Hellenic Journal of Cardiology 59 (2018) 150–154

Contents lists available at ScienceDirect

Hellenic Journal of Cardiology

journal homepage: http://www.journals.elsevier.com/hellenic-journal-of-cardiology/

Review Article

Radial artery as a graft for coronary artery bypass surgery in the era of transradial catheterization

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ARTICLE INFO

Article history:
Received 15 October 2017
Received in revised form
7 January 2018
Accepted 12 January 2018
Available online 31 January 2018

Keywords:
Radial artery
Transradial catheterization
Bypass conduit

ABSTRACT

Radial artery use as a bypass conduit is well established during the past decades, in terms of both patency and safety. On the other hand, transradial catheterization causes a series of structural and functional changes to the vessel itself. Impairment of nitric oxide-dependent vasodilation and notable decrease in radial artery diameter due to intima thickening and hyperplasia, especially during the first 3 months after its cannulation, constitute some of the most important alterations on the radial artery wall and its function after a transradial coronary catheterization procedure. Given the constantly increasing numbers of these transradial catheterization procedures, the authors of this article focus on the current knowledge regarding the potential use of the radial artery as a bypass conduit, after its catheterization, also considering several possible mechanisms on its subsequent structural and functional changes.

1. Introduction

The use of radial artery (RA) as a conduit for coronary artery bypass surgery was first proposed in 1973 by Carpentier et al.[1] Two years later, the same group reported a 35% incidence of narrowing or occlusion of the RA used as a graft for coronary artery bypass surgery. Consequently, they recommended that the use of this graft should be discontinued.[2] In 1992, Acar et al. announced the "revival of the RA" for coronary artery bypass grafting (CABG), after reinvestigating the long-term results from its use and the unexpected discovery of noticeable patency rates in patients on long-term vasodilation treatment with diltiazem. The authors concluded that the RA "may serve as a reasonable alternative to other types of conduits to complement the left internal mammary artery (LIMA)".[3] Carpentier himself then stated that "… it is interesting to see a better understanding of the pathogenesis of arterial spasm as well as that new drugs have changed our view on a conduit that we condemned 20 years earlier". He therefore also recommended RA as a second-choice conduit for CABG, after the pedicled mammary artery.[3] During the past years, there have been numerous publications further supporting the role of the RA as a safe and efficient option for CABG,[4–6] exhibiting satisfactory patency rates.[5, 7–10] The Society for Thoracic Surgery database shows that 6% of CABG patients in the USA received a RA graft as a bypass conduit in 2008.[11]

On the other hand, RA has been increasingly used as the preferable arterial access route during coronary angiography and/or angioplasty, during the past decade, owing to its numerous advantages over the femoral artery approach such as (a) reduction in bleeding complications, (b) earlier patient mobilization, (c) lower mortality rates, and (d) reduced cost because of shorter hospitalization stay.[12–18] These transradial (TR) procedures, however, may be the cause of structural and functional abnormalities of the cannulated RA, probably making its selection for bypass artery graft not suitable.

In this mini review, we will focus on the current knowledge on the use of RA as a bypass artery conduit after its catheterization and the subsequent structural and functional changes.

1.1. Radial artery wall layers

The RA wall consists of 4 layers: (i) a thin, continuous layer of endothelial cells, the *intima*, (ii) a single internal elastic *lamina*, (iii) a thick layer of packed smooth muscle cells, the *media*, and (iv) the outer layer, the *adventitia* (Fig. 1).

Abbreviations: RA, Radial artery; TR, Transradial; LIMA, Left internal mammary artery; CABG, Coronary artery bypass grafting; RITA, Right internal thoracic artery; SVG, Saphenous vein graft.

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Peer review under responsibility of Hellenic Society of Cardiology.

https://doi.org/10.1016/j.hjc.2018.01.009

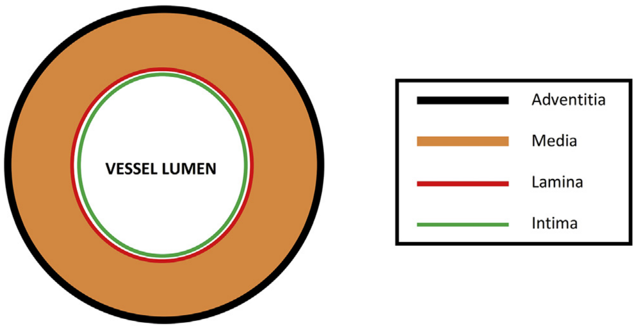

Fig. 1. The radial artery wall layers (transverse section).

