

Coronary artery bypass grafting in diabetic patients: Should we still use the saphenous vein graft? A review of literature in the past 15 years

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ABSTRACT

The burden of diseases associated with diabetes mellitus is dramatic: adults with diabetes mellitus are 2 to 4 times more likely to have cardiovascular diseases than those without it, and at least 65% will die because of diabetes complications. The revascularization strategy in these types of patients included percutaneous coronary interventions with bare metal stents or medicated stents and surgical coronary artery bypass grafting (CABG), but it is well known that in the diabetic patient with two or more vessel disease, the surgical strategy allows the best mid- and long-term results. Moreover, benefits of CABG surgery are limited by life expectancy of the most common type of graft, the saphenous vein (SV). Nearly 40 years after the introduction of bypass surgery, the rate of vein graft failure remains at high levels. Several arterial conduits had been studied as alternative conduits to SV: the Right Internal Thoracic Artery (RITA), the Radial Artery (RA), the Gastroepiploic Artery (GEA) and the Inferior Epigastric Artery (IEA), 40 years ago. The aim of our article is to review the scientific literature of the past 15 years to answer this question: are we ready to treat the diabetic patient, with a completely arterial revascularization, avoiding the use of the great saphenous vein grafts?

Keywords: Total Arterial Revascularization; Coronary Artery Bypass Grafting; Diabetes; Review

1. INTRODUCTION

The burden of diseases associated with diabetes mellitus is dramatic: adults with diabetes mellitus are 2 to 4 times more likely to have cardiovascular diseases than those

without it, and at least 65% will die because of diabetes complications [1].

The national burden of cardiovascular diseases caused by diabetes mellitus is increasing, at an unprecedented rate in all western countries [1,2].

Cardiovascular disease in diabetics is clinically challenging because they tend to be extensive with multivessel involvement [3,4].

It is why surgical revascularization has been reported to be well suited for diabetic patients [5,6].

Typically, the elderly are the patients waiting for coronary artery bypass grafting (CABG) surgery with diabetes mellitus. Female gender is increasing in the diabetic population. Diabetic patients often have a history of hypertension and myocardial infarction. Frequently, they have manifestations of congestive heart disease, resulting in NYHA classification III-IV. It has been shown that diabetic patients have a smaller vessel diameter [7], and statistically they have three-vessel disease more frequently and a lower left ventricular ejection fraction [8, 9].

The revascularization strategy in these types of patients included percutaneous coronary interventions with bare metal stents or medicated stents and surgical coronary artery bypass grafting, but it's well known that in the diabetic patient with two or more vessel disease, the surgical strategy allows the best mid- and long-term results [10].

Moreover, the benefits of CABG surgery remain limited by the life expectancy of the most common type of graft, the saphenous vein. Nearly 40 years after the introduction of bypass surgery, the rate of vein graft failure remains at high levels [11].

The introduction of the left internal thoracic artery (LITA) graft radically changed the long term patency

and survival of patients who underwent CABG [12]. This conduit has shown a remarkable patency rate in several long-term series all around the world. So the introduction of the first arterial conduit has opened to the research of others arterial conduits which could be used with the same results of the LITA.

Several arterial conduits had been studied as alternative ones to saphenous vein (SV): the right internal thoracic artery (RITA), the Radial Artery (RA), the gastroepiploic artery (GEA) and the inferior epigastric artery (IEA) [13].

The aim of our article is to review the scientific literature of the past 15 years to answer to this question: are we ready to treat the diabetic patient with a completely arterial revascularization, avoiding the use of the great saphenous vein grafts?

2. MATERIALS AND METHODS

Our search strategy was: Medline 2002 to 2013 using pubmed interface (total arterial) and (CABG) and (diabetes).

More than 35 articles were found; from these 24 articles were identified as providing the best evidence to answer the question (Table 1).

