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Obesity and COVID-19: An analysis of the relationship between obesity and outcomes of tracheostomy secondary to COVID-19

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University in
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Abstract

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Introduction: Tracheostomy has been an essential tool in management of severe COVID-19. Even before the COVID-19 pandemic, optimal timing and surgical approach has been debated; intense research on best practices for tracheostomy of the critically ill COVID-19 patient has persisted over the past two years. Because obesity alters anatomy and immune function, managing COVID-19 patients with body mass index >30 has been a special focus of investigation.

Methods: Hazard ratios (HR) for mortality, prolonged ventilator dependence and prolonged hospitalization were compared for patients with BMI above and below or equal to 30. HR for the same were calculated for open versus closed surgical approach, interacting with BMI.

Results: BMI > 30 alone did not independently predict mortality, ventilator independence, or hospital discharge over a 90-day follow-up period. Nevertheless, open tracheostomy technique and having a P/F ratio before tracheostomy of under 100 were associated with an increased hazard of hospital discharge when interacting with the BMI category.

Conclusion: More research is needed to determine how best to manage critically ill COVID-19 patients with high BMIs, especially when a tracheotomy is considered.

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Chapter One

Literature Review

1.1 Introduction

For most people, COVID-19 causes moderate illness and symptoms including (but not limited to) fever, dry cough, chills, shortness of breath, and fatigue (CDC, 2022). However, as the name implies, SARS-CoV-2 can also cause life-threatening complications, such as acute respiratory distress syndrome (ARDS), especially among persons with cardiovascular disease, chronic respiratory conditions, obesity, and other non-communicable diseases.

Severe disease in a few, combined with the rapid spread of COVID-19, has put considerable strain on both human and material resource availability in healthcare. In an effort to decrease suffering and improve the outcomes of patients during this pandemic, much research has been conducted pertaining to management of the critically ill patient with COVID-19. Tracheostomy has been an essential tool in management of severe COVID-19 and optimizing patient outcomes has become paramount. Defining optimal surgical approaches for, and timing of tracheostomy for best outcomes was an active area of research even before the pandemic. COVID-19 and its management have made these questions particularly relevant.

In this retrospective chart review study, I aim to add to the body of surrounding tracheostomy, specifically in obese patients. These patients, due to genetics, environmental circumstances, or lifestyle choices represent a vulnerable population.

1.2 Obesity in COVID-19

The effect of obesity on morbidity and mortality associated with COVID-19 has attracted growing attention from researchers and clinicians. A 2020 study by Nakeshbandi and colleagues of 684 patients with COVID-19 in New York City found that obese patients faced a risk of intubation up to 2.4 times that of their average weight counterparts. Interestingly, they found that mortality was statistically significantly increased in males (RR: 1.4) but there was no observed difference in females. A meta-analysis conducted in December of 2020 found similar results, with the risk ratio for mechanical ventilation increasing to 5.22 for patients with a BMI above 40; additionally, they found that the risk of mortality among obese patients was 1.65 times that of those with an average-range BMI (Yang et al., 2020). Other studies have confirmed the association of increased mortality and obesity (Huang, et al 2020; Du et al, 2021; Abumayyaleh et al, 2021). Many studies have found an increase morbidity associated with obesity, including the risk of severe cases of COVID-19, hospitalization, and the need for intensive care (Yang et al, 2020; Pettit et al, 2020; Soeroto et al, 2020; Kwok et al, 2020; Simonnet et al, 2020; Huang et al, 2020; Du et al, 2021; Abumayyaleh et al, 2021).

1.3 Obesity Paradox

In studying the effect of obesity on critical illness-- particularly respiratory illness-- researchers have coined the term "obesity paradox." This term describes the phenomenon of increased morbidity but decreased mortality observed among patients with obesity as compared to their average-BMI counterparts. Researchers dispute the existence of the obesity paradox; several studies have supported its existence, while others have refuted it. Zhi and colleagues conducted a systematic review and meta-analysis in 2016 regarding the obesity paradox in ARDS. They found that obese patients experienced an odds ratio (OR) of 1.75 of having ARDS/AKI and 1.89 of morbidity due to ARDS/ALI. However, obese patients had 0.63 times the odds of dying due to ARDS/AKI. They found that the lowest mortality occurred in the BMI category of 30-39.9, but they found no association with mortality among those with a BMI of 40 or greater. They propose that the lower mortality observed could be explained by immune system dysregulation and an increased tolerance to catabolic stress due to increased fat stores.

De Jong and colleagues seem to agree with this hypothesis. In a 2018 cohort study of 3.6 million adults in the United Kingdom, Bhaskaran and colleagues did not find evidence supporting the obesity paradox. They reported that mortality due to cancer, cardiovascular disease, and respiratory disease reached a minimum around BMI 25. Yang and colleagues also found increased mortality from COVID-19 among those with obesity, which does not support the existence of an obesity paradox in this context. This finding has been confirmed by several other studies (Huang et al, 2020; Abumayyaleh et al, 2021; Du et al, 2021).

Some mechanisms have been proposed to attempt to explain the obesity paradox. Stapleton and colleagues suggest that because adipose tissue produces pro-inflammatory cytokines, obese patients experience immune marker dysregulation which may lead to a more rapidly attenuated cytokine response and increased levels of endogenous anticoagulant. This, they posit, may account for the improved outcomes observed in obese critically ill patients with acute lung injury (ALI). Furuncuoğlu and their team conducted a study in 2016 looking into the effect of obesity on immune cell ratios, immune-inflammatory indices, and platelet circulation. They found that obese patients has higher counts of lymphocytes, white blood cells, neutrophils, and platelets. Additionally, they observed higher immune-inflammatory indices. This would confirm the presence of a proposed pro-inflammatory and/or pro-coagulative state referenced by several papers (Nakeshbandi et al, 2020; Pettit et al, 2020; Schetz et al, 2019; Stapleton et al, 2010; Silverio et al, 2019; Cortes-Telles et al, 2021). While this may seem to refute the obesity paradox, van Eijk and colleagues in 2014 suggested that higher levels of these immune markers may actually "prime" the immune system to mount a more effective response.

The obesity paradox has also been observed during the COVID-19 pandemic. Kwok and colleagues in 2020 found that while obese patients had a higher incidence of mechanical ventilation and severe disease, mortality was not increased. They suggest that instead of BMI, metabolic syndromes (such as hypertension, diabetes, hyperlipidemia, etc) may be more predictive of severe illness and these can be (and often are) experienced by individuals with average-range BMIs. They also found that higher levels of coagulation markers such as D-dimer may be predictive of COVID-19 mortality, in which case an obesity paradox would be supported by Stapleton and colleagues' proposal that those with obesity have higher levels of endogenous anticoagulant.

