Effects of Body Mass Index on Presentation and Outcomes of COVID-19 among Heart Transplant and Left Ventricular Assist Device Patients: A Multi-Institutional Study

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Abstract The coronavirus disease 2019 (COVID-19) pandemic continues to pose a significant threat to patients receiving advanced heart failure therapies. The current study was undertaken to better understand the relationship between obesity and outcomes of SARS-CoV-2 infection in patients with a left ventricular assist device (LVAD) or heart transplant. We performed a retrospective review of patients with a heart transplant or LVAD who presented to one of the participating 11 institutions between April 1 and November 30, 2020. Patients were grouped by body mass index (BMI) into obese (BMI ≥ 30 k/m²) and nonobese cohorts (BMI < 30 kg/m²). Multivariable logistic regression models were used to estimate effects of obesity on outcomes of interest. Across all centers, 162 heart transplant and 81 LVAD patients were identified; 54 (33%) and 38 (47%) were obese, respectively. Obese patients tended to have more symptoms at presentation. No differences in rates of hospitalization or ICU admission were noted. Obese patients with LVADs were more likely to require mechanical ventilation (39% *vs.* 8%, $p < 0.05$). No differences in renal failure or secondary infection were noted. Mortality was similar among heart transplant patients (11% [obese] *vs.* 16% [nonobese], $p = 0.628$) and LVAD patients (12% *vs.* 15%, $p = 1.0$). BMI was not associated with increased adjusted odds of mortality, ICU admission, or mechanical ventilation (all $p > 0.10$). In summary, acute presentations of SARS-CoV-2 among heart transplant and LVAD recipients carry a significantly higher mortality than the general population, although BMI does not appear to impact this. Further studies on the longer-term effects of COVID-19 on this population are warranted. *ASAIO Journal* 2023; 69;43–49

Key Words: transplant, LVAD, COVID-19, SARS-CoV-2, MCS

The ongoing coronavirus (COVID-19) pandemic poses an especially significant health threat to patients treated with advanced heart failure therapies, such as a left ventricular assist device (LVAD) or an orthotopic heart transplant (OHT).[1,2] In addition to requiring high-risk medications such as immunosuppression and anticoagulation, these patients often have significant comorbidities such as diabetes and renal failure, which contribute to general frailty and hemodynamic instability, and portend worse outcomes with coronavirus infection.[3–9]

Obesity has been independently associated with adverse outcomes among patients who require advanced heart failure therapies as well as those who contract COVID-19.[9–15] Proposed mechanisms are multifactorial and include restrictive pulmonary physiology, as well as potentially increased inflammatory cascades because of adipocyte activity.[15,16] However, how obesity affects COVID-19 symptomatology and outcomes among those who have received heart transplants or LVADs are poorly understood.

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We sought to use a multi-institutional registry of COVID-19 presentations in patients with previous heart transplant or LVAD implantation to better describe the risk of obesity in this patient population. We hypothesized that these patients, who already face greater risks and have worse outcomes with COVID-19, might be further negatively affected by the presence of obesity.

Methods

This study was a retrospective review from the 'Trans-CoV-VAD' registry, a prospectively maintained multi-institutional registry of patients with durable LVAD or history of heart transplantation who present with a positive SARS-CoV-2 test in an inpatient or outpatient setting. This study retrospectively analyzed data from this registry between April 1 and November 30, 2020. During this period, 11 centers participated in the registry across 9 states: the University of Pennsylvania (Philadelphia, PA), Ascension St. Vincent Heart Center (Indianapolis, IN), the Cleveland Clinic (Cleveland, OH), the Medical University of South Carolina (Charleston, SC), MedStar Washington Hospital Center (Washington, DC), Mount Sinai Hospital (New York, NY), Northwestern University (Chicago, IL), the University of Michigan (Ann Arbor, MI), Stanford University (Stanford, CA), the University of Pittsburgh (Pittsburgh, PA), and the University of Rochester (Rochester, NY). Each site obtained approval from the local institutional review board. Specific informed consent was waived because of the determination of minimal risk to included patients. Data were collected *via* a review of the patients' electronic medical records, and anonymized data were transmitted for collation and storage at a centralized repository maintained by the University of Pennsylvania. Deidentified data were made available to research staff for retrospective analysis. Data collected included patient demographic and comorbidity information, transplant and VAD-related history, medication history, COVID-19 symptom information and presentation history, and treatment course. Patients with missing height and weight information were excluded.

