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The Impact of Arterial Grafts in Patients Undergoing CABG

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1. Introduction

General population suffers at 2-3% by angina. Incidence of angina in men and women aged 55 to 75 is 9% and 5% respectively. [1]

The prevalence of angina is 24,000 people per million. Almost 1 in 1000 undergoes CABG in the USA. This means that half a million people undergo CABG around the world per year and 1.5 million patients undergo Angioplasty/ stenting (1 to 3).

Without revascularization (angioplasty or bypass) four-year survival of patients one, two or three vessels disease is 92%, 84% and 68% respectively. [2] Moreover, in patients with reduced ejection fraction and heart failure (e.g. stroke) the respective survival rates are 67%, 61% and 42%. [3]

Clearly 5-years survival increases with every form of revascularization treatment. Coronary artery bypass grafting (CABG) remains the gold standard revascularisation strategy for complex 3 vessel coronary artery disease and left mainstem disease.

Recent trials such as the SYNTAX have shown that CABG is superior to PCI in most circumstances of coronary artery disease. Although there are certain anatomical lesions such as isolated left main disease treatment options to be elucidated, CABG remains the gold standard treatment for severe coronary artery disease. Data from studies such as SYNTAX and ART confirmed by the National Cardiothoracic Surgery Database have also shown the low mortality risk of CABG.

These recent evidence has prompted a rewrite of the european guidelines with regards to revascularisation. It is now recommended that no ad hoc PCI to be performed and all cases of severe coronary disease should be discussed in a multidisciplinary setting involving the "Heart team".

Indicatively, with the coronary artery bypass, survival is related to the ejection fraction, according the Cardiothoracic surgeries database of Emory University, where 23960 patients are registered as follows:

	5 years	10 years	15 years
EF \geq 50%	95	80	65
EF 30-50%	78	60	50
EF $<$ 30%	58	38	15

Table 1. Mortality as per Ejection Fraction

So, the main benefit from the bypass (CABG) is not only the symptomatic improvement and avoidance of the risk of a stroke, but also the evident prolongation of the patient's survival. On the other hand, it is obvious that even with CABG, long-term survival is decreasing. Even when reviewing the sudden death risk as a result of CABG, there are three (3) stages.

Years after CABG	Loss (\times 1000)
$\frac{1}{2}$	3.4
1	0.87
5	1.2
10	3.5
15	9.0

Table 2. Risk of death following CABG

There is an early, high-risk period, a period with rapid decrease of the risk and a period after 5 years, with an ascending risk rate. This late phenomenon is related to the atheromatosis of the saphenous vein graft.

2. IMAS versus BIMAS

Arterial and vein grafts are used to perform the CABG surgery. Most patients receive three grafts in a combination of an arterial (LIMA) and vein grafts. [4]

Unfortunately, in the course of time, the atherosclerotic graft disease obstructs vein grafts. It has been shown that approximately 3 months after surgery is developed hyperplasia of the inner lining of the vascular grafts. The atherosclerotic disease of the grafts is characterized by adipose infiltration at the sites of intimal hyperplasia. Indicatively 12% of the vein grafts are occluded within 1 year, 25% within 5 years and 50% within 12 years following surgery. [5], [6] This contributes to the fact that 3% of the patients after undergoing a by-pass surgery require re-surgery in 5 years, 10% in 10 years and 25% in 20 years after the surgery. [7]

Arterial grafts started being systematically used in the 70's. The focus was on the internal mammary artery, which presents great biological properties:

1. Endothelial cells release of nitric oxide (NO), which has vasodilator action and also prevents the accumulation of platelets, the adhesion of neurophils and chemotaxis. NO prevents directly the development of smooth muscle fibers related to the intimal hyperplasia. [8]
2. The protective action of "vasa vasorum"
3. Increased prostacyclin production.
4. Maintenance of the inner elastic layer, which prevents the migration of the smooth muscle cells.
5. The internal mammary artery has a thin middle layer with a few smooth muscle cells, which seem to reduce infiltration in response to the growth factor produced by platelets.

