Current perspectives

Is obesity still a risk factor for patients undergoing coronary surgery?

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Historically, cardiologists and surgeons have considered obesity as a risk factor for mortality and morbidity during cardiac surgery. This factor has in fact been included in the Parsonnet score, one of the first risk stratification systems. This has led to an under-representation of obese patients with severe ischemic heart disease in the surgical population.

A review of the recent literature seems to suggest that obesity is not any longer a risk factor for mortality and morbidity following coronary revascularization. Indeed, obesity is not included in the EuroSCORE, a more recent risk stratification system. Further evidence suggests that the use of off-pump coronary surgery in these patients is associated with a reduced in-hospital mortality and morbidity when compared with conventional coronary surgery with cardiopulmonary bypass and cardioplegic arrest.

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Introduction

Over recent decades the improvement of socio-economic conditions has led to an expansion of the overweight population worldwide. This has been primarily evident in the United States, where by 2000 about 20% of the adult population was obese[1]. European countries are now following the same trend and the prevalence of obesity is increasing rapidly in all age groups.

The American Heart Association recognizes obesity as a major risk factor for coronary artery disease[2,3]. Obesity has been associated with an increased incidence of hypertension, dyslipidemia, type 2 diabetes, stroke, gallbladder disease, osteoarthritis, sleep apnea and respiratory problems, and endometrial, breast, prostate, and colon cancers (Fig. 1)[1].

Historically, cardiologists and surgeons have considered obesity as a risk factor for mortality and morbidity during cardiac surgery and other major surgical procedures[4,5]. Rightly or wrongly, this has led to an under-representation of obese patients with severe ischemic heart disease in the surgical population and this still influences modern decision-making processes[1]. This review discusses the available evidence on obesity as a risk factor for mortality and morbidity following coronary artery bypass graft (CABG) surgery.

Historical perspective

In the early ’80s obesity was considered an independent risk factor for patients undergoing coronary surgery as highlighted by its inclusion among a list of predefined factors used to preoperatively predict the surgical risk associated with the procedure. Indeed, obesity was included in the Parsonnet score system[5], which is still used in many developed countries, and in other systems of risk classification in cardiac surgery[6]. This perception was supported by the findings of several studies[7-9] associating obesity with an increased in-hospital morbidity and mortality. The analysis of the Society of Thoracic Surgeons National Cardiac Surgery Database suggested that obesity was an independent predictor of increased operative mortality in patients undergoing coronary surgery[7]. Wilson et al.[8], in a series of 517 patients, reported obesity as the principal risk factor predisposing to wound infection. Similar results were reported by Shuhaiber et al.[9], who found that the incidence of wound infection was 3 times higher in obese patients undergoing cardiac surgery. Others associated obesity with a higher incidence of respiratory complications and a prolonged ventilation time[10].

In r<etrospect, it is difficult to ascertain whether the importance of overweight and obesity in determining a poor clinical out-

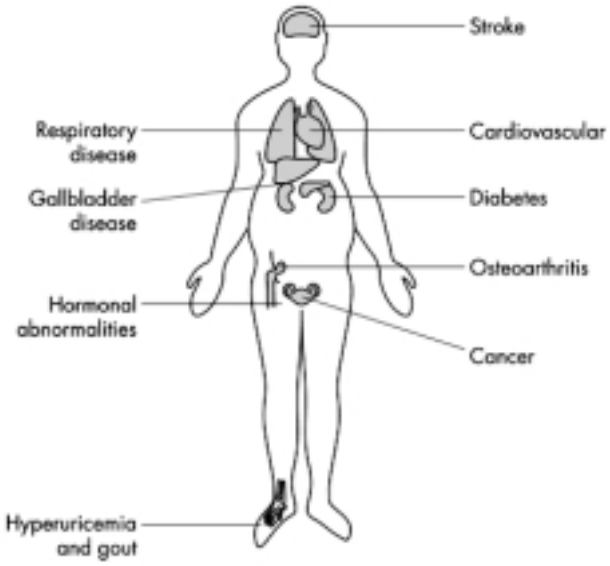

Figure 1. *Physical effects of obesity. Adapted from Campbell[1], with permission.*

come has been misjudged. In the early '80s perfusion, anesthetic and surgical techniques were quite different from those employed nowadays. Hypothermic systemic cardiopulmonary bypass temperature and cold crystalloid cardioplegia for myocardial protection, which have been shown to be inferior to the most recent techniques[11,12], might in part be responsible for the poor clinical outcome.