After the initial query, all patients were stratified into two cohorts based on their body mass index (BMI) at presentation: BMI $<30\,kg/m^2$ (nonobese group) and BMI $\geq 30\,kg/m^2$ (obese group). Heart transplant recipients and VAD patients were examined separately. Outcomes of interest included COVID-19 presentation details, treatments used, and mortality. Continuous variables were expressed as median (interquartile range), whereas categorical variables were expressed as frequency (percent of population). For unadjusted comparisons between groups, the Kruskal–Wallis rank test was used for continuous variables and the χ^2 test or Fisher's exact test was used for categorical variables. Multivariable logistic regression was used to estimate the effect of obesity on outcomes of interest. A restricted cubic spline approach with five knots was used to model any nonlinear effects of BMI. Models were adjusted for age and gender. All statistical analyses were performed using Stata 15 (StataCorp LP, College Station, TX).

Results

Throughout the study period, 243 total patients were identified after excluding three patients for missing height or weight information, of whom 162 had previous heart transplants and 81 had LVADs. Of the heart transplant patients, 54 (33%) were obese, whereas among the LVAD patients, 38 (47%) were obese. Baseline patient characteristics are listed in Table 1, whereas BMI distribution can be found in

Table 1. Patient Demographics and Comorbidities

	Heart Transplant			Ventricular Assist Device		
Patient Characteristics	BMI ≥ 30 (N = 54)	BMI < 30 (N = 108)	*p* Value	BMI ≥ 30 (N = 38)	BMI < 30 (N = 43)	*p* Value
Age at presentation, years	57.3 (46.4–67.8)	61.8 (48.1–68.8)	0.303	52.6 (43.8–63.1)	60.6 (47.2–71.0)	0.083
Age at OHT/VAD, years	51.0 (36.6–60.7)	56.1 (45.0–62.7)	0.057	51.9 (42.7–59.1)	57.5 (43.6–69.6)	0.085
Time since surgery, years	6.3 (2.7–11.3)	5.1 (1.6–13.8)	0.757	1.1 (0.6–3.2)	1.7 (0.6–3.2)	0.476
Female sex	18 (33.3%)	26 (24.1%)	0.212	10 (26.3%)	17 (39.5%)	0.208
Weight, kg	104 (95–118)	77 (70–89)	<0.001*	112 (105–124)	74 (66–84)	<0.001*
Height, m	1.8 (1.7–1.8)	1.8 (1.7–1.8)	0.985	1.7 (1.7–1.8)	1.7 (1.6–1.8)	0.272
Caucasian race	31 (59.6%)	58 (58.6%)	0.565	21 (58.3%)	24 (55.8%)	1.000
Hispanic ethnicity	4 (7.4%)	12 (11.2%)	0.581	3 (8.1%)	4 (9.5%)	1.000
Hypertension	43 (79.6%)	87 (80.6%)	0.889	28 (73.7%)	29 (67.4%)	0.539
Diabetes	24 (44.4%)	54 (50.0%)	0.505	18 (47.4%)	19 (44.2%)	0.774
Atrial fibrillation	5 (9.3%)	9 (8.3%)	0.843	8 (21.1%)	16 (37.2%)	0.112
History of stroke	6 (11.1%)	11 (10.2%)	0.856	8 (21.1%)	9 (20.9%)	0.989
COPD	5 (9.3%)	11 (10.2%)	0.852	2 (5.3%)	1 (2.3%)	0.598
Interstitial lung disease	5 (9.3%)	4 (3.7%)	0.161	0 (0%)	0 (0%)	NA
Home oxygen use	3 (5.6%)	2 (1.9%)	0.334	0 (0%)	0 (0%)	NA
Smoking history	14 (25.9%)	28 (25.9%)	1.000	15 (39.5%)	20 (46.5%)	0.523
Chronic dialysis	1 (1.9%)	9 (8.3%)	0.167	2 (5.3%)	1 (2.3%)	0.598
ACEi/ARB medication use	26 (50.0%)	35 (34.0%)	0.054	18 (52.9%)	22 (53.7%)	0.951
Cardiac diagnosis			0.535			0.855
Amyloid cardiomyopathy	2 (3.8%)	2 (1.9%)				
Congenital heart disease	0 (0%)	4 (3.9%)		0 (0%)	1 (2.4%)	
Familial cardiomyopathy	3 (5.7%)	6 (5.8%)		3 (8.8%)	2 (4.9%)	
Hypertrophic cardiomyopathy	3 (5.7%)	4 (3.9%)		1 (2.9%)	2 (4.9%)	
Ischemic cardiomyopathy	6 (11.3%)	23 (22.1%)		10 (29.4%)	14 (34.2%)	
Other Nonischemic	37 (69.8%)	61 (58.7%)		19 (55.9%)	22 (53.7%)	
Sarcoid cardiomyopathy	1 (1.9%)	2 (1.9%)		1 (2.9%)	0 (0%)	
Viral cardiomyopathy	1 (1.9%)	2 (1.9%)		0 (0%)	0 (0%)	