2. Functional and morphological alterations of the RA after TR procedures

The effect of radial sheath insertion on RA function was assessed by Burstein et al. in 22 patients who underwent elective coronary angiography or angioplasty with a 6-French (6-F) sheath through the right RA.[19] RA function was assessed using ultrasound to measure flow-mediated dilation (FMD). In all cases, the left RA was studied as a control. Patients were studied before sheath insertion, immediately after sheath insertion, and 6 weeks after sheath insertion. The authors concluded that radial sheath insertion results in immediate and persistent blunting of FMD, suggesting severe vasomotor dysfunction, which is sustained for many weeks post-sheath insertion.[19] The impairment in the vasodilating properties of the RA seems to be the same, regardless of radial sheath type (hydrophilic or uncoated).[20] There are reports, however, that the depression in nitrate-mediated vasodilation (NMD) is completely reversible after a period of approximately 3[20] to 12 months.[21] On the other hand, Yan et al. reported that TR coronary procedures decrease both FMD and NMD, even 3 months after the TR procedure, resulting in immediate and persistent blunting on the vasodilatory function of the RA.[22] In a meta-analysis of 12 published studies until April 2017, TR catheterization also caused a significant reduction in the endothelium-dependent vasodilatory properties of the cannulated RAs, in 490 patients. The impairment of the vasodilatory properties of the cannulated RAs persisted for several months after catheterization.[23]

Apart from the functional impairment of the RA after a TR procedure, the procedure itself seems to cause a series of morphological alterations on the vessel itself. Wakeyama et al. studied the RAs of 100 consecutive patients who had undergone TR procedures, using intravascular ultrasound.[24] They noted that the RA lumen in patients who had undergone more than one TR procedures was constantly smaller than in those with only one TR procedure owing to greater degree of intima and media thickening. Furthermore, the RA injury was more profound in the distal part than in the proximal part of the RA wall.[24] An optical coherence tomography study clearly demonstrated that repeated TR procedures constitutes an independent predictor of RA intimal thickening, in both the proximal and distal segments.[25] Intimal tears and medial dissections were among the most common mechanisms of acute RA injury.[25] Table 1 summarizes all the aforementioned studies evaluating the functional and morphological alterations on the RA after its catheterization.

It is estimated that 2.8% of the cannulated RAs evaluated 1 month after a TR procedure develop persistent occlusion.[26] The incidence of RA occlusion is greater (5.5%) when the evaluation is performed at least 1 week after the TR procedure and even higher (7.7%) within 24 hours from the TR procedure.[27] Some of the reported risk factors for RA diffuse stenosis or no-flow are small RA size before the TR procedure, use of sheaths larger than the RA diameter itself, delay in post-procedure sheath removal, diabetes mellitus, and neglecting the use of anticoagulants during the procedure.[28–30] Intimal thickening and hyperplasia seem to be the first response to the endothelial injury after a TR procedure, followed by adventitia inflammation and tissue necrosis, mainly in the distal part of the artery, closer to the puncture site.[20,30] Intimal hyperplasia is considered as the end-stage result of the migration of smooth muscle cells from the media and through the lamina, to the intima.[30,31] As a consequence, the internal RA diameter is significantly decreased right after the TR procedure, with either a partial restoration of its original size 3 months post-TR procedure,[25] or even a continuous reduction in the lumen's size after a mean duration of 95 days.[28] In all the aforementioned studies, the diameter of the cannulated RAs decreased and remained smaller than their original size, regardless of the time interval (mean of 3 to 12 months) after the TR procedure,[21,25,28] mainly due to RA structural changes. Fig. 2 shows a schematic presentation on the reported mechanisms of functional and morphological alterations of the RA, after its catheterization. Fig. 3 represents a RA ultrasound image of a patient subjected to TR catheterization in our department, 1 week after the procedure.

