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Review

Bilateral internal mammary artery grafting in obese: Outcomes, concerns and controversies

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HIGHLIGHTS

- The relationship between obesity and coronary artery disease is presented.
- The impact of obesity on outcomes after CABG is discussed.
- The pros and cons and outcomes of BIMA grafting in obese patients are presented.

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ABSTRACT

Obese patients are generally considered unsuitable to receive bilateral internal mammary arteries (BIMA) during coronary artery bypass grafting (CABG) due to the perceived vulnerability to sternal wound infection and lack of evidence supporting long-term survival benefit. However, no consistent evidence currently discourages the use of BIMA in obese patients. The present review questions the common perception that obesity unacceptably increases the risk of sternal wound complications in patients receiving BIMA grafting. Moreover, the use of skeletonization harvesting technique is expected to further minimize such a risk. Our institutional experience confirmed that BIMA grafting is a safe strategy which does not increase operative mortality and does not significantly affect the incidence of sternal wound complications. On the other hand, a long term benefit in terms of overall survival and freedom from repeat revascularization from the use of BIMA was found.

1. Background

Obesity is an increasing public health issue in the United States (US) and in western countries. Obesity is defined by National Institute of Health as a body mass index (BMI) $\geq$30 kg/m^2. By these criteria, in 1960 approximately one in every ten Americans was obese, a number which has since tripled. Perhaps most concerning, morbid obesity (defined as $\geq$40 kg/m^2) has increased in prevalence from 1% of the population to 6% [1,2]. The importance of obesity as a public health problem is difficult to underestimate; by some accounts it is destined to overtake smoking as the leading cause of preventable death in western countries and it may halt the improvements in life expectancy at a national level according to the World Health Organization. Accordingly the prevalence of obesity nearly doubled from 1980 to 2008, with more than 1.4 billion adults being overweight and more than half a billion obese [3]. At least 2.8 million people die annually as a result of being overweight or obese [4].

2. Obesity and coronary artery disease

Obesity is associated with a host of cardiovascular risk factors and it is associated with a 3-fold increased risk of coronary artery disease (CAD) [5]. While in all likelihood obesity is a risk factor for CAD in itself, it is most importantly associated with a cluster of conditions that contribute directly and indirectly to the development and progression of CAD [6]. Obesity is associated with insulin resistance and type 2 diabetes mellitus, through dietary indiscretion and endocrine activity of adipose tissue [6]. Central adiposity, has been associated with elevated levels of circulating

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proinflammatory cytokines [7], most notably interleukin 6 (produced by adipocytes) which stimulates platelet activity and secretion of C-reactive protein which enhances insulin resistance [8,9]. Furthermore, prevalence of arterial hypertension, another risk factor for CAD, is elevated in obesity not only due to the endocrine effect but also due to increased circulating blood volume and total peripheral resistance [10,11]. Higher BMI is associated with dyslipidemia, including low levels of high density lipoprotein cholesterol (HDL-C) and high levels of triglycerides (TGs) and higher levels of small, dense, atherogenic low density lipoprotein cholesterol [12–14]. Accordingly a reduction in body weight and in mean body mass index showed to positively affect patients lipid profile, type 2 diabetes, sleep apnea, arterial blood pressure as well as to reduce left ventricular mass [15].

Finally, obesity is associated with psychological stress, which in itself is an independent risk factor for CAD [16].

3. Coronary artery bypass grafting in obese patients

As a consequence of high incidence of CAD in patients with increased BMI, a large number of obese patients are referred for CABG nowadays. In the past obese patients have traditionally been considered at higher risk of perioperative morbidity and mortality after CABG, and, occasionally, they have not even been considered suitable for surgery solely because of their obese status. In contrast there are only sporadic past series confirming this hypothesis. Lindhout et al. [17] comparing 924 patients with BMI <30 and 206 patients with BMI ≥30 reported a hospital mortality rate of 3.4% and 1% respectively. Kuduvalli et al. [18] reported on 3429 patients with BMI <30 and 1284 patients with BMI ≥30 undergoing CABG and found an operative mortality rate of 1.6% group and 2.1% respectively.