Values presented as median (interquartile range) or frequency (percent of population).

*Statistical significance at $p < 0.05$.

ACEi/ARB, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blockers; BMI, body mass index; COPD, chronic obstructive pulmonary disease; OHT, orthotopic heart transplant; VAD, ventricular assist device.

Supplemental Figure 2 (Supplemental Digital Content 1, http://links.lww.com/ASAIO/A846). Median age at presentation was 57 and 62 among obese and nonobese OHT patients, respectively ($p = 0.303$), and 53 and 61 among obese and nonobese VAD patients ($p = 0.083$). Race and comorbidity burden were relatively similar between obese and nonobese cohorts. Most patients received transplants for an underlying nonischemic cardiomyopathy diagnosis.

The immunologic history of heart transplant patients at the time of presentation with COVID-19 is listed in Table 2. A slight trend toward more historical acute cellular and antibody-mediated rejection episodes requiring treatment was noted among obese patients. Immunosuppression regimens varied across centers, but a majority of both obese and nonobese patients were on tacrolimus (86.8% *vs.* 80.8%, respectively). Steroid use was noted in approximately half of the patients and did not significantly differ between obese and nonobese patients. Clinical histories of LVAD patients at the time of presentation are given in Table 3. Similarly, a majority of patients had underlying nonischemic cardiomyopathy. Most patients had a HeartMate 3 device (72.7% obese *vs.* 51.2% nonobese), followed by HeartWare HVAD (18.2% obese *vs.* 34.2% nonobese). Roughly one-third of patients in each BMI group had a history of previous early right ventricular failure requiring intervention, in addition to similar rates of historical bleeding complications.

COVID-19–related presentation characteristics for both heart transplant and LVAD patients are detailed in Table 4. Of the cardinal COVID-19 symptoms assessed, obese heart transplant patients had slightly higher rates of cough (65% *vs.* 52%, $p = 0.124$), myalgias (57% *vs.* 30%, $p = 0.001$), and headache (45% *vs.* 21%, $p = 0.002$) compared with nonobese patients. Incidences of the most common symptoms in each cohort are depicted in Figure 1. LVAD patients had similar symptom distributions between obese and nonobese cohorts, although slightly more diarrhea was noted in obese patients (21% *vs.* 10%, $p = 0.209$). Timing of symptom onset with respect to medical evaluation is depicted in Supplementary Figure 2 (Supplemental Digital Content 1, http://links.lww.com/ASAIO/A846. Most symptoms occurred within 5 days preceding presentation, and no appreciable differences between obese and nonobese patients were noted. Similarly, no obvious trend in inflammatory markers was observed between obese and nonobese cohorts.

