

Use of Radial Artery Grafts for Coronary Artery Bypass Grafting

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ABSTRACT

Coronary artery bypass grafting (CABG) is the primary surgical treatment for coronary artery disease (CAD). However, long-term clinical practice has confirmed the poor long-term patency of saphenous vein grafts (SVG), prompting surgeons to investigate alternatives, such as the use of radial artery (RA) grafts. In this report, we review and discuss the current status of radial artery application during CABG and current controversies in the field. Ultimately, evidence indicates that RA-CABG is associated with good long-term patency and is suitable for patients with severe stenosis. However, the compensatory capacity of the ulnar artery should be assessed prior to RA harvesting. Given that the RA is prone to spasms, routine application of calcium channel blockers is recommended. Several studies also have indicated that sequential grafting is an effective method for maximizing radial artery application and that patency rates are similar for the radial artery and right internal mammary artery. In contrast, the use of the bilateral internal mammary arteries is technically more demanding and exhibits a significant volume-outcome relationship. The decision to use the right internal mammary artery or radial artery should be based on individual patient characteristics and the experience of the surgical team.

INTRODUCTION

Coronary atherosclerotic heart disease (CAD) represents the leading cause of death worldwide [Khan 2020]. Coronary artery bypass grafting (CABG) is the primary surgical treatment for CAD and remains the first choice for patients with left main and triple-branch lesions who also have diabetes [Habib 2015; Farkouh 2012], even in cases of heart failure or a left ventricular ejection fraction (LVEF) <35% [Velazquez 2016]. In 1964, Kolesov et al. [Kolesov 1965] first anastomosed the left internal mammary artery (LIMA) with the left anterior descending (LAD) artery, initiating modern CABG. Three years later, Favalaro et al. [Favalaro 1968] achieved good results using the saphenous vein (SV) for CABG, while Loop et al. [Loop 1986] reported excellent clinical results following the use of

the LIMA for CABG, laying the foundation for contemporary CABG. However, long-term clinical practice has confirmed the poor long-term patency of SVG, with patency rates of less than 80% and 70% at 1 and 5 years postoperatively, respectively, and less than 50% at 10 years postoperatively [Sabik 2011]. Given the superior long-term patency of the LIMA, arteries including the right internal mammary artery (RIMA), radial artery (RA), and right gastroretinal artery (RGA) have been widely utilized for CABG procedures. In this report, we review and discuss the status of RA applications during CABG and current controversies in the field.

Background: In 1971, Carpentier et al. [Carpentier 1973] performed the first CABG procedure to utilize the RA (RA-CABG). However, because of the high incidence of stenosis or occlusion (35%) within the first 2 years after surgery, the authors recommended abandoning the use of the RA [Geha 1975]. Eighteen years later, Acar et al. [Acar 1992] performed RA-CABG in 104 patients, benefiting from the use of calcium channel blockers (CCBs) and improved no-touch vessel access techniques, with an early patency rate (mean follow up: 9.2 months) of >90% and a postoperative patency rate of 83% over 5.27 (± 1.30) years. The risk of death was also significantly reduced following their procedure when compared with that following SV (odds ratio [OR]=0.77, 95% confidence interval [CI]=0.63-0.94, $P = 0.01$) [Gaudino 2020]. In a systematic review including 20,931 patients with a mean follow-up period of 6.6 years, Gaudino et al. [Gaudino 2019] reported that the survival advantage of RA-CABG was independent of age, sex, and diabetes status.

Evaluating and harvesting of the RA: The length of the RA is sufficient to reach any coronary branch, and the internal diameter matches that of the coronary artery [Barry 2007]. The upper 1/3 of the RA is covered by the brachioradialis muscle, while the lower end is superficially located and easily obtained. As the RA is a muscular artery, RA spasm is the main cause of early graft failure. The purpose of RA evaluation is to verify the intact morphology of the RA and determine whether compensation can be achieved using the ulnar artery (UA). The modified Allen test [Kobayashi 2009] currently is the most widely used method for assessing the compensatory function of the UA, exhibiting a specificity of 91% and a sensitivity of only 54.5% when 6 s is used as the observation point [Jarvis 2000]. Therefore, the use of the RA is safe in most patients with a positive Allen test. However, Zarzecki et al. [Zarzecki 2018] reported that 18.7% of 4,841 patients exhibited an incomplete superficial palmar arch rate, indicating that the assessment of RA based on physiology alone is inadequate.

