Original Article

The effect of demographics and patient location on the outcome of patients with acute respiratory distress syndrome

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Abstract:

OBJECTIVE: Outcome of acute respiratory distress syndrome (ARDS) in relation to age, gender, race, pre-Intensive Care Unit (ICU) location, and type of ICU.

METHODS: Retrospective cohort study of patients enrolled in the ARDS network randomized controlled trials.

RESULTS: A total of 2914 patients were included in these trials. Outcomes were adjusted to baseline covariates including APACHE III score, vasopressor use, cause of lung injury, lung injury score, diabetes, cancer status, body mass index, and study ID. Older patients had significantly higher mortality at both 28- and 60-day (odds ratio [OR] 2.59 [95% confidence interval [CI]: 2.12–3.18] $P < 0.001$ and 2.79, 95% CI: 2.29–3.39, $P < 0.001$, respectively); less ICU and ventilator free days (relative risk [RR] 0.92, 95% CI: 0.87–0.96, $P < 0.001$ and 0.92, 95% CI: 0.88–0.96, $P < 0.001$, respectively). For preadmission location, the 28- and 60-day mortality were lower if the patient was admitted from the operating room (OR)/recovery room (OR 0.65, 95% CI: 0.44–0.95, $P = 0.026$; and OR = 0.66, 95% CI: 0.46–0.95, $P = 0.025$, respectively) or emergency department (OR = 0.78, 95% CI: 0.61–0.99, $P = 0.039$; and OR = 0.71, 95% CI: 0.56–0.89, $P = 0.004$, respectively), but no statistical differences in ICU and ventilator free days between different preadmission locations. Races other than white and black had a statistically higher mortality (28- and 60-day mortality: OR = 1.47, 95% CI: 1.09–1.98, $P = 0.011$; and OR 1.53, 95% CI: 1.15–2.04, $P = 0.004$, respectively). Between whites and blacks, females and males there were no statistically significant differences in all outcomes.

CONCLUSION: Older patients and races other than blacks and whites have higher mortality associated with ARDS. Mortality is affected by patients preadmission location. There are no differences in outcome in relation to the type of ICU, gender, or between blacks and whites.

Key words:

Acute respiratory distress syndrome, demographics, outcome

Acute respiratory distress syndrome (ARDS) is a serious complication associated with critical illness affecting an estimated 150,000 annually in the US and at least 20% of mechanically ventilated patients.[1,2] The outcome of ARDS varies significantly between patients and is influenced by several factors. There are conflicting results in the literature about the predictors of outcome in patients with ARDS. The ARDS network randomized controlled trials provide a unique opportunity to study the different variables affecting outcome of these patients. We have shown that the outcome is affected by cancer status and not influenced by body mass index (BMI) or presence or absence of diabetes mellitus.[3,4] The aim of this study was to analyze the effect of demographic data such as age, race, gender, pre-Intensive Care Unit (ICU) patient location, and type of ICU on outcome of patients with ARDS.

Methods

The ARDS network has conducted several randomized controlled trials to evaluate therapeutic interventions for the management of acute lung injury. These trials have been previously

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Table 1: Summary of the ARDS network trials

	KARMA	LASRS	LARMA	ALVEOLI	FACTT	ALTA
Years	1996-1998	1997-2003	1998-1999	1999-2002	2000-2005	2007-2008
No. of patients	667	180	235	550	1000	282
Intervention	Low tidal volume ventilation/ ketoconazole use in ARDS	Use of steroids in ARDS	Low tidal volume ventilation/Lisofylline use early in ALI/ARDS	High PEEP/ Low FiO_2 vs Low PEEP/High FiO_2 ventilation strategy	PA catheter vs central venous catheter. Conservative vs liberal fluid strategy in management of patient's with ALI/ARDS	Aerosolized albuterol vs saline placebo in patients with ALI/ARDS
Outcome	No effect of ketoconazole on mortality. Improved mortality with low tidal volume ventilation	No change in mortality	No effect of lisofylline on mortality. Improved mortality with low tidal volume ventilation	No change in mortality	No change in mortality	No change in mortality

KARMA = Ketoconazole and respiratory management, LASRS = Late steroid rescue study, LARMA = Lisofylline and respiratory management, ALVEOLI = Assessment of low tidal volume and elevated end-expiratory volume to obviate lung injury, FACTT = Fluids and catheters treatment trial, ALTA = Albuterol for the treatment of acute lung injury

published.[5-10] Table 1 summarizes the relevant features of these trials. Briefly, all patients fulfilled diagnostic criteria for acute lung injury and were mechanically ventilated. Similar inclusion and exclusion criteria were used in all of the trials. The National Institute of Health and the local Institutional Review Boards of each of the sites approved all studies.