3. RESULTS

3.1. The Bilateral Internal Mammary Artery (BIMA) and the Multiple Internal Mammary Artery (MIMA)

RITA possesses the same molecular and cellular characteristics that contribute to a unique resistance to atherosclerosis and extremely high long term patency rates as the LITA. The vasoactivity of this arterial conduit has also well characterized: the RITA produces significantly more prostacilin, a vasodilator and platelet inhibitor, than the saphenous vein and as well as the LITA. The harvest technique is similar to the LITA and it has been proposed as a skeletonized or pedicled graft for the proximal right coronary artery (RCA) or as a skeletonized or pedicled free graft for the branches of the left coronary artery (LCA) as a Y graft anastomosed to the LITA or an another arterial graft as the radial artery (RA) or a venous graft [14].

Both conduits used as a direct graft or a Y graft seem to have a positive effect on the outcome of diabetic patient undergoing CABG procedures.

The practice of using multiple arterial conduits for CABG is supported by reports showing their early operative morbidity and mortality results to be equivalent or better than for CABG with a single arterial graft [15-17].

Formica, *et al.* and Dorman, *et al.* founded a 12 to 15 years improvement in the late outcome of patients who underwent CABG with the use of BIMA [2,18].

Apparently, none of the surgical techniques utilized to perform operations demonstrated a superiority in terms of graft patency, in-hospital and late mortality and morbidity [2,19-21].

LITA and RITA have been used as pedunculated or skeletonized graft, with direct anastomosis on the target vessels or in composite grafts (Y graft), used to perform the revascularization of a single coronary branch or more coronary branches [19,21] but the type of utilized surgical technique didn't influence the outcomes of the surgical therapy.

Dorman, *et al.*, Rankin, *et al.*, Nasso, *et al.*, Parsa, *et al.*, and Loker, *et al.* emphasized how the use of a second arterial graft is sufficient to improve the long term quality of life of the patient and their rate of cardiac related mortality and morbidity [2,19-22].

In all these studies, the incidence of surgical wound infections and mediastinitis is comparable to non-diabetic patients.

Only one study has reported data in contrast to those listed above: Saito, *et al.* [23] compared the use of SIMA versus BIMA in a large sample of 7702 cases with a propensity matched analysis and he found that the use of BIMA did not affect either short-term survival as post-operative mortality was low in both groups or overall morbidity despite higher incidence of deep sternal infection. This study has the limitation of a 30 days post-intervention follow up and the finding of an higher rate of wound infection is not reported in other propensity matched studies [2,22,24,25].

3.2. The Radial Artery (RA)

The use of a radial artery as a conduit for coronary artery bypass grafting was first described by Carpentier in 1973 [26]. Early patency rates were poor and the interest in the use of this conduit faded. The radial artery possesses a pronounced medial layer and is highly vasoreactive. Cosmetic concerns have also been cited as a deterrent for radial artery usage.

Surgeons' interest in radial artery as a graft for CABG has a known revival in the last 20 - 25 years with the improvements of the harvesting techniques [27] and the identification of the pharmacological agents to prevent the graft spasm [13,28].

The long-term outcome after CABG depends on graft patency. Previous angiographic observational studies have shown that the RA achieved excellent short- (96% - 100%), mid- (94% - 97%), and long-term graft patency (84% - 96%) when used as either an aortocoronary bypass or a composite graft [13,29-31].

Patency rates of the RA have exceeded those of SV grafts at all time points and are comparable to other arterial grafts. Many reports have shown better outcomes of the RA compared with the SV [30,32-43], though some

Table 1. List of the selected articles reviewed in our work.

