ORIGINAL ARTICLE

# Etiology and Outcomes of ARDS in the Elderly Population in an Intensive Care Unit in North India

Inderpaul S Sehgal[1], Ritesh Agarwal[2], Sahajal Dhooria[3], Kuruswamy T Prasad[4], Valliappan Muthu[5], Ashutosh N Aggarwal[6]

## Abstract

**Background:** Whether age would impact the outcomes in subjects with acute respiratory distress syndrome (ARDS) remains unclear. Herein, we study the effect of age as a predictor of mortality in ARDS.

**Materials and methods:** We categorized consecutive subjects with ARDS as either $ARDS_{elderly}$ (age >65 years) or $ARDSnon_{elderly}$ (age ≤65 years) admitted to the respiratory intensive care unit (ICU) of a tertiary care hospital in North India between January 2007 and December 2019. We compared the baseline clinical and demographic characteristics, lung mechanics, and mortality between the two groups. We also analyzed the factors predicting ICU survival using multivariate logistic regression analysis.

**Results:** We included 625 patients ($ARDS_{elderly}$, 140 [22.4%] and $ARDS_{nonelderly}$, 485 [77.6%]) with a mean (standard deviation) age (56.3% males) of 40.6 (17.8) years. The $ARDS_{elderly}$ were more likely ($p = 0.0001$) to have the presence of any comorbid illness compared to $ARDS_{nonelderly}$. The elderly subjects had significantly higher pulmonary ARDS than the younger group. The severity of ARDS was however, similarly distributed between the two study arms. There were 224 (35.8%) deaths, and the mortality was significantly higher ($p = 0.012$) in the $ARDS_{elderly}$ than the to $ARDS_{nonelderly}$ ($ARDS_{elderly}$ vs $ARDS_{nonelderly}$, 45 vs 33.2%). On multivariate logistic regression analysis, the baseline sequential organ failure assessment scores, presence of pulmonary ARDS, and the development of new organ dysfunction were the independent predictors of mortality.

**Conclusion:** The outcomes in subjects with ARDS are dependent on the severity of illness at admission and the etiology of ARDS rather than the age alone.

**Keywords:** Acute respiratory distress syndrome, Elderly, Pneumonia, Respiratory failure, Sepsis.

*Indian Journal of Critical Care Medicine* (2021): 10.5005/jp-journals-10071-23878

## Introduction

Acute respiratory distress syndrome (ARDS) is associated with acute onset (<7 days) hypoxemic respiratory failure with bilateral opacities on chest radiograph, either due to the injury to the lung parenchyma or the pulmonary vasculature.[1] ARDS is subclassified as mild (200 < $PaO_2$:$FiO_2$ ratio ≤300), moderate (100 < $PaO_2$:$FiO_2$ ratio ≤200), or severe ($PaO_2$:$FiO_2$ ratio ≤100) based on the degree of hypoxemia.[2] The mortality increases from 27% to as high as 45% with increasing severity of ARDS.[2] Apart from the severity of hypoxemia, several other factors affect ARDS outcomes, including the driving pressure, arterial $PaCO_2$, the strategy used for mechanical ventilation, and others.[3-7] There is limited information regarding the effect of age on mortality in ARDS.[8-10]

Most clinical trials generally exclude elderly subjects with ARDS. In fact, major trials of ARDS do not address the issue of age-related mortality in ARDS.[7,11,12] Previous trials have merely mentioned the mean age in comparator groups and have not explored the mortality in the elderly.[7,11,12] With increasing global age, the proportion of elderly ARDS is likely to increase in the intensive care units (ICUs).[13] Although the principles of ARDS management are similar in elderly patients, the resolution of ARDS and the outcomes might be different in the elderly population. The elderly subjects have an age-related decline of the physiological reserve and a higher prevalence of comorbid illness.[14,15] These changes further enhance the stress due to acute illnesses, thereby increasing the risk of mortality in critically ill elderly patients.[15,16] We hypothesized that old age would independently affect the outcomes in subjects with ARDS. Our objective was to compare the clinical characteristics and the ICU outcomes of elderly (age >65 years) subjects with ARDS.

[1-6]Department of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India

**Corresponding Author:** Inderpaul S Sehgal, Department of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India, Phone: +91-172-2746825, e-mail: ipdoc_2000@yahoo.com; inderpgi@outlook.com

**How to cite this article:** Sehgal IS, Agarwal R, Dhooria S, Prasad KT, Muthu V, Aggarwal AN. Etiology and Outcomes of ARDS in the Elderly Population in an Intensive Care Unit in North India. Indian J Crit Care Med 2021;25(6):648–654.

