Does the anthropometric profile influence infection morbidity after coronary artery bypass grafting?

Running Title: Anthropometric profile and CABG

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ABSTRACT

Background: Infection after cardiovascular surgery is multifactorial. We sought to determine whether the anthropometric profile influence the occurrence of infection after isolated coronary artery bypass grafting (CABG).

Methods: Between January 2011 and June 2016, 1,777 consecutive adult patients were submitted to isolated coronary artery bypass grafting. Mean age was 61.7 ± 9.8 years and 1,193 (67.1%) were males. Patients were divided into four groups according to the Body Mass Index (BMI) classification: underweight (BMI<18.5 kg/m^2: N=17, 0.9%), normal range (BMI 18.5 – 24.99 kg/m^2: N=522, 29.4%), overweight (BMI 25 – 29.99 kg/m^2: N=796, 44.8%) and obese (>30 kg/m^2: N=430, 24.2%). In-hospital outcomes were compared and independent predictors of infection were obtained through multiple Poisson regression with robust variation.

Results: Independent predictors of any infection morbidity were female sex (RR 1.47, P=0.002), age > 60 years (RR 1.85, P<0.0001), cardiopulmonary bypass > 120 minutes (RR 1.89, P=0.0007), preoperative myocardial infarction < 30 days (RR 1.37, P=0.01), diabetes mellitus (RR 1.59, P=0.0003), ejection fraction < 48% (RR 2.12, P<0.0001) and blood transfusion (RR 1.55, P=0.0008). Among other variables, obesity, as well as diabetes mellitus, were independent predictors of superficial and deep sternal wound infection.

Conclusions: Other factors rather than the anthropometric profile are more important in determining the occurrence of any infection after CABG. However, surgical site infection has occurred more frequently in obese patients. Appropriate patient selection, control of

modifiable factors and application of surgical bundles would minimize this important complication.

INTRODUCTION

Obesity is a growing worldwide health care problem due to changes in life style patterns and feeding habits. However, there are certainly disparities in frequency, according to stark geographical and social inequalities around the world[1]. This is mainly attributed to the level of development status, demographic density, gross domestic product, cultural practices and the impact of preventive medicine on a given community.

Obesity increases health-care costs[2], since many of them have associated medical problems such as hypertension, diabetes, hyperlipidemia, cardiovascular disease, chronic kidney disease and cancer[3,4]. Obesity is a risk factor for coronary artery disease[5] and many obese patients require coronary artery bypass grafting (CABG)[6,7]. The literature shows conflicting results regarding the impact of obesity on outcomes after CABG[8-10]. Although obesity is a risk factor for cardiovascular disease, it has been suggested that obese patients with established cardiovascular disease may have a more favorable prognosis than non-obese patients, which was called “obesity paradox”[11,12].

Surgical site infection prevalence is higher in obese patients. That holds true for most surgical specialties, including cardiac surgery. On the other hand, the adoption of multidisciplinary bundles to prevent surgical site infection have mitigated this problem in most procedures, including bariatric surgery[13]. In regard to cardiac surgery, few reports aimed at determining differences in infection burden according to patient’s body mass index after the implementation of the World Health Organization surgical safety checklist, which have proved that one of the greatest benefits was lowered surgical site infection rates[14].

The aim of this study is to determine whether the anthropometric profile influence the occurrence of infection morbidity after isolated coronary artery bypass grafting.

PATIENTS AND METHODS

Patients

Between January 2011 and June 2016, 1,777 consecutive adult patients were submitted to isolated coronary artery bypass grafting in a single institution. Mean age was 61.7 ± 9.8 years (range 29 – 88 years) and 1,193 (67.1%) were males.

Data were in part retrieved from the prospective cardiovascular surgery registry and in part from each electronic patient's medical record. These data were approved by the Institutional Review Board, which granted its use for research purposes with patient consent waived.

Definitions of study groups and outcomes

Body mass index (BMI) was calculated in every patient according to the World Health Organization definition as the weight in kilograms divided by the square of the height in meters.

In order to determine the association of outcomes of coronary artery bypass grafting in relation to patient's anthropometric profiles at index hospitalization, we divided the patients into four groups according to the BMI classification: underweight (BMI<18.5 kg/m^2), normal range (BMI 18.5 – 24.99 kg/m^2), overweight (BMI 25 – 29.99 kg/m^2) and obese (>30 kg/m^2). Groups were compared in terms of preoperative and intraoperative profiles, as well as postoperative outcomes.