Author and Periodical	Goal	Design: Number of patients Type of study Mono-Multicenter Randomized Follow-up	Type of Conduits	Angiogram Follow up/Patency Rate	Primary Endpoint	Conclusion
Locker, <i>et al.</i> 2012	Compare Multiarterial CABG group to LITA + SV group outcomes	No. Pts: 8622 Diabetic/Non Diabetic Type of study: retrospective analysis Centers Involved: one center Randomization: None Follow up: 15 years	LITA-RITA-RA-SV	None	<ul style="list-style-type: none"> • Perioperative Mortality • Late Mortality 	In patients undergoing isolated coronary artery bypass graft surgery with LITA to left anterior descending artery, arterial grafting of the non-left anterior descending vessels conferred a survival advantage at 15 years compared with SV grafting.
Mediratta, <i>et al.</i> 2013	To determine the factors that contribute to in-hospital mortality and long-term survival in young patients (aged less than 65) undergoing CABG	No. Pts: 5967 Diabetic/Non Diabetic under 65 years Type of study: retrospective analysis of a perspective database Centers Involved: one center Randomization: None Follow up: 7.9 years	LITA-RA-SV	None	<ul style="list-style-type: none"> • Perioperative Mortality • Late mortality 	Significant factors determining long-term survival in the under-65-year group include: age, atrial fibrillation, diabetes (diet and insulin controlled), LV function, cerebrovascular disease, dialysis, LITA usage, "urgent" operation status, CKMB and peripheral vascular disease.
Rankin, <i>et al.</i> 2007	To assess 20-year clinical benefits of MIMA grafting and to evaluate the possible effects of two different MIMA configurations	No. Pts: 867 Diabetic/Non Diabetic Type of study: retrospective analysis Centers Involved: 2 Centers Randomization: None Follow up: 20 years	LITA-RITA-MIMA	None	<ul style="list-style-type: none"> • all-cause death • subsequent PCI • MI • ReDo CABG 	Data confirm clinical benefits of MIMA grafting in multivessel coronary disease to 20 years of follow-up.
Saito, <i>et al.</i> 2013	To evaluate early outcomes of bilateral internal mammary artery (BIMA) compared with single IMA (SIMA) in patients who underwent isolated coronary artery bypass grafting (CABG)	No. Pts: 12229 Diabetic/Non Diabetic Type of study: retrospective analysis of a perspective database Centers Involved: 210 centers Randomization: None Follow up: perioperative (max 30 days after CABG)	LITA-BIMA-SV	None	<ul style="list-style-type: none"> • Perioperative Mortality • Perioperative Morbidity 	BIMA did not affect either short-term survival, or overall morbidity despite higher incidence of deep sternal infection Note: BIMA (Bilateral Internal Mammary Artery).
Schwann, <i>et al.</i> 2009	initial report of the early and late outcomes of sequential RA grafts in a large contemporary CABG series	No. Pts: 4663 Diabetic/Non Diabetic Type of study: retrospective analysis Centers Involved: 2 centers Randomization: None Follow up: 5.3 years	LITA-RA-SV	Yes (symptoms driven) Patency rate: 71% for RA	<ul style="list-style-type: none"> • Late Survival • Patency rate of RA graft assessed by Angiography 	Sequential RA grafting is a safe method for maximizing arterial revascularization and is associated with excellent 10-year survival that seems to be superior to conventional or ITA/SV CABG results.
Schwann, <i>et al.</i> 2013	To determine whether the use of the radial artery (RA) vs the saphenous vein (SV) as the second grafting conduit with the internal thoracic artery (ITA) confers a late-survival advantage in diabetes mellitus (DM)	No. Pts: 2281 Diabetic Type of study: retrospective analysis Centers Involved: one center Randomization: None Follow up: 16 years	RA-SV	None	<ul style="list-style-type: none"> • Long term all causes mortality and morbidity 	RA grafting confers a significant late-survival advantage and, thus, supports its liberal use in DM patients undergoing multivessel CABG.