Several mechanisms have been proposed to explain the discrepancy in outcomes between obese patients and those with average BMIs. One popular theory postulates that those with high BMIs had lower levels of circulating cytokines and higher levels of circulating tumor necrosis factor (TNF) and interleukins (Stapleton et al, 2010). In a 2020 paper by Simonnet and colleagues, researchers suggested that due to these increased levels, people with obesity may experience an impaired immune response. Zhi and colleagues similarly suggest that people with obesity experience immune dysregulation including abnormal neutrophil activity, which they propose in turn causes an abnormal immune response. Another paper by van Eijk and colleagues suggests the proposed pro-inflammatory state experienced by people with obesity actually primes their immune system, ultimately leading to the lower mortality rates sometimes observed among obese patients compared to average weight patients. More research is needed to determine the clinical significance of the observed increased immune markers in obese patients.

The other mechanism proposed by several research teams relates to the unique anatomy of individuals with increased abdominal fat accumulation. De Jong and colleagues describe this hypothesis in great detail in their 2020 paper. The researchers suggest that increased abdominal fat puts pressure on the diaphragm, which then causes upward displacement of the diaphragm, thereby decreasing lung volume. They theorize that the resulting decrease in functional residual capacity (FRC) makes patients more prone to airway closure and atelectasis. They specify that this is of increased concern among obese patients who are anesthetized or sedated, where continuous airway closure combined with increased pressure in the lungs due to the weight of the thoracic cavity can lead to alveolar collapse, which would lead to acute hypoxemia. Barrera and colleagues further describe reduced lung and chest wall compliance and increased airway resistance observed in patients with obesity.

Some researchers believe that fat distribution plays a more important role than BMI in predicting airway related difficulties (De Jong et al, 2020). In a 2017 paper by Littleton and colleagues, researchers suggest that men tend to have more thoracic and abdominal fat, which supports the finding of increased mortality in men described in Nakeshbandi's paper referenced in the first paragraph of this section.

1.4 Ventilating Obese Patients

There are several unique considerations necessary to provide adequate care for obese patients. De Jong and colleagues extensively describe protocols for ventilating obese patients in their 2020 paper. According to this paper, those with obesity may experience cranial displacement of the diaphragm due to increased chest wall mass, leading to decreased functional residual capacity (FRC). They found that FRC decreases on average up to 15% per 5 unit increase in BMI. The authors also note that diaphragm displacement in obese patients worsens with supine positioning, and they suggest that these patients should always be in the seated position or proned. Further, diaphragm displacement leads to increased pressure needed to open closed respiratory units, which is often measured as a decrease in lung compliance. They posit that since higher pressure is needed to adequately recruit the alveoli in obese patients, there is a higher likelihood of atelectasis resulting in a shunt, which would greatly inhibit carbon dioxide elimination. The authors point out that an individual experiencing a severe shunt would not benefit from increased oxygenation, and increased oxygen concentration causes alveoli to collapse more rapidly during an airway closure. This issue is exacerbated, the authors theorize, under anesthesia during which obese patients experience continuous airway closure. Obese patients are generally more difficult to intubate, and the authors include that sedation of these patients can result in further reduced FRC.

As mentioned above, higher pressure is often required to achieve adequate alveolar recruitment in patients with obesity (De Jong et al, 2020). The authors mention that if pressure is too high, patients will experience a decrease in venous return which will result in decreased cardiac output and thereby decreased systemic blood pressure. The researchers note that because of this, obese patients may experience hemoinstability, increasing the need for fluids and vasopressors. Additionally, these patients could experience barotrauma such as pneumothorax, further complicating the course of treatment. Calculating positive end-expiratory pressure (PEEP) for obese patients should be further studied, as the authors highlight the existence of several conflicting studies. One study the authors describe found no increase in recruitibility or oxygenation when PEEP was increased from 5 to 15 cmH_2O. A contrasting study they cite found an improvement in lung elastance and oxygenation when using a higher PEEP (22 compared to 13 mmH_2O). In the same study, patients experienced improvements in gas exchange, respiratory mechanics, and survival when their PEEP calculation was personalized on a case-by-case basis. De Jong and colleagues emphasize the importance of measuring transpulmonary and intra-abdominal pressure for each patient and using these unique values to calculate the appropriate PEEP.

Section 1.5: Tracheostomy

The tracheostomy procedure, creating an opening in the trachea and inserting a tube, has been an important tool for ventilating patients for centuries, even before the use of mechanical ventilation. In current practice, patients who require extensive mechanical ventilation or have failed to wean from the ventilator are transitioned to a tracheostomy to decrease patient discomfort, allow discontinuation of sedation, increase hygiene, and improve patient communication (Barahs et al, 2021; Ghattas et al, 2021).

Ideal timing for tracheostomy has not been definitively determined. Guidelines have ranged widely depending on context. In terms of COVID-19, initial guidelines were 2 to 3 weeks of intubation before tracheostomy due to concern of transmission to healthcare workers through aerosolization during the procedure. Several studies have since demonstrated that with proper precaution, transmission during the procedure is minimal to non-existent (Ferro et al, 2021; Angel et al, 2020; Chao et al, 2020, Battaglini et al, 2021). The current pandemic has sparked much research into tracheostomy timing and patient outcomes. Ho and colleagues found that those who received early tracheostomies experienced fewer intensive care unit (ICU) days. Additionally, Ghattas and colleagues found that those who received early tracheostomies (less than 10 days of intubation) experienced lower mortality (RR 0.83), but this association disappeared when they changed the "early" cut-off to seven days of intubation. Conversely, Ferro and colleagues conducted a systematic review and meta-analysis of tracheostomy outcomes among COVID-19 patients in 2021 and found that there was no difference in mortality or time to decannulation between early (less than 14 days of intubation) and late tracheostomies (greater than 14 days). Battaglini and colleagues similarly found no difference in survival among those who received a tracheostomy before day 15 and those who received one after. More research is needed to identify the ideal timing of tracheostomy, however each patient should be treated according to their health needs.