**Source of support:** Nil

**Conflict of interest:** None

## Materials and Methods

We included all individuals diagnosed with ARDS admitted to the intensive care unit of Department of Pulmonary Medicine of our institute between February 1, 2001 and December 31, 2019. We use a specifically designed computer software to prospectively enter the patient data.[17,18] We calculated the acute physiology and chronic health evaluation (APACHE II) scores and sequential organ failure assessment (SOFA) scores using baseline values. Each subsequent day in respiratory intensive care unit (RICU) was calendar day timed from 8:00 a.m. to 8:00 a.m. of the next day. We calculated the delta SOFA as described previously.[19] We were granted a waiver for informed consent due to anonymized data's retrospective use by the Institute Ethics Committee.

We used the American-European Consensus Conference criteria for acute lung injury and ARDS (before January 1, 2013) and Berlin definition (after 2013) for diagnosing ARDS.[2]

All the patient records were screened for study inclusion. We excluded repeat ICU admissions from the analysis. We used a low tidal volume strategy to ventilate all our patients. We used midazolam and atracurium during the initial 48–72 hours to facilitate mechanical ventilation.[20] In addition we provided stress ulcer and deep venous thrombosis prophylaxis as per the ICU protocol. The subjects were given enteral nutrition.

We recorded the following information: (a) demographic profile; (b) etiology of ARDS; (c) baseline APACHE II and SOFA scores; (d) daily SOFA score including the maximum SOFA score attained during RICU stay; (e) duration of mechanical ventilation; (f) worst values of the following physiologic and ventilator parameters recorded daily including $PaO_2$:$FiO_2$ ratio, positive end-expiratory pressure (PEEP), plateau pressure (Pplat), driving pressure (Pplat minus PEEP) and peak inspiratory pressure (PIP) (Ppeak); (g) ICU and hospital length of stay (LOS); and (h) final outcome.

We categorized subjects with age >65 years as $ARDS_{elderly}$, and those with age ≤65 years as $ARDS_{nonelderly}$, based on previous studies and the World Health Organization definition of the elderly.[9,21,22] We compared the ICU outcomes between elderly and nonelderly subjects with ARDS. We also investigated parameters that predicted mortality in subjects with ARDS.

### Statistical Analysis

We used statistical software package (SPSS for MS-Windows, version 22.0, IBM Inc., Armonk, New York, United States) to perform statistical analysis. We used the Chi-square test and the Student's *t*-test (or Mann–Whitney *U* test), or analysis of variance (or Kruskal–Wallis) for comparing the differences between categorical and continuous variables, respectively. We have described the normally and non-normally distributed data as mean with standard deviation (SD), and median (interquartile range), respectively. We performed a multivariate logistic regression analysis to identify the factors affecting survival. The variables found significant ($p$ <0.1) on the univariate analysis were entered in a multivariate logistic regression model to derive adjusted odds ratio and confidence limits. The level of significance was expressed as probability values ($p$ value) and the odds ratio [95% confidence intervals(CIs)]. We constructed survival curves to study the effect of the category of ARDS on RICU stay using Kaplan–Meier curves. We used the log-rank test to study the differences between the survival curves. We used the mixed model technique for repeated measures analysis of variance to compare the trends in lung mechanics (static lung compliance, $PaO_2$:$FiO_2$ ratio) and ventilatory parameters (PIP, PEEP, plateau pressure, and driving pressure); the within-groups factor was the time (baseline to day 5 of RICU stay), and the between-groups factor was age ($ARDS_{elderly}$ vs $ARDS_{nonelderly}$). We considered a $p$-value of less than 0.05 to be statistically significant.

