Disparities in Lung Protective Ventilation in the United States

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Abstract

Background: Lung-protective ventilation is often used in critically ill patients with acute respiratory failure, including those without acute respiratory distress syndrome. While disparities exist in the delivery of critical care based on gender, race, and insurance status, it is unknown whether there are disparities in the use of lung-protective ventilation. The objective of our study was to determine whether gender-, racial / ethnic-, or insurance status-based disparities exist in the use of lung-protective ventilation for critically ill mechanically ventilated patients in the United States (U.S.).

Methods: This was a secondary data analysis of the U.S. Critical Illness and Injury Trials Group Critical Illness Outcomes Study, a prospective multi-center cohort study conducted from 2010 - 2012. The dependent variable of interest was the proportion of patients receiving tidal volume > 8 mL/kg predicted body weight (PBW). The independent variables of interest were gender, insurance status, and race / ethnicity.

Results: Our primary analysis included 1,595 mechanically ventilated patients from 59 intensive care units (ICUs) in the U.S. Women were more likely to receive tidal volumes > 8 ml/kg PBW than men (odds ratio [OR] = 3.25, 95% confidence interval [CI] = 2.58 – 4.09), though this relationship was substantially weakened after adjusting for gender differences in height (OR = 1.26 95% CI = 0.94 – 1.71). The underinsured were significantly more likely to receive tidal volume > 8 ml/kg PBW than the insured in multivariable analysis (odds ratio = 1.54, 95% confidence interval = 1.16 – 2.04). The prescription of > 8 ml/kg PBW tidal volume did not differ by racial or ethnic categories.

Conclusions: In this prospective nationwide cohort of critically ill mechanically ventilated patients, women and the underinsured were less likely than their comparators to receive lung protective ventilation, with no apparent differences based on race / ethnicity alone. Differences in height between men and women do not fully explain this disparity. Future research should evaluate whether implicit bias affects tidal volume choice and other management decisions in critical care.

Background

Disparities exist in healthcare delivery and clinical outcomes among critically ill patients based on gender, race, and insurance status[1-7].

Lung protective ventilation is often used for patients with acute respiratory distress syndrome (ARDS) and also for patients without ARDS[8], with several studies indicating lower risk of lung injury and other adverse outcomes in non-ARDS patients [9-11]. To date, there are no studies that have specifically investigated whether tidal volumes differ based on gender, race, or insurance status among unselected critically ill mechanically ventilated patients.

The goal of this study was to explore whether race, sex, and insurance status influenced the use of lung protective ventilation. To accomplish this goal, we conducted a pre-planned secondary analysis of

The United States Critical Illness and Injury Trials Group-Critical Illness Outcomes Study (USCIITG-CIOS), a multicenter, prospective cohort study designed to evaluate the impact of ICU protocols on patient outcomes[12,13]. Preliminary analyses from this study have been previously published in abstract form[14].

Methods

Study Design, Setting, and Patients

The details of USCIITG-CIOS have been previously described[12,13]. In brief, this was a prospective cohort study of 6,179 critically ill adult patients from 59 primarily academic intensive care units (ICUs) across the United States (see Acknowledgements). Participating ICUs enrolled newly admitted patients one day per week, with 5-10 days between enrollment days, between July 2010 and March 2012. Data collection elements included demographic characteristics, height, and mechanical ventilation settings abstracted from review of the electronic medical record by trained study personnel at each participating center. Mechanical ventilation parameters were collected from the respiratory flowsheets of the medical record at a single time point at approximately 8:00 am the day of data collection. Patients present in the ICU during the prior data collection day, or discharged before the first data collection day, were not enrolled. All participating sites received approval from their institutional review boards for data collection with a waiver of informed consent.

Exposure variables

The independent variables of interest were gender (women vs. men), race / ethnicity, and insurance status. Race was nominally categorized as White (the base category), African American, Asian-Pacific Islander, and American Indian/Alaskan Native. Ethnicity was binarily categorized as not Hispanic or Latino or Hispanic or Latino. Under-insured patients were those with Medicaid-only coverage, self-pay, or unknown insurance, and insured patients were those with any Medicare or commercial/ private insurance[2]. We also performed a sensitivity analysis that excluded Medicare patients to reduce the likelihood of confounding by age and comorbid conditions[4].

Outcome variable

The primary outcome variable was prescription of a tidal volume / predicted body weight (VT/PBW) > 8 mL/kg. We chose this outcome because it is a threshold that defines a potentially injurious ventilator setting and may be differentially applied in patients based on gender, insurance status, or race/ethnicity.

Statistical analysis

Our primary analysis was a complete case analysis that included patients with non-missing values for race, ethnicity, tidal volume, and height. We also performed a secondary analysis that included patients with missing values for these variables using multiple imputation. The details of the multiple imputation methods are presented in the Supplementary Methods and Table E17 of the online data supplement.

Descriptive statistics were performed for all dependent and independent variables of interest. Continuous variables with a normal and skewed distribution are reported as mean ± standard deviation or median [interquartile range], respectively. Categorical variables are expressed as proportions. Relationships between dichotomous variables were examined using the Chi-square test and relationships between continuous variables were analyzed using the Kruskal-Wallis test. We used clinical judgment and prior literature to construct directed acyclic graphs conceptualizing covariables that might confound or mediate relationships between the independent and dependent variables of interest[15-17]. These covariables were included together with the predictor variable of interest in multivariable logistic regression models. The outcome variable was VT/PBW > 8 mL/kg. The "cluster" option in Stata was used for estimation of the variance-covariance matrix in all logistic models. This option relaxes the assumption of independent observations within groups, adjusting the standard errors and confidence intervals, to account for the possibility that care of patients within individual ICUs was correlated[18].