In terms of technique, two protocols exist. First is the classical open tracheostomy, which is a surgical procedure that often requires an operating room. The other technique is called the percutaneous dilational tracheostomy (PDT), which can be performed bedside. For PDT, an incision is made where the tracheostomy is to be placed, and a series of tracheostomy tubes increasing in size are passed through until the desired size is reached. This can also be performed using the Ciaglia Blue Rhino device, which is a horn shaped tool used to dilate the incision to the appropriate width. The PDT has become favorable due to its convenience and lower cost. Outcome comparison between the two techniques is an area of debate among medical professionals, and research on the topic is scant. One study by Ghattas and colleagues found that PDT was associated with fewer complications. Another study by Farlow and colleagues found that those who received PDT experienced fewer days until decannulation, however Ferro and colleagues found no difference in mortality, time to decannulation, or postoperative complications between the two methods. Battaglini and colleagues also found no improvement in outcomes based on tracheostomy technique. Similarly, Ho and colleagues found no association between probability of death in the hospital and tracheostomy timing or technique. Overall, PDT seems to be equivalent to open tracheostomy in terms of safety and patient outcomes, even offering benefits in some cases. This is an important finding, as open tracheostomies are more expensive and more resource intensive than PDT, so it may be more advantageous to use PDT when appropriate.

Obese patients who are potential candidates for tracheostomy require additional considerations. Due to variations in neck anatomy, most patients undergoing open tracheostomy required extended tracheostomy tubes, according to Barrera and colleagues; the same is likely true for

PDT. The same study found that recognizing key anatomical landmarks may be more difficult in those with obesity, so special care must be taken when performing the procedure. The researchers also found that underweight and obese patients experienced more complications at 30 days post-tracheostomy than average BMI patients. The previously mentioned study by Ghattas and colleagues found no difference in 30 day complications for obese patients. For the most part, tracheostomy appears to be safe for obese patients, assuming all appropriate precautions are considered.

According to Ghattas and colleagues, tracheostomy decreases the work of breathing along with decreasing the need for sedation. As mentioned previously, obese individuals experience increased work breathing and sedation can decrease FRC, so these benefits alone are worthy of consideration. Additionally, issues like trouble identifying anatomical structures can be worked around using tools like ultrasound and bronchoscopy, which are already commonly employed to confirm tracheostomy placement (Ghattas et al, 2021).

1.6 Conclusion

Patients with obesity experience unique circumstances that require careful consideration. These patients must be cared for on a personalized level, as research has shown that this will improve their health outcomes (De Jong et al, 2020). Tracheostomy in these patients has the potential to decrease discomfort, airway resistance, and work of breathing while increasing patient comfort and quality of communication (Barash et al, 2021; Ghattas et al, 2021). Additionally, utilization of tracheostomy for patients with obesity could eliminate the need for sedation, thereby improving their FRC (De Jong et al, 2020). More research is needed in the area to definitively determine complication rate among obese patients, ideal timing, and ideal technique.

Chapter Two

Obesity and COVID-19: An analysis of the relationship between obesity and outcomes of tracheostomy secondary to COVID-19

Julia Spychalski, B.S.

2.1 Abstract

Introduction: Tracheostomy has been an essential tool in management of severe COVID-19. Even before the COVID-19 pandemic, optimal timing and surgical approach has been debated; intense research on best practices for tracheostomy of the critically ill COVID-19 patient has persisted over the past two years. Because obesity alters anatomy and immune function, managing COVID-19 patients with body mass index >30 has been a special focus of investigation.

Methods: Hazard ratios (HR) for mortality, prolonged ventilator dependence and prolonged hospitalization were compared for patients with BMI above and below or equal to 30. HR for the same were calculated for open versus closed surgical approach, interacting with BMI.

Results: BMI > 30 alone did not independently predict mortality, ventilator independence, or hospital discharge over a 90 day follow-up period. I did find, however, that open tracheostomy technique and having a P/F ratio before tracheostomy of under 100 were associated with an increased hazard of hospital discharge when interacting with the BMI category.

Conclusion: More research is needed to determine the ideal treatment course of critically ill patients with high BMIs.

2.2 Introduction

The novel coronavirus of 2019 (SARS-CoV-2), the culprit for coronavirus disease of 2019 (COVID-19), has become central to public health over the last couple of years. This disease has claimed the lives of millions, and has unfortunately followed the well-known pattern of disproportionately impacting the most vulnerable populations. In the US, this includes those who have been historically oppressed, primarily People of Color and those living in disadvantaged areas.

Individuals with high body mass indices (BMIs) have unfortunately fallen into a socially stigmatized category. Social stigma brings with it many health problems, both mental and physical. Studies have produced conflicting results regarding the survival outcomes experienced by those with high BMIs-- some referencing the “obesity paradox,” some refuting it. The obesity paradox has been described simply as an observed increase in morbidity but a decrease in mortality among patients with high BMIs. More research is needed in the area of critical care medicine for patients with high BMIs in order to determine how to provide the best possible care and close the gap of morbidity experienced by these patients.

2.3 Methods

Data Collection

Patients were enrolled in the study through retrospective chart review of institutions within the United States as well as in Bolivia and Spain. Institutions in the United States included Grady Memorial Hospital, Riverside Health System, Memorial Sloan Kettering Cancer Center, Zuckerberg San Francisco General Hospital, University of Missouri Health Center, and Mercy Health Research. The two institutions outside of the United States were Clínica Foianini in Bolivia and Royo Villanova Hospital in Spain. Participants had to have been 18 years old or older, admitted to the hospital for inpatient care during the time period of March 1st, 2020 to March 31st, 2021, and have received a tracheostomy secondary to COVID-19 diagnosis during the same hospital admission. Patients who received tracheostomies for reasons other than COVID-19 (such as esophageal malignancy, pre-existing tracheostomy tube change, etc) were excluded.

Chart review was conducted for the period including the tracheostomy and the following 90 days for each patient. All data were deidentified and stored using the Research Electronic Data Capture tool (REDCap). The collection of this data was approved by Emory's Institutional Review Board as well as the Institutional Review Boards of each institution. Data collected included patient demographics, ambulatory characteristics, prior conditions, peri-procedural complications, post-procedural complications, ventilator settings, procedure details, admission and discharge dates, and relevant lab values and medications.

Selection of Outcomes

The primary outcome of this study was mortality within 30 and 90 days of follow-up. The beginning of the follow-up period was defined as the day of hospital admission, and the end was defined as either date of death or date of hospital discharge; Patients who did not receive the outcome within 30 or 90 days (depending on the analysis) were censored. Secondary outcomes included time to decannulation and hospital length of stay (LOS). Time to decannulation was measured as the number of days between the date of intubation and the date of tracheostomy removal (decannulation). Hospital LOS was measured as the time between the date of hospitalization and the date of discharge from the hospital, whether to long-term acute care or to home. Patients who died prior to discharge or decannulation were excluded from the analysis of these outcomes.