Continued

<p>Hwang, <i>et al.</i> 2010</p>	<p>To evaluate the influence of diabetes mellitus (DM) on 5-year angiographic results and long-term clinical outcomes in patients who underwent total arterial off-pump coronary revascularization for multi-vessel coronary disease</p>	<p>No. Pts: 558 Diabetic/Non Diabetic Type of study: retrospective analysis Centers Involved: one center Randomization: None Follow up: 5 years</p>	<p>LITA-RITA-RA-rGEA Only OPCABG</p>	<p>Yes Patency rate (in DM group): Early: 98.2% 1-Year: 95.3% 5-Year: 94.6%</p>	<ul style="list-style-type: none"> • Long-term survival • cardiac deaths • major advanced cardiovascular or cerebral events 	<p>Diabetes mellitus did not affect 5-year angiographic results, long-term survival, and clinical events in patients with multivessel coronary disease who underwent total arterial off-pump revascularization.</p>
<p>Hoffman, <i>et al.</i> 2013</p>	<p>using radial artery (RA) conduit(s) would improve outcomes and long term survival for diabetic patients undergoing CABG with Left Internal Thoracic Artery (LITA) and RA grafts, with or without additional saphenous vein (SV) when compared with outcomes for patients bypassed with LITA and SV but no RA</p>	<p>No. Pts: 1843 Diabetic/Non Diabetic Type of study: retrospective analysis Centers Involved: one center Randomization: None Follow up: 15 years Propensity matched study</p>	<p>LITA-RA-SV</p>	<p>None</p>	<ul style="list-style-type: none"> • all cause mortality determined from the Social Security Death Index 	<p>For diabetic patients having CABG with LITA, use of radial artery conduit adds a substantial and sustained survival advantage compared to LITA and vein. Optimal revascularization for diabetics with multi vessel disease is redefined.</p>
<p>Dorman, <i>et al.</i> 2012</p>	<p>we studied the long-term results of BIMA versus SIMA grafting in a large population of diabetic patients in whom BIMA grafting was broadly applied</p>	<p>No. Pts: 828 Diabetic Type of study: retrospective analysis Centers Involved: one center Randomization: None Follow up: 30 years Propensity matched study</p>	<p>LITA-RITA SIMA versus BIMA</p>	<p>None</p>	<ul style="list-style-type: none"> • Long-term survival • cardiac deaths • major advanced cardiovascular or cerebral events 	<p>Compared with SIMA grafting, BIMA grafting in propensity score-matched patients provides diabetics with enhanced survival without any increase in perioperative morbidity or mortality Note: SIMA: Single Internal Mammmary artery-BIMA: Bilateral Internal Mammmary Artery.</p>
<p>Zacharias, <i>et al.</i> 2009</p>	<p>Compared with SIMA grafting, BIMA grafting in propensity score-matched patients provides diabetics with enhanced survival without any increase in perioperative morbidity or mortality</p>	<p>No. Pts: 4743 Diabetic/Non Diabetic Type of study: retrospective analysis Centers Involved: one center Randomization: None Follow up: 12 years Propensity matched study</p>	<p>LITA-RITA-RA-SV</p>	<p>None</p>	<ul style="list-style-type: none"> • Long-term survival • cardiac deaths • major advanced cardiovascular or cerebral events 	<p>All-arterial revascularization is associated with significantly better 12-year survival compared with the standard single ITA with saphenous vein CABG operation, in particular for triple-vessel disease patients. The completeness of revascularization of the underlying coronary disease is critical for maximizing the long-term benefits of arterial-only grafting.</p>
<p>Singh, <i>et al.</i> 2008</p>	<p>This study examines the impact of diabetes on graft patency, 1-year postcoronary artery bypass grafting, using data from a multicenter randomized trial</p>	<p>No. Pts: 561 Diabetic/Non Diabetic Type of study: retrospective analysis on a multi-center randomized trial Centers Involved: a multi-center randomized trial Randomization: Yes Follow up: 12 years</p>	<p>LITA-RA-SV</p>	<p>Yes; 1 year angiographic follow up of RA grafts Diabetic: 85.6% Non Diabetic: 90.3%</p>	<ul style="list-style-type: none"> • 1 year mortality • Redo for revascularization • Myocardial infarction • 1 year rate of angiographic occlusion in RA vs SV 	<p>Coronary artery bypass grafting occlusions were more common among diabetics versus nondiabetics at 1-year angiography, mainly because of more frequent SV graft failure in diabetics. Radial artery, compared with SV grafting, is protective in both diabetic and nondiabetic patients.</p>

