ORIGINAL ARTICLE

Relationship Between Body Fat and Morbidity and Mortality in Cardiac Surgery

Relación entre la grasa corporal y la morbimortalidad en cirugía cardíaca

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ABSTRACT

Objective: There is a potentially protective effect of obesity when it coexists with cardiovascular disease. This is known as the "obesity paradox", which might be explained by anthropometric measurements as an unreliable marker of body fat.
Objective: The aim of this study was to estimate body fat with a non-invasive method and study its relationship with morbidity and mortality in cardiac surgery.
Methods: We conducted a prospective and observational study in adult patients undergoing cardiac surgery. Demographic, anthropometric and clinical variables together with the estimation of body composition using bioelectrical impedance analysis were used to analyze their association with length of hospital stay and adverse events after cardiac surgery.
Results: The analysis of 98 patients revealed a direct relationship between the percentage of body fat and length of hospital stay, independently of age, sex, body mass index and preoperative risk (coefficient of 0.27, p = 0.021). In addition, patients who had mediastinitis showed significantly higher body fat (31.55 ± 0.64% vs. 27.13 ± 7.9%, p <0.001), and patients who died had a tendency to have larger fat mass (36.05 ± 3.19% vs. 27.20 ± 7.82%, p = 0.08).
Conclusion: Increased body fat assessed with bioelectric impedance analysis was related to higher morbidity in cardiac surgery. Although this result is biologically plausible, larger studies are necessary in order to definitively establish the "body mass index paradox".

Keywords: Cardiac Surgical Procedures – Obesity - Body Mass Index - Body Composition - Prognosis.

RESUMEN

Introducción: Existe un efecto potencialmente protector de la obesidad cuando coexiste con la enfermedad cardiovascular, conocido como "paradoja de la obesidad". Es posible que se deba a que las medidas antropométricas no sean un marcador fidedigno de la grasa corporal. En este estudio, proponemos estimar la grasa corporal con métodos no invasivos y estudiar su relación con la morbimortalidad en cirugía cardíaca.
Métodos: Llevamos a cabo un estudio prospectivo y observacional en pacientes adultos sometidos a cirugía cardíaca. Analizamos variables demográficas, antropométricas y clínicas junto con la estimación de la composición corporal a través de la impedancia bioeléctrica, para relacionarlas con los días de internación y eventos adversos luego de la cirugía cardíaca.
Resultados: En el análisis de 98 pacientes, encontramos una relación directa entre el porcentaje de grasa corporal y los días de internación, independiente de la edad, el sexo, el índice de masa corporal y el riesgo prequirúrgico (coeficiente de 0,27, p: 0,021). Además, los pacientes que presentaron mediastinitis tuvieron una grasa corporal significativamente mayor (31,55 ± 0,64% contra 27,13 ± 7,9%, p < 0,001), y los pacientes que fallecieron presentaron una tendencia a presentar más masa grasa (36,05 ± 3,19% contra 27,20 ± 7,82%, p: 0,08).
Conclusiones: La mayor cantidad de grasa corporal estimada por análisis de impedancia bioeléctrica se relacionó con una mayor morbilidad en la cirugía cardíaca. A pesar de que esto es biológicamente plausible, sería necesario llevar a cabo estudios de mayor tamaño para poder esclarecer definitivamente la "paradoja del índice de masa corporal".

Palabras clave: Procedimientos quirúrgicos cardíacos - Obesidad - Índice de masa corporal - Composición corporal - Pronóstico.