## Results

We admitted 780 subjects with ARDS during the study period. We included 625 ($ARDS_{elderly}$, 140 [22.4%] and $ARDS_{nonelderly}$, 485 [77.6%]) subjects for further analysis. We excluded the remaining subjects due to survival for <24 hours, ambiguity in the diagnosis and etiology of ARDS, and the presence of insufficient information. The mean (SD) age of the study population (males, $n$ = 352 [56.3%]) was 40.6 (17.8) years and was significantly higher in the $ARDS_{elderly}$ (67.3 vs 32.9 years). Serum glucose was significantly higher in the ARDSelderly ($ARDS_{elderly}$ vs $ARDS_{nonelderly}$; mean ± SD, 150.5 ± 98.7 vs 129.3 ± 79, respectively; $p$ = 0.009) at admission (Table 1). Comorbid illnesses were frequent in the $ARDS_{elderly}$ ($p$ = 0.0001) than $ARDS_{nonelderly}$. The mean ± SD APACHE II score at baseline was not different between the two arms ($ARDS_{elderly}$ vs $ARDS_{nonelderly}$, 19.2 ± 7.8 vs 18.4 ± 8.2, respectively; $p$ = 0.327). We did not find any difference in the APACHE II score even after recalculating the APACHE II score without age ($ARDS_{elderly}$ vs $ARDS_{nonelderly}$, 16.4 ± 8.9 vs 17.4 ± 7.9, respectively; $p$ = 0.238). We found no difference in the severity of illness at admission (baseline SOFA score) between the two groups (Table 1).

The elderly subjects had significantly higher pulmonary ARDS than the younger counterparts, who were more likely to suffer from extrapulmonary ARDS. The most common cause of ARDS in the elderly was community-acquired pneumonia (47%, 66/140), while sepsis (43.5%, 211/485) was the most common cause of ARDS in the younger subjects. There was no difference in the baseline $PaCO_2$, $PaO_2$:$FiO_2$ ratio, and static lung compliance or the severity of ARDS between the two study arms. Most of the subjects were managed with positive pressure ventilation (noninvasive ventilation or invasive mechanical ventilation); the type of ventilatory support was similar between the two study groups. The mean ± SD plateau pressure ($ARDS_{nonelderly}$ vs ARDS $_{elderly}$, 24.3 ± 6.2 vs 22.3 ± 5.9; $p$ = 0.004) and applied PEEP (ARDSnonelderly vs ARDS elderly, 8.4 ± 4.6 vs 7 ± 3.3; $p$ = 0.012) were significantly higher in the $ARDS_{nonelderly}$ arm than $ARDS_{elderly}$. However, there was no difference in the baseline peak airway pressures and the driving pressures (Table 1). There was no difference in the trends of $PaO_2$:$FiO_2$ ratio between the two groups during the initial 5 days of RICU stay (Fig. 1). The plateau pressure reduced significantly with time (days 0 through 5) in both the groups and were significantly lower in the $ARDS_{elderly}$ compared to the ARDS nonelderly at all time. The driving pressure reduced during the RICU stay in $ARDS_{elderly}$, while it increased in $ARDS_{nonelderly}$ during RICU stay. There were no significant differences in other parameters between the two groups. We found no difference in the duration of ICU and hospital LOS between the two groups. There were 224 (35.8%) deaths, and the mortality was significantly higher ($p$ = 0.012) in the $ARDS_{elderly}$ compared to $ARDS_{nonelderly}$ ($ARDS_{elderly}$ vs $ARDS_{nonelderly}$, 45 vs 33.2%).

In the univariate model, the factors that predicted survival included female gender, presence of comorbid illness, baseline serum glucose, baseline SOFA score, delta SOFA, $PaCO_2$, $PaO_2$:$FiO_2$ ratio, use of invasive mechanical ventilation, peak airway pressure, pulmonary ARDS, $ARDS_{elderly}$, and the severity of ARDS (Table 2). However, in the multivariate logistic regression analysis, the only variables that predicted outcome were the baseline SOFA score, the development of new organ dysfunction (delta-SOFA score), and pulmonary ARDS (Table 2).

We plotted the survival curves for patients with ARDSelderly and $ARDS_{nonelderly}$ vis-à-vis the RICU stay (Fig. 2). The mean RICU stay in patients with $ARDS_{nonelderly}$ was 9.3 days (95% CI, 8.5–10 days; range 1–64 days) vs 10.6 days (95% CI, 3.1–12.1 days; range 1–47 days) days in patients with $ARDS_{elderly}$, and was not statistically different in the two groups (log-rank test, $p$ = 0.284).