The historical perception of obesity as a risk factor has also influenced the decision-making process regarding the type of conduit to be used for coronary grafting. Mammary artery grafts have been shown to achieve a better long-term patency than saphenous vein grafts, and their continued use, even bilaterally, is encouraged[13]. However, the perception of obesity as a risk factor for wound infection in patients undergoing bilateral mammary artery harvesting, has limited its use. Hazelrigg et al.[14] studied in the late '80s the relationship between sternal wound infection and internal mammary grafting in a logistic regression analysis of a series of 2582 patients (726 undergoing bilateral mammary artery grafting). They found that bilateral mammary grafting was associated with an increased incidence of wound complications in patients with concomitant pneumonia, obesity, re-exploration, use of the intra-aortic balloon pump or diabetes. Yet this study did not take into account a variety of other patient-, anesthetic-, and surgical-related factors, which have more recently been linked to wound infection[15].

Current perspective

Over the last years the view that obesity is a risk factor in cardiac surgery has been challenged by evidence suggesting that these patients do not present with more complications when compared to norm-weight patients. Christakis et al.[16], in a retrospective study on a population of 7025 patients, showed that gender, but not body mass index (BMI), was a significant independent predictor of operative mortality and low-output syndrome, after adjusting for other preoperative risk variables. Similar results were obtained by Brandt et al.[17] who concluded that severe obesity did not necessarily adversely affect perioperative mortality and morbidity and by Moulton et al.[18] who, in a series of 2299 patients analyzed with a multivariate logistic regression model, found that with the exception of superficial wound infection and atrial dysrhythmias, obesity was not a risk factor for an adverse outcome. It is notable that obesity is neither included in the more recent EuroSCORE risk stratification method[19] nor in the New Zealand priority scoring system[20]. On the other hand, Prasad et al.[21], in a comparison of 250 obese patients vs 250 age- and sex-matched controls with a normal BMI, found obesity to be an independent risk factor for perioperative morbidity. On the same lines, Engelman et al.[22] reported that a BMI > 30 kg/m^2 was associated with an increased incidence of deep sternal wound infection, saphenous vein harvest site infection, and atrial arrhythmias.

More recently, we investigated the impact of body size on the early and late clinical outcomes in a concurrent cohort study of 4372 consecutive patients undergoing CABG[23]. Main outcomes were early death, perioperative myocardial infarction, infective, respiratory, renal and neurological complications, transfusion, duration of ventilation, intensive care unit and hospital stay. Multivariable analyses compared the risk of outcomes between five different BMI groups after adjusting for casemix. The five groups included: 3.0% underweight (BMI < 20 kg/m^2), 26.7% normal weight (BMI ≥ 20 and < 25 kg/m^2), 49.7% overweight (BMI ≥ 25 and < 30 kg/m^2), 17.1% obese (BMI ≥ 30 and < 35 kg/m^2) and 3.6% severely obese (BMI ≥ 35 kg/m^2). Compared to the normal weight, overweight and obese groups included more women, diabetics and hypertensives, but fewer patients with severe ischemic heart disease and a poor ventricular function. Similar findings were observed in other studies[16,18,24]. Underweight patients were more likely to die in hospital (odds ratio-OR 4.0, 95% confidence interval-CI 1.4 to 11.1), have a renal complication (OR 1.9, 95% CI 1.0 to 3.7) or stay in hospital longer > 7 days (OR 1.7, 95% CI 1.1 to 2.5). Overweight, obese and severely obese patients were not at a higher risk of adverse outcomes, and were less likely to require transfusion (ORs from 0.42 to 0.86).

Other studies have also found major imbalances in the distribution of the extent of coronary disease and comorbidity among BMI groups, with almost every one finding obese patients undergoing CABG/cardiac surgery to be younger, on average, than non-obese patients[16,18,24].

Obesity and off-pump coronary surgery

The advent of beating heart coronary surgery has heralded one of the greatest changes in the long history of coronary surgery[25-30]. Its potential of minimizing the incidence of morbidity due to the avoidance of cardiopulmonary bypass and cardioplegic arrest might satisfy the continuously requested improvements in high-risk patient treatment, reduction of costs and resources while maintaining quality of care.

