right gastroepiploic artery, the inferior epigastric artery, and the radial artery. The assumption is that although the performance of one or two arterial ITA grafts is superb, more arterial grafts should perform better in the long-term follow-up. Several studies concerning the use of the radial artery bypass grafts have documented excellent clinical results and satisfactory short- and mid-term patency rates at restudy angiography, supporting its continued use as a bypass conduit. However, a note of caution concerning radial artery conduit patency rate have appeared in few recent reports. Thus, in this paper, we summarize the current evidence about the radial artery as a conduit in CABG surgery, with special emphasis on the clinical results.

Keywords: CABG; Surgery; Arterial grafts

1. Introduction

The clinical and prognostic benefits of coronary artery bypass grafting (CABG) for some subgroups of patients with ischemic heart disease are well accepted, and worldwide every year almost 1 million patients undergo coronary revascularization [1]. CABG provides excellent short- and intermediate-term results, but long-term outcome is strongly influenced by the fate of the vascular conduits used.

Ten years after CABG, 90% of internal thoracic artery (ITA) grafts are patent and disease free, while about 50% of the saphenous vein grafts (SVG) are occluded, and 25% have been severely stenosed [2]. Impressive long-term patency of the left internal thoracic artery—left anterior descending coronary artery (LITA—LAD) graft, coupled with proven long-term survival benefit, has led to its becoming a 'golden standard' of CABG. Significantly better CABG survival when both ITA conduits are used concomitantly compared with a single ITA has been reported [3].

Thus, the use of arterial conduits has expanded beyond the ITAs to include the right gastroepiploic artery, the inferior epigastric artery, and the radial artery (RA). Acar and colleagues [4] strongly recommended revival of the RA conduit (almost completely abandoned due to high occlusion rate reported by Carpentier and colleagues [5] in 1971) having detected several patent RA grafts up to 18 years after the initial myocardial revascularization. Several studies [6—8] have documented excellent clinical results and satisfactory short- and mid-term patency rates at restudy angiography of radial artery conduits used for CABG. One long-term angiographic study has demonstrated disease-free patency rate of the radial artery graft of 88%, 9 years after surgery [9]. These reports led many other groups to reassess the role of this conduit in coronary bypass procedures.

2. Advantages of the radial artery conduit

Several anatomopathological features present the radial artery conduit as an excellent graft to be used in coronary revascularization:

(a) it is easy to harvest it parallel with the ITA;
(b) it is long enough to be used as a conduit to any coronary territory;
(c) it is adapted to higher arterial pressures and large enough in caliber to match most of the coronary arteries;
(d) it is easy to handle due to its thick muscular wall;
(e) it can be harvested in a majority of patients (obesity, diabetes mellitus, chest wall and mediastinal radiation or previous laparotomy do not apply to radial artery harvesting).

3. Potential disadvantages of the radial artery conduit

Removal of the radial artery poses the risk of ischemic complications to the hand, particularly the thumb and index finger. An incomplete superficial palmar arch, RA dominance of the superficial palmar arch and absence or malfunction of the ulnar artery may lead to hand ischemia with RA harvesting. The frequency of an incomplete superficial palmar arch is reported to range from 6% to 34%. Thus, before harvesting the RA it is mandatory to assess the adequacy of the ulnar collateral circulation to the hand. Methods to detect adequate forearm collateral flow include the clinical modified Allen test, pulse oximetry, digital blood pressure measurement, flow measurement with plethysmography, segmental pressure measurements, laser Doppler flowmetry, modified Allen test with Doppler ultrasonography and color Doppler with pulsed wave spectral trace of flow [11,12]. At present, most studies have examined the Allen test or a variation on this test as an index of the immediate safety for harvesting the RA. Concerns with the adequacy of forearm collateral circulation, raised by the preoperative testing method, have excluded RA harvest in range from 5% to 11.6% [13].

If there are no other contraindications before harvesting (RA plaque on ultrasound, damaged RA due to trauma of previous cannulations, the presence of an arterio-venous fistula for hemodialysis, vasculitis, carpal tunnel syndromes or Raynaud’s disease), removal of the RA does not result in any symptoms of hand ischemia or motor dysfunction. Mid-term (few to 24 months) follow-up studies have demonstrated chronic enlargement of the remaining artery (ulnar artery [12] or rather interosseous [14] artery) to compensate blood supply of the forearm.