Although Doppler echocardiography can aid in the assessment of RA morphology and compensatory UA flow,

Received March 6, 2022; received in revised form March 23, 2022; accepted April 28, 2022.

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guidelines for assessing whether the RA can be harvested remain lacking. Sullivan et al. [Sullivan 2003] considered a small internal diameter of the RA, diffuse sclerosis of the canal wall, failure of UA compensation during RA pressure closure, and no significant increase in peak UA flow velocity as contraindications to RA harvesting. Manabe et al. [Manabe 2005] reported that, despite the compensatory expansion of the UA after RA harvesting, patients exhibited a 20% reduction in forearm blood flow, when compared with the preoperative value. When examining Doppler echo findings for the UA 22 years after patients had undergone RA harvesting, Royse et al. [Royse 2018] observed compensatory expansion of the UA without the aggravation of UA atherosclerosis. Other studies have reported that RA harvesting does not reduce hand sensation or grip power [Holman 2013]. Currently, RA harvesting is mostly performed in the non-dominant arm, and a study of 173 patients by Ua-Anusorn et al. [Ua-Anusorn 2020] noted that the incidence of early postoperative hand complications (bleeding, hematoma, incisional infection, neurological complications, etc.) was higher in for the bilateral RA group than the unilateral RA group (28.1% vs. 8.3%). However, evidence suggests that hand perception scores do not significantly differ between the distal dominant and nondominant sides (8.78 ± 1.45 vs. 8.66 ± 1.00), indicating that bilateral RA harvesting is safe and effective [Chen 2019].

The open radial artery harvest (ORAH) technique mostly has been performed using the method described by Reyes et al. [Reyes 1995] in 1993, in which a longitudinal incision is made from the medial aspect of the biceps tendon to the area between the radial carpal flexor tendon and the radial styloid process. The subcutaneous fat and deep fascia are then opened at the wrist to expose the RA, free the RA branches, and ligate them with titanium clips, minimizing the use of an electric knife. In 1998, Psacioglu et al. [Psacioglu 1998] applied an ultrasonic scalpel to improve RA harvesting, avoiding ligation of the vessels and the thermal damage caused by the electric knife, thereby shortening harvesting time and reducing RA spasm. However, no studies have attempted to validate whether these approaches can maintain endothelial cell integrity [Uysal 2019]. Connolly et al. [Connolly 2002] applied their endoscopically harvested radial artery harvesting (ERAH) technique in 300 patients, reporting that this minimally invasive technique resulted in a more aesthetic incision while reducing postoperative forearm pain and the probability of wound infection [Tamim 2020]. The 2017 International Society for Minimally Invasive Cardiothoracic Surgery (ISMICS) meeting [Ferdinand 2017] noted that there was no significant difference between ERAH and ORAH, in terms of major adverse cardiovascular events (MACEs) (OR=0.54, 95% CI=0.20-1.46) or distant patency rates (OR=1.58, 95% CI=0.92-2.71, $P = 0.05$). As such, ERAH routinely is recommended [Kiaii 2017].

PATIENTS AND METHODS

Patient selection: Retrospective studies have indicated that RAs are more susceptible to flow competition than SVG, and that the long-term patency rate of RAs is positively

correlated with the degree of target vessel stenosis [Gaudino 2016]. Additional studies have identified the degree of target vessel stenosis as an independent risk factor [Desai 2004] for RA patency. While some studies have reported no differences in RA patency or MACEs for proximal anastomosis to the ascending aorta or LIMA Y ($P = 0.05$) [Barner 2012; Gaudino 2016], another study [Watson 2013] utilizing LIMA Y grafts produced erroneous results because they did not take LIMA patency into account.