In two recent randomized controlled trials, we demonstrated that performing coronary surgery on the beating heart without the extracorporeal circulation reduces in-hospital morbidity in elective patients[25,26]. The use of a high quality prospective database at our institution also created the opportunity to evaluate the effectiveness of this technique in overweight patients using a cohort study design[27]. The definition of overweight was based on BMI, since it is the body size measurement that best correlates with the body fat content[31]. Patients with a BMI ≥ 25 kg/m^2 were classified as overweight as specified by the American Heart Association guidelines[2]. To take account of imbalances in prognostic factors, propensity scores were calculated to estimate the probability of allocation to on-pump or off-pump groups, as predicted by all the known characteristics of the entire cohort of obese patients. Finally, multivariable comparisons were carried out using multiple logistic regression. A total of 2844 patients with a BMI ≥ 25 kg/m^2 underwent CABG (674 off-pump, 23.7%) with an increase in the proportion of off-pump surgery during the study period (Fig. 2)[27]. After adjustment for prognostic variables, the ORs for many of the adverse outcomes investigated still indicated significant benefit of off-pump surgery (point estimates of ORs 0.35 to 0.79, $p < 0.05$), i.e. hospital deaths, neurological complications, transfusion requirement, postoperative hemoglobin, intensive care unit and hospital length of stay (Table I)[27]. The magnitude of the differences between groups in terms of in-hospital morbidity was quite striking, with the odds of some outcomes being reduced by more than half and the odds of several other outcomes by one third to one half.

Our explanations for such impressive findings are that first, the greater inflammatory activation and subsystem organ dysfunction observed in elective patients undergoing on-pump surgery as compared to off-pump coronary surgery[28-30] may be even more pronounced in overweight patients. Secondly, obesity has been shown to be independently associated with coronary endothelial dysfunction even in patients with normal or mildly diseased coronary arteries[32]. This dysfunction may be amplified by the cardiopulmonary bypass-related inflammatory response[33-35]. Thirdly, the increased hemodilution associated with conventional on-pump coronary surgery and the resultant greater oncotic pressure gradient may favor fluid extravasation, which increases the likelihood of postoperative lung edema with deleterious effects on lung mechanisms and tissue oxygenation[36].

Summary and clinical implications

Obesity is often considered to be a risk factor for perioperative morbidity and mortality with cardiac surgery and other major surgical procedures despite controversial evidence in the literature.

The under-representation of obese patients in the current surgical population remains unexplained. Rejection of some obese patients for surgery would be consistent with the findings of the Appropriateness of Coronary Revascularization study, which indicated that coronary revascularization is under-used in the UK[37].

There are at least three possible reasons why obesity is still considered as an important risk factor for morbidity following CABG: 1) the "power" and influence of analyses from national databases and perceived

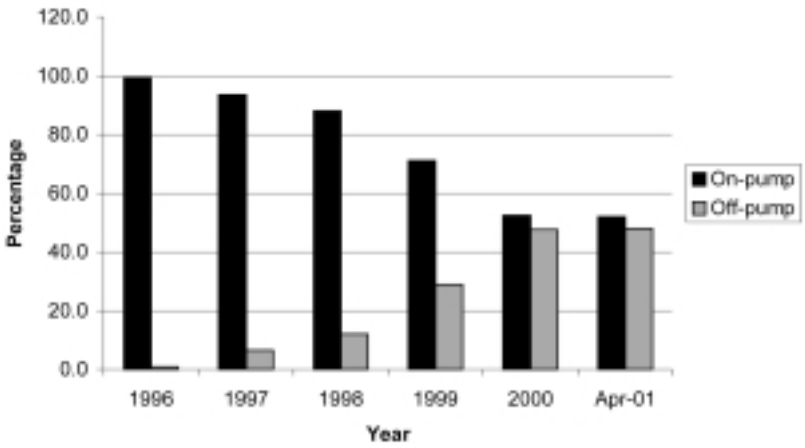

Figure 2. *Percentage of overweight patients (body mass index ≥ 25 kg/m^2) distributed by year. Adapted from Ascione et al.[27], with permission.*

Table I. Effect of off-pump vs on-pump surgery on postoperative outcome; unadjusted and adjusted effect sizes.