We had authorized access to the original data for each of these studies. This manuscript was prepared using Ketoconazole and Respiratory Management in ALI/ARDS (KARMA), Late Steroid Rescue Study (LASRS), Lisofylline and Respiratory Management in ALI/ARDS (LARMA), Assessment of Low tidal Volume and elevated End-expiratory volume to Obviate Lung Injury (ALVEOLI), Fluids And Catheters Treatment Trial (FACTT), and Albuterol for the Treatment of Acute lung injury (ALTA) research materials obtained from the National Heart, Lung, and Blood Institute (NHLBI) Biologic Specimen and Data Repository Information Coordinating Center. The findings of this study do not necessarily reflect the opinions or views of the KARMA, LASRS, LARMA, ALVEOLI, FACTT, and ALTA investigators or the NHLBI.

For the purpose of this analysis, we included only patients who had P/F ratio <300 to fulfill the Berlin definition of ARDS.[11] The data were stratified in relation to demographics (age, race, and gender), pre-ICU patient location, and the type of ICU. Other data points extracted included vasopressor use, etiology of ARDS, lung injury score as well as APACHE score. We also included cancer status since it was found important in our previous analysis of the data.[3]

For age, patients were divided into two groups 16–59 years and 60–89 years. Regarding race patients were divided into white (reference), black and others. The race was self-identified by the patients or relatives. Pre-ICU patient locations were classified into floor/stepdown unit (reference), emergency department (ED), operating room (OR)/recovery room, and others. The ICU locations were classified into mobile ICU (MICU)/critical care unit (CCU) (reference), surgical ICU (SICU)/cardiac SICU, neuro ICU, burn, trauma, and mixed ICU.

The primary outcome for our analysis was mortality at 28-day after enrollment in the study in relation to age, gender, race, pre-ICU, and type of ICU. The secondary outcomes were 60-day mortality, ventilator-free days, and ICU-free days. The ventilator-free days were defined as the number of days of at least 48-h unassisted breathing during the first 28 days after enrollment.

Statistical analysis

Patient's baseline characteristics across six studies were reported descriptively. Continuous data are presented as medians with ranges. Categorical data are reported as frequencies and percentages. In an effort to minimize the false positives due to multiple testing, all variables were specified *a priori* to be clinically sound. These variables included age (<60 and ≥60), gender, ethnic (white, black, and other), pre-ICU location, type of ICU, APACHE III, vasopressor use, cause of lung injury (pneumonia, severe sepsis, aspiration, trauma, and others), lung injury score, cancer status, BMI, diabetes mellitus, and study ID.

The univariate analysis of association between age (<60 and ≥60), gender, ethnic (white, black, and other), pre-ICU location, and type of ICU and clinical outcomes including 28-day mortality, 60-day mortality, categorized ventilation free days in weeks, categorized ICU-free days in weeks, were tested for significance using a Chi-square test or Fisher's exact test where appropriate.

Purposeful multivariable logistic regression model and multivariable zero-inflated negative binomial regression model were then used to evaluate the effect of above-mentioned patient baseline characteristics on clinical outcomes including 28- or 60-day mortality and ventilation free days or ICU-free days, respectively.

Because of missing values in our set of covariates, all the multivariable models were carried out after 15 multiple imputations using the R package mice. All *P* values are 2-sided with a significance level of 0.05. The results of these analyses should be regarded only as descriptive findings, and multiple testing were not adjusted. All calculations were performed with R version 3.0.2.

Results

A total of 2914 patients were included in these trials. Five patients with P/F >300 were excluded from analysis. Table 2 describes the baseline characteristics of these patients.