On the other hand, recent surgical series have challenged the notion that obesity is per se a risk factor for operative mortality after CABG (Table 1). A retrospective analysis by Engel et al. [19] on 10,590 patients undergoing CABG reported comparable 30 day mortality rate among normal weight or overweight (BMI<30) and obese (BMI ≥30) group (2.3% and 2.03%). Van Straten et al. [20] found that 30 day mortality was 2.3% and 2.4% in 8120 patients with BMI<30 and 2010 patients with BMI ≥30 respectively after CABG. Finally we previously reported that early mortality was not affected by obesity regardless of the patients' risk profile in a group of 9931 patients with BMI <30 and 3821 patients with BMI ≥30 (2.58% and 2.20% respectively) [21].

Moreover, some studies showed obese patients to be associated with a trend toward lower in-hospital mortality when compared to normal weight patients. Reeves et al. [22] reported a mortality rate of 0.86% versus 0.99% in 3336 patients with BMI <30 and 903 patients with BMI ≥30. The study of Stamou et al. on a population composed by 1521 patients with BMI <30 and 965 patient with BMI ≥30 found an operative mortality rate of 4.67% and 2.70% respectively [23]. However, the apparent protective effect of obesity on early mortality is most likely related with a better overall risk profile of obese patients including younger age [21].

However, long term results of CABG in obese patients have been reported to be still unsatisfactory. In the Bypass Angioplasty Revascularization Investigation trial [24] 5-year mortality progressively increased by up to fivefold with greater obesity, with an adjusted risk ratio (RR) of 1.0 for normal weight group, 1.52 for obese with BMI between 30 and 35 and 1.73 for obese with BMI ≥35. In the study by Kuduvalli et al. [18], the four years mortality rate was 6.9% in normal weight group and 7.2% in obese group. Finally, we previously reported that patients with BMI ≥30 had a higher risk of late death compared to normal weight subjects (hazard ratio, 1.22; 95%CI, 1.07–2.66; P = 0.006).

4. Reason for poorer outcomes after CABG in obese patients

The poorer outcomes in obese patients are probably due their accelerated atherosclerotic graft disease. Wee et al. examined the relationship between obesity and progression of graft atherosclerosis among 1314 patients enrolled in the Post Coronary Artery Bypass Graft Clinical Trial (post CABG). They found that a higher BMI was associated with a higher likelihood of angiographic progression [24]. Substantial progression of atherosclerosis in vein grafts might partially explain the higher incidence of subsequent cardiovascular events in obese patients [25].

5. Improving CABG results using BIMA

The use of a second internal mammary artery (IMA) over saphenous vein grafts (SVG) has been proposed to overcome the unsatisfactory patency rate of SVG [26,27]. According to the literature, 90% of internal thoracic arteries remain patent at 10 years after surgery, while only 50% of SV graft remain patent [28,29].

In the study by Tatoulis et al. with 5766 patients undergoing right internal thoracic artery (RIMA), the overall ten-year RIMA patency is 90% whereas the SVG patency is 50.7% [30]. Moreover, the use of the secondary IMA has been associated with improved clinical outcomes including better overall late survival [31].

The angiographic superiority of RIMA over SVG has been related to its reduced susceptibility to atherosclerosis. Its striking resistance to the development of atherosclerosis can be attributed to many factors: structurally its endothelial layer shows fewer fenestrations, lower intercellular junction permeability, greater antithrombotic molecules such as heparin sulfate and tissue plasminogen activator, and higher endothelial nitric oxide production, which are some of the unique ways that make the IMA impervious to the transfer of lipoproteins, which are responsible for the development of atherosclerosis [32–42]. Finally, surgical techniques may positively as well as negatively affect the patency of IMA and SVG thus playing a major role in graft failure after coronary bypass surgery [43,44].

Table 1
Impact of obesity on in-hospital mortality and incidence of deep sternal wound infection in observation studies.