For all these reasons, the internal mammary artery, contrary to other vascular grafts, is not affected by intimal hyperplasia.

IMA's attrition rate compared to the saphenous vein is given in the following table:

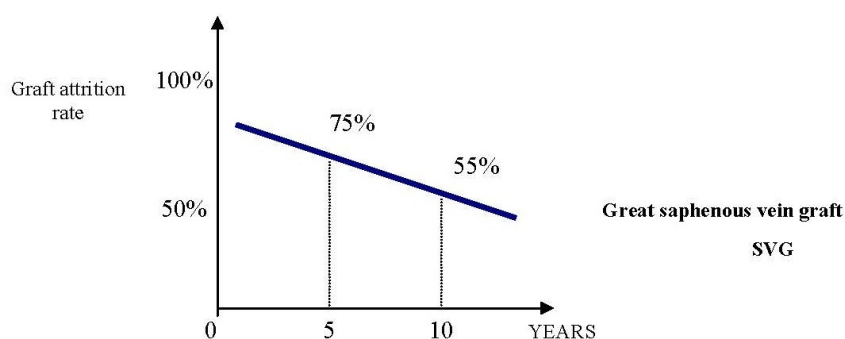
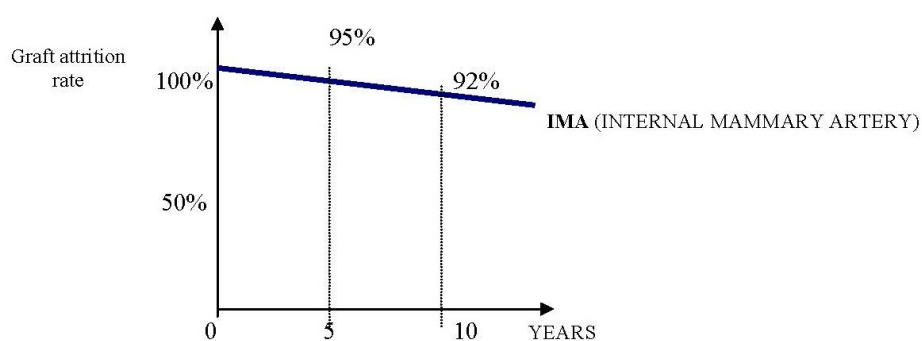


Table 3. IMA and SVG attrition rate over 10 year period

It was only a decade after the systematic use of the internal mammary artery and specifically in 1986 that a benchmark publication came from the Cleveland Clinic [9]: In an extensive retrospective study they compared the clinical outcomes and angiography findings of 2306 patients who received single internal mammary artery (IMA) graft on the left anterior descending artery (LAD) with additional vein grafts and 3265 patients who received only vein grafts. The mean follow-up time was 8.7 years. It was found that patients on whom the internal mammary artery had been used as a graft had lower perioperative mortality rates, less re-surgery rates, smaller chances of recurrent angina or infraction and higher 10-year survival.

A second study followed, by Acinapura et al [10] in which 2100 patients were followed-up for 5 years. The study showed that:

	Patency	Recurrent angina	Re-syrgery
Internal mammary artery	96%	18%	0.5%
Vein graft	67%	31	6.3

Table 4.

Ten-year mortality rate was 10% for the IMA group and 22% for the vein grafts group.

On the same grounds, Cameron and colleagues [11] compared 479 patients with single internal mammary artery graft to 4888 patients with solely vein grafts over a period of more than 15 years. They showed that the use of a single internal mammary artery graft was an independent prognosis factor that promoted survival, especially in older patient, with a reduced LV function.

Conclusively, the use of the internal mammary artery on the anterior descending branch is indicated irrespectively to the age and to the ejection fraction. Moreover, the use of the IMA in patients with a low ejection fraction improves long-term survival.

Because of the ostensible biological similarity of the left and right internal mammary artery, many were those who believed that the use of the two internal mammary arteries as grafts could yield additional benefits.

The patency of the 2 internal mammary (left & right) artery grafts is over 90% in 10 years. The reasonable question posed is: "Why don't we use more arterial grafts during a by-pass surgery?"