3. Radial artery as a conduit for coronary artery bypass surgery

The RA has emerged as an excellent alternative arterial graft, after internal mammary artery harvesting. It represents a safe and efficient option,[4–6] exhibiting similar patency rates with internal mammary arteries[7–8] and even better rates, when compared with vein grafts.[5,9,10] In one of the largest reported series with RA usage in CABG, Tranbaugh et al. reported similar patency rates between RA and left internal thoracic artery (82% vs 85%) in 278 patients with 420 RA grafts after an average observation of 5 years.[5] Furthermore, RA grafts exhibited very low rates of reintervention and were consistently superior to saphenous vein (SV) grafts, in terms of patency, especially when applied in a target coronary vessel with severe stenosis (>80%–90%). Other studies have also documented similar patency rates between the right internal thoracic artery (RITA) and RA,[7,8] with the exception of moderate stenoses (50%–60%), where both RITA and RA grafts are more likely to fail owing to competitive flow.[5] It seems that the most appropriate conduit for a circumflex or a right coronary artery with a moderate stenosis (50%–60%), is a SV graft.[5]

As reported by several large meta-analyses, the superiority of the RA graft patency when compared with SV grafts becomes more evident after the first year and especially in the midterm and long term.[32–34] There are some recently published studies arguing against the use of RA over SV grafts, as a second-choice conduit, because of a neutral survival benefit.[35–36] Both these studies had a mean follow-up time of less than a decade, with 9.2 years for IMA+SVG group, 11.2 years for IMA+RA grafts, 9.2 years for bilateral IMA grafts, in the Swedish nationwide registry study,[35] and a mean follow up of 8 years for the propensity score-matched study of the RA as an additional arterial conduit during in situ bilateral internal mammary artery grafting.[36] It seems that the survival benefit from the selection of the RA graft over the SV graft becomes more apparent in the later years (after the decade)[37] and especially when used in younger patients with a reasonable long-term life expectancy, aiming for a total arterial revascularization.[38]

We should bear in mind that the RA is a “muscular” artery (due to its thick media) and thus extremely prone to spasm, especially after mechanical stimuli.[39] Consequently, there are substantial technical differences in both the preparation and harvesting of the RA graft, when compared to SV harvesting. Careful RA harvesting

Table 1
Studies evaluating the functional and morphological alterations of the radial artery after its catheterization

Author (year of publication)	N (Number of patients)	Results
Stella et al. (1997)	563 (prospective)	2.8% of cannulated radial arteries develop persistent occlusion 1 month after transradial procedures
Wakeyama et al. (2003)	100	Repeated transradial procedures cause a progressive narrowing of the radial artery lumen, especially in its distal part, due to intima and media thickening
Madssen et al. (2006)	30	Radial artery diameter is diminished one year after transradial coronary angiography, while its vasodilatory properties are preserved
Burstein et al. (2007)	22	Radial sheath insertion results in immediate and persistent blunting of flow mediated dilation
Staniloae et al. (2009)	34	Transradial catheterization induces intimal hyperplasia, medial inflammation and tissue necrosis, limited to the puncture site
Dawson et al. (2010)	35	The depression in nitrate-mediated vasodilation is completely reversible after a period of 3 to 12 months
Yonetsu et al. (2010)	69	Repeated transradial procedures is an independent predictor of radial artery intimal thickening in both the proximal and distal segment, assessed via OCT
Yan et al. (2014)	65	Both flow and nitrate mediated dilation of the radial artery are compromised even 3 months after the transradial procedures
Rashid et al. (2016)	31,345 (66 studies, review & meta-analysis)	Radial artery occlusion estimated at 7.7% at 24hours, 5.5% at>1 week follow-up. Higher doses of heparin reduced occlusion rates
Antonopoulos AS et al.	490 (12 studies, meta-analysis)	Transradial catheterization causes a reduction in endothelium dependent response of the cannulated RA, which persists for several months