Authors	Year	Country	N patients BMI <30	N patients BMI ≥30	Operative mortality rate BMI <30	Operative mortality rate BMI ≥30	DSWI BMI <30	DSWI BMI ≥30
Benedetto [20]	2013	UK	9931	4032	2.20%	2.58%	uk	uk
Stamou [22]	2011	USA	1521	965	4.67%	2.7%	0.6%	1.2%
Van Straten [19]	2010	USA	8120	2010	2.3%	2.4%	uk	uk
Engel [18]	2009	USA	6172	4418	2.3%	2.03%	0.2%	0.2%
Lindhout [16]	2004	NL	206	924	1%	3.4%	8.3%	4.4%
Reeves [21]	2003	UK	3336	903	0.86%	0.99%	0.71%	0.66%
Kuduvalli [17]	2002	UK	3429	1284	1.6%	2.1%	uk	uk

DSWI: deep sternal wound infection; BMI: Body mass index, uk: unknown.

6. Evidence and concerns in using BIMA in obese patients

The advantage from the use of a secondary IMA over SVG is anticipated to be more pronounced in obese patients as a consequence of their accelerated atherogenic graft disease [25,45]. However, surgeons continue to be reluctant to perform bilateral internal mammary artery (BIMA) grafting in obese patients and the use of BIMA in obese patients has not been previously investigated.

The main reason for underutilization of BIMA in obese patients is the potential additive effect of BIMA harvesting and obesity in increasing the vulnerability to deep sternal wound infection (DSWI) [46,47,48].

Interestingly, despite the common perception that obesity might represent a major risk for sternal wound complication, the current evidence is still controversial.

Stamou et al. [23] reported a DWSI rate of 0.4% in group with BMI <30 and 0.8% in group with BMI ≥30 patient. Engel et al. [19] found DSWI rate of 0.2% and 0.2% in patients with BMI <30 and BMI ≥30 respectively. Reeves et al. [22] showed a similar DSWI incidence of 5.4% and 4.5% in subjects with BMI <30 and BMI ≥30 respectively.

On the other hand, BIMA harvesting has been reported to increase the risk of sternal wound complications including DSWI. However the evidence is still limited by paucity of randomized studies available. Early outcomes of Arterial Revascularization Trial have been recently reported [49]. A total of 1548 patients were randomized to receive BIMA and 1554 patients received singular internal mammary artery grafting (SIMA). Authors found a trend towards an increased rate of sternal wound reconstruction in BIMA group (1.9% and 0.6%). It should be underlined that authors did not provide the definition of sternal wound reconstruction which might be influenced by technical aspect in sternotomy closure such as experience of performing surgeon (trainee versus attendant surgeon). Moreover, no information was reported on the harvesting technique in the two groups which may influence the incidence of sternal wound complication. Finally, the recommended classification of sternal wound complication as defined by the Centers for Disease Control and Prevention [50] was not adopted in this trial. On the other hand, conflicting results have been reported by observational studies investigating the impact of BIMA harvesting on sternal wound infection. Gansera and colleagues [51] compared 4462 patients receiving BIMA with 4204 patients receiving SIMA bypass and they found a higher rate of DSWI in BIMA than in SIMA group (0.7% vs 0.2%; respectively). Elmistekawy and colleagues [52] compared 3581 patients receiving SIMA grafting with 359 patients receiving BIMA grafting and they reported a DSWI rate of 1.3% and 3.1% respectively and a rate of superficial SWI of 2.2% and 5.6% respectively.

In the study by Walkes et al. [53], 158 patients undergoing BIMA grafting were compared to 911 patients having SIMA bypass. Authors reported a rate of mediastinitis of 4.4% and 2.2% in the BIMA and SIMA group.

Puska et al. [54] compared the outcomes of 812 patients undergoing BIMA grafting and 2715 patients undergoing SIMA grafting, reporting a similar rate of DSWI (1.2% vs 1.0% respectively). Grau et al. [55] compared 928 undergoing BIMA grafting to 928 patients undergoing SIMA grafting, reporting a DSWI rate of 0.3% in both groups. Galbut et al. [56] compared 1137 BIMA patients to 1137 SIMA patients and they found that DSWI rate was 1.5% and 1.1% in BIMA and SIMA groups respectively. Loannidis et al. [45] reported on 867 patients undergoing BIMA grafting and 930 patients undergoing SIMA grafting. DSWI rate was 1.3% and 0.4% in the BIMA and SIMA group respectively. Kelly et al. [57] compared 1079 patients undergoing BIMA grafting and 6554 patients undergoing SIMA grafting. Overall DSWI rate was 1.2% in the BIMA group and 0.7% in the SIMA group. Finally Stevens et al. [58] reported a DSWI rate of 1.4% and 1.2% in the BIMA and SIMA groups respectively.