Table 2: Baseline patient characteristics by study

Variable	KARMA (*n*=667)	LASRS (*n* =180)	LARMA (*n*=235)	ALVEOLI (*n*=550)	FACTT (*n*=1000)	ALTA (*n*=282)
Age, median (range)	51 (18,89)	47 (16,89)	49 (18,86)	50 (16,88)	49 (17,89)	52 (17,89)
Gender (*n*, %)						
Male	392 (59)	89 (49)	145 (62)	302 (55)	534 (53)	156 (55)
Female	275 (41)	91 (51)	90 (38)	248 (45)	466 (47)	126 (45)
Race (*n*, %)						
White	482 (72)	131 (73)	179 (76)	413 (75)	641 (64)	217 (77)
Black	118 (18)	28 (16)	37 (16)	77 (14)	217 (22)	46 (16)
Others	67 (10)	21 (12)	19 (8)	60 (11)	142 (14)	19 (7)
Pre-ICU location (*n*, %)						
Floor/Stepdown	226 (34)	27 (15)	65 (28)	174 (32)	308 (31)	78 (28)
ER	174 (26)	44 (24)	73 (31)	166 (30)	353 (35)	121 (43)
OR/Recovery room	104 (16)	11 (6)	31 (13)	82 (15)	91 (9)	28 (10)
Others	162 (24)	98 (54)	66 (28)	127 (23)	247 (25)	55 (20)
Missing	1 (0)	0 (0)	0 (0)	1 (0)	1 (0)	0 (0)
Patient location (*n*, %)						
MICU/CCU	392 (59)	116 (64)	148 (63)	333 (61)	679 (68)	168 (60)
SICU/Cardiac SICU	131 (20)	19 (11)	41 (17)	98 (18)	105 (10)	33 (12)
Neuro ICU	11 (2)	4 (2)	1 (0)	10 (2)	13 (1)	3 (1)
Burn	16 (2)	5 (3)	6 (3)	10 (2)	6 (1)	4 (1)
Trauma	75 (11)	28 (16)	25 (11)	44 (8)	44 (4)	16 (6)
Mixed ICU	42 (6)	8 (4)	14 (6)	55 (10)	153 (15)	58 (21)
Vasopressor use (*n*, %)	269 (40)	56 (31)	78 (33)	156 (28)	330 (33)	141 (50)
Missing	3 (0.45)	2 (1.11)	2 (0.85)	18 (3.27)	1 (0.1)	0 (0)
Cause of lung injury (*n*, %)						
Sepsis	178 (27)	36 (20)	58 (25)	120 (22)	233 (23)	77 (27)
Pneumonia	205 (31)	63 (35)	84 (36)	221 (40)	471 (47)	107 (38)
Aspiration	96 (14)	30 (17)	38 (16)	85 (15)	149 (15)	54 (19)
Trauma	74 (11)	23 (13)	22 (9)	45 (8)	74 (7)	23 (8)
Others	114 (17)	28 (16)	33 (14)	79 (14)	73 (7)	21 (7)
Cancer (*n*, %)	30 (4)	3 (2)	14 (6)	20 (4)	49 (5)	9 (3)
Diabetes mellitus (*n*, %)	84 (13)	26 (14)	42 (18)	83 (15)	173 (17)	61 (22)
Missing	7 (1.05)	0 (0)	0 (0)	7 (1.27)	33 (3.3)	0 (0)
BMI (*n*, %)						
Underweight	34 (5)	1 (1)	8 (3)	20 (4)	36 (4)	13 (5)
Normal	251 (38)	52 (29)	80 (34)	191 (35)	293 (29)	81 (29)
Overweight	191 (29)	49 (27)	67 (29)	144 (26)	264 (26)	86 (30)
Obese	120 (18)	54 (30)	56 (24)	122 (22)	249 (25)	86 (30)
Severely obese	26 (4)	16 (9)	17 (7)	28 (5)	74 (7)	14 (5)
Missing	45 (6.75)	8 (4.44)	7 (2.98)	45 (8.18)	84 (8.4)	2 (0.71)
LIS, median (range)	2.75 (1,4)	3.25 (2,4)	2.75 (0.667,4)	2.75 (1.25,4)	2.75 (0.5,4)	2.708 (0.5,4)
APACHE III, median (range)	81 (22,178)	85.5 (16,155)	86 (30,195)	91 (0,191)	91 (17,205)	90.5 (32,185)

ICU = Intensive care unit, Pre-ICU location, location prior to admission to ICU, ER = Emergency room, OR = Operating room, MICU = Medical ICU, CCU = Cardiac medical patients, SICU = Surgical ICU, BMI = Body mass index, LIS = Lung injury score

Age

On univariate analysis, there was significant statistical difference in the mortality rate, with 28-day mortality being higher among older age group (39.44% vs. 18.49%, $P < 0.001$, Chi-square test). The 60-day mortality for old age group was 45% and for younger age group 21% ($P < 0.001$, Chi-square test) [Figure 1]. The older age group had less ICU free days [Figure 2] and less ventilator-free days [Figure 3] (both $P < 0.001$, Chi-square test). The multivariable logistic regression results showed a statistically significant higher mortality at both 28 days and 60 days for older age group (OR for 28-day mortality = 2.59, 95% confidence interval [CI]: 2.12–3.18, $P < 0.001$; OR for 60-day mortality = 2.79, 95% CI: 2.29–3.39, $P < 0.001$) [Table 3]. The multivariable negative binomial regression showed there were statistically significant more ICU-free days and ventilator-free days for younger age group (older age group; relative risk [RR] for ICU-free days = 0.92, 95% CI: 0.87–0.96, $P < 0.001$; RR for ventilator-free days = 0.92, 95% CI: 0.88–0.96, $P < 0.001$) [Table 3].