## Discussion

This study highlights that while the elderly subjects had greater comorbid illnesses and more pulmonary ARDS than the younger subjects, they did not experience higher mortality than their younger counterparts. Only a few studies have investigated the effect of age

**Table 1:** Baseline characteristics, ventilatory parameters, and outcomes of patients with ALI/$ARDS_{elderly}$ and ALI/$ARDS_{nonelderly}$

| *Parameters* | *Total (n = 625)* | *$ARDS_{elderly}$ (n = 140)* | *$ARDS_{nonelderly}$ (n = 485)* | *p value* |
|---|---|---|---|---|
| **Demographic profile** | | | | |
| Male gender, *n* (%) | 352 (56.3) | 86 (61.4) | 266 (54.8) | 0.177 |
| Age, in years | 40.6 ± 17.8 | 67.3 ± 7 | 32.9 ± 11.4 | 0.0001 |
| [$]Any comorbidity, *n* (%) | 176 (28.2) | 83 (59.3) | 93 (19.2) | 0.0001 |
| **Laboratory parameters** | | | | |
| Plasma glucose | 134 ± 84.2 | 150.5 ± 98.7 | 129.3 ± 79 | 0.009 |
| Hemoglobin, g/dL | 10.9 ± 3 | 11.1 ± 2.9 | 10.9 ± 3 | 0.451 |
| Serum albumin, mg/dL | 2.3 ± 2.5 | 2.3 ± 1.4 | 2.3 ± 2.8 | 0.855 |
| **ICU severity scores** | | | | |
| Baseline APACHE II score | 18.6 ± 8.1 | 19.2 ± 7.8 | 18.4 ± 8.2 | 0.324 |
| Baseline APACHE II score without age | 17.2 ± 8.2 | 16.4 ± 8.9 | 17.4 ± 7.9 | 0.238 |
| SOFA score at admission | 7.8 ± 3.6 | 7.2 ± 3.3 | 7.9 ± 3.7 | 0.058 |
| Delta-SOFA score | 2 ± 2.9 | 2.2 ± 3.1 | 1.9 ± 2.9 | 0.370 |
| **Respiratory parameters** | | | | |
| $PaCO_2$ | 39.1 ± 13.8 | 39.3 ± 14.7 | 39.1 ± 13.5 | 0.881 |
| $PaO_2$:$FiO_2$ ratio | 167.9 ± 67.8 | 171.9 ± 69.9 | 166.8 ± 67.2 | 0.430 |
| Cstat at RICU admission, mL/cm $H_2O$ | 25.3 ± 12.1 | 27.6 ± 12.3 | 24.8 ± 12 | 0.109 |
| **Type of respiratory support** | | | | 0.094 |
| Oxygen supplementation | 140 (22.4) | 40 (28.6) | 100 (20.6) | |
| Noninvasive ventilation | 25 (4) | 8 (5.7) | 17 (3.5) | |
| Invasive mechanical ventilation | 460 (73.6) | 92 (65.7) | 368 (75.9) | |
| **Ventilator parameters** | | | | |
| PIP, cm of $H_2O$ | 28 ± 8.1 | 26.8 ± 7.6 | 28.3 ± 8.2 | 0.087 |
| Plateau pressure, in cm of $H_2O$ | 23.9 ± 6.2 | 22.3 ± 5.9 | 24.3 ± 6.2 | 0.004 |
| PEEP, cm of $H_2O$ | 8.2 ± 4.4 | 7 ± 3.3 | 8.4 ± 4.6 | 0.012 |
| Driving pressure, cm of $H_2O$ | 5.3 ± 3.9 | 6.1 ± 4 | 5.7 ± 3.9 | 0.421 |
| **Type of ARDS** | | | | 0.0001 |
| *Extrapulmonary ARDS | 312 (49.9) | 48 (34.3) | 264 (54.4) | |
| [#]Pulmonary ARDS | 313 (50.1) | 92 (65.7) | 221 (45.6) | |
| **Severity of ARDS** | | | | 0.440 |
| Mild | 209 (33.4) | 52 (37.4) | 157 (32.4) | |
| Moderate | 306 (49) | 62 (44.6) | 244 (50.3) | |
| Severe | 110 (17.6) | 26 (18.6) | 84 (17.3) | |
| **Outcomes** | | | | |
| Mortality, *n* (%) | 224 (35.8) | 63 (45) | 161 (33.2) | 0.012 |
| ICU length of stay, in days | 9.6 ± 8.8 | 10.6 ± 8.9 | 9.3 ± 8.8 | 0.121 |
| Hospital length of stay, in days | 18.9 ± 48 | 22.7 ± 59.6 | 17.8 ± 44.1 | 0.283 |