Abbreviations

BIA	Bioelectrical impedance analysis	**IQR**	Interquartile range
BMI	Body mass index	**SD**	Standard deviation

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INTRODUCTION

Overweight and obesity are directly associated with the incidence of cardiovascular disease. (1) Usually, body mass index (BMI) is used for their identification in epidemiological studies, defining overweight as BMI ≥25 and obesity as BMI ≥30. Although this measurement is easy to perform, it presents many limitations since it does not accurately reflect the body composition of an individual. In a study relating anthropometric measurements with mortality in 49,476 women and 4,944 men, only a very low BMI or high percentage of body fat correlated with mortality, but not a high BMI. (2)

The relationship between BMI and mortality becomes even more complex in patients with established cardiovascular disease. A potentially protective effect of obesity when it coexists with cardiovascular disease has been demonstrated by several retrospective and prospective epidemiological studies, (3, 4) a phenomenon known as the "obesity paradox". (5) There are many possible explanations, but one of the most accepted sustains that in reality BMI, when used as a surrogate of body fat, acts as a confounder in the relationship between excessive adiposity and increased mortality. (6) Since it does not directly measure body fat, BMI would only be an imperfect marker of adiposity, and more accurate measurements of body fat could be more useful. (7) Thus, the "obesity paradox" would be reduced to the "BMI paradox".

There is special interested in studying what happens in patients undergoing cardiac surgery. For example, lower morbidity and mortality after coronary revascularization surgery has been reported in obese patients compared with those presenting normal weight. (8, 9) However, BMI is not taken into account in cardiac surgery risk scores developed in Europe and Argentina (EuroSCORE and ArgenSCORE). (10, 11)

The aim of this study was to evaluate the relationship between body fat and morbidity of patients undergoing cardiac surgery, and to determine whether there is an independent relationship with BMI, age and sex.

METHODS

A prospective, observational study was carried out in the coronary care unit of a high-complexity private hospital of the Autonomous City of Buenos Aires. All patients over 18 years of age undergoing cardiac surgery between August 1, 2018 and July 31, 2019 were invited to participate. Dialysis patients, with limb amputations or pacemakers, and those not granting their consent to participate, were excluded from the study.

Age, sex, height and weight were obtained from the clinical history. Body mass index was calculated as the ratio between weight in kilograms and the square of height in meters. In addition, relevant patient history (diabetes, renal failure, previous cardiac surgery, pulmonary disease, functional class, pulmonary hypertension, peripheral vascular disease, number of vessels with coronary artery disease and left ventricular ejection fraction), surgery characteristics (type of surgery, priority, use of cardiopulmonary bypass) and presurgical risk calculated using the EuroSCORE and the ArgenSCORE were recorded.

Fat mass was estimated through bioelectrical impedance analysis (BIA), a simple, low-cost and non-invasive method to estimate body composition through the analysis of body resistance to a low-level alternate electric current. (12) Bioimpedance measurements were obtained with a standard tetrapolar bioimpedance meter (BIA 310, Biodynamics Corp., Seattle, USA, series number 409903), at a frequency of 50 kHz, with the patient lying in supine position, without contact with metallic objects and with the arms and legs at 30° from the midline. Measurements were performed placing two electrodes in the right arm with a 5 cm separation and two in the right leg also with a 5 cm separation, 24 hours prior to surgery and in fasting conditions.

The primary endpoint was length of hospital stay after surgery. Secondary endpoints were postoperative complications (heart failure, cardiogenic shock, vasoplegia, atrial fibrillation, mediastinitis, type V infarction and death).

Statistical analysis

Continuous variables were expressed as mean and standard deviation (SD) or median and interquartile range (IQR) according to their distribution, and categorical variables as absolute and relative frequencies. Continuous variables were compared using Student's t test for normal unpaired samples or the Wilcoxon test for non-parametric samples, and categorical samples were compared using the chi-square test. Normality of distributions was assessed by histogram observation, skewness and kurtosis and finally, using the Shapiro-Wilk test. Correlations were evaluated with Pearson's coefficient, with prior exclusion of outliers using the bagplot method. Finally, a linear regression model was built to establish the relationship between body fat and days of hospital stay, independently of sex, age, BMI and the ArgenSCORE (the latter was incorporated to the model after its logarithmic transformation due to its distribution). A p value <0.05 was considered significant. All calculations were performed using R 3.6.1 statistical software.