Acute hand ischemia with serious motor deficiency was reported in two articles [15,16], presenting the same patient with identical angiographic material. In that single case angiographic examination confirmed ulnar artery agenesis although perioperative tests had established adequate collateral circulation. Circulation was restored by performing brachioradial bypass grafting using reversed cephalic vein [15,16].

In a prospective, randomized study, Hata and colleagues [17] have suggested that sharp dissection with scissors and clips may be better for early postharvest forearm circulation and can decrease the incidence of hand numbness. However, there were no differences among the three methods (traditional dissection, electrocautery, or ultrasonic scalpel) with respect to forearm circulation 12 months after radial artery harvesting.

The most common complications noted, occurring in 2.6% to 15.2% of patients [12,18], are sensory abnormalities, especially cutaneous paresthesia and/or numbness in the radial distribution of sensory nerves (lateral antebrachial cutaneous nerve, superficial branch of the radial nerve) due to nerve injury from direct trauma, edema or carpal tunnel hematoma. Long-term persistence of the symptoms were recorded in 10% of the patients, but were considered a ‘constant and significant source of discomfort’ in only 1% of patients (without a significant limitation in hand activities) [18].

Gaudino and colleagues [19,20] have recently brought to our attention a new and alarming perspective on the possible chronic consequences of radial artery removal on the forearm circulation. Twenty-five [19] and 39 patients [20] submitted to radial artery removal (nondominant arm) for CABG underwent serial echo-Doppler evaluation of the flow and morphology of the forearm arteries until 10 years follow-up. The peak systolic velocity as well as the intima-media thickness of the ulnar artery has always been higher on the operated side, and this difference reached statistical significance at 10 years follow-up. There was a significantly higher prevalence of atherosclerotic plaques in the ulcer artery of the operated versus control arm (7/25 vs 0/25; p = 0.03, and 11/39 vs 0/39; p = 0.005, respectively). Thus, the authors concluded that radial artery removal for CABG surgery leads to a chronic increase in ulnar flow accompanied by increased intima-media thickness and accelerated atherosclerotic disease. These findings may have potentially important implications for surgical indications and patient management, especially in young patients with a long life expectancy.

Patients who had undergone endoscopic RA harvesting have been reported to have significantly fewer major complications (hematomas, wound infections, neuralgias) than patients who underwent the open RA harvesting technique [21].

In patients with coronary artery disease, RA atherosclerotic involvement is more frequent (up to 6.9%) than that of the gold standard ITA [22]. The RA that is heavily calcified poses technical difficulties intraoperatively apart from indicating a doubtful long-term patency.

It is commonly agreed upon that RA harvest must be performed with gentle mobilization of the RA, with light traction, minimal touch and minimal diathermy or ultrasonic dissection, thus diminishing endothelial trauma related to harvesting process. The RA is expected to be more vasospastic (reported rate of 4–10%) compared to other arterial grafts [23] due to its characteristics of being a type III artery (He’s [24] classification) and of having predominantly α-adrenergic receptors. The propensity for the RA to go into spasm is likely due to the higher density of muscle cells in the media of this vessel resulting in a significantly higher maximal contractile force in response to vasoconstricting agents (norepinephrine, serotonin, endothelin I, and angiotensin II) generated in response to endothelial damage and dysfunction due to inflammatory response to cardiopulmonary bypass or surgical stress, as well as exogenously administered inotropes or vasoconstrictors [23]. Systemic vasodilators were suggested and empirically used with the beginning of the revival of the interest of the RA, but were found to be ineffective and
unnecessary by later reports [25]. Currently, the propensity of the RA to spasm has greatly been reduced using topically different categories of vasodilators, including calcium channel blockers, the phosphodiesterase inhibitors, α-adrenergic antagonists as well as drug mixtures. Clinically useful agents should ideally be effective against a wide variety of endo and exogenously delivered substances causing receptor-mediated as well as receptor-independent vasoconstriction of the RA graft [23]. Currently, no single topical antispasmodic agent fulfills all the criteria necessary to prevent RA vasospasm in perioperative period. Verapamil—nitroglycerin solution is effective against a broad range of vasoconstricting agents [23], but its relatively short duration of effects (up to 5 h) limits its usefulness in the clinical practice. Phenoxybenzamine is a more effective agent to prevent α-adrenergic spasm, but has little effect on vasoconstriction caused by noncatecholamine vasoactive mediators. Its prolonged duration [23] of action (up to 18 h in vitro) as well as the ability to prevent catecholamine-mediated vasoconstriction, recommends it as a useful agent in the immediate postoperative period, especially in CABG patients requiring inotropic support. Finally, a combination of agents may be appropriate to combat vasospasm of the RA graft and thereby reduce the likelihood of early graft failure.