*Includes sepsis, acute pancreatitis, multiple transfusions, and malaria; [#]Includes community-acquired pneumonia, aspiration pneumonia, vasculitis, tuberculosis, fat embolism, drowning, and paraquat poisoning; [$]Includes diabetes mellitus, hypertension, chronic renal failure, chronic liver disease, immunosuppression, and malignancy. APACHE II, acute physiology and chronic health evaluation II; ARDS, acute respiratory distress syndrome; Cstat, static lung compliance; $PaCO_2$, partial pressure of carbon dioxide in arterial blood; $PaO_2$, partial pressure of oxygen in arterial blood; $PaO_2$:$FiO_2$ ratio, the ratio of partial pressure of arterial blood to the fraction of oxygen in inspired air; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; SOFA, sequential organ failure assessment

on outcomes in subjects with ARDS.[8,9,21,22] Notably, some of these studies were conducted before the landmark ARDSnet trial.[7-9] Thus, a better understanding of the etiology and factors predicting outcomes in elderly subjects with ARDS is required. The proportion of elderly subjects with ARDS in our study was 22% and was lower than the previous studies (up to 60%).[8,9,22] The lower prevalence of elderly subjects in our study could be due to the lower life expectancy of the Indian population compared to the western countries. It could also be due to a general perception of poor outcomes and physicians' reluctance to admit the elderly to the ICU.[14]

The common etiology of ARDS in the elderly subjects was pneumonia, while sepsis was the most common cause of ARDS in younger individuals. In general, the incidence of pneumonia is higher in the elderly than in the young and is associated with higher mortality.[21,23-25] Even in the current study, the presence of pneumonia and pulmonary ARDS was an independent predictor of mortality. The elderly subjects required lower PEEP and driving pressure than the younger individuals, possibly due to the difference in ARDS etiology between the two arms. It has been previously shown that a higher PEEP is required for

