

Morpho-Functional Features of the Radial Artery: Implications for Use as a Coronary Bypass Conduit

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Since its reintroduction in the early 1990s the radial artery has gained a major role in coronary surgery, currently representing a valid alternative to the right internal thoracic artery as a second arterial graft. However, its peculiar morphologic and functional features have both surgical and clinical critical implications that must be taken into account. In this review we summarize the

current totality of evidence on the biologic characteristics of the radial artery, such as its histopathology, vaso-reactivity, and remodeling, and discuss their potential implications for use as a coronary bypass conduit.

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The radial artery (RA) was reintroduced in coronary surgery in the early 1990s and currently represents an alternative to the right internal thoracic artery (ITA) as a second arterial conduit. The RA has peculiar morphologic and functional features that distinguish it from the other arterial grafts, with major surgical implications. In this review we analyze the published evidence on the main biologic characteristics of the RA and summarize the current knowledge on the topic.

Material and Methods

In March 2014 the PubMed database was searched using the definition “radial artery coronary surgery,” “radial artery morphology,” “radial artery vasoreactivity,” “radial artery vasodilatation,” “radial artery patency,” and “radial artery remodeling.” All relevant abstracts were reviewed and the function “related articles” was used for all included manuscripts. Careful reference cross-check was performed for all selected studies.

Results

Histopathology

The RA is a muscular conductance artery; according to the functional classification of arterial grafts proposed by He [1], it belongs to type III limb arteries (Fig 1A and 1B).

In humans the mean length of the RA is 20.5 cm (range 15.2 to 23.5 cm) and the mean diameter is 2.0 mm [2]. This length is sufficient to reach all potential target vessels and the diameter is larger than that of all other arterial conduits used in coronary artery surgery.

Histologically, the main feature of the RA is the thick tunica media [3] (Figs 2 and 3). Several authors have demonstrated that its thickness is greater than that of the ITA and of the inferior epigastric artery and similar to that of the gastroepiploic artery [4]; comparative histopathologic studies have shown that compared with the ITA the RA has a significantly greater intimal area, medial area, and intima to media ratio [2].

Although relatively spared, the RA is not completely free from atherosclerosis (ATS); the prevalence of ATS and intimal hyperplasia is known to be higher in the RA than in the ITA [5]. The presence of atherosclerotic plaques has been described in 5% to 15% of RAs of unselected coronary artery bypass (CABG) candidates [2, 6]; age, smoking, peripheral vascular disease, and diabetes have all been identified as significant predictors of RA ATS [2, 6].

Beside ATS, the RA can be affected by a peculiar type of calcific disease of the media (Mönckeberg calcification). The estimated prevalence of medial calcification in the RA is around 25% and the identified risk factors coincide with those of RA ATS [5, 7].

Of note, no relationship seems to exist between irregularities of the RA at preoperative echographic evaluation and the angiographic patency when the artery is used as a CABG conduit [8].

Vasoreactivity

Although the causes and molecular mechanisms of spasm in arterial grafts are still largely unknown, it is usually accepted that spasm is an extreme form of vasoconstriction and is related to hyper-reactivity of the conduits to constrictor stimuli. In this regard He and colleagues [9] have proposed to classify the vasoconstrictors that cause spasm in arterial grafts into 2 types: type I vasoconstrictors are endothelin (ET), thromboxane A₂ (TXA₂), prostaglandin F_{2α}, and α₁-adrenoceptor agonists; they are the most potent and act even in the presence of

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Abbreviations and Acronyms

5-HT	= 5-hydroxytryptamine
ATS	= atherosclerosis
ATII	= angiotensin II
CABG	= coronary artery bypass graft
ET	= endothelin
ITA	= internal thoracic artery
LD	= luminal diameter
NO	= nitric oxide
RA	= radial artery
SV	= saphenous vein
TXA2	= thromboxane A2

intact endothelium. Type II vasoconstrictors instead (eg, 5-hydroxytryptamine) are less potent and can play a role in arterial graft vasospasm only in the case of endothelial damage; although all arterial grafts react to these vasoconstrictors, substantial differences have been observed among different arteries in their reactivity.