Outcome	Unadjusted effect size*			Adjusted effect size§°#		
	OR**	95% CI	p	OR**	95% CI	p
Deaths	0.34#	0.16 to 0.71	0.004	0.37§#	0.18 to 0.77	0.008
Myocardial infarction	1.23	0.58 to 2.58	0.59	2.29§	0.91 to 5.76	0.08
Inotrope support	0.63	0.51 to 0.78	< 0.001	0.81°	0.63 to 1.03	0.08
Intra-aortic balloon pump	0.37	0.14 to 1.01	0.05	0.39§	0.14 to 1.15	0.09
Arrhythmia	0.63	0.46 to 0.87	0.005	0.73°	0.51 to 1.04	0.08
Postoperative VF/VT	0.11	0.01 to 0.88	0.04	0.14§#	0.01 to 1.47	0.10
Pulmonary complication	0.64	0.45 to 0.91	0.01	0.83°	0.56 to 1.23	0.35
Chest infection	0.48	0.26 to 0.89	0.02	0.83§	0.42 to 1.66	0.60
Neurological complications	0.29	0.11 to 0.76	0.01	0.35§	0.12 to 1.00	0.05
Permanent stroke	0.00§§	–	–	–§§	–	–
Transient stroke	0.15#	0.02 to 1.46	0.10	0.23§	0.02 to 2.56	0.23
Infective complications	0.85	0.40 to 1.78	0.66	1.01§	0.43 to 2.39	0.98
Septicemia	0.51	0.15 to 1.75	0.28	0.63§	0.15 to 2.54	0.51
Renal complications	1.07	0.64 to 1.80	0.79	1.49§	0.81 to 2.72	0.20
Dialysis required	0.68#	0.32 to 1.42	0.30	0.90§#	0.44 to 1.85	0.78
Gastrointestinal complications	0.60	0.18 to 2.00	0.40	0.55§	0.15 to 2.03	0.37
Multisystem failure	0.00§§	–	–	–§§	–	–
Re-operation bleeding tamponade	0.57	0.30 to 1.06	0.08	0.56§	0.28 to 1.10	0.09
Blood loss > 1000 ml	0.64	0.51 to 0.81	< 0.001	0.81°	0.62 to 1.05	0.11
Any RBC transfusion (0 vs ≥ 1 U)	0.26	0.20 to 0.33	< 0.001	0.40°	0.30 to 0.52	< 0.001
Any PLT transfusion (0 vs ≥ 1 U)	0.37	0.25 to 0.54	< 0.001	0.48§	0.32 to 0.73	0.001
Any FFP transfusion (0 vs ≥ 1 U)	0.35	0.22 to 0.54	< 0.001	0.46§	0.29 to 0.75	0.002
Postoperative hemoglobin < 10 g/dl	0.44	0.36 to 0.55	< 0.001	0.55°	0.43 to 0.70	< 0.001
Ventilated ≥ 10 hours	0.67	0.54 to 0.83	< 0.001	0.86°	0.67 to 1.10	0.22
ICU stay > 1 day	0.54	0.41 to 0.70	< 0.001	0.69°	0.51 to 0.94	0.02
ICU or HDU stay > 2 days	0.56	0.45 to 0.69	< 0.001	0.79°	0.62 to 0.99	0.04
Postoperative length of stay > 7 days°°	0.49	0.38 to 0.62	< 0.001	0.67°	0.51 to 0.88	0.004

CI = confidence interval; FFP = fresh frozen plasma; HDU = high dependency unit; ICU = intensive care unit; OR = odds ratio; PLT = platelets; RBC = red blood cells; VF = ventricular fibrillation; VT = ventricular tachycardia. * OR adjusted only for consultant team carrying out the operation (except where indicated#); ** unadjusted ORs were based on a sample size of up to 2844, and adjusted ORs on a sample size of up to 2743 (propensity scores could not be calculated for 101 patients who had ≥ 1 prognostic factor missing), with a maximum of 1.2% missing data for any outcome except blood loss, transfusion requirement and postoperative hemoglobin; these latter outcomes were not documented during the first year (20% of patients); § estimates of ORs for off vs on-pump surgery adjusted for: quintiles of propensity score (see text) and consultant team (except where indicated#); ° ORs adjusted for: quintiles of propensity score (see text), consultant team, presence of unstable angina, previous myocardial infarction, hypercholesterolemia, left main stem stenosis > 50%, extent of coronary disease, number of grafts and body mass index group; # ORs were not adjusted for consultant team because one or more teams did not observe any events; §§ CIs could not be calculated, and a multivariable model could not be estimated, because there were no events among off-pump patients; °° excluding length of stay for 21 patients who died in hospital. Adapted from Ascione et al.[27], with permission.

methodological problems with single center studies; 2) the inclusion of obesity in the Parsonnet score; 3) the difficulty for physicians in partitioning the complex effects of other risk factors that may often be associated with obesity. There are also further possible explanations. First, obese patients may die younger without developing severe disease. If so, one would expect similar imbalances across BMI groups in different institutions, since the etiology and progression of ischemic heart disease is the same across the developed world. This reason could explain why the obese patients undergoing CABG in our study were, on average, younger than patients with a normal weight but not why they had less severe ischemic heart disease. Second, cardiologists or cardiac surgeons may tend to select obese patients for surgery in a different way from non-obese patients, i.e. they may be less likely to consider obese than normal weight patients for surgery when they have less favorable risk profiles. Inadvertent discrimination of this kind against obese patients could arise because of the prevailing view that obesity is a risk factor for mortality and morbidity following CABG.

However, findings of previous studies and our own lead us to conclude that obesity is not a risk factor for mortality and morbidity following CABG. Furthermore, the results of our study suggest that off-pump surgery is safe and effective and is associated with a reduced in-hospital mortality and morbidity in overweight patients when compared with conventional coronary surgery with cardiopulmonary bypass and cardioplegic arrest.

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