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Formica, <i>et al.</i> 2004	We present our experience with total arterial myocardial revascularization with bilateral internal thoracic artery (BITA) and right gastroepiploic artery (rGEA)	No. Pts: 174 Diabetic/Non Diabetic Type of study: retrospective analysis Centers Involved: one center Randomization: None Follow up: 9 years	LITA-RITA-rGEA	None	<ul style="list-style-type: none"> • Death • recurrence of angina • occurrence of cardiac-related events. 	This study indicates that the myocardial revascularization in young patients with three-vessel disease using exclusively pedicle BITA and rGEA provides excellent 9-year patient survival and improvement in terms of freedom from return of angina pectoris and freedom from any cardiac-related event. These results encourage the more extensive use of BITA and rGEA in selected patients with three-vessel coronary disease.
Suma, <i>et al.</i> 2007	Assessing the use of rGEA for CABG	No. Pts: 1352 Diabetic/Non Diabetic Type of study: retrospective analysis Centers Involved: one center Randomization: None Follow up: 15 years	rGEA in combination with others conduits	Yes 15 years patency rate for rGEA; 96%	<ul style="list-style-type: none"> • Perioperative mortality and morbidity • Early, midterm, late survival • Early, midterm, late rGEA patency 	GEA graft is a suitable conduit with acceptably good patency rate to the distal right or circumflex coronary artery.
Parsa <i>et al.</i> 2013	To assess single institutional outcomes with multiple internal thoracic artery grafting for guidance with future clinical decisions	No. Pts: 19482 Diabetic/Non Diabetic Type of study: retrospective analysis Centers Involved: one center Randomization: None Follow up: 15 years	LITA-RITA MIMA versus SIMA	None	<ul style="list-style-type: none"> • Subsequent AMI or MI • Postoperative PCI • ReDo CABG • All causes death 	This study confirms improved patient's outcomes with multiple internal thoracic artery grafting.
Cho, <i>et al.</i> 2010	To evaluate early and 1-year results of arterial Y composite grafts anastomosed to the in situ left internal thoracic artery were studied. Off-pump CABG only	No. Pts: 320 Diabetic/Non Diabetic Type of study: retrospective analysis Centers Involved: one center Randomization: None Follow up: 1 year	LITA-RITA-rGEA rGEA-LITA (Y graft) versus RITA-LITA (Y graft)	Yes 1 year follow up rGEA patency rate: 97% RITA patency rate: 95%	<ul style="list-style-type: none"> • Perioperative Mortality and morbidity • Patency rate at 1 year with angiographic follow up 	Construction of Y composite grafts using the RITA or RGEA showed comparable results including patency rates early and 1 year postoperatively.
Nasso, <i>et al.</i> 2009	To evaluate the effect of a double arterial graft on the outcome of CABG operations and investigate which second choice arterial conduit its better for improving outcomes	No. Pts: 626 Diabetic/Non Diabetic Type of study: retrospective analysis Centers Involved: two centers Randomization: Yes Follow up: 2 year	LITA-RITA-RA-SV	None	<ul style="list-style-type: none"> • In Hospital outcome • 2 years freedom from all cause death and adverse cardiac event free survival 	Revascularization with 2 arterial conduits offers better midterm event-free survival than a single arterial graft, irrespective of which second-choice arterial conduit is used (radial artery or right thoracic artery), the simultaneous use of saphenous vein grafts, and the patient's age.
Schwann, <i>et al.</i> 2008	To evaluate the use of RA as second choice conduit in revascularization of diabetics patients	No. Pts: 1516 Diabetic Type of study: retrospective analysis Centers Involved: one center Randomization: None Follow up: 2 year	LITA-RA-SV	None	<ul style="list-style-type: none"> • Early, mid term survival of diabetic patients after CABG 	Using radial as a second arterial conduit as opposed to vein grafting did not confer a survival benefit in diabetics.