Let's answer through a short review of the recent literature:

1. Calafiore [12] from Italy showed 99% patency of the 2 internal mammary arteries as shown in angiographies, at 18 months.
2. Accola et al [13] showed that in young patients, BIMAS could be safely used without putting them at higher risk of perioperative morbidity or mortality.

3. A Belgian study [14] showed 97% patency of the 2 internal mammary arteries as shown in angiographies in 161 patients at 7.5 years after by-pass.
4. Buxton [15] analyzed 962 patients and found that the patency of the right internal mammary artery is better when used for left coronary by-pass. Moreover, he underlined that arterial grafts shall by-pass a coronary artery with stenosis over 90% (to avoid the risk of competitive flow). Passing the RITA to the left, either anterior to the aorta or through the transverse sinus, did not influence patency
5. The same conclusions, meaning the use of the BIMAS on the left coronary system, were reached in a study by Schmidt [16].
6. B. Lytle [17] from Cleveland showed that the use of 2 internal mammary grafts is better than the use of a single mammary artery, regarding longer survival and lower re-surgery & recurrent angina or infraction rates. In addition, the study mentions that the benefit of the second internal mammary artery is evident 12 years after by-pass and offers a cumulative benefit. In patients with diabetes and those with a low LV ejection fraction the study showed even greater benefit regarding survival.
7. The BIMA shows no benefits in the first 4 years, however after 15 years occurrence of recurrent angina is decreased from 36% to 27%. [18]
8. Finally, the statistically strongest study comes from Oxford [19]. It is an extensive meta-analysis of seven studies. Taggard et al compared 11,200 patients with a single internal mammary artery graft versus 4,700 patients with BIMA. This study as well reached the same conclusions and showed prolonged survival when BIMA grafts were used.

Finally, it shall be underlined that all the above studies are retrospective and no prospective control studies exist till now for the single internal mammary VS the bilateral internal mammary grafting.

3. The radial artery

The fact that radial artery grafts were patent for over 18 years after surgery [20] has been the basis to re-recruit the RA (radial artery) as a graft for CABG. There is low in situ atherosclerosis incidence for this artery, however the thickened middle lining, with the abundant cells of smooth muscle fibers (contrary to the internal mammary artery) increased intimal hyperplasia of this vessel.

Angiography studies of middle time duration showed 90% patency rate in 1 year [21], 83% in 5 years [22] and over 80% in 8 years.

Although these results are encouraging, the databases should be interpreted with caution. The majority of the studies are retrospective analyses and the rate of the grafts used for follow-up via angiography varies in these studies. The recent study by Possati [23] with 92% angiographic follow-up for over 8 years, contains the most well-documented database to this day.

Two prospective randomized control studies comparing the radial artery (RA) to other grafts by means of a full angiographic follow-up are the RAPS [24] (Radial Artery Patency Study) and RSVP (Radial artery versus Saphenous Vein Patency Study) and are still in progress.

The RAPCO (Radial Artery Patency and Clinical Outcome) [25] is a prospective randomized study that compares the radial artery (RA) to grafts from the great saphenous vein and the free grafts from the right internal mammary artery. All patients received grafts from the LIMA to the LAD and then they were randomized and received either the radial artery or the right internal mammary artery on a second target in patients less than 70 years old and either the radial artery or the great saphenous vein (again within a second target) in patients aged over 70.

The 5year angiographic patency of the radial artery and the right internal mammary artery was 95 and 100% respectively, and of the saphenous vein and the radial artery it was 87% and 94% respectively.

4. Problems related to the radial artery

The tendency for vasospasm is due to the thick muscle wall of the vessel. Prevention is achieved by fine handling and the use of focal agents during denudation (papaverine / phenoxybenzamine solutions) followed by amlodipine 5mg x 1 for one year after surgery.

5. The disadvantages of arterial grafts

The sternum infection rates when using BIMA grafts is vastly variable. Lytle reports 2.5% incidence of inflammation of the sternotomy incision when using bilateral internal mammary arteries compared to 1.4% in the group of single internal mammary artery graft. [26] Grossi and colleagues [27] published an increase of the incidence of inflammation of the sternal incision when factor 2 exists and a lot higher rate of chances, increased by 13.9% when there is concurrent diabetes. Kouchoukos [28] published that other risk factors showing an increase of the inflammation are obesity, severe chronic obstructive pulmonary disease and prolonged mechanical ventilation.

