

Impact of body mass index on surgical coronary revascularization for ischaemic heart failure: insights from STICHES

Nicholas S. Hendren¹, Lin Zhong², Ian J. Neeland¹, Katherine C. Michelis¹, Mark H. Drazner¹, W.H. Wilson Tang³, Ambarish Pandey¹ and Justin L. Grodin^{1*}

¹Division of Cardiology, Department of Internal Medicine, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Suite E5.310F, Dallas, TX 75390-8830, USA; ²Division of Bioinformatics, Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, TX, USA; ³Department of Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH, USA

Abstract

Aims Patients with obesity and ischaemic heart failure may counter-intuitively have better outcomes compared with patients with normal body weight due to an ‘obesity paradox’. This study sought to determine if body mass index (BMI) impacts the treatment effects or safety outcomes of the treatment of ischaemic heart failure with coronary artery bypass grafting (CABG).

Methods and results We obtained and reviewed the Surgical Treatment of Ischaemic Heart Failure (STICHES) data for 1212 patients. We categorized obesity by the World Health Organization (WHO) classes to define baseline characteristics and test for treatment interactions for the primary and secondary STICHES outcomes by treatment groups. While CABG decreased the risk of death, there was no evidence of treatment interaction by BMI per 5 kg/m² ($P = 0.83$) or WHO obesity class. For the overall cohort, there was no interaction by WHO obesity class for the cumulative incidence of death in either the medical therapy or CABG plus medical therapy (P -interaction = 0.90). There was a non-significant trend for higher BMI and a lower risk of death [hazard ratio 0.92, 95% confidence interval (CI) 0.85–1.00, $P = 0.051$]. Increasing body size (per 5 kg/m²) was associated with return to the operating room (odds ratio 2.48, 95% CI 1.45–4.26, $P < 0.001$) and infectious mediastinitis (odds ratio 2.09, 95% CI 1.10–3.97, $P = 0.024$) at 30 days but not other 30 day safety outcomes.

Conclusions The benefit of CABG vs. medical therapy for ischaemic heart failure was consistent regardless of BMI or WHO obesity class for death or secondary clinical outcomes. However, higher BMI was associated with some short-term post-CABG complications.

Keywords Obesity paradox; Ischaemic heart failure; CABG

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*Correspondence to: Justin L. Grodin, Division of Cardiology, Department of Internal Medicine, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Suite E5.310F, Dallas, TX 75390-8830, USA. Tel: 214-648-6741; Fax: 214-645-2480.

Email: justin.grodin@utsouthwestern.edu

Introduction

Prior analyses of patients with coronary artery disease and systolic heart failure have observed an ‘obesity paradox’, where obese patients paradoxically have more favourable outcomes compared with normal-weight individuals.^{1,2} Furthermore, additional observations of contemporary surgical registries have observed an obesity paradox in patients undergoing cardiac surgery.³ Despite these prior