Mediation analysis was conducted according to the methods of Pearl et al[19] to probe relative contributions of gender and height on tidal volume > 8 ml/kg PBW. Statistical analyses were conducted with Stata version 14.2 (2015. *Stata Statistical Software* College Station, TX: StataCorp LP).

Results

Patient Characteristics

We enrolled 6,179 critically ill patients from 59 intensive care units, of which 2,513 patients received mechanical ventilation. Race was missing in 193 patients, tidal volume in 689 patients, and height in 147 patients. After exclusion of patients with one or more of these missing variables, 1,595 patients remained for the complete case analysis (Figure 1). The characteristics of mechanically ventilated subjects in the complete case analysis are shown in Tables 1 and 2. The hospital / ICU characteristics of these patients are shown in Tables E6 and E7 of the online data supplement.

Complete Case Analysis

Relationship between Gender and Provision of Lung Protective Ventilation (Table 3 and Figure 2)

Unadjusted tidal volumes were lower in women vs. men (400 [360-450] mL vs. 500 [450-550] mL, Figure 2). However, women received higher tidal volume than men when adjusted for predicted body weight (7.6 [6.7-8.6] mL/kg in women vs 6.7 [6.0 - 7.6] in men) and were more likely to receive tidal volumes above 8 ml/kg PBW (40% of women vs. 17% of men, odds ratio = 3.42 [2.67 – 4.40]).

Our hypothesized causal diagram indicated that height may mediate the association between gender and lung protective ventilation[20] (Figure 3). When we adjusted for patient height, the association between gender and tidal volume > 8 ml/kg PBW was substantially weakened (odds ratio [OR] = 1.28 [0.91 – 1.80), demonstrating that height was a strong mediator of the gender – tidal volume relationship. However, to examine whether gender plays a role in tidal volume choice in subgroups of taller and shorter patients, we

performed stratified analysis with dichotomous height classification using the median height of 5 feet 7 inches of all patients. We found that gender-based differences in tidal volume > 8 ml/kg PBW occurred both in shorter patients (odds ratio [OR] = 1.66, 95% confidence interval [CI] = 1.13, 2.42) and taller patients (OR = 1.82, 95% CI = 1.14 – 2.91). This suggests that gender continued to play a role in tidal volume selection despite gender-differences in height. In other words, height did not fully confound the association between gender and tidal volume. Furthermore, the effect estimate for gender was similar across height categories (as above, 1.66 vs 1.82). The lack of heterogeneity between these effect sizes indicates that height is not a significant effect-modifier for the gender-tidal volume relationship; that is, we did not find an interaction between height and gender in predicting tidal volume.

Mediation analysis further explored the relationship between gender and height in predicting tidal volume. (see Supplementary Methods and Tables E1-E5 in the online data supplement). This analysis indicates that a direct effect of female gender on choice of tidal volume was operative in approximately 39% of cases where the provision of tidal volume > 8 ml/kg PBW was related to related to gender and/or height. Likewise, an indirect mediation pathway, where gender affects height which in turn affects tidal volume choice, was operative in 59% of cases where the provision of tidal volume > 8 ml/kg PBW was related to related to gender and/or height.

Our hypothesized causal diagram (Figure 3 and Table E8 in the online data supplement) modeled age and comorbidity as variables that could be associated with height (the mediator) and tidal volume choice (the outcome)[21,22]. Multivariable analysis with these covariables demonstrated similar findings to the analysis adjusting for height alone (Table 3). These results indicate minimal influence of age and comorbidity on the gender-height-tidal volume relationship.

Relationship between race / ethnicity and lung protective ventilation (Table 4)

Unadjusted and PBW-adjusted tidal volumes were similar among racial and ethnic categories (Table 4). These findings were similar after adjustment for gender, insurance status, and comorbidity (Table 4; also see Figure 3 illustrating the proposed causal pathway involving these covariables, and Table E9 detailing relationships between these covariables and race/ethnicity).

Relationship between insurance status and lung protective ventilation (Table 3)

PBW-adjusted tidal volumes were slightly higher in underinsured compared to insured patients (Table 3). There were slightly more underinsured patients receiving tidal volume > 8 ml/kg IBW when compared to insured patients (31% vs 26%, OR = 1.26, 95% CI = 0.92 – 1.74).

We considered age, race / ethnicity, comorbidity, and ICU admission after elective surgery as potential confounders of the relationship between insurance status and lung protective ventilation (Figure 3 and Table E10)[22,23]. The association between underinsurance and tidal volume above 8 ml/kg PBW was stronger after adjusting for these covariables (OR = 1.56, 95% CI = 1.16 – 2.10, Table 2). This masking of the true association is explained by the confounding effects of age and ICU admission after elective

surgery. Both of these variables are “negatively” associated with the independent variable of interest (under-insurance) and “positively” associated with the outcome of interest (tidal volume above 8 ml/kg PBW); that is, older patients and the patients admitted to ICU after elective surgery were less likely to be underinsured (negative association), and more likely to receive tidal volume > 8 ml/kg PBW (positive association). Associations with this directionality were not observed for the race/ethnicity and comorbidity covariables, so they were less likely to explain this confounding (Table E10). Indeed, a more parsimonious multivariable logistic regression model including only age and ICU admission after elective surgery showed a similar association between underinsurance and high tidal volume (OR for under-insured patients receiving tidal volume > 8 ml/kg = 1.60, 95% CI = 1.18 – 2.18).

Sensitivity analysis examining the relationship between insurance status and lung protective ventilation excluding Medicare patients (n = 689) demonstrated similar findings, with multivariable analysis showing that underinsured patients were 71% more likely to receive non-lung protective ventilation than insured patients (online data supplement Table E11).