Tracheostomy timing was defined as early (before 14 days of ventilator dependence) or late (after 14 days). Technique was either open (surgical) or percutaneous (dilational). BMI category was defined using a cut-off of 30 kg/m^2 (> 30 and ≤ 30). Ventilator requirement measures included the ratio of partial pressure of oxygen (PaO_2) to fraction of inspired oxygen (FiO_2) and positive end-expiratory pressure (PEEP). Disease severity was measured using the Sequential Organ Failure Assessment (SOFA). Having 3 or more comorbidities was identified as a confounder, as this variable was associated with both having a BMI of over 30 and mortality, ventilator dependence, and hospital discharge. The presence of obesity on admission was included as a comorbidity; thus, one to two comorbidities was analyzed separately from three or more comorbidities to avoid complete separation with the obesity factor.

Statistical Analysis

Survival analysis and Cox Proportional Hazards methods were used to obtain hazard ratio estimates. Fisher exact tests were used in univariate analysis. Bivariate analysis was used to compare demographics, tracheostomy timing and technique, comorbidities, and disease severity by BMI category. Power was calculated using a two-sample t-test. Statistical significance was determined with an alpha cut-off of $p=0.05$. All analyses were conducted using R version 4.1.2.

Tracheostomy technique and timing, presence of comorbidities, ventilator requirements (PaO_2/FiO_2, PEEP before and after tracheostomy), and disease severity score (SOFA) were analyzed to assess potential interaction with BMI category to affect mortality. Sensitivity analyses were observed at BMI values of 35 and 40 (data not provided). The presence of comorbidities was used to adjust for possible confounding.

2.3 Results

Patient Population

Of the 314 patients in the study, 157 had a body mass index (BMI) of greater than 30. Of those with a BMI > 30, 60% were male, 48% were Black or African American, and 27% identified as Hispanic or Latinx. Patients with BMIs of over 30 were disproportionately younger than 65, Bolivian, and were more frequently Black or African American, and diagnosed with 3 or more comorbidities.

Table 1. Population Characteristics

Characteristic		Overall (n=314)	BMI > 30 (n=157)	p-value
Age	≥ 65 years	132 (42%)	54 (34%)	0.01
Sex	Male	199 (63%)	94 (60%)	0.24
Country	US	276 (88%)	147 (94%)	< 0.01
	Bolivia	31 (10%)	6 (4%)	
	Spain	7 (2%)	4 (3%)	
Race	Black	120 (38%)	76 (48%)	< 0.01
	White	114 (36%)	48 (31%)	
	Other	23 (7%)	6 (4%)	
	Unknown	52 (17%)	26 (17%)	
Ethnicity	Hispanic/Latinx	56 (18%)	27 (17%)	0.81
	Unknown	2 (1%)	9 (6%)	
Comorbidities	Hypertension	216 (69%)	114 (73%)	0.18
	Respiratory Related	74 (24%)	41 (26%)	0.35
	Heart Disease	59 (19%)	29 (19%)	0.99
	Diabetes	124 (40%)	69 (44%)	0.13
	Unknown	2 (1%)	1 (1%)	0.37
	≥ 3 Comorbidities	138 (44%)	96 (61%)	< 0.01
	No Comorbidities	30 (10%)	11 (7%)	0.18
Tracheostomy Timing	Early	85 (27%)	33 (21%)	0.02
Tracheostomy Technique	Open	75 (24%)	41 (26%)	0.43

*For race/ethnicity, patients may have identified as both hispanic/latinx and a race category

The majority (90%) of patients had at least one comorbidity. Significantly more individuals in the BMI > 30 category had 3 or more comorbidities compared to individuals with a BMI below 30 (61% vs 27%; $p < 0.01$). Most patients in both categories had late tracheostomies but slightly more patients with a BMI of over 30 had late tracheostomies(73% BMI ≤ 30; 79% BMI > 30;

p=0.02).The majority of patients in both BMI categories had percutaneous tracheostomies. Hypertension was the most common comorbidity at 69% prevalence, followed by diabetes (40% prevalence), with no significant difference in prevalence among the BMI categories.

Mortality Hazard

Having a BMI of over 30 was not found to affect the hazard of mortality over the 30- or 90-day follow-up period independently (HR: 0.45, p=0.13; HR: 0.66, p=0.09). Overall, having a BMI of over 30 was not associated with a difference in mortality hazard (Figure 1a & 1b). None of the measured interactions impacted the hazard of 90-day mortality in a statistically significant way. These findings were consistent after multivariable analysis. Having a BMI of over 30 and a PEEP requirement of less than 9 after tracheostomy was found to contribute the highest hazard of 30-day mortality. Having a BMI of greater than 30 and a P/F ratio of less than 100 before tracheostomy was found to have the highest hazard for 90-day mortality (3.29, p=0.21), and this effect remained upon multivariable analysis (3.17, p=0.23); again, this effect did not achieve statistical significance. The hazard was also increased for having a BMI of over 30 and a P/F ratio of less than 100 after

Table 2. 30- and 90-day Mortality Hazard

Interaction Term	30-day HR Adjusted for Comorbidities (95% CI)	p-value	90-day HR Adjusted for Comorbidities (95% CI)	p-value
BMI > 30 alone	0.45 (0.18-1.24)	0.13	0.66 (0.41-1.07)	0.09
P/F Pre-trach < 100	1.46 (0.07-28.81)	0.81	3.17 (0.49-20.55)	0.23
P/F Post-trach < 100	0.59 (0.04-8.83)	0.70	2.77 (0.69-11.05)	0.15
P/F Improvement**	0.90 (0.09-9.30)	0.93	1.93 (0.59-6.29)	0.28
PEEP Pre-trach < 9	1.41 (0.23-8.79)	0.71	1.79 (0.69-4.64)	0.23
PEEP 72 hr Post-trach < 9	10.31 (1.14-93.11)	0.04	1.64 (0.61-4.40)	0.33
PEEP Improvement***	0.78 (0.09-6.94)	0.82	0.95 (0.32-2.77)	0.92
Early Trach	2.70 (0.42-17.31)	0.30	1.50 (0.55-4.09)	0.43
SOFA > 10	0.13 (0.01-1.81)	0.13	1.35 (0.42-4.36)	0.61
Open Trach*	--	--	1.69 (0.45-6.36)	0.44

*Some values designated "--" could not be measured due to insufficient sample size.
**P/F Improvement was defined as an increase in P/F ratio after tracheostomy
***PEEP Improvement was defined as a decrease in PEEP after tracheostomy

tracheostomy after univariate (1.97, p=0.33) and multivariate (2.77, p=0.15) analysis, although this difference was not statistically significant.

Hazard of Ventilator Independence

A BMI of over 30 was not independently significantly associated with an increased hazard of ventilator liberation after univariate analysis (0.63, p=0.15). Overall, having a BMI of over 30 was associated with a decreased 30-day probability of ventilator independence (Figure 1c), but this association was not statistically significant. It should be noted that the proportional hazards assumption was violated between 40 and 50 days of follow-up (Figure 1c & 1d).