Outcomes assessed included intraoperative support (myocardial ischemic time, cardiopulmonary bypass time, when applicable), postoperative all cause in-hospital mortality and morbidity (defined in accordance with the Society of Thoracic Surgeons National Database: http://www.sts.org/registries-research-center/sts-national-database/adult-cardiac-surgery-database/data-collection). MACE was consistent with major trials on coronary surgery safety, which included death, stroke and myocardial infarction. Sepsis was defined as infection with evidence of altered organ perfusion, expressed as tachycardia, fever or hypothermia, tachypnea with hypotension (systolic blood pressure < 90 mmHg or decrease from baseline systolic blood pressure > 40mmHg). Line infection was documented by Infectious Disease team and was characterized by bacteremia with positive blood and line culture tips. Urinary tract infection was documented by Infectious Disease team after a positive urine culture. Deep sternal wound infection was any chest wound infection that affect the sternum and/or mediastinum, usually manifested by drainage from the mediastinal incision, elevated temperature and sternal dehisce. Superficial wound infection was defined as any wound infection other than mediastinitis, with purulent drainage and institution of therapy. Wound may dehisce or be opened by surgeons.

The indication for surgery followed a heart team decision on an individual basis. The choice of conduits and the conduction of the operation were at the discretion of the attending surgeon. Institution's protocols were strictly followed in terms of intraoperative and postoperative management, which was universally applied in all patients. Study was observational.

Data analyses

Categorical variables are summarized as frequencies and percentages and continuous variables as means ± standard deviations (SD), or as equivalent 15th, 50th (median), and 85th percentiles (for consistency with ±1 SD) when data were skewed. Categorical outcomes were compared using either χ^2 or Fisher's exact test and continuous outcomes by the Wilcoxon rank-sum nonparametric test. Independent predictors of infection were obtained through multiple Poisson regression with robust variation. Data were analyzed into two steps: bivariable and multiple, being calculated their prevalence ratios with correspondent 95% confidence intervals. Initially, simple Poisson regression was applied in order to adjust each covariable. Those with $P<0.25$ were retained and included into multiple Poisson regression. The final model included only covariables with $P<0.05$. The body mass index was included as an independent variable of interest, in order to verify its association with any infectious morbidity adjusting for possible confounders. Multicollinearity between independent variables was determined, being significant if the tolerance indicator was higher than 0.6. All analyses were performed using SAS® (Cary, NC, USA) statistical software version 9.4.

RESULTS

Overall mean weight and height were 72.6 kg ± 13.2 kg and 162 cm ± 9 cm, respectively. According to the BMI classification, 1,777 patients were divided into four study groups: underweight (N=17, 0.9%), normal weight (N=522, 29.4%), overweight (N=796, 44.8%) and obese (N=430, 24.2%).

Preoperative profiles of study groups were compared (Table 1). Male sex was predominant in all groups, except the underweight. Obese group comprised the youngest (59.8 years ± 9.9 years) population in comparison with other groups. The proportion of patients operated in the setting of unstable angina (36.4%) or within a month of an episode of acute myocardial infarction (23.5%) was considered relatively high. Normal weight patients were operated more frequently in those scenarios than the other groups. Obese patients had more hypertension (90.6%), diabetes (25.9%) and hyperlipidemia (56.1%), being operated more frequently in the presence of stable angina. There were no differences among study groups on coronary anatomy and left ventricle ejection fraction. Intraoperative profiles (Table 2) demonstrated that the majority of patients (91.9%) were submitted to on-pump coronary bypass. Cardiopulmonary bypass duration and ischemic times were similar among study groups. There were no differences in terms of the number of treated vessels (overall mean 3 ± 0.9/patient, P=0.51) and in the use of one (overall 96.8%, P=0.56) or two internal thoracic arteries (overall 11.6%, P=0.2).

Outcomes are demonstrated in Table 3. Thirty-day mortality was similar between groups (underweight 0%, normal weight 1.9%, overweight 1% and obese 1.6%, P=0.17), as well the occurrence of MACE (underweight 11.8%, normal weight 5.2%, overweight 4.6% and obese 5.6%, P=0.53). Normal weight patients had greater requirement of intra-aortic balloon pump (P=0.004) and developed more frequently acute kidney injury (P=0.03), probably due to the higher proportion of acute coronary syndrome in this group. Prolonged mechanical ventilation, defined as the requirement of tracheostomy was similar among study groups (P=0.17).