Among 377 patients with diabetes, multi-arterial coronary artery bypass grafting (MABG) was superior to single arterial coronary artery bypass grafting (SABG) (hazard ratio [HR]=0.74, 95% CI=0.58-0.96) [Schwann 2018], and similar study has suggested that arterial graft patency and long-term clinical outcomes in patients with diabetes are better when the RA is used than when SVG is used [Raza 2017]. In a sub-analysis of data from the Radial Artery Patency Study (RAPS), Tam et al. [Tam 2018] reported that the use of the RA (relative to the SV) resulted in better outcomes in terms of MACE (11.8% vs 5.6% $P = 0.15$) and event-free survival (log-rank $P = 0.14$), and there were no significant differences in cumulative patency rates at 7.7 (± 1.5) years post-procedure (log-rank $P = 0.69$). In a propensity-matched analysis of 283 female patients, Dimitrova et al. [Dimitrova 2013] reported a 36% reduction in all-cause mortality at 15 years in the RA-CABG group (vs. SV). Pullan et al. [Pullan 2015] integrated data for 13,369 patients, who underwent RA-CABG between 1997 and 2012, noting that RA improved survival in male patients only and that female patients did not benefit from RA. The lack of early diagnosis in women due to atypical patient symptoms and the presence of other comorbidities (hypertension, diabetes, peripheral vascular disease, and chronic lung disease) at the time of presentation prompted physicians to forgo the use of additional arterial grafts [Attia 2017]. Although sex may be an independent risk factor for reduced benefit, some studies indicate those female patients may still benefit from CABG [Dimitrova 2013]. In a study of 13,334 patients, Tranbaugh et al. [Tranbaugh 2017] observed a significant benefit of CABG in patients under 70 years of age (HR: 0.77, $P < 0.01$), although there was no significant improvement in survival in patients over 70 years of age (HR: 0.95, $P = 0.35$). In their study of older adults undergoing RA-CABG, Habib et al. [Habib 2012] reported a 53% reduction in the 12-year risk of death relative to SABG in patients over 70 years of age. Given the superior performance of arterial grafts, RA-CABG can still be applied selectively in older adults treated at experienced centers.

Application of antispasmodic drugs: Antispasmodic drugs are an essential part of performing RA-CABG, and the application of antispasmodic drugs directly drives RA revival. Acar et al. [Acar 1998] routinely used papaverine to prevent RA spasms, while Yoshizaki et al. [Yoshizaki 2008] compared the abilities of verapamil-nitroglycerin (VG) and papaverine to prevent RA spasms in a study including 215 patients. One-year postoperative angiography results suggested that patency rates were better in the VG group, and both topical application of papaverine (OR=4.55, $P = 0.037$) and RCA grafts (OR=3.71, $P = 0.041$) were identified as independent risk

factors for RA occlusion. In their study of 72 patients undergoing RA-CABG, He et al. [He 2008] observed that administration of nicardipine-nitroglycerin (NG) significantly inhibited RA contraction (32.5–76.4%, $P < 0.05$), while Watanabe et al. [Watanabe 2014] demonstrated the superior diastolic effect of fasudil vs. VG in patients undergoing RA-CABG ($P = 0.001$). Other drugs used to prevent RA spasm include phosphodiesterase inhibitors, phenoxybenzamine (α -receptor antagonist), and chlorpromazine [Rudzinski 2013; Shipulin 2017]. However, all vasodilators work by specific mechanisms to relax the blood vessels. No single vasodilator is sufficient to prevent or treat all arterial graft spasms, and a combination of vasodilators is used for different spasm mechanisms to obtain the best results [Langenaeken 2021]. To date, only a few RCTs have evaluated the effect of postoperative CCBs on patency and clinical outcomes in RA-CABG, and in most cases, the use of CCBs did not improve long-term patency or reduce MACEs [Patel 2006]. Data from a Canadian study that included 27 cardiac centers showed that, despite a lack of evidence-based support, oral verapamil was routinely administered to 95% of patients for 6–12 months after RA-CABG [Myers 2003]. A study that examined intravascular ultrasonography findings 10 years after surgery suggests that, as the RA lumen expands after transplantation, the RA gradually loses its morphologic function as a muscular vessel, becomes more histologically oriented to elastic arteries, and has diminished vasoactive properties [Gaudino 2005]. Another study reported that the use of β -receptor antagonists and angiotensin-converting enzyme inhibitors (ACEIs)/acetylcholine receptor blockers (ARBs) is limited, as they can exacerbate the adverse effects of CCBs [Gaudino 2019]. Further RCTs are also required to verify whether CCB use can improve the long-term patency of the RA in patients undergoing RA-CABG.