Table 3. 30- and 90-day Ventilator Independence Hazard

Interaction Term	30-day HR Adjusted for Comorbidities (95% CI)	p-value	90-day HR Adjusted for Comorbidities (95% CI)	p-value
BMI > 30 alone	0.83 (0.46-1.48)	0.52	0.82 (0.64-1.17)	0.60
P/F Pre-trach < 100	1.06 (0.10-11.17)	0.96	5.01 (1.11-22.52)	0.04
P/F Post-trach < 100*	--	--	0.95 (0.18-4.96)	0.95
P/F Improvement**	3.40 (0.58-20.08)	0.18	1.07 (0.46-2.48)	0.87
PEEP Pre-trach < 9	2.50 (0.79-7.90)	0.12	1.35 (0.66-2.76)	0.41
PEEP 72 hr Post-trach < 9	1.76 (0.39-8.05)	0.47	1.03 (0.45-2.35)	0.94
PEEP Improvement***	0.52 (0.17-1.66)	0.27	0.87 (0.44-1.74)	0.70
Early Trach	0.58 (0.19-1.70)	0.32	0.72 (0.35-1.46)	0.36
SOFA > 10	0.52 (0.11-2.54)	0.42	0.39 (0.14-1.08)	0.07
Open Trach	2.87 (0.82-10.06)	0.10	2.15 (1.07-4.35)	0.03

*Some values designated "--" could not be measured due to insufficient sample size.
**P/F Improvement was defined as an increase in P/F ratio after tracheostomy
***PEEP Improvement was defined as a decrease in PEEP after tracheostomy

A P/F ratio of less than 100 and receiving an open tracheostomy were significantly associated with increased 90-day hazard of ventilator independence during the 90 day follow-up period after univariate analysis (5.01, p=0.04; 2.15, p=0.03), although these estimates violate the proportional hazards assumption. A SOFA score of greater than 10 was associated with decreased 90-day hazard of ventilator liberation (0.39, p=0.07), just shy of statistical significance.

No other interaction terms were found to have an effect on the hazard of 30- or 90-day ventilator liberation before or after multivariate analysis.

Hazard of Hospital Discharge

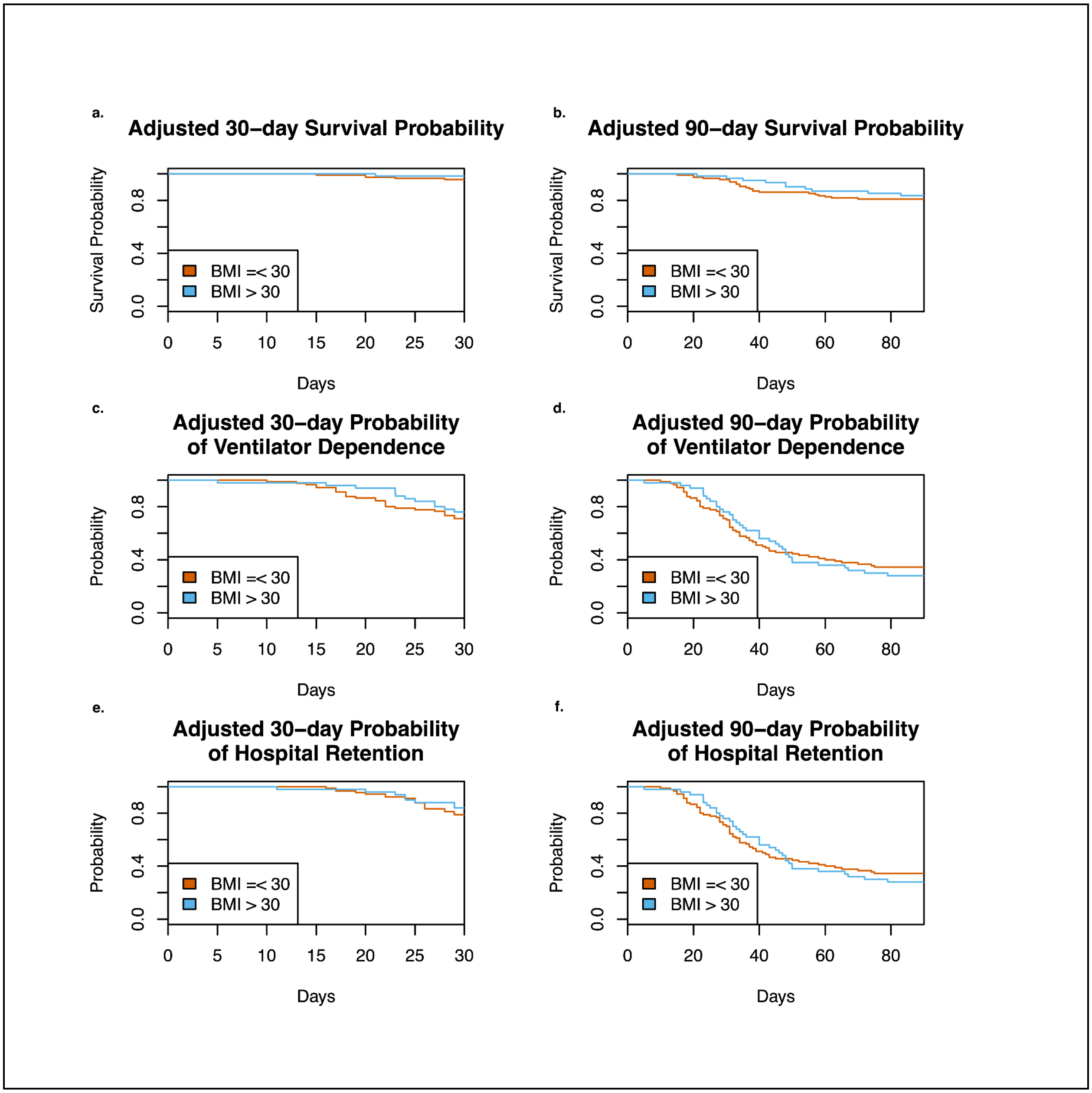
A BMI of greater than 30 was not found to independently impact the hazard of hospital discharge over the 30 or 90 day follow-up period (0.61, p=0.19; 0.99 (0.63). It should be noted that between 40 and 50 days of follow-up, the proportional hazards assumption was violated (Figure 1d & 1e). Having a SOFA score of greater than 10 was associated with a lower hazard of 90-day hospital discharge before (0.37, p=0.04). and after (0.33, p=0.03) multivariable analysis, although these estimates did not meet the proportional hazards assumption. Having a PEEP requirement of less than 9 before and after tracheostomy was associated with an increased hazard of 30 day hospital discharge (3.37, p=0.07; 4.09, p=0.07), but these results were not statistically significant.