Additional sensitivity analyses included the addition of severity of illness, presence of ARDS, and mode of mechanical ventilation to the models. None of these variables appreciably affected our results (online data supplement Tables E12 – E14). We also constructed hierarchical models nesting patients within their ICUs. These analyses confirm that our models using ICU clustering accounted for possible differences in care received by patients within individual ICUs (Online Data Supplement Table E15).

Multiple Imputation Analysis

This analysis combined the patients in the complete case analysis with the 918 patients with one or more missing values for height, tidal volume, or race/ethnicity, yielding 2,513 patients (online data supplement Table E16).

The imputation model accounted for baseline differences between patients with vs without missing values (online data supplement Table E16). Imputed values were similar to the values recorded in the complete cases (Online Data Supplement Table E18).

The association between gender and tidal volume > 8 ml/kg PBW was similar in magnitude to that observed in the complete case analysis, but now statistically significant in the multivariable logistic regression model including height (OR = 1.37, 95% CI = 1.03 – 1.83, online data supplement Table E19).

Likewise, the relationship between insurance status and tidal volume above 8 ml/kg PBW was of similar magnitude to that observed in the multivariable analysis of the complete cases (OR = 1.42, 95% CI = 1.06 – 1.89, online data supplement Table E19). This relationship was similar when exclusively analyzing 1,455 non-Medicare patients in this dataset (OR = 1.48, 95% CI = 1.09 – 2.02, Online Data Supplement Table E20).

There remained no significant associations between tidal volume above 8 ml/kg PBW and racial / ethnic categories in this larger multiple imputation dataset (online data supplement Table E19).

Discussion

In this multicenter prospective cohort study of critically ill patients with respiratory failure in the U.S., we found that women were less likely to receive lung protective ventilation compared to men. While height differences between men and women mediate a large portion of this effect, our analysis suggests that gender also has its own direct effect on tidal volume choice. Furthermore, we found that underinsured patients were less likely to receive lung protective ventilation than insured patients after accounting for other imbalances between these groups.

The gender disparity we observed in tidal volume is consistent with Han and colleagues' finding that women with sepsis and ARDS are less likely to receive lung protective ventilation than men[20], a finding they attributed to the shorter height of women. Our study reinforces these findings in a separate prospective and multicenter cohort of unselected mechanically ventilated critically ill patients. Our findings confirm that height is an important mediator of the association between female gender and high tidal volume delivery.

Height-based differences in care delivery like the one described here could play a role in the inverse relationship that has been observed between height and mortality in the critically ill[24]. These differences may be exacerbated by overestimating height in shorter patients, thus exposing them to excessive tidal volumes[25]. Our dataset did not specify whether heights were measured or estimated. If estimated, our results may be biased toward underestimating the frequency of high tidal volumes in shorter patients, many of whom are women.

It is tempting to conclude that height differences are sufficient to explain the gender difference in tidal volume that we observed. However, our mediation analysis suggests that a direct effect of female gender on tidal volume choice contributed to 39% of the cases in which high tidal volume was related to gender and/or height. Furthermore, the gender difference in tidal volume was even observed in taller patients with height ≥ 5'7". Finally, our multiple imputation analysis in the larger sample size indicated that gender was associated with tidal volume > 8 mL/kg PBW even after adjusting for height. These three findings suggest that gender is an important determinant of tidal volume choice, not fully explained by gender-based differences in height.

Sex differences in the PBW formula are an additional factor that could contribute to this gender disparity, providing different PBW-based tidal volumes for women vs men of the same height. For example, the 8 ml/kg PBW tidal volume is 493 mL for women 5'7" in stature vs 529 mL for men of the same height. If the tidal volume is set at 500 mL for both, only women receive a tidal volume > 8 ml/kg PBW. Although sex-based PBW formulas may be unnecessary for other applications[26], they are appropriate for tidal volume optimization because of sex-differences in lung volume[27,28]. Creating ventilator algorithms that calculate and deliver tidal volumes bases on clinician-entered values for sex, measured height, and desired ml/kg PBW tidal volume could more consistently provide lung protective ventilation than the current practice of ordering absolute unadjusted tidal volume[29].

A remaining factor that could contribute to the observed gender disparity may be implicit bias in treatment delivery. A number of previous studies have reported gender-based disparities in ICU care, with less aggressive treatment in women vs. men[3,30,31]. These studies document that women are less likely than men to receive prompt antibiotic therapy, deep venous vein thrombosis (DVT) prophylaxis, mechanical ventilation, dialysis, and full code status. Further work is warranted to identify gender bias in critical care, define its effect on treatment decisions, and test strategies for its elimination.

We found that underinsured patients were less likely than insured patients to receive lung protective ventilation. To our knowledge this insurance-based disparity in tidal volume has not been reported previously, though insurance status-based differences in other ICU processes of care are well-known[2,4,32]. Access to acute care probably does not account for this disparity, since all patients were receiving critical care at the time of enrollment in our study. Likewise, differences in ICU quality are unlikely to explain our findings, since robust variance estimation with ICU-level clustering in our logistic models accounted for the possibility that patients within individual ICUs are correlated. Finally, different treatment preferences or beliefs are unlikely to explain these findings, because tidal volume is not a value sensitive decision and it is improbable that patient or surrogate decision maker preference could have influenced tidal volume choice. It is possible that clinicians' implicit biases influenced their adherence to lung protective ventilation[33,34], negatively impacting underinsured patients. Prior studies have demonstrated that treatment decisions by clinicians in acute care are influenced by socioeconomic status-based implicit bias[35,36]. Further work is warranted to identify whether insurance-based bias exists in critical care, define its effect on treatment decisions, and test strategies for its elimination.