It has recently been shown that adenoviral-mediated gene transfer (suggesting a possible future clinical application), causing overexpression of nitric oxide synthase in human RA, can minimize RA vasospasm through the inhibition of voltage-dependent as well as receptor-dependent pathways [26].

In order to prevent delayed vasospasm, oral calcium channel antagonists have been recommended for as long as 1 year after surgery for patients receiving RA conduits. Gaudino and colleagues in prospective, randomized studies have confirmed that calcium channel blocking therapy started immediately after surgery and continued for the first postoperative year [27] as well as beyond 1 year [28] did not affect either radial artery conduit patency or clinical outcomes.

However, the role of calcium channel blocking therapy in the early postoperative period, when radial artery tendency to spasm is thought to be maximal, has yet to be clarified, and its use remains routine in many centers.

4. Optimal grafting strategy

There is accumulating evidence [29—31] that grafting the RA to coronary targets with moderate stenoses (<70%) results in statistically significantly reduced conduit patency. Furthermore, in a prospective, randomized study, Desai and colleagues [31] have recently presented that targeted coronary arteries with stenosis of ≥90%, as compared with those coronary-vessel lesions with stenosis of 70—89%, were associated with a lower rate of occlusion of the radial artery conduit (5.9% vs 11.8%, p = 0.03). The concept of competitive flow [23] suggests that graft flow is influenced by native coronary flow. Grafted conduits may, therefore, fare better in conditions of poor native coronary flow, i.e. in the case of high-grade stenosis or occlusion of targeted coronary arteries.

Some studies [29,30] have identified target location as predictor for conduit failure, thus lower angiographic patency rates for RA grafts to both the circumflex and right (statistically significant) coronary arteries were reported. These findings remain controversial because there are many studies confirming that target vessel location does not influence RA conduit patency [8,9,31].

There are few options to perform the proximal RA anastomosis. The most commonly used are to the aorta as an aortocoronary conduit or to another graft (usually ITAs) as a composite conduit (in a T or Y fashion). It has been speculated that the histologic and structural characteristics of the RA can render this conduit particularly prone to vessel wall ischemia and consequent intimal proliferation, especially when exposed to the hemodynamic stress due to the sharp increase in dp/dt present in the initial part of the ascending aorta. For this reason some authors have advocated performing the proximal anastomosis of RA grafts to a vascular region with a lower dp/dt, such as an ITA graft [32].

Maniar and colleagues [30] have reported that the site of proximal anastomosis does not appear to influence RA conduit patency. In their study, angiographic (average period to reangiogram 26.1 months) RA conduit patency in aortocoronary versus composite configuration demonstrated no significant difference (72.0% vs 70.5%). Other authors [7,33] have reported excellent midterm (average period to reangiogram 16.2 and 36.8 months, respectively) RA conduit patency (96.8% and 91.9%, respectively) in aortocoronary configuration. Matchless results (patency rate of 99%) were reported [32] for composite configuration (average period to reangiogram 35 months). However, composite configuration might be considered as a form of sequential grafting, as inflow from one conduit is derived to at least two coronary beds.

5. Follow-up studies

Since the 1990s, several authors [6—9] have demonstrated encouraging mid-term as well as long-term results of the RA conduit in coronary artery bypass surgery. However, these results must be interpreted with caution. Almost all the data are from retrospective, nonrandomized studies, and, unfortunately, lack sufficient scientific rigor to allow meaningful conclusion to be drawn, as evidence-based medicine mandates the prospective randomized trials as the most accurate tool for determining a treatment benefit compared with a control population [34].