Table 4. 30- and 90-day Hospital Discharge Hazard

Interaction Term	30-day HR Adjusted for Comorbidities (95% CI)	p-value	90-day HR Adjusted for Comorbidities (95% CI)	p-value
BMI > 30 alone	0.61 (0.30-1.27)	0.19	0.99 (0.81-1.43)	0.63
P/F Pre-trach < 100*	--	--	0.58 (0.15-2.30)	0.44
P/F Post-trach < 100*	--	--	0.84 (0.11-6.13)	0.86
P/F Improvement**	0.81 (0.11-6.19)	0.84	1.42 (0.68-3.01)	0.35
PEEP Pre-trach < 9	3.37 (0.89-12.76)	0.07	1.59 (0.88-2.88)	0.13
PEEP 72 hr Post-trach < 9	4.09 (0.88-19.05)	0.07	1.42 (0.72-2.80)	0.31
PEEP Improvement***	0.52 (0.11-2.54)	0.42	1.18 (0.65-2.16)	0.58
Early Trach	0.55 (0.15-2.06)	0.38	0.94 (0.51-1.73)	0.84
SOFA > 10	0.25 (0.03-1.86)	0.18	0.33 (0.13-0.88)	0.03
Open Trach	1.01 (0.24-4.29)	0.99	1.02 (0.55-1.89)	0.95

*Some values designated "--" could not be measured due to insufficient sample size.
**P/F Improvement was defined as an increase in P/F ratio after tracheostomy
***PEEP Improvement was defined as a decrease in PEEP after tracheostomy

Figure 1. 30- and 90-day Survival Curves for Each Outcome



2.4 Discussion

Obesity was not found to be an independent predictor of 90-day mortality, ventilator independence, or hospital discharge after tracheostomy in COVID-19 patients. This finding is supported by previous studies (Abumalayyeh, 2020; Zhi 2016). Further, the association did not change when the BMI cut-off was moved from 30 to 35, then to 40 (data not shown). A paper by

Yang and colleagues published in 2020 suggests that the effects of having a high BMI are more pronounced after 40 (Yang, 2020). The finding in this paper could be due to the fact that the population under study contained very few individuals with a BMI of over 40, so detecting a significant difference was not possible. Since a difference in mortality was not observed in this study, there was no detected evidence of an obesity paradox, consistent with a 2020 study by Abumalayyeh and colleagues (Abumalayyeh et al, 2020). The obesity paradox has, however, been observed in other studies (Zhi et al, 2016; Schetz et al, 2019; Huang, et al, 2020).
In this study, a difference in the probability of ventilator dependence was not observed among BMI categories. Barrera and colleagues conducted a study in 2020 that is inconsistent with this finding (Barrera, 2020). In that study, however, all patients had received open tracheostomies, which was not the case in the current study.

Interestingly, in this study, open tracheostomy was associated with an increased probability of ventilator independence over the 30 and 90 day follow up periods, which is inconsistent with the Barrera study and a previous study by Ferro and colleagues (Barrera et al, 2020; Ferro et al, 2021). The increase in ventilator dependence among patients with BMIs of over 30 observed in these studies could be explained by doctor's perceptions of increased risk for patients with BMIs over 30 (Stapleton, 2010).

Neither tracheostomy technique nor timing affected the probability of mortality or hospital discharge over the 90 day follow-up period. Having a BMI of over 30 did not change this finding. This is consistent with other studies (Ho et al, 2012; Ghattas et al, 2020). If there truly is not a difference in outcomes based on tracheostomy timing and technique, this could suggest a benefit of conducting early, percutaneous tracheostomies; Early tracheostomy could provide improved patient hygiene, comfort, and communication, while percutaneous technique could serve as a cost-saving alternative to surgical placement (Ghattas et al, 2021). Of course, each case should be carefully considered and any decision on timing or technique should be based on the individual patient's needs and the physician's discretion.

This study has some limitations. First, the study was likely underpowered due to the small sample size, which could explain the paucity of statistically significant findings (76% power to detect a moderate effect of 0.3 given the study population). It is possible that important differences could be detected with a larger sample. Second, data on patient positioning and fat distribution was not available. Patient positioning is hypothesized to have an important impact on patient outcomes involving respiratory diseases, especially for patients with high BMIs (De Jong et al, 2020). Additionally, fat distribution is thought to play a much larger role in outcomes than BMI alone (Littleton, 2017; Huang, 2020). Finally, our study involved a large proportion of non-white patients, and access to healthcare is inequitable in the United States for non-white individuals (Riley, 2012). This could have had an unmeasured effect on both the route of treatment and the outcome.

The findings in this study suggest that BMI alone is not predictive of worse outcomes in patients with COVID-19 who received tracheostomies. There is likely much more that goes into disease severity than BMI or body weight. The social stigma surrounding high BMI is often itself a source of poor health, anxiety, and healthcare inequity (Phelan, 2015). Findings like the ones in this study show that the size of someone's body is not sufficient to make a health-based judgment, much less a social judgment.

2.5 Conclusion

The needs of patients with BMIs over 30 are unique and require more research. Android distribution of body weight can impact intra-abdominal and transpulmonary pressure, which increases pressure on the airway, leading to the observed increase in airway collapse seen in some patients with high BMIs (De Jong et al, 2020). Because of the difficulty in collecting measurements of these factors, the determination of pressure support needs for those with high BMIs are often estimated; and these estimates are often based on a higher BMI than is actually observed (De Jong, 2020). Patients have been shown to have better outcomes when these pressure support needs are personalized (De Jong, 2020).

In order to adequately provide care for critically ill patients with high BMIs, we must make efforts to learn how to care specifically for these patients. More research is needed in the area of critical care for patients with high BMIs in order to address the increased morbidity experienced by these patients as seen in other studies (Zhi et al, 2016l; Simonnet et al, 2020; Huang et al, 2020; Du et al, 2020; Ghattas et al, 2021; Abumayyaleh et al, 2021).

Future Directions of Research

Further research is needed to determine the effect of obesity on patient outcomes related to tracheostomy. While this study did not detect any influence, it is possible and indeed likely that a study with a larger sample size may shed more light on these results. Future studies should also explore the effects of fat distribution, patient positioning, and nutrition. More comprehensive data surrounding tracheostomy technique and timing should be collected and analyzed, as these questions remain unanswered.