We did not find racial or ethnic differences in the application of lung protective ventilation. These results are surprising in the context of numerous studies demonstrating significant racial differences in critical care and outcomes[2,37-39]. Our regression models were clustered by ICU, accounting for potential correlations in processes of care within these ICUs. Prior studies have shown that racial differences in critical care outcomes are attenuated after adjustment for the site (and, by extension, the quality) of care delivery [40,41]. That said, even our unadjusted analyses did not show differences in lung protective ventilation by race or ethnicity (Table 2).

Our negative findings may relate to the limitations of our study. Our racial designations were gleaned from the medical records by data abstractors at each site. It is unknown whether these racial designations were consistently recorded in the medical records using the preferred method of self-report[42]. In addition, the medical records frequently contained ambiguous terminology that could not be confidently classified into one of the standard designations[43], contributing to the high number of missing values in our dataset. Even though we did not observe racial / ethnic differences in tidal volume, our analyses demonstrated that minority populations are over-represented among the underinsured (Table E9) and therefore remain at risk for high tidal volume ventilation. [32].

Our cohort included all mechanically ventilated patients. Lung protective ventilation is considered best practice in ARDS, though it is not invariably applied, with average tidal volume of 7.8 ml/kg in ARDS patients across 50 countries[8]. In patients without ARDS, lung protective ventilation may not be the standard of care, but several studies support its use in these patients as well, showing lower levels of pro-inflammatory cytokines, lower radiographic evidence of lung injury, shorter hospital stays, and less post-operative pulmonary complications[10,11,44-46]. A randomized controlled trial showed no differences in clinical outcomes when patients were randomized to low vs. intermediate tidal volume[47], but a large amount of overlap in tidal volume between groups may have biased these results toward the null[48]. Regardless of whether universally accepted in non-ARDS acute respiratory failure, differences in the application of lung protective ventilation in these demographic groups are an important signal of disparities in ICU care.

Strengths and Limitations

Our study has several strengths, particularly the prospective cohort design, manual data abstraction, large sample size, and nationwide ICU representation from 35 medical centers. There are several limitations to our study. First, our observational study design does not permit conclusions about whether there is any causal basis for the associations we observed between tidal volume and gender, height, or insurance status. Likewise, we cannot rule out residual confounding by other unmeasured variables that may explain these associations. Our use of causal models to define potential confounders may be over-simplified and miss important covariables that could be responsible for our findings[15]. For example, we were unable to determine which patients in this dataset had ARDS, and its presence would influence tidal volume. If ARDS were differentially distributed amongst our demographic groups, this could confound our findings. However, consistent demonstration of disparities in processes of care across different studies increases the likelihood of that the similar associations we report are robust [2-4,6,20,35]. Our findings thus add to the evidence suggesting women, shorter people, and the underinsured are treated differently in U.S. ICUs. Second, our cohort included predominantly academic institutions, so its applicability to patients in community hospital may be limited. Third, we collected each patient's ventilator data only once, and it may have been on any day from 1-10 of their ICU stay. This "snapshot" of tidal volume delivery may not accurately reflect the volume received throughout their treatment with invasive mechanical ventilation. Fourth, height, race, and gender were taken from the medical record without specification about how they were originally ascertained. We are unsure whether race and ethnicity were consistently obtained by the recommended method of self-report[42]. If not, there is risk of non-differential ascertainment bias and possible obscuration of true racial differences[49]. Likewise, heights may have been inaccurate if they were estimated instead of measured, with over-estimation particularly likely in women,[25] and accompanying risk of differential ascertainment bias. If so, gender-differences in lung protective ventilation may be even larger than we report here. Fifth, it is important to note that the associations we identify in this study may have changed considerably since 2010 – 2012 when our data was obtained. Investigating these questions in a contemporary cohort is an important next step to determine whether the disparities present a decade ago are entrenched over time.

Conclusions

Analysis of this large prospective cohort study uncovered important disparities in the provision of lung protective ventilation in the U.S. Women were less likely to receive lung protective ventilation compared to men, an association largely but not fully explained by the shorter height of women. Furthermore, we find a robust association between under-insurance and non-adherence to lung protective ventilation especially after accounting for other imbalances between patients with different insurance types. Tidal volume prescription is a clinical management decision; our findings suggest this decision may be biased by demographic and phenotypic factors such as insurance status, gender, and height. Additional research is required to confirm these findings, evaluate the extent to which implicit bias determine processes of ICU care, and test interventions to eliminate these disparities.

Declarations

Ethics approval and consent to participate: All participating sites received approval from their institutional review boards for data collection with a waiver of informed consent (see acknowledgements section below for list of participating sites).

Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request and conditional on the approval from the Critical Illness Outcomes Study Publication Committee.

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Authors' contributions: MLM contributed to the study design, performed data analysis, and drafted the manuscript. CMQ and AKB participated in study design and were major contributors in writing the manuscript. APP designed and led the study, analyzed and interpreted the data, edited and finalized the manuscript, and takes responsibility for all aspects of the work. All authors read and approved the final manuscript.