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Santos, <i>et al.</i> 2002	To compare the results of composite Y-grafts of the radial artery (RA) and the right gastroepiploic artery (RGEA) proximally anastomosed to the left internal thoracic artery (LITA) for CABG, evaluated through angiography, in a prospective randomized study	No. Pts: 60 Diabetic Type of study: prospective randomized study Centers Involved: one center Randomization: Yes Follow up: perioperative	LITA-RITA-RA-r-GEA Composite arterial grafts' outcome comparison	YES Between the 7Th and the 15Th postoperative day	<ul style="list-style-type: none"> • Early complications after CABG (perioperative AMI, cardiac death, infection) • Early graft patency 	Radial artery had better early results than right gastroepiploic artery. Use of the LITA as inflow graft seems not to affect its good patency. Use of the RGEA as composite graft should not be encouraged.
Hassanein, <i>et al.</i> 2010	The objective of this study is to demonstrate the safety and potential advantages of bilateral mammary coronary revascularization in patients older than 65 years	No. Pts: 415 Diabetic/Non Diabetic Type of study: propensity score analysis Centers Involved: one center Randomization: Yes Follow up: perioperative	BIMA-SV	None	<ul style="list-style-type: none"> • Early complications after CABG (perioperative AMI, cardiac death, infection, neurological complications) • Early graft patency 	Bilateral internal mammary artery revascularization can be safely performed in patients older than 65 years. T-graft configuration without aortic anastomosis is particularly beneficial in this age group since it avoids aortic manipulation, which is an important risk factor for postoperative stroke.
Tranbaugh, <i>et al.</i> 2012	16-year experience in 1851 consecutive patients undergoing isolated CABG, using the RA after the LITA to LAD graft to better define the outcomes, long-term survival, patency, and need for rein-tervention after RA grafting	No. Pts: 1851 Diabetic/Non Diabetic Type of study: retrospective study Centers Involved: one center Randomization: None Follow up: 15 years	LITA-RITA-RA-SV	Yes (symptoms driven) Patency rate: LITA: 85% RITA: 80% RA: 82%	<ul style="list-style-type: none"> • Early complications after CABG (perioperative AMI, cardiac death, infection, neurological complications) • Long term outcomes • Early-mid-long term patency rates 	RA grafting is a highly effective revascularization strategy providing excellent short and long-term outcomes with very low rates of reintervention. RA patency is similar to LITA patency and is much better than SV patency. RA grafting should be more widely utilized in patients undergoing CABG.
Desai, <i>et al.</i> 2004	To determine the relative patency rate of radial-artery and saphenous-vein grafts in a randomized trial with a 1-year follow-up	No. Pts: 561 Diabetic/Non Diabetic Type of study: randomized trial study (RAPS) Centers Involved: 13 centers Randomization: None Follow up: 1 year	LITA-RA-SV	Yes 1 year after the operation Patency rate RA 91.8% SV 86.4%	<ul style="list-style-type: none"> • Early patency rate of RA versus SV 	Radial-artery grafts are associated with a lower rate of graft occlusion at one year compare with the saphenous-vein grafts. Because the patency of radial-artery grafts depends on the severity of native-vessel stenosis, such grafts should preferentially be used for target vessels with high-grade lesions.
Possati, <i>et al.</i> 2003	To asses the long term patency rate of RA graft	No. Pts: 90 Diabetic/Non Diabetic Type of study: perspective study Centers Involved: one center Randomization: None Follow up: 10 years	LITA-RA-SV	Yes 10 years after the operation Patency rate RA 91.6% LITA 97.5%	<ul style="list-style-type: none"> • Long term patency of the RA graft anastomosed to ascending aorta 	Ten years after surgery, RA grafts have excellent patency and perfect patency rates. Appropriate surgical technique and correct indication are the key factors for long-term RA patency.

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Collins, <i>et al.</i> 2008	We performed a single-center prospective randomized trial comparing the angiographic patency of radial artery and saphenous vein aortocoronary bypass grafts at 5 years after surgery	No. Pts: 90 Diabetic/Non Diabetic Type of study: perspective study Centers Involved: one center Randomization: None Follow up: 10 years	LITA-RA-SV	Yes 5 years after the operation Patency rate: RA 98,3% SV 86,4%	<ul style="list-style-type: none"> • Midterm patency rate of RA graft versus SV graft 	Radial artery aortocoronary bypass grafts to a stenosed branch of the circumflex coronary artery have an excellent patency rate at 5 years. This was significantly better than the patency rate for saphenous vein grafts and comparable to reported patency rates for internal thoracic artery grafts.
Tranbaugh, <i>et al.</i> 2010	The second best conduit for coronary artery bypass graft surgery is unclear. We sought to determine if the use of a second arterial conduit, the radial artery, would improve long-term survival after CABG using the left internal thoracic artery and saphenous vein	No. Pts: 4721 Diabetic/Non Diabetic Type of study: retrospective study Centers Involved: one center Randomization: None Follow up: 14 years	LITA-RA-SV	None	<ul style="list-style-type: none"> • Early, mid and long term survival of patients after CABG 	Using the LITA, SV, and a RA conduit for CABG results in significantly improved long-term survival compared with using the LITA and SV. The use of two arterial conduits offers a clear and lasting survival advantage, likely due to the improved patency of RA grafts. We conclude that RA conduits should be more widely utilized during CABG.

reported similar long-term graft patency [44-47].