Infection morbidity

In univariable analysis (Table 3), obese patients had greater proportion of superficial wound infection (P=0.01), and a tendency of more deep sternal wound infection (P=0.06) and any infection morbidity (P=0.06), when compared with the other groups.

Multivariable regression (Table 4) identified as independent predictors of any infection morbidity female sex (RR 1.47 95%CI 1.14 – 1.88, P=0.002), age greater than 60 years-old (RR 1.85 95%CI 1.44 – 2.39, P<0.0001), duration of cardiopulmonary bypass greater than 120 minutes (RR 1.89 95%CI 1.3 – 2.73, P=0.0007), preoperative myocardial infarction < 30 days (RR 1.37 95%CI 1.07 – 1.75, P=0.01), diabetes mellitus (RR 1.59 95%CI 1.24 – 2.04, P=0.0003), ejection fraction less than 48% (RR 2.12 95%CI 1.47 – 3.07, P<0.0001) and need of blood transfusion (RR 1.55 95%CI 1.2 – 2, P=0.0008). The anthropometric profile was not significantly associated with infection (P=0.12), after adjusting for possible confounders. However, obese patients had 35% more infection than normal weight patients, and almost reached statistical significance in the multivariable model (RR 1.35 95%CI 1 – 1.81, P=0.0507). Tolerance indicator varied between 0.88 and 0.96, indicating that there is no multicollinearity between independent variables.

In order to analyze specifically surgical site infection, two additional multivariable models were created, on superficial wound infection (Table 5) and on deep sternal wound infection (Table 6). Independent predictors of superficial wound infection were female sex (RR 1.95 95%CI 1.42 – 2.69, P<0.0001), cardiopulmonary bypass duration greater than 120 minutes (RR 2.44 95%CI 1.47 – 4.03, P=0.0005), diabetes mellitus (RR 1.9 95%CI 1.35 – 2.67, P=0.0002), ejection fraction less than 48% (RR 2.19 95%CI 1.32 – 3.62, P=0.002), and obesity (RR 1.89 95%CI 1.21 – 2.96, P=0.005). Tolerance indicator varied between 0.97 and 0.99, indicating that there is no multicollinearity between independent variables. Independent predictors of deep sternal wound infection were diabetes mellitus (RR 2.58 95%CI 1.43 – 4.65, P=0.002), chronic obstructive pulmonary disease (RR 3.99 95%CI 1.53 – 10.42, P=0.005), blood transfusion (RR 2.21 95%CI 1.25 – 3.93, P=0.007) and obesity (RR 2.1 95%CI 1.11 – 3.96, P=0.02). Tolerance indicator varied between 0.98 and 0.99, indicating that there is no multicollinearity between independent variables.

DISCUSSION

The present study demonstrated that other factors rather than the anthropometric profile are more important in determining the occurrence of any infection after coronary artery bypass grafting. However, obese patients are associated independently with more surgical site infection, either superficial and deep sternal wound infection. Therefore, the influence of the anthropometric profile seems more relevant on the surgical site infection than in any other type of infection.

Published literature[15,16] on the influence of anthropometry in coronary artery bypass patients focus mainly on major morbidity and mortality. Results from these studies show controversial results. Our data supports that abnormal BMI was not associated with higher mortality and major cardiovascular adverse events, nor it confers benefit as has been reported[17].

When other morbidities are studied, Devarajan[14] and colleagues found that BMI > 30 kg/m^2 was associated with increased pulmonary morbidity, but not infection morbidity. That was explained by a commonly observed restrictive lung pattern[18,19] aggravated or not with congestive heart failure, chronic inflammatory state related to metabolic syndrome and cytokine-mediated inflammatory response to cardiopulmonary bypass. These authors considered that potential pulmonary complications are usually treatable and not associated with mortality. Although our data did not look at this particular problem in detail, it appears that there was no major differences on the need of tracheostomy and nosocomial pneumonia according to BMI.