Table 2. Heart Transplant History and Immunosuppression at Presentation

Patient Characteristics	BMI ≥ 30 (N = 54)	BMI < 30 (N = 108)	*p* Value
Transplant to infection interval, years	6.3 [2.7–11.3]	4.8 [1.6–13.8]	0.7
History of acute cellular rejection			0.076
1 Episode	8 (14.8%)	16 (14.8%)	
2 Episodes	5 (9.3%)	2 (1.9%)	
3 Episodes	2 (3.7%)	3 (1.9%)	
4 Episodes	1 (1.9%)	0 (0%)	
History of antibody-mediated rejection			0.089
1 Episode	3 (5.6%)	5 (4.6%)	
2 Episodes	1 (1.9%)	0 (0%)	
3 Episodes	2 (3.7%)	0 (0%)	
4 Episodes	NA	NA	
Immunosuppressant use			
Cyclosporin	4 (7.6%)	15 (14.4%)	0.302
Tacrolimus	46 (86.8%)	84 (80.8%)	0.344
Dose, mg	4 [2.5–7]	4.5 [2–7.75]	<0.01
Sirolimus	7 (13.2%)	13 (12.5%)	1.000
Everolimus	2 (3.8%)	1 (1.0%)	0.264
Mycophenolate	35 (66.0%)	59 (56.7%)	0.261
Dose, mg	1000 [1000–2000]	1440 [1000–2000]	0.20
Prednisone	26 (49.1%)	51 (49.0%)	0.998
Dose, mg	5 [5–7.5]	5 [5–10]	0.06

Values presented as frequency (percent of population).
BMI, body mass index.

Table 3. Ventricular Assist Device and Clinical History

Patient Characteristics	BMI ≥ 30 (N = 38)	BMI < 30 (N = 43)	*p* Value
Device			0.191
Heartmate II	3 (9.1%)	6 (14.6%)	
Heartmate III	24 (72.7%)	21 (51.2%)	
Heartware HVAD	6 (18.2%)	14 (34.2%)	
Post-VAD complications			
RV failure	11 (32.4%)	14 (34.2%)	0.870
Pulmonary hypertension	2 (6.1%)	3 (7.3%)	1.000
GI bleeding	5 (14.7%)	14 (34.2%)	0.066
Other bleeding	4 (11.8%)	4 (10.0%)	1.000
Post-VAD stroke	5 (14.7%)	8 (19.5%)	0.761

Values presented as frequency (percent of population).
BMI, body mass index; GI, gastrointestinal; RV, right ventricle; VAD, ventricular assist device.

Patient outcomes are detailed in Table 5. The overall rate of hospitalization was 56%. Slightly more intensive care unit (ICU) utilization was noted among obese LVAD patients, while similar incidences were noted among transplant patients. Obese patients had more mechanical ventilation use in both heart transplant (34.6% *vs.* 23.3%, $p = 0.278$) and LVAD (39.1% *vs.* 7.7%, $p = 0.015$). Two heart transplant patients received ECMO support, one of whom was obese. No differences in rates of secondary infection or need for renal replacement therapy were noted, whereas one obese LVAD patient suffered an outflow graft obstruction/stenosis (HeartMate 3). Overall mortality was 13.6% among heart transplant patients and 12.3% among LVAD patients, with similar distributions between obese and nonobese cohorts. Mortality was higher among hospitalized patients (23.0% and 20% in the OHT and VAD cohorts, respectively). Outcomes data stratified by LVAD device type can be found in Supplementary Table 1 (Supplemental Digital Content 1, http://links.lww.com/ASAIO/A846). When modeled *via* a linear or restricted cubic spline approach, obesity was not predictive of worsening mortality in OHT (linear model adjusted odds ratio (AOR) 0.99 [0.91–1.08], $p = 0.846$) or LVAD (linear model AOR 0.99 [0.89–1.09], $p = 0.795$) patients. Similarly, obesity was not predictive of ICU stay in OHT (linear model AOR 1.00 [0.92–1.10], $p = 0.918$) or LVAD (linear model AOR 1.05 [0.97–1.13], $p = 0.237$) patients after adjustment. Finally, obesity was not predictive of ventilator use in OHT (linear model AOR 1.07 [0.97–1.17], $p = 0.158$) or LVAD (linear model AOR 1.08 [0.98–1.18], $p = 0.092$) patients after adjustment. Estimated AOR for mortality *vs.* BMI as modeled with restricted cubic splines is depicted in Figure 2 (all $p > 0.05$).