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Tables

Table 1. Patient characteristics by sex and insurance status (complete case analysis)*

Variable	Study population n = (1,595)	Women (n = 710)	Men (n = 885)	Under-insured (n = 338)	Insured (n = 1,257)
Age (years)	61 (51 – 71)	62 (52 – 73)	60 (50 – 70)	52 (41 – 59)	64 (54 – 74)
APACHE II score	21 (16 – 26)	21 (16 – 25)	21 (16 – 26)	19 (14 – 24)	21 (16 – 26)
SOFA score	7 (4 – 10)	6 (4 – 9)	7 (5 – 10)	6 (4 – 10)	7 (4 – 10)
Hospital mortality†	437 (30%)	191 (28%)	246 (30%)	86 (30%)	351 (30%)
Hospital length of stay (days)†	17 (10 – 30)	17 (10 – 29)	17 (10 – 31)	17 (9 – 33)	17 (10 – 30)
ICU length of stay (days)†	10 (5-18)	10 (5 – 17)	10 (5 – 10)	10 (5 – 18)	10 (5 – 18)
Comorbid conditions					
Heart failure	271 (17%)	135 (19%)	136 (15%)	54 (16%)	217 (17%)
COPD	423 (26%)	212 (30%)	211 (24%)	67 (20%)	356 (28%)
Cancer	338 (21%)	139 (20%)	199 (22%)	43 (12%)	295 (23%)
Chronic kidney disease	261 (16%)	125 (18%)	136 (15%)	39 (12%)	222 (18%)
Chronic liver disease	183 (11%)	72 (10%)	111 (12%)	48 (14%)	135 (11%)
HIV/AIDS	59 (4%)	23 (3%)	36 (4%)	29 (9%)	30 (2%)
Admission diagnosis category					
Respiratory	865 (54%)	389 (55%)	476 (54%)	184 (54%)	681 (54%)
Infectious	472 (30%)	229 (32%)	243 (27%)	114 (30%)	391 (30%)
Cardiovascular	467 (29%)	200 (28%)	267 (30%)	98 (26%)	395 (30%)
Gastrointestinal	236 (15%)	102 (14%)	134 (15%)	51 (14%)	202 (15%)
Trauma	101 (6%)	27 (4%)	74 (8%)	40 (11%)	71 (5%)
Endocrine	101 (6%)	48 (7%)	53 (6%)	30 (8%)	78 (6%)
Other	235 (15%)	106 (15%)	129 (14%)	48 (13%)	203 (16%)
Admission source					
Emergency department	715 (45%)	322 (45%)	393 (44%)	196 (58%)	519 (41%)

Hospital floor	315 (20%)	131 (18%)	184 (21%)	60 (18%)	255 (20%)
Operating room	255 (16%)	105 (15%)	150 (17%)	31 (9%)	224 (18%)
Outside hospital	252 (16%)	123 (17%)	129 (15%)	45 (13%)	207 (16%)
Other	58 (4%)	29 (4%)	29 (3%)	6 (2%)	52 (4%)

* Values refer to median (interquartile range) or number (percentage)

† Mortality status, ICU length of stay, and hospital length of stay were missing in 114 patients.

Table 2. Patient characteristics by racial and ethnic categories*

		Race				Ethnicity	
Variable	**Study population n = (1,595)**	**White (n = 1,113)**	**Black (n = 424)**	**Asian (n = 51)**	**American Indian / Alaska native (n = 7)**	**Non-Hispanic or Latino (n = 1,544)**	**Hispanic or Latino (n = 51)**
Age (years)	61 (51 – 71)	62 (52 – 74)	58 (48 – 67)	65 (54 – 78)	55 (53 – 61)	61 (51 – 72)	58 (37 – 67)
APACHE II score	21 (16 – 26)	21 (16 – 25)	20 (16 – 26)	21 (17 – 24)	23 (20 – 27)	21 (16 – 26)	21 (17 – 25)
SOFA score	7 (4 – 10)	7 (4 – 10)	7 (4 – 10)	7 (4 – 10)	9 (5 – 10)	7 (4 – 10)	7 (5 – 11)
Hospital mortality†	437 (30%)	293 (28)	120 (30)	22 (43)	2 (33)	427 (30)	10 (20)
Hospital length of stay (days)†	17 (10 – 30)	17 (10 – 30)	18 (9 – 31)	14 (6 – 36)	16 (15 - 20)	17 (10 – 30)	16 (8 – 34)
ICU length of stay (days)†	10 (5-18)	10 (5 – 17)	10 (5-18)	10 (4 – 21)	12 (5 – 20)	10 (5 – 18)	8 (4 – 20)
Comorbid conditions							
Heart failure	271 (17%)	167 (15)	99 (24)	4 (8)	1 (14)	266 (17)	5 (10)
COPD	423 (26%)	309 (28)	104 (24)	9 (18)	1 (14)	416 (27)	7 (14)
Cancer	338 (21%)	263 (23)	62 (15)	11 (22)	2 (28)	331 (21)	7 (14)
Chronic kidney disease	261 (16%)	141 (13)	113 (27)	7 (14)	0 (0)	258 (17)	3 (6)
Chronic liver disease	183 (11%)	121 (11)	53 (12)	7 (14)	2 (28)	173 (11)	10 (20)
HIV/AIDS	59 (4%)	14 (1)	44 (10)	0 (0)	1 (14)	58 (4)	1 (2)
Admission diagnosis category							
Infectious	472 (30%)	291 (26)	168 (40)	12 (24)	1 (14)	460 (30)	12 (24)
	467 (29%)	300	150	16	1 (14)	462 (30)	5 (10)

Cardiovascular		(27)	(35)	(31)			
Gastrointestinal	236 (15%)	170 (15)	60 (14)	5 (10)	1 (14)	231 (15)	5 (10)
Trauma	101 (6%)	73 (6)	24 (6)	3 (6)	1 (14)	98 (6)	3 (6)
Endocrine	101 (6%)	64 (6)	35 (8)	2 (4)	0 (0)	98 (6)	3 (6)
Other	235 (15%)	166 (15)	59 (14)	8 (16)	2 (28)	230 (15)	5 (10)
Admission source							
Emergency department	715 (45%)	444 (40)	246 (58)	22 (43)	3 (43)	685 (44)	30 (59)
Hospital floor	315 (20%)	215 (19)	86 (200)	11 (22)	3 (43)	305 (20)	10 (20)
Operating room	255 (16%)	201 (18)	44 (10)	9 (18)	1 (14)	249 (16)	6 (12)
Outside hospital	252 (16%)	212 (19)	33 (8)	7 (14)	0 (0)	248 (16)	4 (8)
Other	58 (4%)	41 (4)	15 (4)	2 (4)	0 (0)	57 (4)	1 (2)

* Values refer to median (interquartile range) or number (percentage)

† Mortality status, ICU length of stay, and hospital length of stay were missing in 114 patients.