In this paper, the proportion of patients operated in the setting of unstable angina (36.4%) or within a month of an episode of acute myocardial infarction (23.5%) reflects a very particular health system that lacks an efficient primary prevention. Our hospital is the only one that have a cardiac surgery program for the public health system in an area of 3 million inhabitants. Patients are initially diagnosed and treated at different local hospitals, and subsequently transferred to our heart center for advanced care. That means prolonged preoperative hospitalization, untreated chronic deficiency anemia, frequent issues of multi-resistant bacteria colonization and poor glycemic control. Those issues explain the higher prevalence of infection than it is reported in the literature. In spite of that, our hard end-points of morbidity and mortality are adequate for this particular patient profile.

It is uncertain the association between infection and BMI after CABG. Some authors[7-10] have reported increased risk of superficial and deep sternal wound infection with obesity, as well as the use of bilateral internal thoracic artery, prolonged operative time and prolonged mechanical ventilation. These data are dated almost a decade. During this timeframe, cardiac surgical care has evolved, particularly in the development of surgical safety checklists and hospital bundles[20,21] that provide a structured way of improving the processes of care in order to ultimately improve patient outcomes. The

American Association for Thoracic Surgery developed best practice guidelines[22] in the prevention of sternal wound infections that include preoperative *Staphylococcus* decolonization using mupirocin and appropriate body soaps, prophylactic antibiotic coverage, maintaining strict serum glucose under control, treatment of all extra-thoracic infections before CABG, avoidance of bone wax, skeletonized thoracic artery harvesting and endoscopic vein harvesting. It is uncertain the universal adherence to this best practice guidelines in all institutions, and consequently on infection outcomes. Despite all the efforts of institutional quality improvement programs, there are uncontrolled issues that are difficult to attain such as emergency operations, those in cardiogenic shock, those with preoperative anemia and poor glycemic control, and frail patients that cannot ambulate independently.

Independent predictors of any infection morbidity identified in this paper have support in the literature. Female gender, age greater than 60 years, duration of cardiopulmonary bypass greater than 120 minutes, preoperative myocardial infarction < 30 days, diabetes mellitus, ejection fraction less than 48% and need of blood transfusion[23,24]. The anthropometric profile was not significantly associated with infection (P=0.12), after adjusting for possible confounders. Independent predictors of surgical site infection identified in this paper also have support in the literature, such as diabetes mellitus[25], chronic obstructive pulmonary disease[26], blood transfusion[27] and obesity[28].

Limitations of the study

This is a retrospective cohort of patients with its inherited limitations. Although the use of BMI as a proxy for body fat percentage due to obesity is controversial, it is a simple measure and used in the investigation to classify patient populations. The low number of patients in the underweight group (N=17) may influence the results, particularly in the multivariable model. Exclusion of the latter of the multivariable model would determine the significance of obesity as an independent predictor of any infection after CABG. On the other hand, it has been proven that the greatest influence of obesity was on surgical site infection. Intraoperative and postoperative care were at discretion of the attending physician, and it was not uniformly applied throughout our cohort in terms of following current guidelines on prevention and treatment of infection after CABG.

CONCLUSIONS

Other factors rather than the anthropometric profile are more important in determining the occurrence of any infection after CABG. However, surgical site infection has occurred more frequently in obese patients. Appropriate patient selection, control of modifiable factors and application of surgical bundles would minimize this important complication.

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Table 1 – Preoperative data according to the study group

	Underweight (N=17)	**Normal (N=522)**	**Overweight (N=796)**	**Obese (N=430)**	**P**
Demographics					
Age (years, mean ± sd)	60.3 ± 13	63 ± 9.7	62 ± 9.7	59.8 ± 9.9	<0.0001
Male sex (%)	8 (47.1%)	361 (69%)	550 (69%)	267 (62%)	0.01
Weight (kg, mean ± sd)	47.6 ± 5.9	61.8 ± 8	72.7 ± 8.5	86.9 ± 11	<0.0001
Height (cm, mean ± sd)	163 ± 9.8	164 ± 8.9	163 ± 8.9	162 ± 9.4	0.13
Symptoms					
Funcional class (NYHA)					0.92
I	17 (100%)	470 (90%)	716 (90%)	391 (91%)	
II	0	27 (5.1%)	59 (7.4%)	31 (7.2%)	
III	0	22 (4.2%)	17 (2.2%)	8 (1.9%)	
IV	0	2 (0.5%)	2 (0.3%)	0	
Presentation					
Acute myocardial infarction	5 (29.4%)	149 (28.6%)	181 (22.8%)	83 (19.4%)	0.008
Unstable angina	6 (35.3%)	217 (41.7%)	281 (35.4%)	142 (33%)	0.03
Stable angina	11 (64.7%)	304 (58.3%)	514 (64.6%)	288 (67%)	0.03
Number of diseased vessels					0.98
One	1 (5.8%)	23 (4.4%)	30 (3.8%)	21 (4.9%)	
Two	3 (17.6%)	110 (21.1	171 (21.6%)	91 (21.3%)	
Three	13 (76.5%)	388 (74.5	590 (74.6%)	316 (73.8%)	
Left main disease	0	36 (16.7%	54 (17.2%)	20 (13%)	0.49