Patients with high BMIs often present with more complex cases, and therefore more research is needed in the future to determine how to adequately care for these patients. Unique ventilation needs and anatomical variations are under-studied, and this could explain the increased morbidity and mortality observed in some studies. Additionally, more work could be focused on determining mechanisms by which high BMI interacts with survival and ventilator needs are essential to maximizing the quality of care provided to these patients. Current research has failed to come to a consensus on mechanistic characteristics of high BMI and critical care outcomes.

Finally, more research should be conducted to evaluate the benefits and disadvantages of open versus percutaneous tracheostomy. Considerations such as cost, resource usage, and patient outcomes should be included in the analysis. A definitive answer to this question remains unknown, and knowledge of this answer could save the already strained healthcare system time, money, and resources.

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Appendix

A.1 Supplemental Tables

Supplemental Table 1. 30-day Mortality Hazard

Interaction Term	Independent Contribution (95% CI)	p-value	Crude HR of Interaction (95% CI)	p-value	HR Adjusted for Comorbidities (95% CI)	p-value
Confounder: Comorbidities (≥3)	7.65 (1.64-35.66)	0.01				
BMI > 30 alone	0.65 (0.16-2.63)	0.54	0.72 (0.29-1.80)	0.48	0.45 (0.18-1.24)	0.13
P/F Pre-trach < 100	1.78 (0.15-21.70)	0.65	1.73 (0.09-34.11)	0.72	1.46 (0.07-28.81)	0.81
P/F Post-trach < 100	0.43 (0.03-5.62)	0.52	0.28 (0.02-4.14)	0.36	0.59 (0.04-8.83)	0.70
P/F Improvement*	0.37 (0.07-1.82)	0.22	1.13 (0.11-11.69)	0.92	0.90 (0.09-9.30)	0.93
PEEP Pre-trach < 9	6.59 (0.57-76.68)	0.13	1.32 (0.21-8.16)	0.77	1.41 (0.23-8.79)	0.71
PEEP 72 hr Post-trach < 9	0.10 (0.01-0.71)	0.02	8.39 (0.94-75.09)	0.06	10.31 (1.14-93.11)	0.04
PEEP Improvement**	1.53 (0.34-6.95)	0.58	0.75 (0.08-6.69)	0.80	0.78 (0.09-6.94)	0.82
Early Trach	5.69 (1.17-27.72)	0.03	2.68 (0.42-17.21)	0.30	2.70 (0.42-17.31)	0.30
SOFA > 10	3.89 (0.63-1.99)	0.14	0.15 (0.01-2.06)	0.16	0.13 (0.01-1.81)	0.13
Open Trach***	0.19 (0.02-	0.17	--	--	--	--

*P/F Improvement was defined as an increase in P/F ratio after tracheostomy
**PEEP Improvement was defined as a decrease in PEEP after tracheostomy
***Some values designated "--" could not be measured due to insufficient sample size.

Supplemental Table 2. 90-day Mortality Hazard

Interaction Term	Independent Contribution (95% CI)	p-value	Crude HR of Interaction (95% CI)	p-value	HR Adjusted for Comorbidities (95% CI)	p-value
Confounder: Comorbidities (≥3)	2.26 (1.15-4.42)	0.02				
BMI > 30 alone	0.57 (0.28-1.13)	0.11	0.85 (0.55-1.34)	0.49	0.66 (0.41-1.07)	0.09
P/F Pre-trach < 100	0.75 (0.18-3.15)	0.69	3.29 (0.51-21.30)	0.21	3.17 (0.49-20.55)	0.23
P/F Post-trach < 100	2.39 (0.87-6.55)	0.09	1.97 (0.50-7.73)	0.33	2.77 (0.69-11.05)	0.15
P/F Improvement*	0.62 (0.30-1.27)	0.19	2.11 (0.65-6.88)	0.21	1.93 (0.59-6.29)	0.28
PEEP Pre-trach < 9	0.60 (0.22-1.66)	0.32	1.78 (0.69-4.59)	0.24	1.79 (0.69-4.64)	0.23
PEEP 72 hr Post-trach < 9	0.98 (0.36-2.68)	0.97	1.55 (0.58-4.16)	0.38	1.64 (0.61-4.40)	0.33
PEEP Improvement**	0.88 (0.39-1.97)	0.75	0.92 (0.32-2.71)	0.89	0.95 (0.32-2.77)	0.92
Early Trach	0.85 (0.39-1.87)	0.69	1.44 (0.53-3.91)	0.48	1.50 (0.55-4.09)	0.43
SOFA > 10	1.32 (0.58-3.01)	0.51	1.57 (0.49-5.03)	0.45	1.35 (0.42-4.36)	0.61
Open Trach	0.46 (0.17-1.22)	0.12	1.91 (0.51-7.16)	0.34	1.69 (0.45-6.36)	0.44

*P/F Improvement was defined as an increase in P/F ratio after tracheostomy
**PEEP Improvement was defined as a decrease in PEEP after tracheostomy

Supplemental Table 3. 30-day Ventilator Independence Hazard

Interaction Term	Independent Contribution (95% CI)	p-value	Crude HR of Interaction (95% CI)	p-value	HR Adjusted for Comorbidities (95% CI)	p-value
Confounder: Comorbidities (≥3)	0.43 (0.15-1.18)	0.10				
BMI > 30 alone	0.58 (0.24-1.40)	0.22	0.72 (0.43-1.20)	0.21	0.83 (0.46-1.48)	0.52
P/F Pre-trach < 100	2.10 (0.48-9.14)	0.32	1.11 (0.11-11.63)	0.93	1.06 (0.10-11.17)	0.96
P/F Post-trach < 100*	0.62 (0.10-4.02)	0.62	--	--	--	--
P/F Improvement**	1.53 (0.53-4.39)	0.43	3.36 (0.57-19.80)	0.18	3.40 (0.58-20.08)	0.18
PEEP Pre-trach < 9	4.32 (0.93-20.15)	0.06	2.49 (0.79-7.86)	0.12	2.50 (0.79-7.90)	0.12
PEEP 72 hr Post-trach < 9	1.30 (0.30-5.69)	0.73	1.78 (0.39-8.13)	0.46	1.76 (0.39-8.05)	0.47
PEEP Improvement***	3.68 (1.37-9.89)	0.01	0.52 (0.17-1.66)	0.27	0.52 (0.17-1.66)	0.27
Early Trach	4.85 (2.03-11.60)	< 0.01	0.58 (0.20-1.70)	0.32	0.58 (0.19-1.70)	0.32
SOFA > 10	2.87 (1.00-8.32)	0.05	0.46 (0.10-2.20)	0.33	0.52 (0.11-2.54)	0.42
Open Trach	0.19 (0.04-0.85)	0.03	2.74 (0.79-9.57)	0.11	2.87 (0.82-10.06)	0.10