**Table 2:** Comparison of parameters between survivors and nonsurvivors

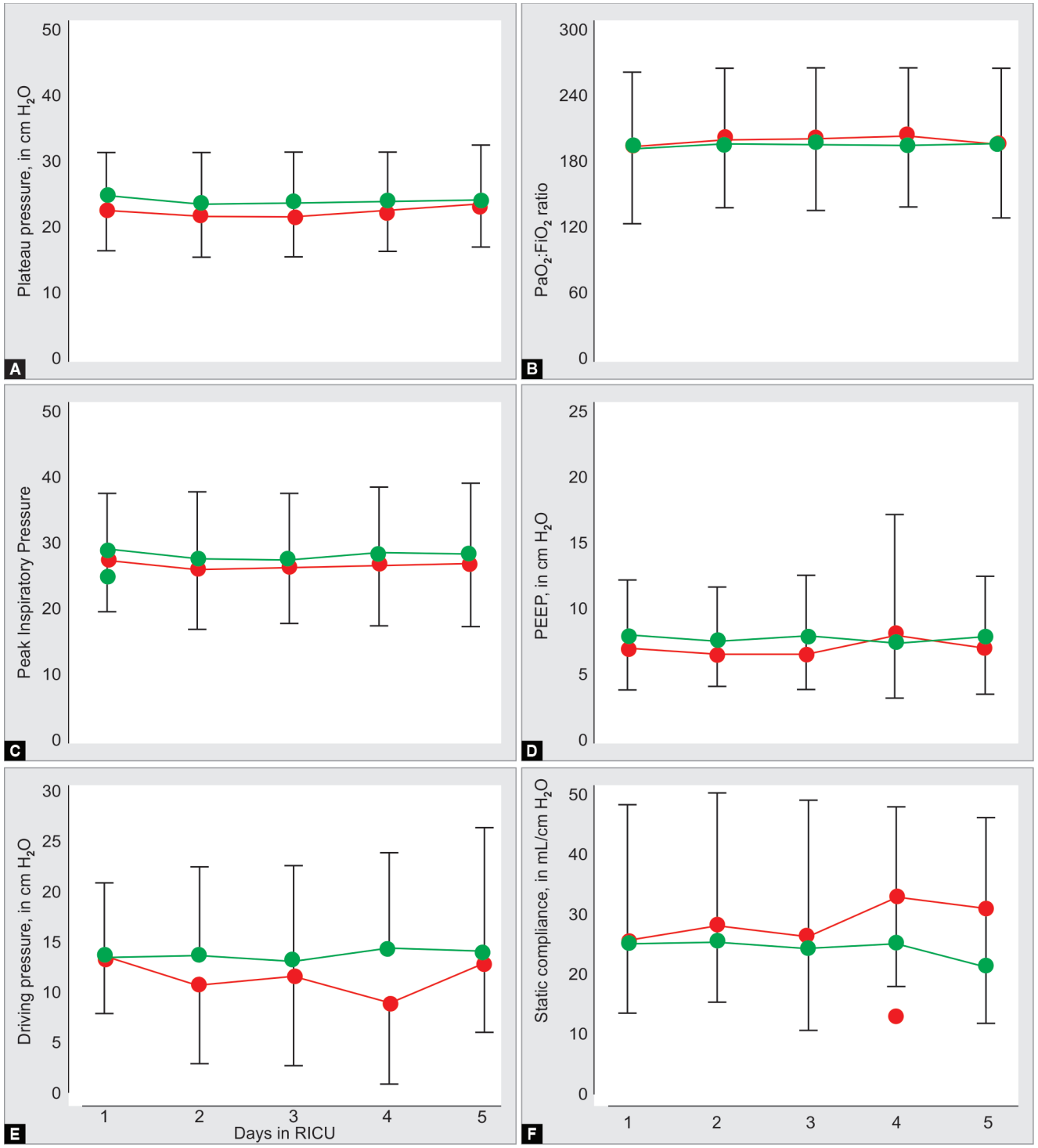
| *Parameters* | *Survivors (n = 401)* | *Nonsurvivors (n = 224)* | *p value* | *Crude OR (95% CI)* | *Adjusted OR (95% CI)* |
|---|---|---|---|---|---|
| Female gender, *n* (%) | 189 (47.1) | 84 (37.5) | 0.023 | 0.67 (0.48–0.94)* | 0.76 (0.5–1.2) |
| Comorbid illness[$] | 95 (23.7) | 81 (36.2) | 0.001 | 1.8 (1.3–2.6)* | 1.5 (0.9–2.5) |
| **Laboratory parameters** | | | | | |
| Plasma glucose | 126.2 ± 76.7 | 148.1 ± 94.7 | 0.002 | 1 (1–1.01)* | 1 (0.99–1) |
| Hemoglobin, g/dL | 11 ± 3 | 10.9 ± 3.1 | 0.905 | 0.99 (0.9–1.1) | |
| Serum albumin, mg/dL | 2.3 ± 2.5 | 2.3 ± 2.6 | 0.686 | 1.01 (0.9–1.1) | |
| **ICU severity scores** | | | | | |
| SOFA score | 7.2 ± 3.4 | 8.8 ± 3.8 | 0.0001 | 1.1 (1.1–1.2)* | 1.1 (1.1–1.2)* |
| Delta-SOFA score | 1.4 ± 2.1; 0 (0–2) | 3.2 ± 3.7; 2 (0–5) | 0.0001 | 1.2 (1.1–1.3)* | 1.4 (1.3–1.5)* |
| **Respiratory parameters** | | | | | |
| $PaCO_2$ | 41.8 ± 16.3 | 37.6 ± 11.9 | 0.0001 | 1 (1.01–1.03)* | 1 (0.9–1) |
| $PaO_2$:$FiO_2$ ratio | 175.7 ± 67.7 | 154 ± 65.9 | 0.0001 | 0.99 (0.99–1)* | |
| Cstat at RICU admission, mL/cm $H_2O$ | 24.4 ± 10.9 | 25.8 ± 12.8 | 0.300 | 0.99 (0.97–1) | |
| **Type of respiratory support** | | | 0.014 | | |
| Noninvasive support[#] | 119 (29.7) | 46 (20.5) | | Reference | Reference |
| Invasive mechanical ventilation | 282 (70.3) | 178 (79.5) | | 1.6 (1.1–2.4)* | 1.3 (0.7–2.2) |
| **Ventilator parameters** | | | | | |
| Peak airway pressure, cm of $H_2O$ | 27.3 ± 7.9 | 29.1 ± 8.3 | 0.012 | 1.03 (1–1.1)* | 1 (0.9–1) |
| Plateau pressure, in cm of $H_2O$ | 23.6 ± 5.8 | 24.5 ± 6.8 | 0.138 | 1.02 (0.9–1.1) | |
| PEEP, cm of $H_2O$ | 8.1 ± 4.7 | 8.3 ± 3.9 | 0.702 | 1.01 (0.9–1.1) | |
| Driving pressure, cm of $H_2O$ | 5.9 ± 4.1 | 5.8 ± 3.6 | 0.102 | 0.99 (0.94–1) | |
| **Type of ARDS** | | | 0.016 | | |
| Extrapulmonary ARDS | 215 (53.6) | 97 (43.3) | | Reference | Reference |
| Pulmonary ARDS | 186 (46.4) | 127 (56.7) | | 1.5 (1.1–2.1)* | 2 (1.3–3.1)* |
| **Category of ARDS** | | | 0.012 | | |
| ARDSnonelderly | 324 (80.8) | 161 (71.9) | | Reference | Reference |
| ARDSelderly | 77 (19.2) | 63 (28.1) | | 1.6 (1.1–2.4)* | 1.4 (0.8–2.4) |
| **Severity of ARDS** | | | 0.001 | | |
| Mild | 150 (37.5) | 59 (26.3) | | Reference | Reference |
| Moderate | 194 (48.5) | 112 (50) | | 1.5 (1–2.1)* | 1.5 (0.9–3.3) |
| Severe | 56 (14) | 53 (23.7) | | 2.4 (1.5–3.9)* | 1.7 (0.9–2.5) |