Gender

On univariate analysis, there was no significant statistical difference between males and females mortality at 28 days (25.77% versus 23.72%, $P = 0.219$, Chi-square test) but there was a statistically significant higher mortality for males at 60 days (30.16% vs. 26.36%, $P = 0.027$, Chi-square

Table 3: Results of multivariable regression models after multiple imputations

Variable	28-day mortality[a]		60-day mortality[a]		ICU-free days[b]		Ventilator-free days[b]	
	OR (95% CI)	*P*	OR (95% CI)	*P*	RR (95% CI)	*P*	RR (95% CI)	*P*
Age								
16-59 years	Ref.		Ref.		Ref.		Ref.	
60-89 years	2.59 (2.12,3.18)	<0.001	2.79 (2.29,3.39)	<0.001	0.92 (0.87,0.96)	<0.001	0.92 (0.88,0.96)	<0.001
Gender								
Male	Ref.		Ref.		Ref.		Ref.	
Female	0.94 (0.78,1.14)	0.538	0.85 (0.7,1.02)	0.083	1.04 (1,1.08)	0.046	1.02 (0.98,1.06)	0.25
Race								
White	Ref.		Ref.		Ref.		Ref.	
Black	1.1 (0.85,1.41)	0.479	1.16 (0.91,1.47)	0.242	1.05 (0.99,1.1)	0.1	1.03 (0.98,1.08)	0.305
Others	1.47 (1.09,1.98)	0.011	1.53 (1.15,2.04)	0.004	0.96 (0.9,1.02)	0.214	0.97 (0.92,1.04)	0.424
Pre-ICU location								
Floor/Stepdown	Ref.		Ref.		Ref.		Ref.	
ED	0.78 (0.61,0.99)	0.039	0.71 (0.56,0.89)	0.004	1.04 (0.99,1.1)	0.101	1.04 (0.99,1.1)	0.086
OR/Recovery room	0.65 (0.44,0.95)	0.026	0.66 (0.46,0.95)	0.025	1.01 (0.94,1.08)	0.852	1.02 (0.95,1.09)	0.589
Others	0.7 (0.55,0.91)	0.007	0.72 (0.57,0.93)	0.01	1.01 (0.96,1.06)	0.775	1.02 (0.96,1.07)	0.558
Patient location								
MICU/CCU	Ref.		Ref.		Ref.		Ref.	
SICU/Cardiac SICU	0.9 (0.65,1.24)	0.518	0.94 (0.7,1.28)	0.713	0.95 (0.89,1.01)	0.089	0.96 (0.91,1.02)	0.23
Neuro ICU	0.77 (0.32,1.84)	0.553	1.06 (0.48,2.33)	0.889	0.97 (0.83,1.15)	0.745	1 (0.85,1.17)	0.973
Burn	1.26 (0.58,2.75)	0.557	1.22 (0.57,2.6)	0.604	0.96 (0.82,1.13)	0.662	1.03 (0.88,1.2)	0.726
Trauma	0.76 (0.5,1.17)	0.217	0.77 (0.51,1.15)	0.204	0.95 (0.88,1.02)	0.176	1 (0.92,1.07)	0.919
Mixed ICU	0.73 (0.52,1.03)	0.069	0.75 (0.54,1.04)	0.082	0.99 (0.94,1.06)	0.854	1.01 (0.95,1.07)	0.794

ICU = Intensive care unit, Pre-ICU location; location prior to admission to ICU, ED = Emergency department, OR = Operating room, MICU = Medical ICU, CCU = Cardiac medical patients, SICU = Surgical ICU. [a]Multivariable logistic regression, OR = Adjusted odds ratio (95% CI). [b]Multivariable zero-inflated negative binomial regression, RR = Adjusted rate ratio (95% CI) for count component. Each model was adjusted for baseline covariates, APACHE III, vasopressor use, cause of lung injury, lung injury score, diabetes mellitus, cancer status, BMI, and study ID