Table 4. Clinical Characteristics at Presentation

	Heart Transplant			Ventricular Assist Device		
	BMI ≥ 30 (N = 54)	BMI < 30 (N = 108)	*p* Value	BMI ≥ 30 (N = 38)	BMI < 30 (N = 43)	*p* Value
COVID sentinel symptoms						
Fever	30 (56.6%)	51 (49.5%)	0.401	14 (41.2%)	17 (41.5%)	0.980
Cough	34 (65.4%)	54 (52.4%)	0.124	15 (44.1%)	19 (46.3%)	0.847
Dyspnea	29 (54.7%)	46 (44.7%)	0.234	15 (44.1%)	17 (41.5%)	0.817
Chest pain	7 (13.5%)	10 (9.7%)	0.480	6 (17.7%)	6 (14.6%)	0.723
Abd pain	7 (13.2%)	8 (7.8%)	0.275	4 (11.8%)	2 (4.9%)	0.401
Myalgias	30 (56.6%)	31 (30.1%)	0.001*	7 (20.6%)	10 (24.4%)	0.695
Diarrhea	22 (41.5%)	33 (32.0%)	0.241	7 (20.6%)	4 (9.8%)	0.209
Anosmia	4 (7.7%)	11 (10.7%)	0.775	5 (14.7%)	5 (12.2%)	1.000
Fatigue	29 (54.7%)	49 (47.6%)	0.398	12 (35.3%)	14 (34.2%)	0.917
Headache	24 (45.3%)	22 (21.4%)	**0.002***	5 (14.7%)	6 (14.6%)	1.000
Respiratory rate	20 (18–24.5)	20 (18–22)	0.525	18 (18–20)	18 (18–21)	0.629
Temperature (F)	99.4 (98.6–100.6)	99.2 (98.4–100.8)	0.606	98.7 (98.1–100.4)	98.2 (97.5–100.2)	0.095
Labs on presentation						
WBC	5.9 (4.4–9.4)	6.0 (4.2–7.5)	0.426	6.5 (4.1–9.1)	6.2 (4.5–8.7)	0.899
Ferritin	700 (389–1,121)	689 (264–1,850)	0.893	198 (95–715)	541 (335–916)	0.066
Procalcitonin	0.3 (0.10–2.61)	0.61 (0.10–1.86)	0.829	0.43 (0.07–0.68)	0.72 (0.06–6.92)	0.382
CRP	72.8 (19.5–107.3)	24.7 (9.3–54.3)	0.225	20.8 (9.1–108.9)	31.8 (6.9–199)	0.527

Values presented as median (interquartile range) or frequency (percent of population).
*Statistical significance at $p < 0.05$.
BMI, body mass index; CRP, C-reactive protein; WBC, white blood cell count.