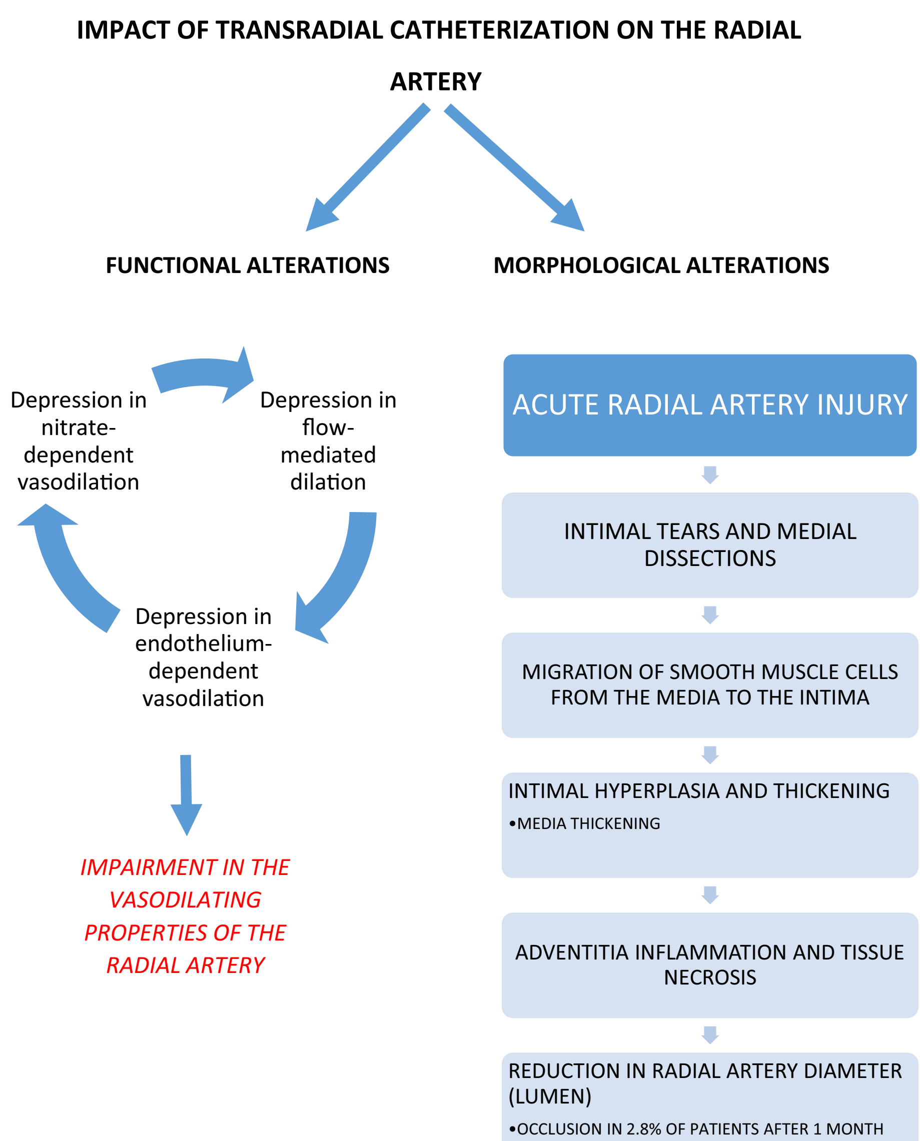

Fig. 2. Schematic presentation of the mechanisms of RA alterations.

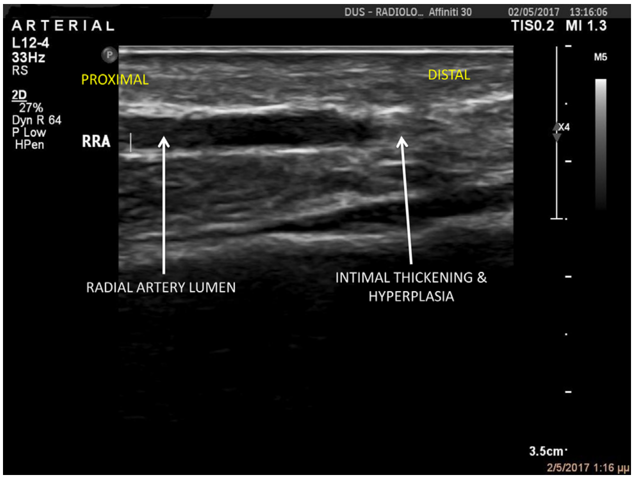

Fig. 3. Radial artery ultrasound 1 week after its catheterization.

with its satellite veins, minimizing physical injuries to the vessel wall, applying hydrostatic instead of mechanical dilation, along with the more extensive use of vasodilators (such as calcium channel blockers) led to the "revival" of the RA as a conduit and resulted in higher patency rates at 9 months (93%), as previously discussed.[3] Preoperative evaluation of the forearm circulation using the ultrasound, the Allen test and pulse oximetry provides us with an accurate estimation of the RA morphology and represents an important tool in the RA graft selection process.[40]

4. Previously cannulated RAs as CABG conduits

Despite the robust evidence regarding the patency rates of RA grafts, there is little evidence on the patency of previously cannulated RA grafts as CABG conduits. As previously described, TR interventions cause a series of functional and morphological alterations on the RA, including nitrate-responsiveness decrease, intimal thickening, hyperplasia, inflammation, and RA diameter reduction.