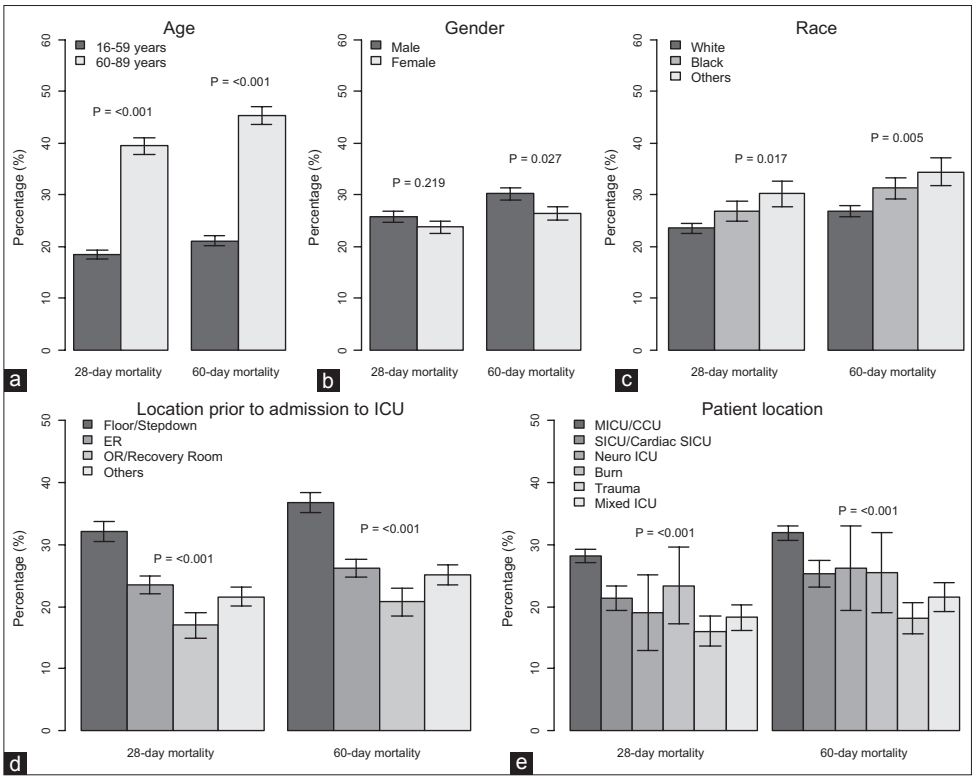

Figure 1: Mortality rate by age group (a), gender (b), race (c), location before admission to Intensive Care Unit (d), and patient location (e); Chi-squared test was used to calculate *P* values. The bar plots represent mortality rate (%) ± standard error from groups defined by each variable

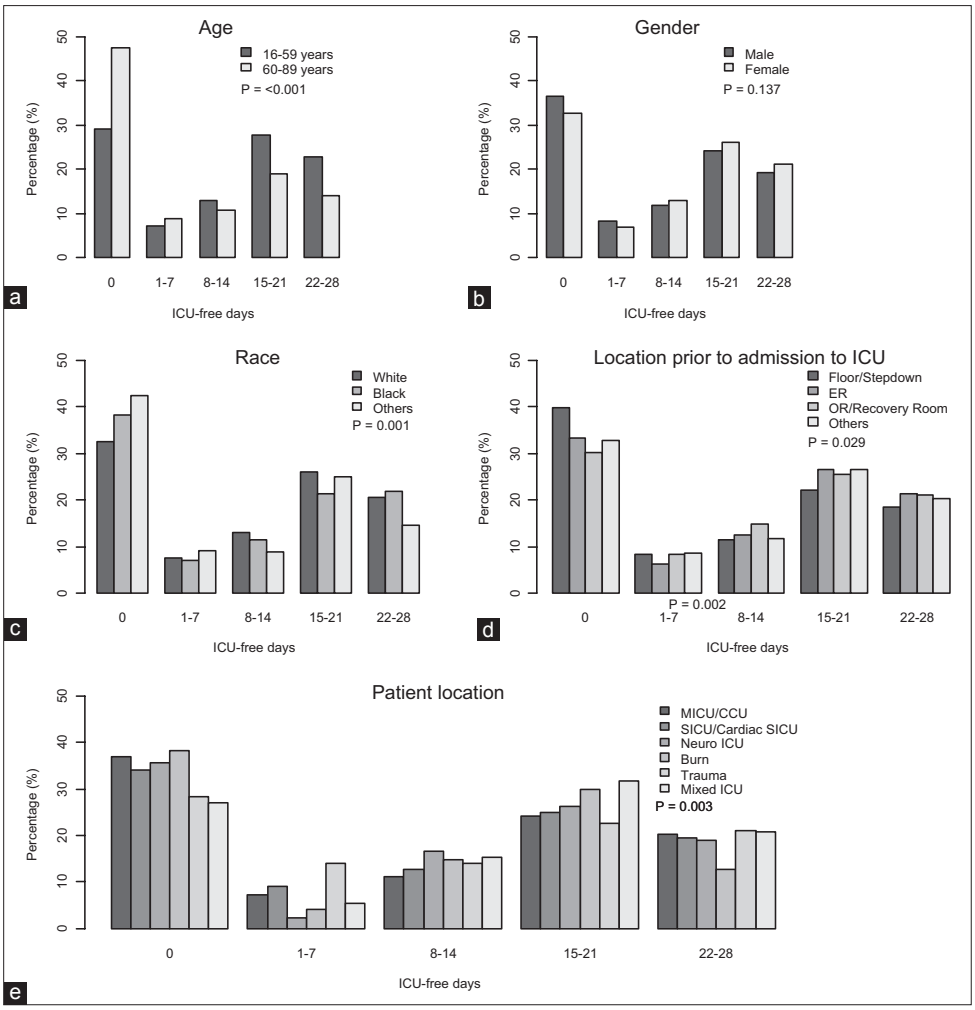

Figure 2: Percentage of patients with 0, 1–7, 8–14, 15–21, and 22–28 Intensive Care Unit-free days during the first 28 days after enrollment by age group (a), gender (b), race (c), location prior to admission to Intensive Care Unit (d), and patient location (e); either Chi-squared test or Fisher's exact test was used to calculate *P* values

test) [Figure 1]. There was no statistically significant difference in the categorized ICU free days [Figure 2] or ventilator-free days [Figure 3] in relation to gender. The multivariable logistic regression results did not show a statistically significant difference for 28 days (OR = 0.94, 95% CI: 0.78–1.14, *P* = 0.538) as well as 60 days mortality (OR = 0.85, 95% CI: 0.7–1.02, *P* = 0.083). There were statistically significant more ICU-free days for females (RR = 1.04, 95% CI: 1.00–1.08, *P* = 0.046) but not for ventilator-free days [Table 3] from multivariable negative binomial model.