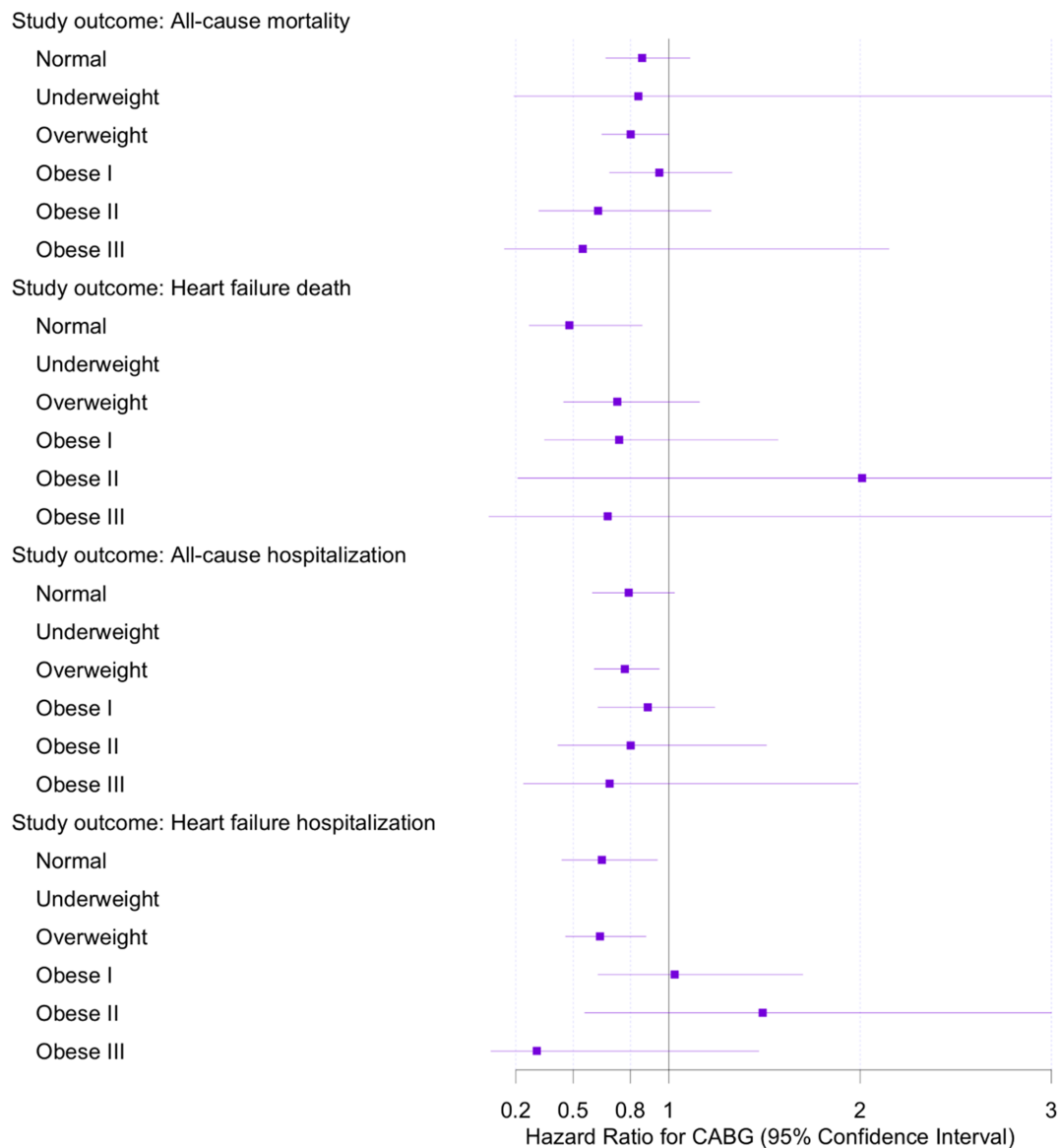
observations, it is uncertain if obesity modifies the benefit of coronary artery bypass grafting (CABG) in ischaemic heart failure. Obesity may associate with favourable outcomes following CABG due to increased metabolic reserves, attenuated activation of the renin–angiotensin system, and increased blood pressure, allowing for titration of cardioprotective medications.⁴ Alternatively, obesity may increase the risk of post-operative complications and a prolonged hospital stay.⁵

Methods

The STICHES dataset was obtained from the National Heart, Lung, and Blood Institute’s Biologic Specimen and Data Repository Information Coordinating Centre via an approved proposal by our institutional review board. All patients provided written consent for their respective studies, and the protocols were approved by the institutional review board at each site. This study complies with the Declaration

of Helsinki. Briefly, STICHES randomized patients with an ejection fraction < 35% and coronary artery disease amenable to CABG between July 2002 and May 2007 to either medical therapy (*N* = 602) or medical therapy plus CABG (*N* = 610).⁶ We categorized obesity by the World Health Organization (WHO) classes to define baseline characteristics. BMI was analysed by treatment groups (medical therapy vs. medical therapy plus CABG) as a continuous variable and WHO obesity classes to test for treatment interactions for the primary and secondary STICHES outcomes. Next, we

Figure 1 Forest plot for coronary artery bypass grafting (CABG) vs. medical management for ischaemic heart failure by World Health Organization obesity classes by outcome. Hazard ratios are displayed by World Health Organization obesity classes: underweight (*n* = 9), normal (*n* = 387), overweight (*n* = 518), Class I obesity (*n* = 220), Class II obesity (*n* = 58), and Class III obesity (*n* = 20). Solid lines represent 95% confidence intervals. Hazard ratio < 1 favours CABG. World Health Organization obesity classes: underweight (<18.5 kg/m²), normal (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), Class I obesity (30.0–34.9 kg/m²), Class II obesity (35.0–39.9 kg/m²), and Class III obesity (≥40.0 kg/m²).



evaluated and analysed the combined cohort as a continuous variable and WHO obesity classes to test for treatment interactions for the primary and secondary STICHES outcomes by treatment groups.

Results

All 1212 individuals within STICHES had available BMI data in the combined medical and CABG groups with a median value of 27 (interquartile range 24–30) kg/m². Median age was 60 (54–67) years with a left ventricular ejection fraction (LVEF) of 27% (21–33%). Higher baseline BMI was associated with higher frequency of White race (P -trend < 0.001), higher New York Heart Association class (P -trend = 0.031), and higher prevalence of diabetes (P -trend 0.001), hyperlipidaemia (P -trend < 0.001), and hypertension (P -trend < 0.001). Higher baseline BMI was also associated with higher insulin (P -trend < 0.001) and diuretic use (P -trend 0.032) but lower clopidogrel use (P -trend = 0.009).