*Statistically significant; [#]Include oxygen supplementation and noninvasive ventilation; [$]Includes diabetes mellitus, hypertension, chronic renal failure, chronic liver disease, immunosuppression, and malignancy. APACHE II, acute physiology and chronic health evaluation II; ARDS, acute respiratory distress syndrome; Cstat, static lung compliance; $PaCO_2$, partial pressure of carbon dioxide in arterial blood; $PaO_2$, partial pressure of oxygen in arterial blood; $PaO_2$:$FiO_2$ ratio, the ratio of partial pressure of arterial blood to the fraction of oxygen in inspired air; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; SOFA, sequential organ failure assessment

the extrapulmonary compared to the pulmonary ARDS.[26,27] The resolution of respiratory failure and lung mechanics was similar in the two groups; this contradicts that with a poor physiological reserve, the elderly subjects are more likely to require longer periods for recovery than their younger counterparts.[15,16] In fact, the ICU and hospital stay were also similar in the two groups.

The mortality (45%) in the elderly subjects with ARDS in our study was lower than those in previous studies (60–85%).[9,10,15,28] Higher mortality could be due to the inclusion of subjects with HIV infection, active malignancy, and cirrhosis.[9] The lower mortality in the elderly may also be due to the universal use of low tidal volume strategy and differences in ARDS etiology in our study. In another study, the SOFA score and the lung mechanics (PIP) rather than the age were predictors of mortality.[21] Another study of ARDS secondary to trauma also demonstrated organ dysfunction at baseline rather than age to be a predictor of survival.[22] Even in our study, higher severity of illness at baseline (SOFA score) was independently associated with a higher odds of death. Another factor that predicted mortality in our study was the delta-SOFA score, which signifies the development of new organ dysfunction. An increase in delta SOFA has been previously shown to be associated with an increase in ICU mortality and follows a linear pattern.[29]

Intuitively, the presence of comorbid illness should affect outcomes in elderly subjects. However, the presence of comorbid illness did not impact the clinical outcomes in the current study. In a previous study, the mere presence of comorbidity was not associated with higher mortality in subjects with ARDS.[30] However, a Charlson's comorbidity score of >4 predicted higher mortality.[30] In another study, comorbid illness, such as COPD, chronic steroid use, and presence of diabetes mellitus, was not associated with a higher mortality.[9,31] The presence of hyperglycemia has been associated with poor outcomes in critically ill subjects.[32] The elderly subjects in the current study had significantly higher plasma glucose levels. However, on a multivariate logistic regression analysis,




**Figs 1A to F:** Time course of plateau pressure (left top panel), peak inspiratory pressure (left middle panel), driving pressure (left lower panel), $PaO_2$:$FiO_2$ ratio (right top panel), PEEP (right middle panel), and static lung compliance (right lower panel) from baseline to day 5 in the two groups of patients. The plateau pressure reduced significantly with time (days 0 through 5) in both the groups and significantly lower in the elderly than the younger subjects at all time points. The driving pressure reduced in the elderly and increased in the younger subjects during RICU stay. There were no significant differences in other parameters between the two groups. Circles = mean values; error bar = SD. The hollow circle represents $ARDS_{elderly}$, and the solid circle represents $ARDS_{nonelderly}$

higher plasma glucose at admission did not predict mortality, possibly due to better glucose control in the ICU after admission.[31]

