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Review

Bilateral internal mammary artery grafting: Rationale and evidence

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HIGHLIGHTS

- BIMA grafting associated with better long-term outcomes.
- BIMA grafting provides incremental beneficial effect with time.
- BIMA grafting associated with relatively few drawbacks.

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ABSTRACT

Coronary artery bypass graft (CABG) surgery remains the preferred mode of revascularization in patients with complex multi-vessel coronary artery disease. The left internal mammary artery (IMA) and saphenous vein are the most commonly utilized conduits in CABG surgery and are still considered to be the gold standard by most surgeons. However, there is emerging evidence that use of bilateral IMAs is associated with significantly better long-term outcomes and the benefit increases with time from surgery. In spite of this incremental beneficiary effect, most surgeons are reluctant to use both IMAs, because it is technically more demanding, time-consuming and is associated with marginally higher sternal wound infection rates. This review highlights the histological features, physiological characteristics and genomics of IMAs that provide the basis for the use of these vessels during CABG surgery. Additionally, the superiority of the bilateral IMAs with regard to patency and long-term outcomes is also discussed in detail. Furthermore, the safety of using bilateral IMAs with regard to early postoperative outcomes with special reference to deep sternal wound infections has been addressed. The present review provides enough evidence to convince more surgeons about the advantages of bilateral IMA grafting.

1. Introduction

The initial enthusiasm in the utilization of the left internal mammary artery (LIMA) as a bypass graft was evoked by the encouraging results of the work by Arthur Vineberg in 1946, who tunneled the skeletonized LIMA through the myocardium adjoining the left anterior descending (LAD) artery anticipating the development of collaterals between the side-branches of the LIMA and myocardial vessels, thereby restoring myocardial perfusion [1,2]. After the performance of the first LIMA-LAD anastomosis by a non-suture technique by Goetze and colleagues in 1960 [3], Vasilii Kolesov, a Russian cardiac surgeon, performed the first sutured coronary artery bypass graft (CABG) by anastomosing the LIMA to the LAD in 1964 [4], followed by Spencer the same year in the USA [5], making 2014 the 50th anniversary of contemporary CABG. Reports about the application of bilateral internal mammary arteries (BIMA) for myocardial revascularization can be traced back to the sixties, when Rene Favalaro, considered the 'father' of coronary surgery, described the technique and outcomes of BIMA implants into the myocardium [6,7]. However, with the advent of the use of the saphenous vein as a conduit in CABG [8,9], it became the most commonly utilized graft during the seventies and early eighties [10,11] due to the ease of harvest, better handling properties, excellent procedure reproducibility and favorable immediate outcomes. Nevertheless, use of the LIMA as a graft to the LAD became standard practice after the landmark paper from the Cleveland Clinic group reported that LIMA to the LAD was associated with improved 10-year survival and freedom from recurrent angina, myocardial infarction (MI) and the need for repeat revascularization [12].

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The use of BIMA grafts to revascularize the coronary arteries by conventional direct anastomoses was first reported by Suzuki and associates in 1973 [13]. The first reports on excellent clinical outcomes of BIMA grafting were published by the Cleveland Clinic group as early as 1983 [14]. Increasing evidence about the superior long-term outcomes of CABG with LIMA use [15–17] prompted the cardiac surgical community to utilize both internal mammary arteries (IMA) to achieve greater territorial revascularization. However, regular use of BIMA for coronary revascularization was adopted initially only by few centers [18–22]. Nevertheless, by the turn of the century several groups had evaluated the results of BIMA in multi-vessel CABG surgery comparing them with those achieved by the single IMA, which still continues to be the "gold standard" in CABG surgery [14,23,24]. Despite superior results procured with BIMA grafting [14,24], very few surgeries worldwide are performed with the use of BIMA averaging approximately 20% in Europe and less than 5% in the USA [25]. Even in the pivotal SYNTAX trial, less than a third of patients in the three-vessel disease subgroup received BIMAs [26]. The reluctance to perform BIMA grafting routinely stems from several factors, the major ones being that BIMA grafting is technically more challenging and time-consuming and is associated with a small, but increased risk of sternal wound infections. It is, therefore, extremely essential for the experts in the field of BIMA grafting to spread awareness about the unparalleled benefits of BIMA in the cardiac surgical community. The present review, thus, focuses on the rationale and evidence of utilizing BIMA in CABG surgery.