Radial artery grafting: The 2020 ESC guidelines for the comprehensive management of acute coronary syndrome [Collet 2021] recommend RA as the preferred access for percutaneous coronary intervention (PCI) (Class IA). However, PCI has been shown to lead to endothelial hyperplasia, vascular dysfunction, and endothelial injury [Lim 2014]. Kamiya et al. [Kamiya 2003] reported a reduced early patency rate in the trans-radial coronary procedures (TRA) group, when compared with that in the non-RA route group (77% vs. 98%). Given these findings, the use of RA-CABG after TRA should be avoided as much as possible. Although clinical data are currently insufficient to develop a safe interval, the 2016 The Society of Thoracic Surgeons Clinical Practice Guidelines on Arterial Conduits for Coronary Artery Bypass Grafting [Aldea 2016] recommends a minimum interval of 3 months using post-TRA RA as the graft vessel.

To maximize the use of the RA, Weinschelbaum et al. [Weinschelbaum 1997] performed the first sequential grafting procedure using the RA in 1997. A total of 296 patients (mean grafts: 1.8 ± 0.8) underwent angiography 1–19 months (9.5 ± 6.1) postoperatively, and the authors observed that all grafts were patent. Research has demonstrated that endothelial proliferation is inversely correlated with flow rate and that distal graft patency is correlated with flow rate [Faulkner 1975]. Schwann et al. [Schwann 2009] examined angiography

findings for 122 of 538 patients experiencing a recurrence of symptoms following sequential RA grafting, reporting that failure rates were similar for distal and proximal components (29% vs. 31%). The reported rates were also better than those previously observed for single grafts [Zacharias 2004]. Other studies have demonstrated the use of sequential RA grafts increases bridge vessel flow when compared with that of single vessels, that proximal anastomosis to the ascending aorta does not increase the incidence of coronary steal [Nakajima 2012], and that distal anastomotic patency is unrelated to the degree of anastomotic stenosis, with no increase in distal graft failure rate [Gaudino 2005].

Is the RA the best second graft vessel? The Radial Artery Database International Alliance (RADIAL) [Gaudino 2018] examined angiography data for 652 patients who had undergone RA-CABG at a mean of 4.17 years (± 2.5 years) after surgery, observing that the risk of occlusion (vs. SV) was significantly lower in RAs (HR=0.44, 95% CI=0.28–0.70, $P < 0.001$). The RAPS investigators [Deb 2012] examined angiography findings 7.7 \pm 1.5 years after surgery in 269 patients, also reporting that the rate of complete patency was higher for RAs than for SVG (88.0% vs. 80.3%, $P = 0.03$).

At the 10-year follow up of the Arterial Revascularization Trial (ART) [Taggart 2019], there was no significant difference in mortality or cardiovascular events between the single internal mammary artery (SIMA) and bilateral internal mammary artery (BIMA) groups (HR: 0.96, 95% CI: 0.82–1.12, $P = 0.62$), which may be related to the high crossover rate between the groups, with 15% of the BIMA group using only a SIMA and 20% of the SIMA group using the RA. The Radial Artery Patency and Clinical Outcomes (RAPCO) study [Buxton 2020], which included 394 patients, reported higher patency (80% vs. 89%, HR for graft failure=0.45, 95% CI=0.23–0.88) and survival rates (90.9% vs. 83.7%, HR for death=0.53, 95% CI=0.30–0.95) 10 years after surgery when the RA was used than when the RIMA was used. A meta-analysis of data from 4,400 patients noted a 27% lower risk of late (>4 years) graft vessel occlusion with RIMA vs. RA [Benedetto 2015].

