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**Research Letter**

**Association of obesity with venous thromboembolism and myocardial injury in COVID-19**

**ARTICLE INFO**

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Obesity

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**ABSTRACT**

**Introduction:** Although both obesity and coronavirus disease 2019 (COVID-19) independently induce inflammation and thrombosis, the association between obesity class and risk of thrombosis in patients with COVID-19 remains unclear.

**Methods:** This retrospective cohort study included consecutive patients hospitalized with COVID-19 at a single institution. Patients were categorized based on obesity class. The main outcomes were venous thromboembolism (VTE) and myocardial injury, a marker of microvascular thrombosis in COVID-19. Adjustments were made for sociodemographic variables, cardiovascular disease risk factors and comorbidities.

**Results:** 609 patients with COVID-19 were included. 351 (58%) patients were without obesity, 110 (18%) were patients with class I obesity, 76 (12%) were patients with class II obesity, and 72 (12%) were patients with class III obesity. Patients with class I and III obesity had significantly higher risk-adjusted odds of VTE compared to patients without obesity (OR = 2.54, 95% CI: 1.05–6.14 for class I obesity; and OR = 3.95, 95% CI: 1.40–11.14 for class III obesity). Patients with class III obesity had significantly higher risk-adjusted odds of myocardial injury compared to patients without obesity (OR = 2.15, 95% CI: 1.12–4.12). Both VTE and myocardial injury were significantly associated with greater risk-adjusted odds of mortality.

**Conclusion:** This study demonstrates that both macrovascular and microvascular thromboses may contribute to the elevated morbidity and mortality in patients with obesity and COVID-19.

**Introduction**

Patients with obesity have greater risk of mechanical ventilation and mortality in coronavirus disease 2019 (COVID-19) [1]. COVID-19 has been associated with both macrovascular and microvascular thromboses likely through inflammation induced endothelial cell damage [2,3]. More severe disease and higher mortality rates observed among patients with obesity may be due to their higher risk of thrombosis, as obesity is known to be associated with endotheliopathy and platelet activation [4]. We aimed to elucidate the association between obesity and thrombosis through investigating the rates of venous thromboembolism (VTE) and myocardial injury, a marker of microvascular thrombosis [3], among patients with COVID-19.

**Methods**

Institutional Review Board approval #2000027783 was obtained. This retrospective cohort study used the “Yale COVID-19 Cardiovascular Registry”, which included consecutive patients with COVID-19 hospitalized between March 1st and May 31st 2020. The design of this registry has been previously described [5]. Body mass index (BMI) was operationalized as patients without obesity (BMI < 30.0 kg/m²), patients with class I obesity (BMI 30.0 kg/m²–34.9 kg/m²), patients with class II obesity (BMI 35.0 kg/m²–39.9 kg/m²), and patients with class III obesity (BMI ≥ 40.0 kg/m²). Our main outcomes were VTE verified by imaging through routine clinical practice (either CT scan for pulmonary embolism or ultrasound for deep vein thrombosis), myocardial injury (defined as any troponin T value above 99th percentile upper reference limit during hospitalization), and death or mechanical ventilation. Covariates used for adjustment included age, sex, race, and history of VTE, coronary artery disease, diabetes, hypertension, and hyperlipidemia. Analysis of variance and chi-squared testing was used to evaluate for trends in baseline characteristics, and logistic regression was used to estimate risk-adjusted odds ratios.

**Results**

Of the 609 patients with COVID-19, 351 (58%) patients were without obesity, 110 (18%) were patients with class I obesity, 76 (12%) were patients with class II obesity, and 72 (12%) were patients with class III obesity (Table 1). Overall, the mean age was 66 years, 290 (48%) were female, 312 (51%) were of White race, and 182 (30%) were of Black race. 107 (18%) patients had known coronary artery disease, 240 (39%) patients had diabetes, 369 (61%) patients had hypertension, and 238 (39%) patients had hyperlipidemia on admission. Patients without obesity were significantly older, more likely to be White, less likely to be Black, and less likely to have diabetes than patients with obesity.

Overall, 106 (17%) patients received diagnostic imaging for VTE. Rates of VTE were 4% for patients without obesity, 9% for patients with class I obesity, 4% for patients with class II obesity, and 11% for patients with class III obesity. After adjusting for covariates, patients with class I and III obesity had significantly higher odds of VTE compared to patients without obesity (OR = 2.54, 95% CI: 1.05–6.14 for class I obesity; and OR = 3.95, 95% CI: 1.40–11.14 for class III obesity) (Fig. 1). Unadjusted
Obesity increases the risk of thrombosis by low grade inflammation and oxidative damage, leading to endothelial injury and increased platelet activation [4]. There is growing evidence that a hyper-inflammatory state in COVID-19 also induces endothelial dysfunction [2], and can activate tissue factor leading to platelet upregulation [6]. Hence, higher obesity class may enhance inflammation and be an additive risk factor for thrombosis in patients with COVID-19.

Limitations of our study include underestimation of VTE events, as imaging was not conducted for every patient. In addition, there may be differences in characteristics between those receiving and not receiving imaging within each BMI category. This study demonstrates that greater risk of macrovascular and microvascular thromboses may contribute to the elevated morbidity and mortality in patients with obesity and COVID-19.

Ethical statement ORCP

I have read and have abided by the statement of ethical standards for manuscripts submitted to the Obesity Research & Clinical Practice. Nihar R. Desai, on behalf of the co-authors.

Conflicts of Interest/Disclosures

None.

CRediT authorship contribution statement

Stephen Y. Wang: Conceptualization, Methodology, Formal analysis, Investigation, Writing - original draft, Writing - review & editing, Visualization. Avinainder Singh: Conceptualization, Investigation, Writing - review & editing. Maxwell D. Eder: Investigation, Writing - review & editing. Lina Vadlamani: Investigation, Writing - review & editing. Alfred I. Lee: Writing - review & editing, Supervision. Hyung J. Chun: Writing - review & editing, Supervision. Nihar R. Desai: Conceptualization, Methodology, Resources, Writing - review & editing, Supervision.
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