Only the Cleveland Clinic reported worse graft patency of the RA than the SV [48].

Possati, *et al.* reported the long-term (105 ± 9 months) graft patency of RA grafts in a series of 90 consecutive CABG patients [36].

The RA graft patency was 88%, which was less than that of the LITA (96%), but better than that of the SV (53%). Although these results are encouraging the use of the RA as a complementary arterial conduit with the LITA, there are only a few long-term studies assessing RA graft patency in the setting of a randomized controlled trial.

The Radial Artery Patency Study (RAPS) investigators enrolled 561 patients in 13 centers [49]. In this trial, the RA graft was randomly assigned to bypass in either the right coronary territory or the circumflex coronary territory, with the SV graft used for the opposing territory, which had proximal lesions at least 70% of occlusion diameter narrowing. Angiography for 440 RA grafts and 440 SV grafts was performed in 440 patients in 1 year. They reported that 8.2% of RA grafts and 13.6% of SV grafts were completely occluded ($P = 0.009$). Diffuse narrowing of the graft (string sign) was present in 7.0% of the RA grafts and only 0.9% of SV grafts ($P = 0.001$). The absence of severe native vessel stenosis was a risk of graft occlusion and diffuse narrowing of the RA conduit (70% - 89% proximal stenosis: 81.7%; >90% proximal stenosis: 91.5%). Patency of the RA grafts was similar in the right coronary and circumflex arteries. These is com-

patible with previous reports suggesting that the RA should be limited to grafting to native coronary vessels with a high degree of stenosis (>70%) because of graft sensitivity to competitive flow and diffuse narrowing [50,51].

Diffuse narrowing of the RA graft is thought to be of little or no clinical consequence because the narrowed graft may improve or work well late in the follow-up. However, cardiologists consider the string sign of the RA graft as a failure. As the string sign at 1 year is unfavorable toward a functioning RA or SV graft, 15.2% of RA grafts and 14.5% of SV grafts are occluded or functioning poorly. RA grafting should not be considered in the setting of <75% proximal coronary obstruction, especially in the right coronary branches [52].

The RAPS Investigators also reported that diabetes (RR: 1.45, $P = 0.03$), female gender (RR: 1.78, $P = 0.02$), and small target vessel diameter (RR: 2.28, $P < 0.01$) are multivariate predictors of graft failure [53,54].

Graft occlusion was more common among diabetic patients (14% vs 10%) because of more frequent SV occlusion (19%) than RA occlusion (10%). The RA is protective in the small-sized coronary arteries with diffuse diabetic disease. As regards the gender, RA graft occlusion rate at 1 year was similar in men (8.6%) and women (5.3%) ($P = 0.6$), whereas SV graft occlusion rates were lower in men (12.0%) than in women (23.3%). A history of peripheral vascular disease was associated with an elevated risk of RA occlusion, but not with SV occlusion. On the contrary, angiographic studies of patients at the

Cleveland Clinic found poor graft patency in the RA (51%) compared with the SV (64%). As concerns sex, women had significantly worse RA graft patency (39%) than men (56%) [30].

The Radial Artery Patency and Clinical Outcome (RAPCO) study, was undertaken to compare angiographic patency and cardiac-event-free survival of the RA graft with that of the free RITA and SV during a 10-year period after CABG [55].

The RA was compared with the free RITA in patients <70 years of age and with the SV in patients aged >75 years. The 5-year interim results of this single center trial conducted by Buxton, *et al.* in Australia reported that there were no differences in angiographic graft failure and cardiac events of the patients with the RA compared with the RITA or SV. The 5-year patency rates between the RA and RITA were 95% vs 100%, respectively, and those between the RA and SV were 87% vs 94%. However, these results were based on a small number of angiographic studies, and SV graft patency was very much better than in previous reports. The final results up to 10 years should clarify the long-term RA graft patency.