Table 3. The relationships of lung protective ventilation with gender and insurance status*

	Women (n= 710)	Men (n = 885)	Underinsured (n = 338)	Insured (n = 1,257)
Tidal volume (mL)	400 (360 – 450)	500 (450 – 550)	450 (400 – 500)	450 (400 – 500)
Tidal volume / PBW (mL/kg)	7.6 (6.7 – 8.6)	6.7 (6.0 – 7.6)	7.1 (6.4 – 8.2)	7.0 (6.2 – 8.0)
Tidal volume > 8 ml/kg PBW	288 (40%)	147 (17%)	105 (31%)	330 (26%)
unadjusted odds ratio of tidal volume > 8 ml/kg PBW	3.42 (2.67 – 4.40)	1 (ref)	1.26 (0.92 – 1.74)	1 (ref)
Height-adjusted odds ratio	1.28 (0.91 – 1.80)	1 (ref)	—	—
Multivariable adjusted odds ratio (all variables)	1.28 (0.92 – 1.77)†	1 (ref)	1.56 (1.16 – 2.10)§	1 (ref)

* Values refer to median (interquartile range) or number (percentage)

† Adjusted for age (continuous), height (continuous), total number of comorbidities (0-5).

§ Adjusted for age (continuous), post-operative from elective surgery status, race, ethnicity, total number of comorbidities (0-5).

Table 4. The relationship of lung protective ventilation with race/ ethnicity*

	Race				Ethnicity	
	White (n = 1,113)	Black (n = 424)	Asian (n = 51)	American Indian / Alaska native (n = 7)	Non-Hispanic or Latino (n = 1,544)	Hispanic or Latino (n = 51)
Tidal volume (mL)	450 (400 – 500)	450 (400 – 500)	450 (390 – 500)	350 (300 – 500)	450 (400 – 500)	450 (400 – 500)
Tidal volume / PBW (mL/kg)	7.1 (6.2 – 8.0)	7.07 (6.2 – 8.0)	7.6 (6.4 – 8.3)	6.7 (5.9 – 7.3)	7.1 (6.2 – 8.0)	7.2 (6.4 – 8.2)
Tidal volume > 8 ml/kg PBW	303 (27)	115 (27)	31 (16)	1 (14)	419 (27)	16 (31)
unadjusted odds ratio of tidal volume > 8 ml/kg PBW	1 (reference)	0.99 (0.62 – 1.60)	1.22 (0.61 – 2.44)	0.44 (0.07 – 2.68)	1 (reference)	1.22 (0.49 – 3.08)
Multivariable adjusted odds ratio (all variables) ‡	1 (reference)	0.86 (0.52 – 1.41)	1.30 (0.63 – 1.41)	0.32 (0.05 – 2.00)	1 (reference)	1.08 (0.39 – 2.94)

* Values refer to median (interquartile range) or number (percentage)

‡ Adjusted for gender, insurance status, and total number of comorbidities (0-5).