Race

On univariate analysis, there mortality at 28 days was least for whites (23.51%) followed by blacks (26.87%) followed by others (30.18%) (*P* = 0.017, Chi-square test). For 60-day mortality, it was least among whites (26.81%) followed by blacks (31.29%) followed by others (34.45%) (*P* = 0.005, Chi-square test) [Figure 1]. The group others had the least categorized ICU and ventilator-free days followed by blacks than whites [Figures 2 and 3]. The multivariable logistic regression model resulted no statistically significant differences between white and blacks in 28-day mortality (OR = 1.1, 95% CI: 0.85–1.41, *P* = 0.479) and 60-day mortality (OR = 1.16, 95% CI: 0.91–1.47, *P* = 0.242). However, there was a statistically significant mortality in the group of other races for both 28-day mortality (OR = 1.47, 95% CI: 1.09–1.98, *P* = 0.011) and 60-day mortality (OR = 1.53, 95% CI: 1.15–2.04, *P* = 0.004). There were no statistically significant differences in ICU-free days and ventilator-free days between different groups [Table 3] from multivariable negative binomial model.

Pre-Intensive Care Unit patient location

On univariate analysis, the least 28-day mortality was in patients admitted from the operating room/recovery room (17%) followed by ED (23.57%) and then the floor/stepdown (32.19%) (*P* ≤ 0.001, Chi-square test) [Figure 1]. The 60-day mortality was least for the patients admitted from the operating room/recovery room (20.75%) followed by ED (26.16%) and then the floor/stepdown (36.87%) (*P* < 0.001, Chi-square test) [Figure 1]. The least ICU-free days were for patients admitted from the floor/stepdown unit and the most ICU-free days and ventilator-free days were for patients admitted from the ED or from the operating room/recovery room [Figures 2 and 3]. The multivariable logistic regression showed there was a statistically significant lower 28-day mortality if the patient was admitted from the operating room/recovery room (OR = 0.65, 95% CI:

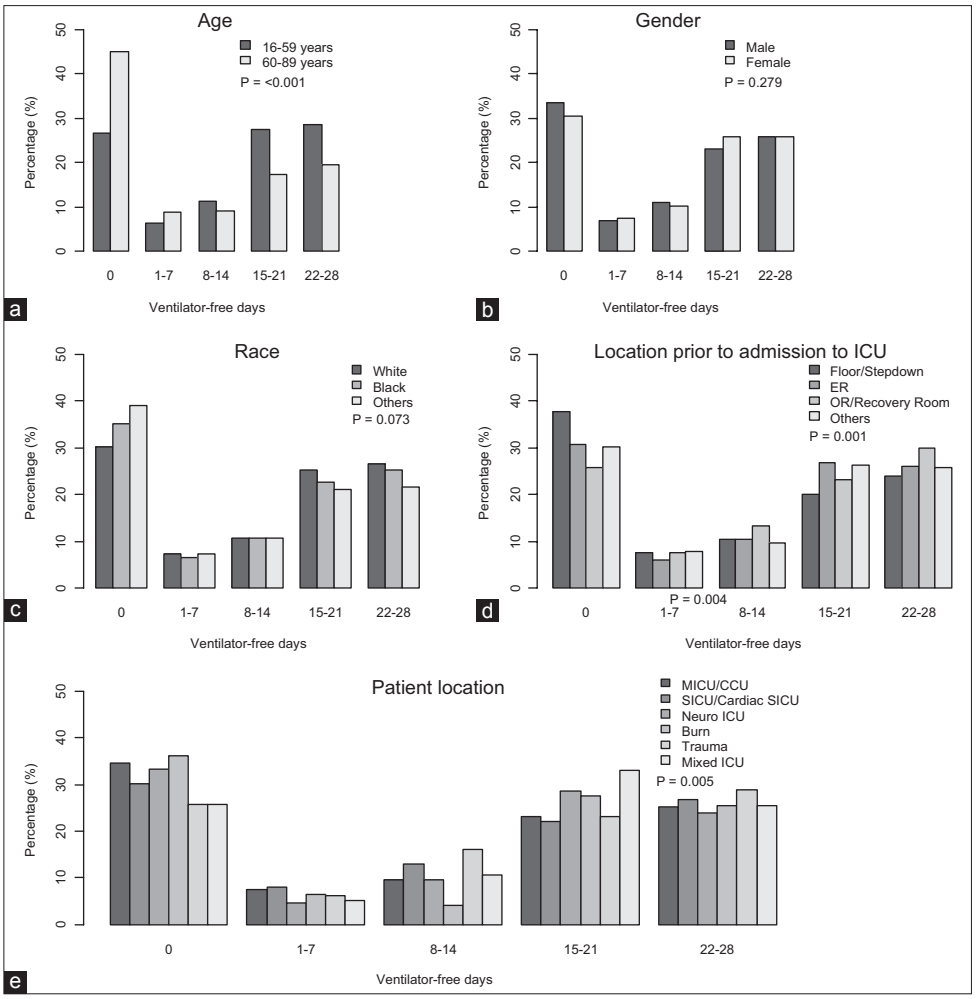

Figure 3: Percentage of patients with 0, 1–7, 8–14, 15–21, 22–28 ventilator-free days during the first 28 days after enrollment by age group (a), gender (b), race (c), location before admission to Intensive Care Unit (d), and patient location (e); either Chi-squared test or Fisher's exact test was used to calculate *P* values

0.44–0.95, *P* = 0.026) followed by the ED (OR = 0.78, 95% CI: 0.61–0.99, *P* = 0.039). The same trend was seen in 60-day mortality (operating room/recovery room: OR = 0.66, 95% CI: 0.46–0.95, *P* = 0.025 followed by ED: OR = 0.71, 95% CI: 0.56–0.89, *P* = 0.004) [Table 3]. There were no statistically significant differences in ICU-free days and ventilator-free days between different groups from multivariable negative binomial regression model [Table 3].

Type of Intensive Care Unit

On univariate analysis, the least 28-day mortality was in the trauma units 16.02% followed neuro ICU 19.05%, followed by SICU/cardiac SICU 21.31%, burn units 23.4%, and MICU/CCU 28.17% (*P* < 0.001). The 60-day mortality was lowest in trauma units 18.2% followed by SICU/cardiac SICU 25.3%, burn units 25.5%, neuro ICU 26.2%, and MICU/CCU 31.9% (*P* < 0.001) [Figure 1]. The categorized ICU-free days and ventilator-free days were mixed and inconsistent between the groups [Figures 2 and 3]. The multivariable logistic regression model and negative binomial regression model showed no statistically significant difference between the different types of ICU in relation to 28 days mortality, 60-day mortality, ICU-free days, and ventilator-free days [Table 3].

Discussion

This analysis shows that certain demographic factors affect the outcome of patients with ARDS with higher mortality in older patients and races other than blacks and whites. On the other hand, there were no differences in outcome in relation to gender or between blacks and whites. In addition, this analysis demonstrates that the pre-ICU patient location impacts outcome with least mortality in those admitted from operating room/recovery, followed by those admitted from ED, and is worst in those who were admitted from floor/step down units. There were no differences in outcomes in relation to the type of ICU the patients with ARDS were treated in.

ARDS is a clinical condition characterized by severe respiratory distress, hypoxemic respiratory failure with bilateral pulmonary infiltrates in the absence of congestive heart failure or fluid overload. The most common risk factor for developing ARDS is severe sepsis; other known risk factors include aspiration of gastric contents, severe trauma, massive blood products, drug overdose, pancreatitis, near-drowning, and inhalation injury.[1,12] The pathogenesis involves diffuse alveolar and capillary endothelial injury that allows proteinaceous interstitial fluid accumulation, loss of functional surfactant

resulting in alveolar collapse resulting in impaired gas exchange.[13] Although mortality has improved significantly in the last two decades, it is still as high as 46% for those with severe ARDS.[14]

There are different factors the affect the outcome of patients with ARDS. Several studies have addressed these factors with variable results.[1,14-27] The aims of this study were to determine the role of demographic data such as age, gender, and race on the outcome and also to study other variables that have not been previously addressed such as pre-ICU patient location and type of ICU.

Age has been shown to be a critical determinant in the incidence of ARDS (16/100,000 person-years in young (15–19 years of age) and 306/100,000 person-years (75–84 years of age), and has been reported to be a risk factor for death among patients with this syndrome.[1,14-17] A study of 256 patients done by Suchyta *et al*. identified age over 55 years as a cutoff above which mortality is significantly increased ($P = 0.002$).[15] Mortality rates among patients between the age 15–19 years has been reported to be 24% which increases above 60% among patients 85 years of age or older.[1,18] The current analysis confirms previous findings about worse outcomes with older age including 28- and 60-day mortality and fewer ventilator and ICU-free days. However, it shows at the same time that the mortality for older patients is better than previous reports (28-day mortality 39% for those older than 60 years). Factors associated with age that may explain worse outcomes include a reduction in respiratory function due to decline in chest wall compliance forced expiratory volume in 1 s, respiratory muscle strength, and diminished response to hypoxia and hypercapnia. Other factors include comorbid illnesses, increased risk of pulmonary infections and delayed tissue repair following an inflammatory injury.[19,20]