Ethical considerations

This project complies with the ethical regulations established by the Declaration of Helsinki for research in human subjects. (13) An informed consent was written, notifying the patients that data from their clinical history would be used and that they would undergo bioimpedance assessments. The protocol was reviewed and approved by the institutional authorities.

RESULTS

A total of 133 patients underwent cardiac surgery during the study period. Eight patients fulfilled the exclusion criteria and one patient was excluded due to pregnancy, though this criterion had not been contemplated a priori. Complete anthropometric and body composition data were obtained from the 124 remaining patients and among these, 98 were valid and finally included in the analysis. These patients presented no significant differences in demographic and clinical variables or events compared with those with incomplete data.

Patient characteristics are shown in Table 1. Most patients were men <60 years of age, undergoing elective coronary artery bypass graft surgery with cardiopulmonary bypass. Anthropometric data and body composition stratified by sex are depicted in Table 2. Men were higher and heavier than women, but with similar BMI. Women presented lower lean mass and higher body fat, with the same total body water. Median hospital stay was 8 days (IQR 6,6 to 11.5 days).

Patients presenting with mediastinitis had greater percentage of body fat compared with the remaining

patients (31.55±0.64% vs. 27.13±7.9 %, p<0.001). No significant differences in body fat were found with respect to heart failure, cardiogenic shock, vasoplegia, atrial fibrillation, type V infarction and bleeding. Body fat was higher, albeit not statistically significant, in patients who died at 30 days (36.05±3.19% vs. 27.20±7.82%, p=0.08).

Figure 1 illustrates a positive correlation of 0.27 (p=0.016) between the percentage of body fat and length of hospital stay, without apparent association with age. It also shows that no patient with body fat <25% was hospitalized for more than 14 days. When body fat was incorporated to a linear regression model (Figure 2) together with age, sex, BMI and the ArgenSCORE to predict the length of hospital stay, the corresponding correlation coefficient was 0.27 (p=0.021). No significant relationship was found between BMI and length of hospital stay. Among all the variables considered, the risk score presented the highest magnitude of association with days of hospitalization (coefficient 1.72, p <0.001). In general, per each 4% increase in fat mass length of hospital stay increased by approximately one day, independently of age, sex, BMI and the ArgenSCORE.

Table 1. Population characteristics

Characteristic (n = 98)	Mean ± SD, median (IQR) o n (%)
Age (years)	58.87 ± 11.85
Men	79 (80.6%)
Functional class.	
I	29 (37.2%)
II	32 (41.0%)
II	14 (17.9%)
IV	3 (3.8%)
LV ejection fraction	52.49 ± 12.36
Chronic renal failure	8 (8.2%)
COPD	9 (9.2%)
Insulin-dependent diabetes	6 (6.1%)
Hematocrit (%)	38.29 ± 4.28
Creatinine (mg/dL)	0.98 (0.85-1.18)
Type of surgery	
CABG	56 (57.1%)
Valve replacement	24 (24.5%)
Combined	9 (9.2%)
Bentall	2 (2.0%)
Others	7 (7.1%)
Cardiopulmonary bypass time (minutes)	74.16 ± 27.13
Priority	
Elective	61 (62.2%)
Urgent	35 (35.7%)
Emergent	2 (2.0%)
Salvage	0 (0.0%)
Use of cardiopulmonary bypass	73 (75.3%)
EuroSCORE	1.04 (0.68-1.81)
ArgenSCORE	2.13 (1.18-4.95)
Mortality	2 (2.0%)

LV: Left ventricular. COPD: Chronic obstructive pulmonary disease. CABG: Coronary artery bypass graft surgery.

