



## 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.

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## 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<sup>2</sup>. 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<sup>2</sup>) 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 anti-thrombotic 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.

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