Echocardiography					
LV ejection fraction (%)	59 [46.5-66]	60 [46-67]	62 [48-68]	62 [50-68]	0.16
Comorbidities					
Hypertension	10 (58.8%)	400(76.8%)	622 (78.5%)	388 (90.6%)	<0.0001
Diabetes	2 (11.8%)	88 (16.9%)	144 (18.3%)	111 (25.9%)	0.002
Hyperlipidemia	3 (17.7%)	252 (48.4%	382 (48.3%)	240 (56.1%)	0.001
COPD	1 (5.9%)	11 (2.1%)	11 (1.4%)	10 (2.3%)	0.44
Previous stroke	0	38 (7.3%)	30 (3.8%)	21 (4.9%)	0.02

Legend: NYHA – New York Heart Association classification; LV – left ventricle; COPD – chronic obstructive pulmonary disease

Table 2 – Intraoperative data according to study group

	Underweight (N=17)	**Normal (N=522)**	**Overweight (N=796)**	**Obese (N=430)**	**P**
Type of CABG					.25
Off-pump	2 (11.8%)	42 (8%)	75 (9.4%)	27 (6.3%)	
On-pump	15 (88.2%)	480 (92%)	721 (90.6%)	403 (93.7%)	
Previous cardiac surgery	0	9 (1.7%)	18 (2.3%)	3 (0.7%)	0.15
CPB time (minutes)	78.5 [49.7-106]	79 [62-100]	76 [60-96]	80 [64.2-100]	0.11
Ischemic time (minutes)	70 [42-92]	65 [50-82]	64 [47-82]	68 [53-84]	0.14
Number of treated vessels	3 [3-4]	3 [2-4]	3 [2-4]	3 [2-4]	0.51
One internal thoracic artery	15 (93.8%)	508 (98.6%)	777 (98.7%)	420 (97.7%)	0.56
Two internal thoracic arteries	0	58 (11.3%)	104 (13.2%)	44 (10.2%)	0.2
Radial artery	0	7 (1.4%)	26 (3.3%)	17 (4%)	0.03
Saphenous vein	15 (93.8%)	476 (92.4%)	713 (90.6%)	395 (91.8%)	0.4

Legend: CABG – coronary artery bypass grafting; CPB – cardiopulmonary bypass

Table 3 – Morbidity and mortality after myocardial revascularization performed according to the study group

	Underweight (N=17)	Normal (N=522)	Overweight (N=796)	Obese (N=430)	P
30-day mortality	0	10 (1.9%)	8 (1%)	7 (1.6%)	0.17
Hospital mortality	0	12 (2.3%)	8 (1%)	9 (2.1%)	0.07
MACE	2 (11.8%)	27 (5.2%)	37 (4.6%)	24 (5.6%)	0.53
Myocardial infarction	0	9 (1.7%)	16 (2%)	8 (1.9%)	0.68
Cerebrovascular accident	2 (11.8%)	8 (1.5%)	13 (1.6%)	9 (2.1%)	0.18
Atrial fibrillation	2 (11.8%)	70 (13.6%)	110 (14.1%)	56 (13.3%)	0.97
Intra-aortic balloon pump	0	23 (4.4%)	12 (1.5%)	6 (1.4%)	0.004
Re-exploration for bleeding	0	6 (1.4%)	15 (2.2%)	4 (1.1%)	0.43
Acute kidney injury	1 (5.9%)	14 (2.7%)	6 (0.8%)	8 (1.9%)	0.03
Prolonged mechanical ventilation*	0	9 (1.7%)	6 (0.8%)	3 (0.7%)	0.17
Sepsis	0	21 (4.1%)	17 (2.2%)	15 (3.5%)	0.15
Deep sternal wound infection	0	7 (1.3%)	11 (1.4%)	11 (2.6%)	0.06
Superficial wound infection	1 (6.3%)	13 (2.5%)	30 (3.8%)	23 (5.3%)	0.01
Nosocomial pneumonia	0	28 (5.4%)	30 (3.8%)	21 (4.9%)	0.37
Urinary tract infection	0	7 (1.6%)	7 (1%)	5 (1.3%)	0.77
Venous central line infection	0	0	2 (0.3%)	2 (0.5%)	0.35
Any infection morbidity	1 (6.3%)	33 (6.5%)	52 (6.5%)	45 (10.5%)	0.06
Intensive care unit stay (days)	2 [2-5]	2 [2-3]	2 [2-3]	2 [2-3]	0.88