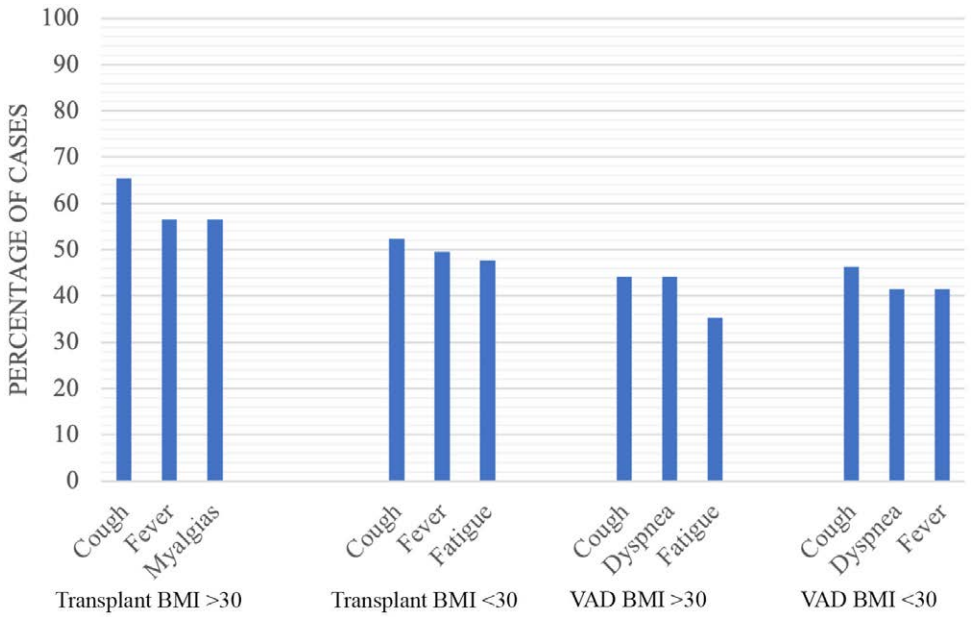

Figure 1. Most common COVID-19 symptoms: frequencies of the three most common COVID-19 symptoms among orthotopic heart transplant and ventricular assist device patient cohorts. BMI, body mass index. full color online

Discussion

In this large multi-institutional study examining the role of obesity on the presentation characteristics and outcomes of OHT and LVAD patients with COVID-19 infection, obese heart transplant patients were often more symptomatic than their nonobese counterparts. High rates of hospitalization were noted in both AHF cohorts, with more ICU and ventilator utilization specifically in obese LVAD patients. Among both OHT and LVAD patients, in-hospital mortality with COVID-19 infection was high (23% and 20%, respectively), and obesity did not appear to influence this; thus, obesity may be relatively de-emphasized when considering risks of complications with COVID-19 infection in advanced heart failure patients.

Advanced heart failure patients are among the highest risk patient population for severe complications from COVID-19 infection, resulting in a low clinical threshold for hospitalization compared with the general population.[1,2] From the earliest descriptive series of COVID-19 infections, preexisting cardiovascular disease has consistently portended worse mortality and hospitalization courses.[6,7,12] Proposed mechanisms for this increased risk are varied and include reduced overall immunity, general frailty, underlying myocardial injury, and reduced hemodynamic capacity to cope with significant sepsis. Several medications taken by these patient populations may also affect infection severity. As the angiotensin-converting enzyme (ACE) 2 acts as the functional receptor for the SARS-CoV-2 virus,

Table 5. Clinical Outcomes of Infection

	Heart Transplant			Ventricular Assist Device		
	BMI ≥ 30 (N = 54)	BMI < 30 (N = 108)	*p* Value	BMI ≥ 30 (N = 38)	BMI < 30 (N = 43)	*p* Value
Admission required	26 (49.1%)	61 (59.2%)	0.226	23 (67.7%)	27 (65.9%)	0.870
Hospital length of stay	13.5 (5–22)	8 (4–23)	0.425	11 (6–39)	6 (4–23)	0.216
ICU stay required	10 (38.5%)	22 (37.9%)	0.963	14 (60.9%)	7 (26.9%)	0.017*
ICU length of stay	15 (13–20)	7 (3–23)	0.268	10 (6–13)	7 (3–10)	0.410
Mechanical ventilation	9 (34.6%)	14 (23.3%)	0.278	9 (39.1%)	2 (7.7%)	0.015*
Ventilator time	13.5 (9.5–20)	9 (3–27)	0.492	10 (6–11)	20, 69**	0.099
ECMO used?	1 (1.6%)	1 (3.9%)	0.530	0 (0%)	0 (0%)	NA
Pulse steroids used	12 (22.6%)	21 (21.0%)	0.814	10 (29.4%)	7 (18.0%)	0.248
Immunosuppression reduced	24 (46.2%)	46 (45.1%)	0.901	NA	NA	NA
Renal replacement therapy	7 (13.2%)	7 (6.9%)	0.191	1 (2.9%)	3 (7.5%)	0.620
New secondary infection	10 (18.9%)	15 (15.2%)	0.556	3 (8.8%)	2 (5.3%)	0.662
GI bleeding	1 (1.9%)	2 (2.0%)	1.000	1 (2.9%)	3 (7.5%)	0.620
Venous thromboembolism	1 (2.2%)	2 (2.3%)	1.000	0 (0%)	0 (0%)	NA
LVAD thrombosis	NA	NA	NA	1 (3.0%)	0 (0%)	0.465
Mortality at time of reporting	6 (11.3%)	16 (15.5%)	0.628	4 (11.8%)	6 (14.6%)	1.000
Mortality among admitted patients	5 (19.2%)	15 (24.6%)	0.782	4 (17.4%)	6 (22.2%)	0.736