The role of race and gender on the development and outcome of ARDS has been previously studied with conflicting results. In a study of the National Center for Health Statistics of 333,004 patients who died from ARDS, the rates of death for men were almost double those for women (8.6/100,000 men as compared to 4.7/100,000 for women, $P < 0.05$).[21] The mortality in blacks was significantly higher than whites and other races. The findings were true for men and women (the mean rate for black men was 12.8/100,000, compared with 9.1/100,000 in white men and for black women was 7.4/100,000, compared with 5.4/100,000 in white women ($P < 0.05$).[21]

The authors of that study hypothesized the higher mortality in men and blacks to be due to factors related to higher risk in these groups for diagnoses that lead to ARDS such as sepsis and trauma, higher risk of developing ARDS during critical illness, and dying from ARDS once they develop the disease. The differences in outcome could also reflect socioeconomic status, the severity of illness or other confounding factors.[21]

In another recent study, men were more likely than women to develop acute lung injury (6.9% vs. 4.7%, $P < 0.001$) and experienced a longer ICU ($P = 0.002$) but not hospital ($P = 0.10$) length of stay. Men who developed acute lung injury had a nonsignificant increase in in-hospital mortality (27.6% vs. 18.5%; $P = 0.08$; 95% CI, 0.94%–2.99%). Whites, compared with blacks, were more likely to develop acute lung injury (6.5% vs. 4.5%, $P = 0.014$); however, there was no difference in acute lung injury associated mortality (24.8% vs. 21.6%, $P = 0.63$). Hispanic ethnicity was associated with neither acute lung injury development (5.6% in Hispanics and 6.6% in non-Hispanics, $P = 0.43$), nor mortality ($P = 0.84$).[22] In an analysis of part of the ARDS network studies and after adjusting for severity of illness, there was no difference in mortality between black and white patients; however Hispanics had higher 60 days mortality (OR = 2.00; 95% CI, 1.37–2.90) and fewer ventilator-free days.[23]

The current analysis of only patients who fulfilled the revised criteria for ARDS shows that there were no differences in outcomes between men and women. Furthermore, there were no differences between blacks and whites in all outcomes; however, races other than blacks and whites had significantly higher 28- and 60-day mortality. The races other than blacks and whites include not only primary Hispanics but also other minorities. It is not clear why this group had higher mortality, but factors may include language barriers affecting seeking medical attention or the care during critical illness. In addition, it is possible that this group may have a higher burden of comorbid illnesses. Further studies are needed to determine whether other races have higher risk for developing or dying from ARDS and the reasons behind these differences.

There are very few studies that analyze the outcome of ARDS in relation to pre-ICU location or type of ICU. A prospective observational study of 296 patients with ARDS reported a significantly lower ICU mortality rate among patients with community-acquired ARDS (diagnosed within 48 h of hospital or ICU admission) as compared to hospital acquired ARDS.[24] Patients in the community acquired ARDS also had higher number of ventilator-free days as well has a higher number of ICU-free days. Our study shows that the mortality outcomes were significantly better in patients admitted to ICU from ED or operating room/recovery room as compared to those admitted from floor/step down units. This has similar implication to the above study in that patients admitted to ICU from the community did better than those who developed ARDS while in hospital for other illnesses. This difference in outcome may be related to slow progression of respiratory failure, trial of other therapies for hypoxia, hospital-acquired complications, or delayed diagnosis among patients on the floor/step down.

The current study also significantly shows that there were no differences in all outcomes in relation to the type of ICU the patients with ARDS were treated in. The type of ICU is likely to correlate with the etiology of ARDS. Some studies have suggested that there is the difference in outcome of ARDS in relation to the precipitating factors. For example, the risk of death from ARDS associated with sepsis and burn were higher than with trauma or neurological complications.[25-27]

The lack of differences in outcome between the different ICUs may reflect standardized care of ARDS (lung protective strategies, pronning, and supportive care) in the modern units.

The strengths of the study are the large number of patients with similar distribution among baseline characteristics. In addition, the original studies were high quality multicenter, randomized, controlled double-blinded prospective studies with robust

design, inclusion criteria and data collection, which provides stronger conclusions. Only patients that fulfilled the current definition of ARDS were included in the analysis. The outcomes included mortality (28 and 60 days) and other indicators of utilization of health-care resources such as ventilator and ICU-free days. There are limitations to this study including the retrospective analysis of published data with the lack of specific data about confounding factors related to our analysis. Also, there is no correlation between the pre-ICU location and type of ICU and etiology of ARDS.

Conclusion

This study provides further insight about predictors of outcome in patients with ARDS. Higher mortality is associated with older patients and races other than blacks and white. Older patients also have fewer ventilator and ICU-free days. Mortality is also impacted by the patient location before ICU admission. On the other hand, there are no differences in outcome in relation to gender or between blacks and white or the type of ICU the patient is treated in.

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Conflicts of interest
There are no conflicts of interest.

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