*Some values designated "--" could not be measured due to insufficient sample size.
**P/F Improvement was defined as an increase in P/F ratio after tracheostomy
***PEEP Improvement was defined as a decrease in PEEP after tracheostomy

Supplemental Table 4. 90-day Ventilator Independence Hazard

Interaction Term	Independent Contribution (95% CI)	p-value	Crude HR of Interaction (95% CI)	p-value	HR Adjusted for Comorbidities (95% CI)	p-value
Confounder: Comorbidities (≥3)	0.69 (0.41-1.19)	0.18				
BMI > 30 alone	0.63 (0.39-1.03)	0.07	0.79 (0.58-1.09)	0.15	0.82 (0.64-1.17)	0.60
P/F Pre-trach < 100	0.98 (0.37-2.58)	0.97	5.05 (1.12-22.67)	0.03	5.01 (1.11-22.52)	0.04
P/F Post-trach < 100	1.56 (0.49-4.95)	0.45	0.92 (0.18-4.80)	0.92	0.95 (0.18-4.96)	0.95
P/F Improvement*	1.01 (0.59-1.72)	0.97	1.08 (0.47-2.50)	0.86	1.07 (0.46-2.48)	0.87
PEEP Pre-trach < 9	1.96 (0.89-4.34)	0.09	1.35 (0.66-2.76)	0.42	1.35 (0.66-2.76)	0.41
PEEP 72 hr Post-trach < 9	1.78 (0.81-3.91)	0.15	1.03 (0.45-2.36)	0.94	1.03 (0.45-2.35)	0.94
PEEP Improvement**	1.77 (0.99-3.17)	0.06	0.87 (0.44-1.73)	0.70	0.87 (0.44-1.74)	0.70
Early Trach	1.94 (1.19-3.18)	0.01	0.73 (0.36-1.47)	0.38	0.72 (0.35-1.46)	0.36
SOFA > 10	2.16 (1.17-4.00)	0.01	0.39 (0.14-1.06)	0.06	0.39 (0.14-1.08)	0.07
Open Trach	0.70 (0.40-1.21)	0.20	2.12 (1.05-4.28)	0.04	2.15 (1.07-4.35)	0.03

*P/F Improvement was defined as an increase in P/F ratio after tracheostomy
**PEEP Improvement was defined as a decrease in PEEP after tracheostomy

Supplemental Table 5. 30-day Hospital Discharge Hazard

Interaction Term	Independent Contribution (95% CI)	p-value	Crude HR of Interaction (95% CI)	p-value	HR Adjusted for Comorbidities (95% CI)	p-value
Confounder: Comorbidities (≥3)	6.96 (0.18-2.72)	0.60				
BMI > 30 alone	1.55 (0.48-4.97)	0.46	0.87 (0.47-1.64)	0.68	0.61 (0.30-1.27)	0.19
P/F Pre-trach < 100*	3.24 (0.60-17.61)	0.17	--	--	--	--
P/F Post-trach < 100*	--	0.99	--	--	--	--
P/F Improvement**	1.76 (0.49-6.27)	0.38	0.76 (0.10-5.81)	0.79	0.81 (0.11-6.19)	0.84
PEEP Pre-trach < 9	0.49 (0.08-3.12)	0.45	3.28 (0.87-12.37)	0.08	3.37 (0.89-12.76)	0.07
PEEP 72 hr Post-trach < 9	1.68 (0.28-10.04)	0.57	4.15 (0.89-19.36)	0.07	4.09 (0.88-19.05)	0.07
PEEP Improvement***	1.13 (0.34-3.71)	0.84	0.54 (0.11-2.64)	0.45	0.52 (0.11-2.54)	0.42
Early Trach	2.28 (0.76-6.86)	0.14	0.58 (0.15-2.16)	0.41	0.55 (0.15-2.06)	0.38
SOFA > 10	2.93 (0.93-9.24)	0.07	0.22 (0.03-1.61)	0.14	0.25 (0.03-1.86)	0.18
Open Trach	0.52 (0.13-2.05)	0.35	0.92 (0.22-3.87)	0.91	1.01 (0.24-4.29)	0.99

*Some values designated "--" could not be measured due to insufficient sample size.
**P/F Improvement was defined as an increase in P/F ratio after tracheostomy
***PEEP Improvement was defined as a decrease in PEEP after tracheostomy

Supplemental Table 6. 90-day Hospital Discharge Hazard

Interaction Term	Independent Contribution (95% CI)	p-value	Crude HR of Interaction (95% CI)	p-value	HR Adjusted for Comorbidities (95% CI)	p-value
Confounder: Comorbidities (≥3)	1.33 (0.83-2.11)	0.23				
BMI > 30 alone	0.89 (0.57-1.39)	0.61	1.01 (0.77-1.33)	0.93	0.99 (0.81-1.43)	0.63
P/F Pre-trach < 100	1.59 (0.72-3.54)	0.25	0.59 (0.15-2.34)	0.46	0.58 (0.15-2.30)	0.44
P/F Post-trach < 100	0.37 (0.10-1.36)	0.13	0.82 (0.11-6.03)	0.85	0.84 (0.11-6.13)	0.86
P/F Improvement*	1.76 (1.08-2.89)	0.02	1.45 (0.69-3.06)	0.33	1.42 (0.68-3.01)	0.35
PEEP Pre-trach < 9	1.95 (0.93-4.08)	0.08	1.59 (0.88-2.89)	0.12	1.59 (0.88-2.88)	0.13
PEEP 72 hr Post-trach < 9	0.40 (0.19-0.84)	0.02	1.39 (0.71-2.74)	0.34	1.42 (0.72-2.80)	0.31
PEEP Improvement**	1.46 (0.90-2.36)	0.13	1.19 (0.65-2.17)	0.57	1.18 (0.65-2.16)	0.58
Early Trach	2.00 (1.28-3.12)	<0.01	0.93 (0.50-1.71)	0.81	0.94 (0.51-1.73)	0.84
SOFA > 10	1.33 (0.75-2.37)	0.33	0.37 (0.14-0.96)	0.04	0.33 (0.13-0.88)	0.03
Open Trach	0.77 (0.47-1.26)	0.30	1.03 (0.56-1.92)	0.90	1.02 (0.55-1.89)	0.95

*P/F Improvement was defined as an increase in P/F ratio after tracheostomy
**PEEP Improvement was defined as a decrease in PEEP after tracheostomy

A.2 Supplemental Figures

Supplemental Figure 1. Unadjusted 30- and 90-day Survival Curves for Each Outcome