2. Rationale and evidence

Although, strong evidence from several observational studies suggestive of survival benefit for BIMA use are available in literature for more than a decade [27,28], no randomized controlled trial (RCT) comparing the results of single IMA (SIMA) with BIMA existed until the Arterial Revascularisation Trial (ART) was undertaken [29]. To date, only the 1-year results of the ART trial have been published [30]. Therefore, there continues to be no definitive evidence in the form of a RCT with regard to the long-term benefits of BIMA grafting, which has been a major contention against the use of BIMA. Nevertheless, excellent long-term clinical outcomes with BIMA use reported by numerous observational studies are not the only rationale for their use. There are various factors discussed in this section that make their utilization efficacious, safe and prudent in majority of patients undergoing CABG.

2.1. Efficacy

The efficacy of the IMA depends upon its physical characteristics, which are chiefly responsible in determining its long-term patency rates and thereby the event-free survival benefit in comparison to other conduits.

2.1.1. Basic properties

2.1.1.1. Histological features: The IMA has a unique histology as compared to the other peripheral arteries in the human body. The internal elastic lamina, being non-fenestrated, is well-developed, thereby shielding the media from harmful luminal stimuli, while simultaneously preventing initiation of intimal hyperplasia by impeding the migration of smooth muscle cells from the media [31]. Additionally, the media has more elastic fibers and less smooth muscle cells than other arteries, which protects against development of atherosclerosis and vasospasm [32] and demonstrates a subdued reaction to known mitogens such as platelet-derived growth factor and pulsatile mechanical stretch [33,34]. The anatomical features of various arterial grafts are mentioned in Table 1.

2.1.1.2. Physiological characteristics: Another unique feature of the IMA is its endothelium, which can produce significantly larger quantities of vasodilators such as nitric oxide and prostacyclin than venous grafts, resulting in greater endothelium-dependent relaxation (EDR) in response to acetylcholine, ADP, and thrombin in patients undergoing CABG [37]. Additionally, EDR factor provides better protection against histamine- and serotonin-induced contractions in IMAs than venous grafts, which could translate to improved graft function and patency of the former [38]. The downstream flow of these endogenously secreted vasodilators into the coronary artery could also have a protective effect distal to the anastomosis, thus retarding the progression of CAD [39] by providing protection against atherosclerosis to the entire target vessel [40].

Thus, the use of BIMA grafting could only compound this effect, especially in patients who undergo total arterial revascularization with two IMAs. Furthermore, several studies have revealed a favorable response from the IMA to pharmacological agents such as milrinone, nitroglycerine and norepinephrine that are commonly used in the immediate postoperative period [41–43]. Apart from the above-mentioned benefits derived from its endothelium, the IMA also has the ability to remodel itself after its use as a bypass graft, resulting in an increase in diameter and concomitantly increased flows over time after CABG. This could also be attributed to endothelium-related mechanisms [44,45]. Even when BIMAs are used in a Y-configuration, the endothelium-dependent and the endothelium-independent vasodilator capacity of the two limbs of the Y-graft IMA configuration appears to be similar 3 years after bypass surgery [46].

2.1.1.3. Genomics: A comparative genome-wide transcriptional analysis of the LIMA, RIMA and the aortic wall revealed that the genes in the annotated atherosclerosis signaling pathway are down-regulated in both IMAs relative to the aorta [47]. Furthermore, signaling pathway genes for eicosanoids, which are signaling molecules associated with pro-inflammatory processes, are also expressed at lower levels in both IMA tissues. This transcriptional

Table 1
Anatomical characteristics of arterial grafts.

Anatomical characteristics	Internal mammary artery [35]	Radial artery [35]	Inferior epigastric artery [36]	Gastroepiploic artery [36]
Mean luminal diameter	1.5 ± 0.36 mm[a]	2.0 ± 0.45 mm[a]	1.1 ± 0.5–2.0 ± 0.4 mm	1.8 ± 0.5–2.7 ± 0.5 mm
Intimal thickness	0.01–0.52 mm	0.05–0.63 mm	Trivial values - 134 ± 131 μm	10 ± 17–50 ± 49 μm
Media	Fewer muscular fibers; greater number of elastic lamellae	Muscular with rare dispersed elastic fibers	Muscular with rare dispersed elastic fibers	Muscular with rare dispersed elastic fibers
Media thickness	0.10–0.60 mm	0.10–0.85 mm	165 ± 70–316 ± 86 μm	155 ± 70–380 ± 116 μm
Number of discontinuities in internal elastic lamina	Very few	Higher and constant	Higher and constant	Higher and constant

[a] Diameter internal to the media: Luminal diameter + Intimal thickness.