Figures

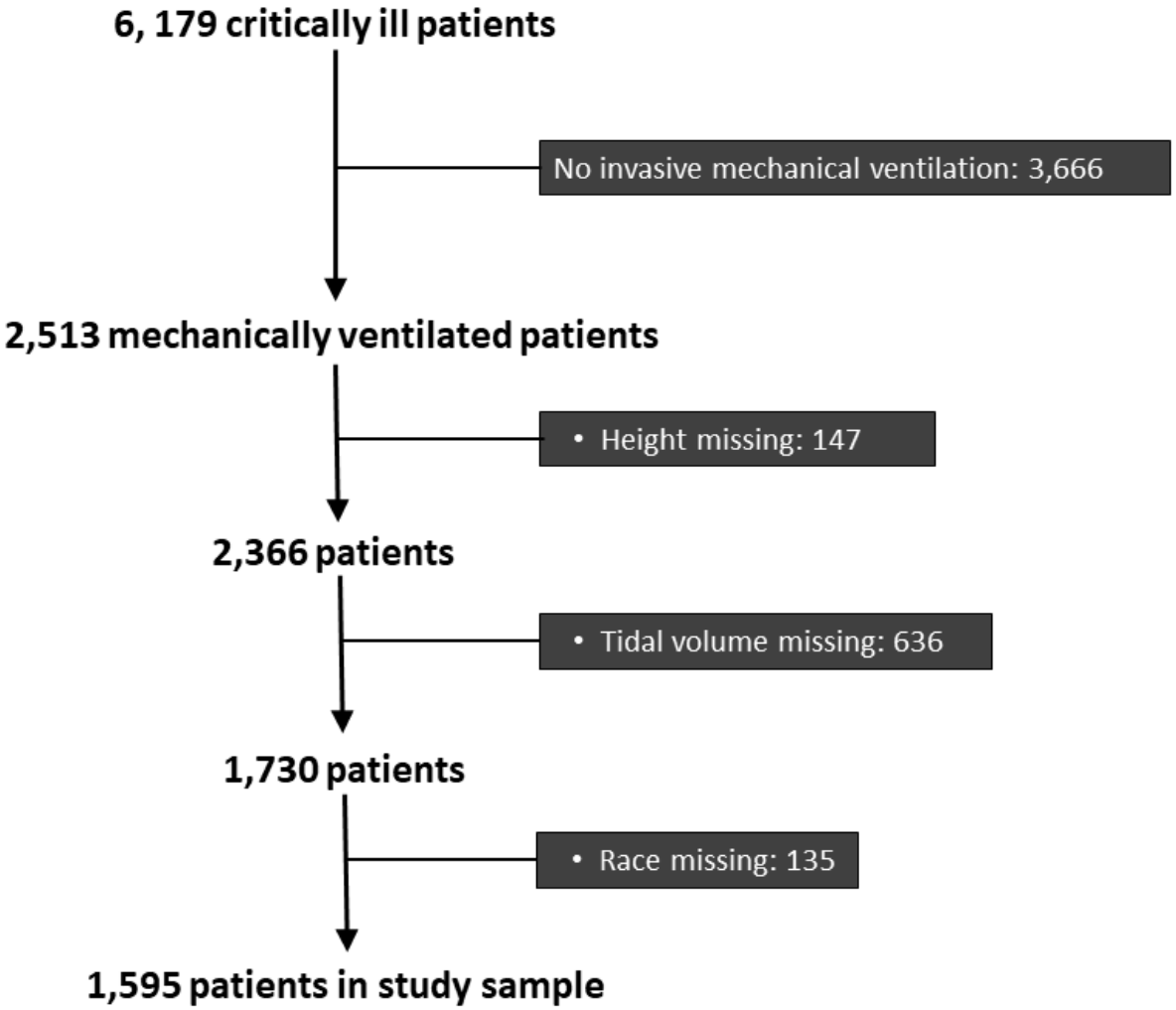

Figure 1

Derivation of study sample.

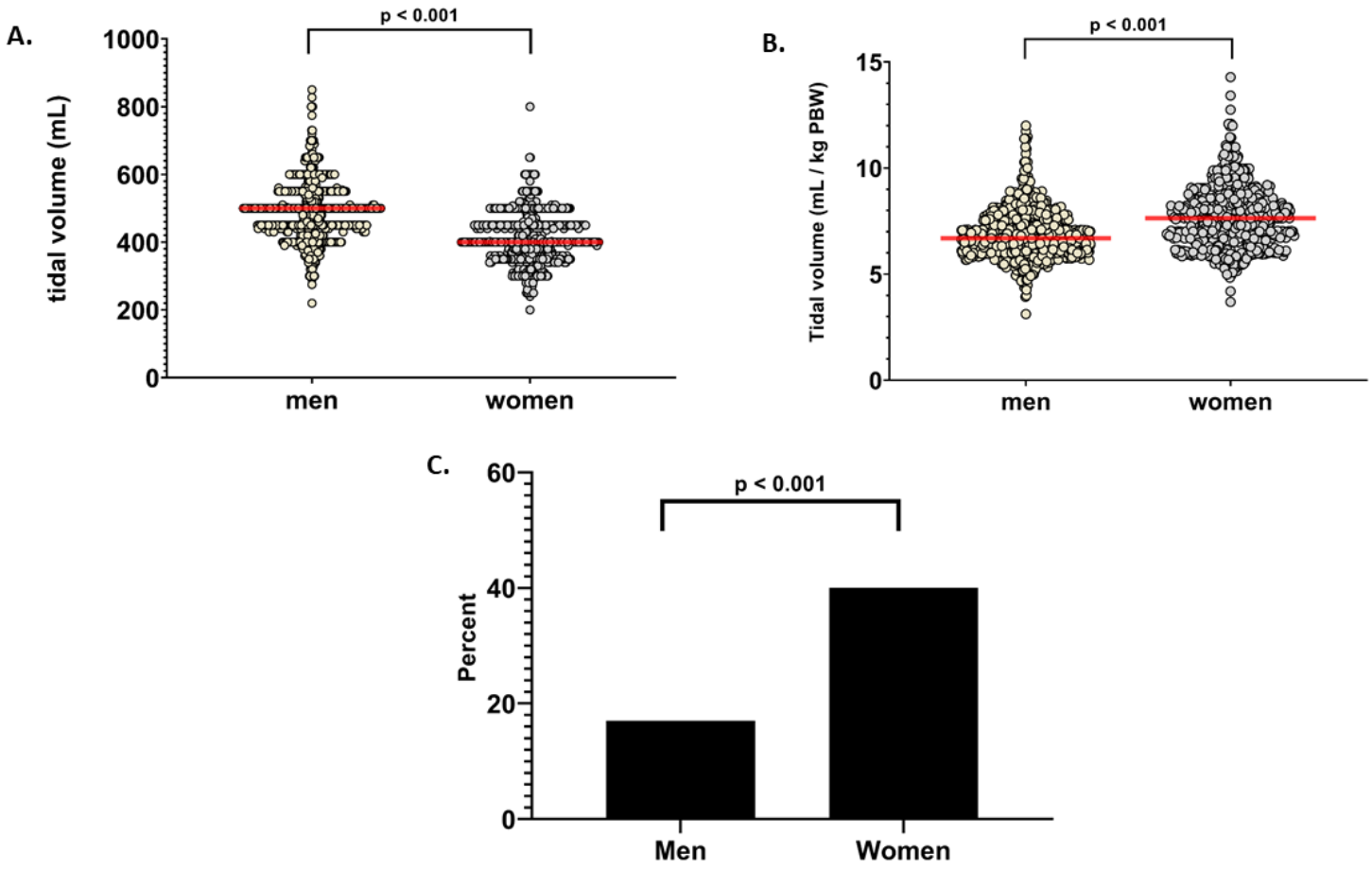

Figure 2

Tidal volume parameters in men vs. women. A. unadjusted tidal volume in men vs. women; B. Tidal volume adjusted for predicted body weight in men vs. women; C. Percentage of men vs. women receiving tidal volume > 8 ml/kg predicted body weight. Dot plots show distributions of values, with the median value indicated by the horizontal line. Comparisons analyzed with the rank-sum test or chi-square test.