The Radial Artery Versus Saphenous Vein Graft Patency (RSVP) trial was a single-center, prospective, randomized clinical trial designed to compare 5-year patency rates of RA and SV aortocoronary grafts to the circumflex coronary artery [56].

At 5 years, 103 patients among 142 enrolled patients underwent angiography. The graft patency of the RA (98.3%) was significantly ($P = 0.04$) better than that of the SV (86.4%). Graft narrowing occurred in 10% of patent RA grafts and 23% of SV grafts ($P = 0.01$).

In conclusion, despite the poor first outcomes of the RA graft, the progress of harvesting techniques and pharmacological therapy to prevent the radial spasm had lead to re-discover a useful arterial conduit with wide application opportunities especially on the left coronary branches with patency rates comparable to the RITA's ones and superior to those of the SV graft.

3.3. The Right Gastroepiploic Artery (rGEA)

The right GEA represents another interesting option as a conduit for CABG. Several studies demonstrated similarities of this conduit with the internal thoracic artery. Of the other possible arterial conduits, the right gastroepiploic artery (r-GEA) has several advantages, such as providing a comparably sized artery-to-artery anastomosis, necessitating no additional incision in the leg or forearm, and histologic similarity to the ITA, which would suggest long-term patency [57,58].

In 1987, Pym and others authors [59], have independently reported their successful clinical application of the GEA graft for CABG, and now over the last 2 dec-

ades, basic research and the clinical application of GEA has widely been undertaken. The GEA graft has a high clinical availability for CABG [60], low incidence of arteriosclerosis [61], and sufficient flow capacity [62].

Its biological and physiological activity have been studied extensively [63,64].

Several investigators have shown that GEA can be used without increased morbidity, particularly in abdominal complications [65,66], and the late survival rate has been excellent in CABG with GEA plus internal thoracic artery grafts [18,56,67,68].

High tendencies to develop vasospasm and competitive flow in moderately stenotic coronary lesions, however, have been indicated as limitations of the in situ RGEA graft, but this tendency to develop spasm seems to be due to the use of pedicled r-GEA, while skeletonized r-GEA appears to have a significantly low rate of spasm [69-72].

Moreover, the length of this vessel, if it is used as a composite graft, allows to reach both coronary systems and to achieve a complete arterial revascularization [69].

Suma, *et al.*, in a study published on Circulation [57], a large series of patients who received a r-GEA graft, demonstrating that r-GEA has a patency rate superior to the SV one.

3.4. The Inferior Epigastric Artery (IEA)

The Inferior Epigastric Artery represents an infrequent arterial conduit used as a free graft for CABG. In our research in PubMed we did not find recent articles or trials about the use of this conduit in CABG so this section of our review is to complete the view of arterial conduits which are used or proposed for total arterial grafting.

For some authors, the artery exhibits favorable physiological vasoreactivity characteristics and its length, diameter and location are rather variable. After it has been harvested, it is treated like a radial artery in terms of preparation. It is used to create composite Y graft usually with an anastomosis with the LITA, RITA or SV [73].

Some authors reported good patency rate in early postoperative follow up, even with angiography [74], but the patients' series and the lack of mid- and long term follow up can't encourage a wide use of this conduit and it absolutely requires others clinical investigations on larger series of patients.

4. CONCLUSIONS

In a review of the literature of the last 15 years, it has been reported the superiority of total arterial coronary grafting in CABG, even in the long term follow-up.

The harvesting of this "addictional" conduit expands

the operating time, but it has been shown that each of them improve the outcome of the coronaric patients undergoing CABG.

Although diabetes is an independent risk factor for coronary artery disease and graft restenosis, the outcome of the diabetic patient is significantly improved by the use of total arterial grafting.

It is also clear that each arterial vessel we described, especially the radial artery, seems to have particular indications and a preferential anastomosis territory. The wide application and the utilization of these vessels need to be proved by multicenter randomized studies in the future.

Our opinion is that the use of total arterial myocardial revascularization should be encouraged, and cardiac surgery is near to avoid the use of saphenos vein graft in the scheduled coronary patient.

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