Arterial grafts shall be avoided in patients with chronic renal dysfunction and those undergoing dialysis (Steal syndrome from the AV fistula, limited survival due to dialysis).

Matsa [29] suggests the use of a skeletonized internal mammary artery (as this technique protects the collateral sternal blood flow). He argues that the complication rate of the sternal incision was the same in diabetic patients and in non-diabetic patients.

The competitive flow is the causal factor for the "string sign" which is rarely observed in arterial grafts. It had been reported when the vessel to be by-passed had not high grade stenosis. Thus, in order to avoid the competitive flow, arterial grafts are usually used only when stenosis is over 90%.

ARTERIAL GRAFTS PATENCY	5 year patency	10 year patency
LITA →LAD	95%	90%
LITA→ other than LAD	90%	80%
RITA→RCA	90%	80%
RITA→LAD	95%	" />90%
Free ITA grafts	90%,	" />80%
Radial artery	80%	70-80%
Right gastroepiploic artery	80%	63%

Table 5. Patency of various arterial grafts over time

6. Studies on total arterial revascularization (tar)

Tavilla et al [30] reported on the 10 year follow-up of 201 CABGs in three-vessel disease using exclusively pedicled bilateral internal thoracic and right gastroepiploic arteries. Ten-year actuarial survival was 87%. The actuarial freedom from angina was 97% and 86% at 5 and 10 years respectively. None of the patients needed a repeat surgical revascularization after leaving the hospital, whereas 9 (5%) patients underwent a percutaneous transluminal coronary angioplasty. At 5 years 86% and at 10 years 69% of the patients remained free of any cardiac-related event.

Nishida [31] reported on total arterial revascularization on 239 patients with the only use of BIMAs and the right gastroepiploic artery (RGEA). ITA grafts were harvested by using the skeletonization technique. Sequential grafting was performed in 64 patients; One patient (0.4%) died of mediastinitis. Graft patency was confirmed angiographically in 230 patients (96%) 2 to 3 weeks after surgery. The patency rate was 97.1% for the left ITA, 99.6% for the right ITA, and 95.5% for the RGEA. Five-year actuarial survival rate was 92.9%, and the cardiac death-free rate was 97.8%.

Finally in a prospective randomized trial on total arterial revascularization, Muneretto et al [32] conducted a TAR study with the use of LIMA in patients over 70 years old. Follow-up was performed at 15 months, and it showed higher arterial patency and freedom from ischemic attacks in the TAR group.

Recommendation for the use of BIMA

In young patients (less than 65 years old)

- not obese and diabetic at the same time
- angiography has shown proper coronary disease (stenosis \geq 90%)

Bilateral IMAs shall go to the left system

Contraindications

- Emergencies
 - Chronic renal dysfunction requiring dialysis
 - Peripheral vascular disease and carotid stenosis
 - Chronic obstructive pulmonary disease
-

Table 6. Indications and Contraindications for the use of BIMA

7. Conclusion

Experience regarding the preference of use of bilateral internal mammary arteries as grafts is growing big. However, despite the fact that the evidences are compelling, the absence of prospective randomization makes them vulnerable to criticism.

The use of bilateral internal mammary arteries can be conducted safely. It can offer long-term symptomatic improvement and also improve survival. Surprisingly, multiple arterial conduits are used in <15% of patients undergoing a CABG, and the radial artery is the most common choice for the second arterial conduit.

The lack of robust protocols for using BITA grafting, contributes to the variations in practises amongst surgeons. Quidelines for BIMA usage, including variables such as age, the type of diabetes, obesity, LV function and the suitability of the coronary anatomy would emergence in the future. More specifically a possible scoring system taking into consideration Syntax score and EuroSCORE maybe able to become a quide for BIMA utilization and that may overcome the difficulty for surgeons to extend the use of BIMA.

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