Several other retrospective studies have suggested that there are no significant differences in long-term patency rates or primary clinical outcomes between RA and RIMA [Gaudino 2019; Spadaccio 2019]. However, the risk of deep sternal wound infection (DSWI) must be considered when using the BIMAs. Although this risk does not increase when the BIMAs are harvested using the skeletal technique [Benedetto 2016], the incidence of DWSI is still higher in patients with obesity and diabetes, especially those requiring insulin for glycemic control [Van den Eynde 2019; Gatti 2017]. Schwann et al. [Schwann 2019] analyzed CABG data from 2004–2015 in the STS database, observing a significant difference in operative mortality between RA-CABG and RIMA-CABG (adjusted OR=0.80, 95% CI=0.69–0.96), as well as significant differences in DWSI (adjusted OR=0.39, 95% CI=0.32–0.46). However, there was no significant difference in mortality between the two transplant strategies in institutions where BIMA accounted for more than 20% of total CABG procedures, and BIMA-CABG was not associated with DWSI risk in institutions where BIMA-CABG accounted for more

than 40% of total CABG procedures. A meta-analysis of 34 studies by Gaudino et al. [Gaudino 2018] indicated that this significant volume-outcome relationship may be related to a more precise selection of treatment strategies among experienced physicians. The application of the BIMA is more difficult, making surgeons less likely to select it [Catarino 2002]. In contrast, the left RA and LIMA can be harvested simultaneously, reducing the operative time. In addition, limited by the length of the IMA, RIMA in situ transplantation may require harvesting of the entire IMA segment, and the distal IMA lumen is relatively narrow and rich in smooth muscle, which may affect the rate of IMA patency [Borovic 2010]. Compared with in situ RIMA transplantation, RA coverage is more extensive, and in situ, RIMA for left coronary system transplantation may increase the risk of bridge injury during secondary surgery [Buxton 2014]. However, RIMA and RA do not represent opposing strategies when performing total arterialized CABG; thus, for centers skilled in BIMA-CABG, decisions should be based on patient life expectancy [Bowdish 2020]. The 2021 AHA guidelines for myocardial revascularization [Lawton 2021] recommend transplantation with the RA instead of the SV for patients with reasonable life expectancy after LIMA-LAD (Class IA).

SUMMARY AND OUTLOOK

Use of the RA during CABG is associated with good patency rates and long-term outcomes, although distal anastomosis is susceptible to flow competition for coronary arteries with severe stenosis. Improved RA access techniques and perioperative prevention of spasms using appropriate drugs are key to ensuring RA patency. However, further studies are required to determine whether the long-term application of CCBs can aid in improving prognosis. Evidence indicates that sequential RA grafts are safe and effective when arterial graft sources are limited and that the use of bilateral RAs does not increase the risk of complications. Furthermore, clinical outcomes are similar when the RIMA and RA are used, although the use of the BIMAs requires consideration of DWSI risk, especially in patients with diabetes. There is also a significant volume-outcome relationship for BIMA-CABG, with a reduced advantage of using the RA in experienced cardiac centers.

Although numerous studies have demonstrated that arterial graft vessels are effective in improving patient survival, the STS database shows that only 10.7% of patients who underwent isolated CABG from 2004 to 2014 received a MABG graft [Schwann 2017]. The RA-CABG learning curve is relatively short, and it is recommended to start with the RA for the first procedure. The preferred choice for the second arterial graft vessel should be based on individual patient characteristics and the experience of the surgical team.

ACKNOWLEDGEMENT

This study was supported by the Yunnan Provincial Clinical Medical Center for Heart Diseases (ZX2019-08-01).

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