The most essential data from mid-term and long-term studies “radial artery patency not superior as expected” (the RA conduit patency equivalent or even worse than SVG patency) are presented in Table 1. Data in Table 2 represent results “radial artery patency superior as expected” (the RA conduit patency better then SVG, not worse than right internal thoracic artery—RITA conduit patency). It should be noticed that RA conduit was used in sequential fashion by some authors (marked with ‘a’ in Tables 1 and 2, greater number of reassessed anastomoses than used grafts—which means more distal anastomoses per graft, up to one-third of RA grafts in the report by Shah and colleagues [33]). Excellent long-term patency rate have been reported for saphenous vein grafts in such construction (85.4% at 10 years) [35].
A note of caution has recently come from Cleveland Clinic in a form of retrospective, symptom-directed angiographic study on RA graft patency, presented by Khot and colleagues [36]. At average follow-up of 1.6±1.4 years RA grafts had a patency rate of only 51.3%, which was significantly lower than that of LITA (90.3%, \( p < 0.0001 \)) or saphenous vein grafts (64.0%, \( p = 0.0016 \)). Although their methodology is flawed (primarily because the sample studied is composed exclusively of patients presenting with angina), the article presents one of the largest angiographic (310 out of approximately 3600 patients, calculated according to data supplied by Khot and colleagues [37]) follow-up studies of RA conduit patency. The importance of the study is that it raises concerns about high RA graft failure at a time when RA conduit use is increasing.

In a retrospective study by Cameron and colleagues [38] (only 50 asymptomatic patients were included) RA graft patency was 88.7% versus 91.7% patency rate of SVG (average period to reangiogram 5.2 years). In addition, in a group of 21 patients who underwent restudy coronary angiography due to recurrent angina the same patency rate for RA conduit (88%) has been found. Therefore, authors concluded that the patency rate of 88% for RA conduit might be a true reflection of patency rate for entire cohort. Unfortunately, authors have overlooked the fact that average period to restudy angiogram was only 2.7 years in symptomatic patients (thus, in all appearance, additional graft failure can be expected in next 2.5 years).

Unfortunately, propensity score [39] statistical technique (used to overcome most of the bias sources of nonmatched

Table 1
The mid- and long-term arterial (ITAs, radial artery) and venous grafts angiographic patency—‘radial artery patency not superior as expected’

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study design</th>
<th>Percentage of patients reassessed</th>
<th>Angiographic patency</th>
<th>Years to reangiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Khot and colleagues [36]</td>
<td>Retrospective</td>
<td>310/3600</td>
<td>51.3%</td>
<td>64.0%</td>
</tr>
<tr>
<td>Cameron and colleagues [38]</td>
<td>Retrospective</td>
<td>16.7/50/300</td>
<td>88.7%</td>
<td>91.7%</td>
</tr>
<tr>
<td>Zacharias and colleagues [40]</td>
<td>Retrospective, propensity score</td>
<td>20.5/190/925</td>
<td>68.2%</td>
<td>63.3%</td>
</tr>
<tr>
<td>Shah and colleagues [33]</td>
<td>Retrospective</td>
<td>4.5/219/4872</td>
<td>90.6%</td>
<td>88.9%</td>
</tr>
<tr>
<td>Buxton and colleagues [42]</td>
<td>Prospective, randomized II groups, RA versus FRITA or SVG</td>
<td>RA 27.9/219/4872 FRITA 20.0/32.9/219</td>
<td>97.4%</td>
<td>95.5%</td>
</tr>
</tbody>
</table>

Table 2
The mid- and long-term arterial (ITAs, radial artery) and venous grafts angiographic patency—‘radial artery patency superior as expected’

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study design</th>
<th>Percentage of patients reassessed</th>
<th>Angiographic patency</th>
<th>Years to reangiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acar and colleagues [6]</td>
<td>Retrospective</td>
<td>5.5/50/910</td>
<td>82.8%</td>
<td>91.5%</td>
</tr>
<tr>
<td>Possati and colleagues [43]</td>
<td>Prospective</td>
<td>20.9/68/325</td>
<td>88.6%</td>
<td>74.0%</td>
</tr>
<tr>
<td>Bhan and colleagues [7]</td>
<td>Retrospective</td>
<td>21.6/62/287</td>
<td>96.8%</td>
<td>98.2%</td>
</tr>
<tr>
<td>Iaco and colleagues [8]</td>
<td>Retrospective</td>
<td>43.9/72/164</td>
<td>95.6%</td>
<td>88.8%</td>
</tr>
<tr>
<td>Calafiore and colleagues [32]</td>
<td>Retrospective</td>
<td>19.8/57/288</td>
<td>99.0%</td>
<td>91.7%</td>
</tr>
<tr>
<td>Possati colleagues [9]</td>
<td>Prospective</td>
<td>27.7/90/325</td>
<td>90.5%</td>
<td>67.1%</td>
</tr>
<tr>
<td>Desai and colleagues [31]</td>
<td>Prospective, randomized</td>
<td>78.4/440/581</td>
<td>Perfect patency 91.8%</td>
<td>86.4%</td>
</tr>
</tbody>
</table>