Values presented as median (interquartile range) or frequency (percent of population).
*Statistical significance at $p < 0.05$.
**Only two observations reported.
BMI, body mass index; ECMO, extracorporeal membrane oxygenation; GI, gastrointestinal; ICU, intensive care unit; LVAD, left ventricular assist device.

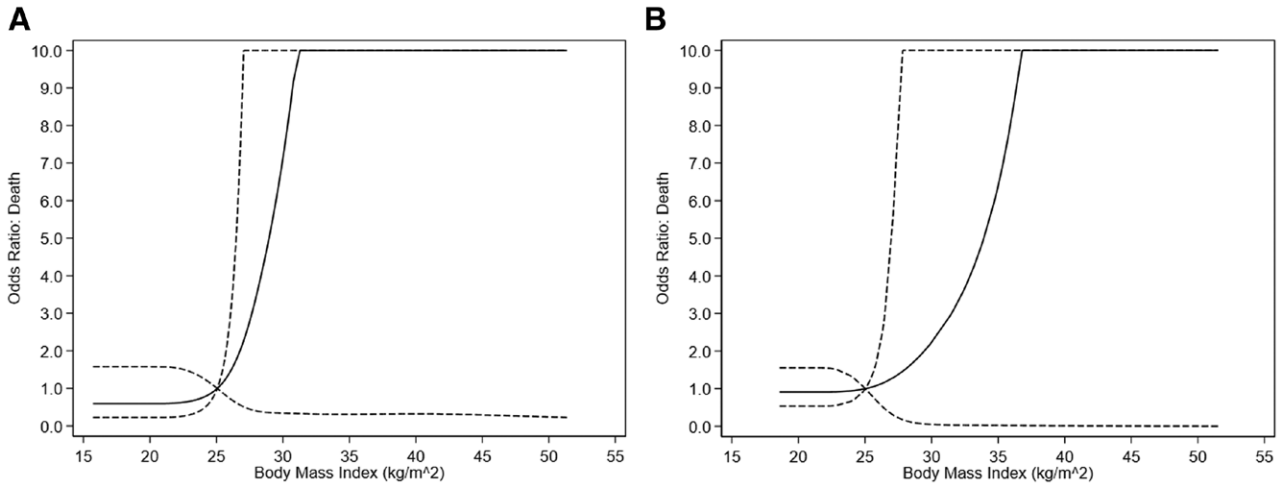

Figure 2. Restricted cubic spline model: Restricted Cubic spline model approximation of adjusted odds ratio for mortality with (**A**) orthotopic heart transplant and (**B**) ventricular assist device patient cohorts with 95% confidence interval (dotted lines). For all models, a reference of body mass index 25 was chosen. Models adjusted for patient age and gender. All models nonsignificant ($p > 0.05$).

theoretical positive and negative effects of ACE inhibitor and an angiotensin receptor blocker I medications have been proposed, though most data have not demonstrated an association between therapy and outcome, including the Blockers of Angiotensin Receptor and Angiotensin-Converting Enzyme inhibitors suspension in hospitalized patients with coronavirus infection trial.[16] The immunosuppressive therapies associated with heart transplantation have as of yet unquantified but putatively increased impact on the severity of infection and vaccination responses, and guidelines for managing these in COVID-19–infected patients are unclear.[17] Furthermore, the low-grade disseminated intravascular coagulation and pulmonary thrombotic microangiopathy associated with COVID-19 infection may be particularly associated with pulmonary emboli and right heart strain, ischemic insult, and coagulopathy.[1,2]