As previously reported, compared with medical therapy, CABG decreased the risk of death, but there was no evidence for a treatment heterogeneity by BMI per 5 kg/m² (P = 0.83) or WHO obesity class (Figure 1). A similar result was seen for secondary outcomes of heart failure death (P -interaction = 0.44), all-cause hospitalization (P -interaction = 0.79), and heart failure hospitalization by continuous BMI (P -interaction = 0.36) and WHO obesity class (Figure 1). Visually, there was no evidence of non-linear treatment interaction by Martingale residuals for BMI and primary or selected secondary outcomes. Within the CABG cohort after adjustment for sex, age, and diabetes, higher BMI (per 5 kg/m²) was associated with return to the operating room [odds ratio (OR) 2.48, 95% confidence interval (CI) 1.45–4.26, P < 0.001] and infectious mediastinitis (OR 2.09, 95% CI 1.10–3.97, P = 0.024) at 30 days but not other 30 day safety outcomes including worsening renal function (OR 0.73, 95% CI 0.43–1.24, P = 0.24), infection (OR 1.05, 95% CI 0.72–1.52, P = 0.81), and return to the operating room for bleeding (OR 0.91, 95% CI 0.53–1.57, P = 0.73).

Within the overall cohort, there was no interaction by WHO obesity class for the cumulative incidence of death in either the medical therapy or CABG plus medical therapy (P -interaction = 0.90). For the whole cohort, higher BMI (per 5 kg/m²) was associated with percutaneous coronary intervention [hazard ratio (HR) 1.27, 95% CI 1.04–1.54, P = 0.02] and all-cause rehospitalization (HR 1.10, 95% CI 1.02–1.18, P = 0.02) but not associated with myocardial infarction, stroke, heart failure death, or heart failure hospitalization (P > 0.15 for all). There was a non-significant trend for higher BMI and a lower risk of death (HR 0.92, 95% CI 0.85–1.00, P = 0.051).

Aims

The aim of this study was to determine if BMI modified the prognostic benefit of CABG for ischaemic heart failure or 30 day safety outcomes in the STICHES dataset.

Conclusions

Our major findings were three-fold. First, we observed no statistically significant heterogeneity by BMI for the impact of CABG in comparison with medical therapy on clinical outcomes in individuals with ischaemic cardiomyopathy. Second, higher BMI in the CABG cohort was associated with return to the operating room and infectious mediastinitis at 30 days but not additional 30 day safety outcomes. Third, for the overall STICHES clinical cohort, we observed a modest association for higher BMI per 5 kg/m² with percutaneous coronary intervention and all-cause rehospitalization but not all-cause death, heart failure death, or heart failure hospitalization.

These findings are in contrast to prior studies that have observed an obesity paradox for patients undergoing cardiac surgery.^{1,3} Johnson *et al.* was a retrospective study of nearly 78 800 patients who underwent cardiac surgery in Canada.⁷ They observed obesity paradox with overweight patients having the lowest post-operative mortality; however, there were significant differences between the Canadian cohort and the STICHES cohort. First, the prevalence of heart failure was reported to be 1.6% in the Canadian cohort compared to 89% with New York Heart Association Classes II–IV heart failure in the STICHES cohort.^{6,7} In STICHES, all patients had an LVEF < 35%, while only half of patients had a reported LVEF, and ~8% had an LVEF < 35% in the Canadian cohort. Patients undergoing CABG with reduced systolic function are inherently different than CABG with preserved systolic function and may have different post-operative clinical outcomes, which may contribute to the observed differences between the prior studies. To our knowledge, no analyses were reported for these patients with a reduced ejection fraction by Johnson *et al.*, and the observations from STICHES may represent the largest analysis testing the impact of BMI on the surgical treatment of ischaemic cardiomyopathy.

In regard to the 30 day post-operative complications, we observed a positive association with higher continuous BMI and infectious mediastinitis; however, it is important to note the low overall event rate in 11/606 surgical patients (1.8%) with five events occurring in patients with a BMI < 30 kg/m². Likewise, 19/606 patients (3.1%) had to return to the operating room for reasons other than bleeding and nine events occurring in patients with a BMI < 30 kg/m². Therefore, despite a positive statistical association with continuous BMI, these findings should be interpreted with caution given the low event rates and that these events did not translate

into statistical differences in all-cause mortality, heart failure death, or heart failure hospitalizations.

In short, patients with ischaemic cardiomyopathy enrolled in a randomized clinical trial for CABG vs. medical therapy are inherently different than a contemporary population undergoing CABG for obstructive coronary artery disease. Our findings suggest that in a randomized select population, the long-term benefits of CABG for ischaemic heart failure may be applicable to patients regardless of BMI, but larger body size may impact some short-term post-operative outcomes and overall prognosis.

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Conflict of interest

None declared.

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