Moreover in a recent report from 1,526,360 patients from the US Nationwide Inpatient Sample who underwent isolated CABG, BIMA grafting was associated with increased risk of DSWI only in patients with severe, chronic diabetes but not in obese patients [59].

On the other hand, it is well known that harvesting technique may have a major impact on sternal wound complications in patients receiving BIMA grafting. Skeletonized BIMA harvesting may reduce the potential vulnerability of obese patients to deep sternal wound infection when BIMA grafting is used. In fact, dividing the collateral branches with hemostatic clips and scissors, this technique enables maintenance of collateral perfusion from the intercostal or the muscular branches, likely being useful to prevent sternal infections [60]. A recent meta-analysis by Dai et al. [61] on 32 observational studies showed that the risk of DSWI in the BIMA group was higher than in the SIMA group (relative risk [RR] 0.62, 95% confidence interval [CI] 0.55–0.71). However, lack of randomized comparison still precludes final conclusion on the size of the effect of BIMA harvesting technique on sternal wound outcomes.

7. Current results for BIMA usage in obese patients

To date no previous studies focused on the impact of BIMA grafting on early and late outcomes in obese patients. We recently reported our institutional experience of BIMA grafting in obese patients [62]. From April 2001 to May 2013 a total of 1522 obese patients received CABG. Of those, using BIMA (n = 229, 15.0%) or SIMA (n = 1293, 85.0%). In the BIMA group the RIMA was used as in situ retrosternal conduit to the left anterior descending artery (LAD) in 135 cases (in these cases, the left internal mammary artery was used as in-situ conduit to graft the diagonal branch in 11 cases and the circumflex territory in 124), as in-situ retroaortic conduit to the circumflex territory in 61 cases, as Y graft to the circumflex territory in 21 cases, to graft to the right coronary artery in 12 cases (6 cases in situ conduit, 6 cases as free conduit). A total of 145/229(63%) patients in the BIMA group received at least a SVG. BIMAs were harvested as skeletonized conduits in 100/229 (43%).

After propensity score matching we found that operative mortality (within 30 days) occurred in 3 (1.3%) and 4 (1.7%) subjects in the matched BIMA and SIMA groups respectively (P = 1). DSWI occurred in 6 (2.6%) and 2 (0.9%) patients in the BIMA and SIMA group respectively (P = 0.2). Among BIMA patients, DSWI occurred in 2/100(2.0%) patients receiving skeletonized BIMAs and 4/129 (3.1%) patients receiving pedicled BIMAs (P = 0.6). After a median follow-up of 4.5 ± 3.3 years. Survival probability was 97.7% ± 1.0 versus 93.2 ± 1.8 at 5 years, and 97.7 ± 1.0 versus 92.1 ± 2.1 at 10 years in the BIMA and the SIMA groups respectively. Compared to SIMA, the use of BIMAs was associated with a significantly lower late mortality rate (Hazard Ratio [HR] 0.35; 95% confidence interval (CI) 0.13–0.97; P = 0.03). Repeat revascularization free survival probability was 93.6% ± 1.7 versus 86.6 ± 2.5 at 5 years and 93.6 ± 1.7 versus 78.9 ± 4.1 at 10 year in the BIMA and the SIMA groups respectively. Compared to SIMA, the use of BIMAs was associated with a significantly lower need for repeat revascularization (HR 0.45; 95%CI 0.23–0.85; P = 0.01).

8. Conclusions

Current evidence for BIMA grafting in obese patients is limited. However, available retrospective series confirmed that the adoption of BIMA grafting in obese patients may be safe and effective. Surprisingly, no consistent evidence confirms the perceived vulnerability to sternal wound infection currently from BIMA usage in obese patients. Moreover, obese patients should be considered a subgroup which more likely benefits from BIMA grafting. However, there is an urgent need for further studies particularly randomized controlled trials with long-term clinical and angiographic follow-up to confirm the benefit from BIMA usage in obese patients.

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Conflict of interest

None.

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