Legend: MACE – major adverse cardiovascular events; * requirement of tracheostomy

Table 4 – Determinants of any infection morbidity by multivariable Poisson regression

Variable	Unadjusted RR (95%CI)	P	Adjusted RR (95%CI)	P
Female sex	1.72 (1.36 – 2.17)	<0.0001	1.47 (1.14 – 1.88)	0.0024
Age > 60 years	1.74 (1.34 – 2.27)	<0.0001	1.85 (1.44 – 2.39)	<0.0001
CPB time > 120 minutes	2.49 (1.72 – 3.59)	<0.0001	1.89 (1.3 – 2.73)	0.0007
CC time > 80 minutes	1.64 (1.2 – 2.25)	0.002	-	-
MI < 30 days	1.46 (1.14 – 1.87)	0.002	1.37 (1.07 – 1.75)	0.01
Diabetes mellitus	1.82 (1.42 – 2.32)	<0.0001	1.59 (1.24 – 2.04)	0.0003
LVEF < 48%	2.2 (1.52 – 3.19)	<0.0001	2.12 (1.47 – 3.07)	<0.0001
COPD	1.93 (1.09 – 3.34)	0.02	-	-
Previous stroke	1.54 (1 – 2.35)	0.04	-	-
Blood transfusion	2.01 (1.6 – 2.54)	<0.0001	1.55 (1.2 – 2)	0.0008

Legend: RR – relative ratio; CI – confidence intervals; CPB – cardiopulmonary bypass; CC – aortic cross-clamping; MI – myocardial infarction; LVEF – left ventricle ejection fraction; COPD – chronic obstructive pulmonary disease

Table 5 – Determinants of superficial wound infection by multivariable Poisson regression

Variable	Unadjusted RR (95%CI)	P	Adjusted RR (95%CI)	P
Female sex	2.14 (1.55 – 2.95)	<0.0001	1.95 (1.42 – 2.69)	<0.0001
CPB > 120 minutes	2.68 (1.61 – 4.46)	0.0001	2.44 (1.47 – 4.03)	0.0005
CCT > 80 minutes	1.83 (1.1 – 2.7)	0.01	-	-
Diabetes mellitus	2.31 (1.66 – 3.21)	<0.0001	1.9 (1.35 – 2.67)	0.0002
LVEF<48%	2.02 (1.21 – 3.38)	0.007	2.19 (1.32 – 3.62)	0.002
Blood transfusion	1.8 (1.3 – 2.49)	0.0004	-	-
Obesity	1.99 (1.28 – 3.1)	0.002	1.89 (1.21 – 2.96)	0.005

Legend: RR – relative ratio; CI – confidence intervals; CPB – cardiopulmonary bypass duration; CCT – aortic cross clamping duration; LVEF – left ventricle ejection fraction

Table 6 – Determinants of deep sternal wound infection by multivariable Poisson regression

Variable	**Unadjusted RR (95%CI)**	**P**	**Adjusted RR (95%CI)**	**P**
Diabetes mellitus	2.94 (1.72 – 5.03)	<0.0001	2.58 (1.43 – 4.65)	0.002
COPD	4.1 (1.57 – 10.7)	0.004	3.99 (1.53 – 10.42)	0.005
Blood transfusion	2.53 (1.47 – 4.35)	0.008	2.21 (1.25 – 3.93)	0.007
Obesity	2.33 (1.25 – 4.37)	0.008	2.1 (1.11 – 3.96)	0.02

Legend: RR – relative ratio; CI – confidence intervals; COPD – chronic obstructive pulmonary disease