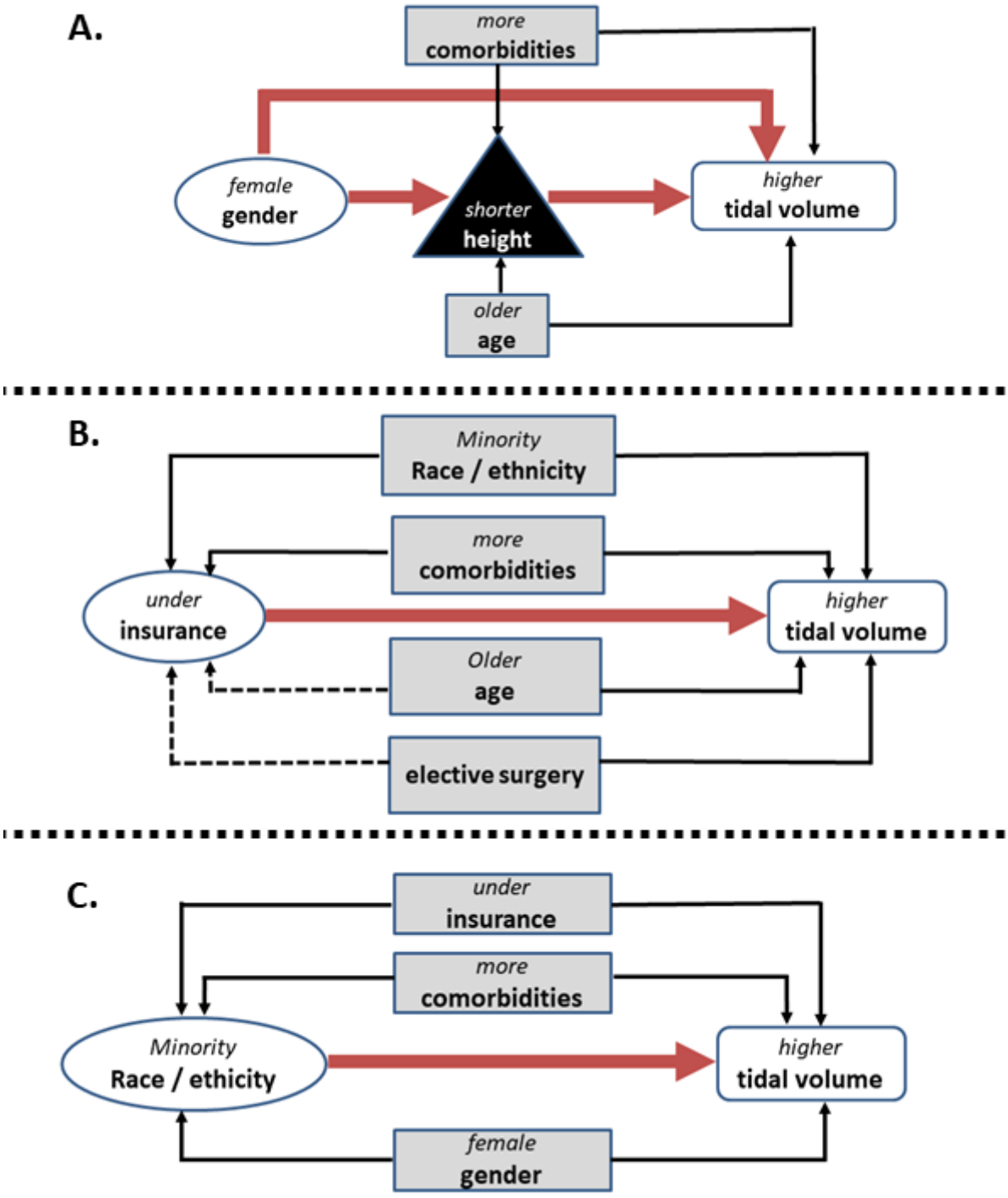

Figure 3

Directed acyclic graphs modeling hypothesized relationships between exposures (ovals) and outcome of interest (rectangles with white background). Proposed causal pathways are diagramed in thick solid arrows. Potential confounders are diagramed in shaded rectangles. Relationships between potential confounders and other variables are diagramed as thin arrows. Positive relationships between potential confounders and other variables are those that increase the probability of the other variable, designated by thin solid arrows. Negative relationships between potential confounders and other variables are those

that decrease the probability of the other variable, designated by thin dashed arrows. Mediators are designated by black triangles.

A. Theorized causal association diagram between female gender (exposure) and higher tidal volume (outcome). There are two possible causal pathways diagramed: one that includes shorter height as a mediator (the indirect path)[20] and one goes directly from female gender to higher tidal volume (the direct path). Medical comorbidities and older age are diagramed as possible confounders of the relationship between height (mediator) and tidal volume (outcome)[21,50].

B. Theorized causal association diagram between under-insurance (exposure) and higher tidal volume (outcome). Minority race/ethnicity and more comorbidities are diagramed as potential confounders sharing positive associations with both the exposure and the outcome[23]. Older age and elective surgery are diagramed as confounders sharing negative associations with under-insurance but positive associations with higher tidal volume[22].

C. Theorized causal association diagram between minority race / ethnicity (exposure) and higher tidal volume (outcome). Under-insurance, more comorbidities, and female gender are diagramed as potential confounders sharing positive associations with the exposure and outcome [23,51].

Supplementary Files

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