Now, 2 years into the COVID-19 pandemic, many descriptive series of infected patients have come to light. Of particular note in the current study is the higher rate of mortality noted among both obese and nonobese OHT and LVAD patients who contract the SARS-CoV-2 virus compared with the general population.[18–23] In a series of 28 heart transplant patients who presented for COVID-19 in New York early in the pandemic, Latif et al. reported a 25% mortality rate although this may have been overestimated because of lack of widespread testing and limited treatment knowledge at the time.[18] An Italian multicenter report from Bottio et al. captured 47 patients across 7 centers between February and July 2020 and noted an almost 30% mortality rate.[19] Despite the more widespread testing capacity and inclusion of both inpatient and outpatient presentations in the current study, overall mortality remained high, further highlighting the vulnerability of this patient population. Similar mortality rates have been observed in other solid organ transplant populations, with a 10-fold increase in mortality compared with the general population.[24–27] The Trans-CoV-VAD

registry summarized the largest series of COVID-19 presentations in OHT and durable LVAD populations; these summaries should serve as a benchmark for estimating morbidity in these cohorts.[28,29]

Obesity has been identified as a risk factor for serious infection and mortality among COVID-19 patients in numerous observational studies.[9,12–15] Various mechanisms of this increased risk have been proposed, including increased incidence of associated comorbidities (hypertension, coronary disease, etc.) and worsened baseline lung function because of associated restrictive physiology or obesity-hypoventilation syndrome. Interestingly, adipocytes are known to highly express ACE-2 receptors; consequently, increased inflammatory responses have been proposed as contributory to morbidity.[30] However, in a single-center observational study of 77 patients hospitalized with severe COVID-19 infection, a sizable array of inflammatory markers and cytokines were similar between obese and nonobese cohorts, suggesting systemic inflammatory responses may be similar.[31] In the current study, obesity was associated with more symptoms at presentation and trends toward increased mechanical ventilation without increased mortality. Although the report may be underpowered to define these markers, these findings are certainly in line with existing literature suggesting more important effects from preexisting cardiovascular comorbidities. Obesity therefore should be relatively deemphasized when considering risk factors for infection in these patients.

The significance of these findings comes at a crucial time as targeted SARS-CoV-2 vaccines are widely available. Specifically, the high rate of mortality in these series illustrates the importance of expanding efforts for full vaccination in these cohorts. As most of these vaccines have been engineered using synthetic mRNA technology, there is no theoretical capability for viral infection in immunocompromised patients. We strongly support the guidance from the International Society of Heart and Lung Transplantation and the American Society of Transplantation encouraging prompt vaccination for these high-risk patients.[32,33]

This study has several limitations that may affect the conclusions drawn. Although multi-institutional in design, an important limitation is that only OHT/VAD patients who presented to hospitals within the participating centers' network were assessed, and this likely biases toward patients with more severe disease. In addition, detailed clinical courses including status before VAD implant/transplant, present severity of illness/cardiac impairment, immunosuppressive adjustments, and adjuvant therapies were not available in the data and thus effects cannot be considered. A significant limitation lies in the sample size of this cohort which limits the statistical power of analyses. However, a paucity of data surrounding COVID-19 infection in advanced heart failure patients exists and comparatively, this multi-institutional cohort represents one of the largest series in this population available. Finally, this study has all the limitations associated with the retrospective cohort study design.

In summary, acute presentations of SARS-CoV-2 among heart transplant and LVAD recipients carry a significantly higher mortality than the general population. Obese heart transplant patients experienced more symptoms than their nonobese counterparts, but obesity did not affect the adjusted risk of mortality in either AHF cohort. Underlying cardiovascular comorbidities may therefore play a larger role in the morbidity of COVID-19 than obesity alone. Expanded efforts to achieve full vaccination in these vulnerable cohorts should be encouraged.

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