Table 2. Anthropometric and body composition data according to sex

Characteristic	Women	Men	p
n	19	79	
Age (years)	62.58 ± 14.01	57.97 ± 11.18	0.129
Height (cm)	157.89 ± 5.78	170.29 ± 6.37	<0.001
Weight (kg)	71.19 ± 14.75	82.58 ± 14.99	0.004
BMI (m/kg2)	28.54 ± 5.51	28.46 ± 4.88	0.950
Lean mass (%)	66.46 ± 7.67	74.28 ± 7.15	<0.001
Fat mass (%)	33.46 ± 7.69	25.72 ± 7.15	<0.001
Total body water (%)	73.67 ± 1.99	73.30 ± 1.74	0.423

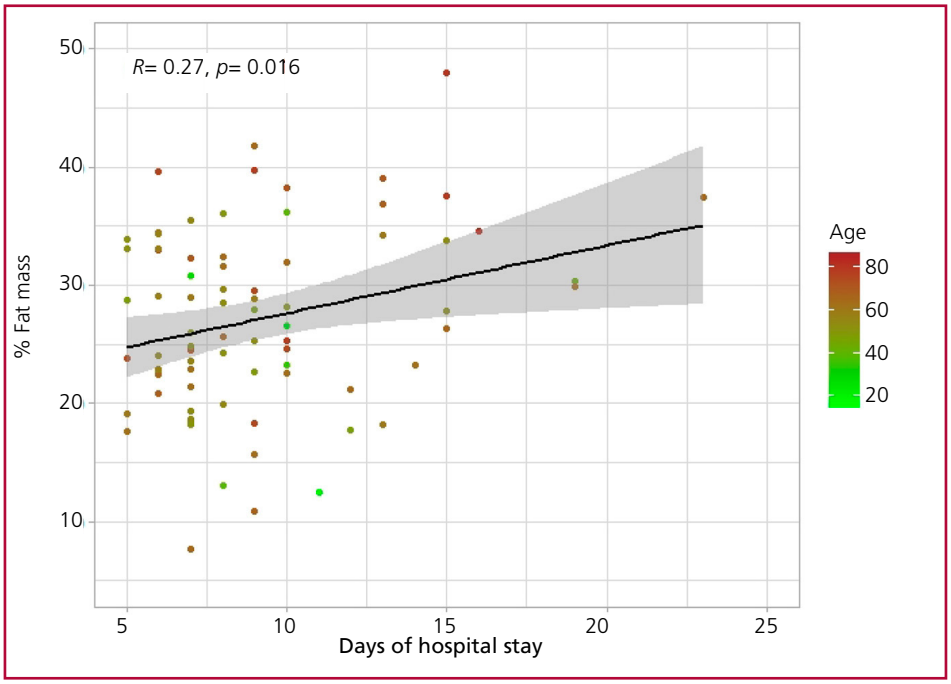

Fig. 1. Relationship between percent fat mass and length of hospital stay, with patient identification according to age.