Considering these, Gaudino et al. assessed the degree of RA damage after TR intervention, in 50 consecutive CABG patients. All patients underwent echo-Doppler evaluation of the RA of the catheterized arm; the contralateral RA was used as control. The distal segment of the RA was submitted to immunohistochemical assessment of endothelial integrity. The authors concluded that although the traumatic lesions after the TR procedure displayed a tendency to heal over time, the RA endothelial integrity and function was incomplete after 1 month. These findings argue against the use of a previously cannulated RA as an arterial conduit.[41]

Watson et al. evaluated 16 previously cannulated RA grafts using multidetector computed tomographic imaging. Their data indicate satisfying RA patency rates, 4 years after surgery.[42] Major drawback of this small study is that the analysis does not clarify which of the two RAs (left or right) was used as a graft for each patient, rendering their results debatable and less valid.

Kamiya et al. studied 67 CABG patients with RA grafting and compared clinical, angiographic, and pathologic results of RA grafting between patients with ($n = 22$) and without ($n = 45$) preoperative TR catheterization. Their results exhibited that TR catheterization caused intimal hyperplasia and reduced early graft patency, without affecting early clinical outcomes. RA graft patency was inversely related with the number of repeated TR catheterizations.[31] More recent data from a retrospective review estimate the long-term patency rates of RA grafts to 59% if they have been previously cannulated, compared to 78% for RA grafts not subjected to catheterization before CABG, indicating significantly lower patency rates for the prior catheterized RA grafts.[43]

5. Comments

Based on the current evidence,[1–43] it is clear that both cardiologists and surgeons should be very careful in the use of the RA in cardiovascular procedures. Cardiologists should be focused to minimize RA damage during TR procedures by choosing small-size catheters along with using appropriate-dose heparin. Surgeons should prefer uncannulated RAs (typically the opposite RA to that catheterized), whereas alternative conduits should be preferred when a RA has been previously and repeatedly cannulated. The harvesting method along with the preparation sequence of the RA remain of utmost importance, while the maximal survival benefit from their use after IMAs and over SV grafts becomes even more evident after the first decade. Total arterial revascularization utilizing IMAs and RA grafts seems more suitable in young patients, with a longer life expectancy. For older patients, with a shorter life expectancy and a circumflex or a right coronary artery with a moderate stenosis (50%–60%), a SV graft seems as the most appropriate conduit after the use of IMA.

TR catheterization causes a series of functional and morphological alterations to the RA. The functional alterations seem to persist for at least 3 to 12 months (mainly loss of vasomotor and vasodilating properties of the RA), or even more, while the morphological alterations seem to persist indefinitely, ranging from a mild narrowing to complete occlusion of the vessel lumen. According to recent data, previously cannulated RAs seem to exhibit statistically less patency rates as graft conduits, when compared with uncannulated RA grafts, in CABG patients. A preoperative evaluation of the forearm circulation with Doppler ultrasound, Allen test, and pulse oximetry is also supported as a reliable method for successful RA graft selection. Further extension of Doppler ultrasound applications on previously cannulated RAs to assess their patency and diameter, along with the avoidance of the use of the distal end of the artery, which typically exhibits the greatest degree of morphological alterations, would probably be useful.

6. Conclusions

Despite the initial difficulties, RA harvesting and its use as an alternative arterial graft conduit is well established during the past two decades. RA patency rates are comparable to those of internal thoracic arteries, which still constitute the first choice during the graft selection process. RA patency rates are superior to those of the SV grafts, particularly in the midterm and long term (after the first year and especially after the decade). TR catheterization causes a decrease in RA diameter, along with a series of structural and functional changes persisting for at least 3 to 12 months. RA grafts from previously cannulated arteries have not been extensively studied, in terms of safety and patency. Although additional retrospective studies would be useful, given the results of Kamiya et al.,[31] Gaudino et al.,[41] and Ruzieh et al.,[43] surgeons should be very cautious whenever they decide to use a previously cannulated RA as a graft conduit, especially if the vessel has been subjected to more than one catheterization.

Conflict of interest

All the authors of this article have no conflicts of interest and did not receive any type of funding for this work.

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