\* Number of anastomosis reassessed.
studies) was employed only in the manuscript of Zacharias and colleagues [40]. Although cumulative 0- to 6-year survival was better for patients with radial artery conduit (vs patients with SVG as second conduit), the angiographic RA conduits patency (1.8 ± 1.4 years to reangiogram) were 68.2%, statistically not better (p = 0.11) than SVG patency rate (63.3%). Low patency rates may stem in part from the fact that the patency data were derived from symptomatic patients exclusively, who reflected a worst-case scenario. Due to possibility of silent graft occlusion, the assumption that symptom-free patients are likely to have more patent grafts does not justify extrapolation of better patency rates to entire cohort. This problem has been discussed only in one manuscript so far. The purpose of that study (Buxton and colleagues [41]) was to compare protocol-directed angiographic patency data from a randomized clinical trial (Radial Artery Patency and Clinical Outcome (RAPCO) study) [42] with symptom-directed angiography patency data in patients who were not included in the randomized controlled trial. Five-year estimates for graft patency were made using survival analyses accounting for interval censoring. The odds ratio for graft failure for nontrial controlled trial. Five-year estimates for graft patency were made using survival analyses accounting for interval censoring. The odds ratio for graft failure for nontrial controlled trial. Five-year estimates for graft patency were made using survival analyses accounting for interval censoring. The odds ratio for graft failure for nontrial controlled trial. Five-year estimates for graft patency were made using survival analyses accounting for interval censoring. The odds ratio for graft failure for nontrial controlled trial. Five-year estimates for graft patency were made using survival analyses accounting for interval censoring. The odds ratio for graft failure for nontrial controlled trial. Five-year estimates for graft patency were made using survival analyses accounting for interval censoring. The odds ratio for graft failure for nontrial

The well-designed prospective, randomized trial (Radial Artery Patency Study (RAPS)) comparing the patency of saphenous vein grafts with that of RA grafts has recently been reported by Desai and colleagues [31]. The radial artery was randomly assigned to bypass the major vessel in either the right coronary territory or the circumflex territory, with the saphenous vein graft used for the opposing territory (control). The target coronary vessels had to be at least 1.5 mm in diameter, with proximal lesions causing narrowing of at least 70% of the diameter. The primary end point was graft occlusion, determined by angiography 8—12 months postoperatively. The angiographic study performed 1 year after surgery (average period to reangiogram 0.9 ± 0.4 years) in this trial demonstrated an occlusion rate of 8.2% for RA conduits and 13.6% for saphenous vein grafts (p = 0.009). However, 7% of RA grafts (vs only 0.9% of SVG) had diffuse angiographic narrowing (the ‘string sign’), resulting in a total ‘bad graft’ rate of 15.2% for RA conduit (vs 14.5% for SVG). Furthermore, perfect graft patency, defined as grafts with thrombolysis in myocardial infarction (TIMI) flow grade 3, was similar (87.7% for RA graft vs 85.7% for SVG, p = 0.37). Multivariable analysis revealed that presence of radial artery string sign was closely related to the perioperative use of α-adrenergic agonists and target vessel stenosis less than 90% [44].

6. The future of the radial artery conduit

The radial artery conduit is becoming increasingly popular (due to excellent patency rates in some mid and long-term studies) as a third arterial conduit in association with LITA and RITA, or as the second in patients with contraindications to bilateral ITA harvesting. However, it is essential not to overlook the notes of caution coming from some reports (i.e., Khot and Zacharias) as these results of radial artery patency are not as good as expected. The most important data are still to come. Prospective, randomized angiographic studies and/or meta-analyses between 10 and 15 years after CABG surgery should determine the position of the radial artery conduit in the future of CABG surgery.

References