The RA is more reactive than the ITA to numerous vasoconstrictor agents, including norepinephrine, 5-hydroxytryptamine (5-HT), angiotensin II (ATII), ET, potassium chloride, phenylephrine, and vasopressin [10-13]; the interaction with endogenous TXA₂ further increases the RA constrictive response to 5-HT [14]. Of note, the response to ET and ATII is higher in the RA than in the ITA even in the presence of a similar degree of endothelial function [11].

Studies in patients have confirmed the observations of organ chamber studies showing an enhanced response of RA grafts to the intra-arterial infusion of 5-HT as compared with ITA grafts [15, 16]; although the reasons for this hyper-reactivity are not fully understood, both the thick muscular media and the intrinsic biologic properties of the RA probably play a role. Both α 1 and α 2 receptors are abundantly present in the RA, as well as histamine 1, urotensin II, angiotensin I, ET, and calcitonin receptors [17-22], while β -adrenoceptors are less represented [23].

It has been shown by histochemistry that endothelial nitric oxide (NO) synthase type III expression is higher in the human ITA than in the RA or in the great saphenous vein (SV) [24]. Other studies have confirmed higher NO synthase protein and messenger RNA levels in the ITA than in the RA [25]. The functional consequence of

these findings is probably the observation that in organ bath studies the basal and stimulated release of NO and endothelium-derived hyperpolarizing factor of the RA is significantly lower than that of the ITA [26, 27] and that the endothelial regulation of vascular contraction is reduced in the RA as compared with the ITA [28]. One study reported enhanced NO-mediated relaxation in the RA compared with the ITA, suggesting a high sensitivity of the artery to NO [29]. Vascular endothelial growth factor induces similar relaxation in the ITA and the RA, although through different pathways [30].

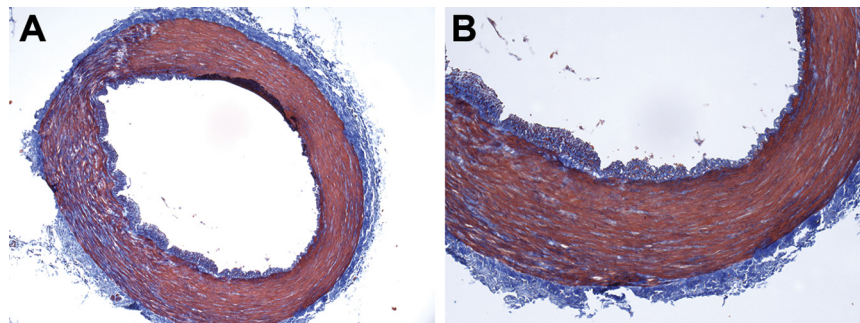
Of note, organ bath studies have shown that the proximal RA is characterized by a greater vasoconstrictor response to potassium chloride, phenylephrine, and ATII, but not to noradrenaline and adrenaline, compared with the distal RA [31, 32]. Although the proximal RA exhibits a greater medial cross-sectional area than the distal part and the higher smooth muscle cell content in the proximal segment can justify the greater vasoconstrictor response, differences in receptor density might also play a role. The limited *in vivo* information, however, does not appear to confirm laboratory data; indeed, it has been reported that RA grafts obtained from the distal portion of the artery have a higher vasoconstrictor response to 5-HT, a greater incidence of the "string" sign, and a lower midterm perfect patency rate than grafts taken from the more proximal part of the artery [33].

Morpho-Functional Features in Specific Patient Populations

It is known that the prevalence of RA calcifications is significantly higher in diabetic than in nondiabetic patients [34]. Moreover the RA intimal thickness index and intima to media ratio are both higher among diabetic patients [35], as well as NO synthase protein expression and von Willebrand factor and ET-1 messenger mRNA levels [35]. Conflicting data exist on the functional characteristics of the RA of diabetic patients. While some authors have reported similar vasoreactive properties for RA rings from diabetic versus nondiabetic patients [36], others have described impaired RA endothelial function and greater response to vasoconstrictors in the former [37].

Comparative morpho-functional studies have demonstrated that in females the RA has a significantly smaller lumen with a greater ratio of intima to lumen area compared with males [38]. On the functional side, RAs from females

Fig 1. Masson's trichrome stain of a segment of radial artery at different magnifications. (A) The thick walled muscular media is evident in red at lower ($\times 5$) magnification. (B) At higher magnification ($\times 10$), in the media some sporadic fibroblasts (in blue) are evident between abundant smooth muscle cells (in red).



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