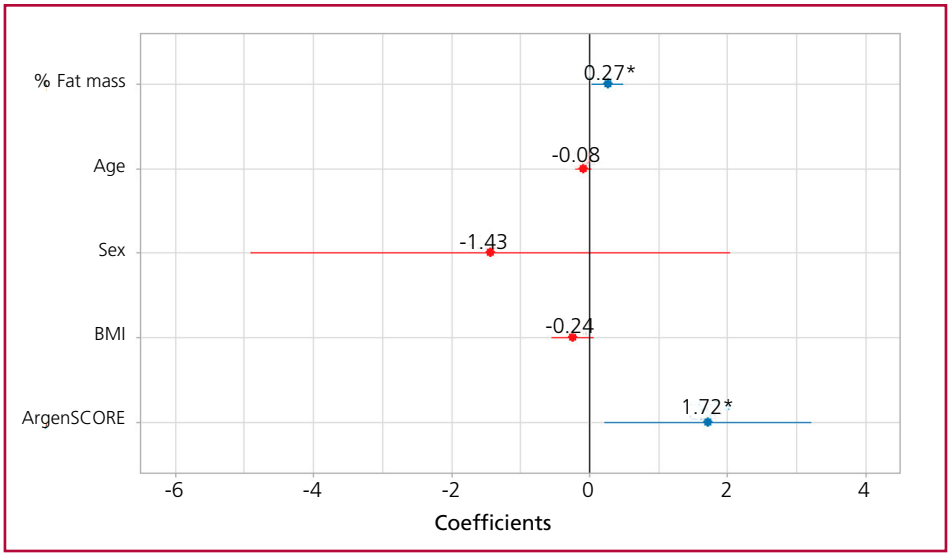

Fig. 2. Coefficients of the linear regression model, considering length of hospital stay (days) with respect to fat mass, age, sex, BMI and the ArgenSCORE (*: p < 0,., **: p <0.01, ***: p <0.001). BMI: Body mass index.

DISCUSSION

According to our data, there is a direct relationship between body fat and morbidity in patients undergoing cardiac surgery, and it is also possibly associated with greater 30-day mortality.

Several studies relate body composition lean mass with events after cardiac surgery. In the BICS study, the phase angle (calculated from the relationship between resistance and reactance as an indicator of general nutritional status) was independently related with higher 30-day mortality. (14) This is due to the correlation between lower phase angle and lower muscle mass, also associated to greater patient frailty. In addition, other studies have shown that a lower lean mass is related with a more prolonged hospital stay and more infections, (15) need for transfusions, (16) higher costs, (17) and in general, more postoperative complications. (18, 19)

This shows that, especially in elderly patients, lean mass as an indicator or frailty and lower resistance to stress is a valuable prognostic marker. However, in younger populations, fat mass may play a more relevant function. There is less evidence on the role of body fat on the outcome after cardiac surgery. A substudy of the BICS trial showed that a combination of elevated fat mass and reduced lean mass (a condition known as "sarcopenic obesity" (20) was related to greater manifestation of adverse events. (21) The investigators suggested that this is due to greater insulin resistance, lower capacity to heal wounds and increased risk of infections in patients with higher fat mass. In another study, visceral adiposity, though not BMI, was associated with reduced heart rate variability in patients with type 2 diabetes undergoing

coronary artery bypass graft surgery. (22) This result indicates that the autonomic function impairment characteristic of diabetic patients is related to their fat mass, and that this could have prognostic impact.

From a molecular viewpoint, adiponectin and leptin play a central role in metabolic homeostasis, and have been associated with the pathophysiology of cardiovascular disease. Adiponectin has insulin-sensitizing, anti-inflammatory and anti-atherogenic effects, (23, 24) while leptin is the cause of various processes associated with cardiovascular disease. (25) In obesity, decreased levels of adiponectin coexist with a rise in leptin, (26) which might explain increased adverse events in patients with greater fat mass. In a study of patients undergoing cardiac surgery, leptin was positively correlated with BMI and fat mass, and negatively with the size of the left atrium and cardiac mass index, while adiponectin was positively correlated with the size of the left atrium and E/e'. (27) According to the authors, it suggests that both markers can participate in cardiac remodeling after cardiovascular surgery and thus impact on the prognosis.

Based on these results from previous studies and our data analysis, we can postulate that body composition estimated with more accurate methods than BMI could be an important risk marker when deciding a surgical procedure.

However, the following limitations of the study should be considered. Sample size was small and did not allow an independent relationship between body composition and mortality. Also, the nature of the BIA method, despite being useful in population samples, is less accurate at an individual level. Absence of data on body fat distribution (waist-hip index) was another limitation as well as the lack of biomarker assessments, as adiponectin and leptin.

CONCLUSIONS

According to the evidence available, body composition is related with complications and mortality after cardiac surgery. We have found an independent relationship between a higher percentage of body fat and length of hospital stay, as well as greater morbidity in patients with increased fat mass. This finding is biologically plausible, but it is necessary to perform larger sample studies in order to incorporate the estimation of body composition to usual surgical risk assessment.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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