Our study has a few limitations. The study was single-centered with the inherent flaws of a retrospective study design. We used an arbitrary cutoff value of 65 years. The number of very old subjects (>80 years) was less; thus, the results of this study may not be applicable to this age-group. The use of an arbitrary age cutoff is likely to ignore the with-in-age group heterogeneity in organ reserves, functional

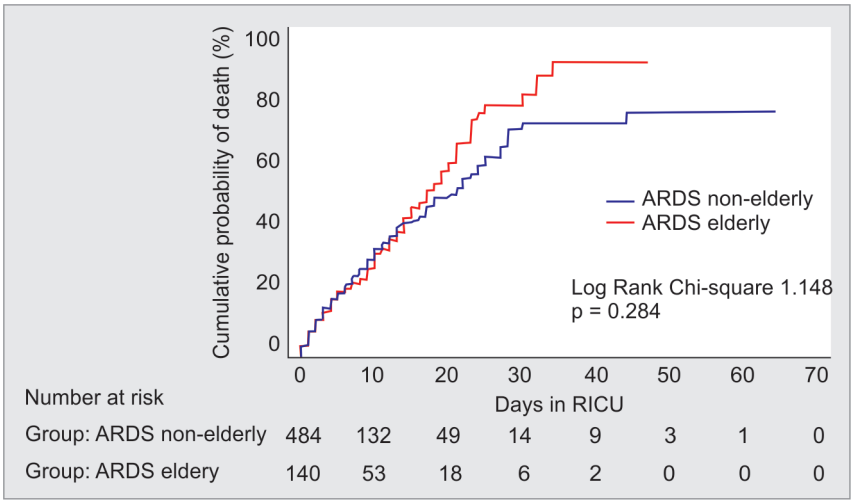



**Fig. 2:** Kaplan–Meier survival curves comparing the cumulative probability of mortality in $ARDS_{elderly}$ and $ARDS_{nonelderly}$ during intensive care unit stay. There was no difference in time to death between the two study arms (log-rank test)

ability, and the ability to tolerate the various treatment.[33] Thus, future studies may consider using an objective measure of frailty, which is more likely to represent the biological age. Finally, we do not have the follow-up details of subjects after discharge from the hospital.

In conclusion, the outcomes in elderly subjects with ARDS are dependent on the severity of illness at admission, the occurrence of new organ dysfunction, and the etiology of ARDS rather than the age. More studies are needed to confirm our findings.

## Author Contributions

Inderpaul S Sehgal—conceived the idea, performed the statistical analysis, drafted and revised the manuscript, and is the overall guarantor

Ritesh Agarwal—provided intellectual content to the manuscript, drafted and critically revised the manuscript for intellectual content

Sahajal Dhooria—drafted and critically revised the manuscript for intellectual content

Kuruswamy T Prasad—drafted and critically revised the manuscript for intellectual content

Valliappan Muthu—drafted and critically revised the manuscript for intellectual content

Ashutosh N Aggarwal—performed the statistical analysis, drafted and revised the manuscript

## Orcid

*Inderpaul S Sehgal* https://orcid.org/0000-0002-6505-6019
*Ritesh Agarwal* https://orcid.org/0000-0003-2547-7668
*Sahajal Dhooria* https://orcid.org/0000-0003-3199-9163
*Kuruswamy T Prasad* https://orcid.org/0000-0001-7690-6595
*Valliappan Muthu* https://orcid.org/0000-0003-0410-8468
*Ashutosh N Aggarwal* https://orcid.org/0000-0001-8556-3600

## References

1. Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. Lancet 1967;2:319–323. DOI: 10.1016/s0140-6736(67)90168-7.
2. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. Acute respiratory distress syndrome: the Berlin definition. JAMA 2012;307(23):2526–2533. DOI: 10.1001/jama.2012.5669.
3. Ferguson ND, Fan E, Camporota L, Antonelli M, Anzueto A, Beale R, et al. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. Intensive Care Med 2012;38(10):1573–1582. DOI: 10.1007/s00134-012-2682-1.
4. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med 2015;372(8):747–755. DOI: 10.1056/NEJMsa1410639.
5. Nin N, Muriel A, Penuelas O, Brochard L, Lorente JA, Ferguson ND, et al. Severe hypercapnia and outcome of mechanically ventilated patients with moderate or severe acute respiratory distress syndrome. Intensive Care Med 2017;43(2):200–208. DOI: 10.1007/s00134-016-4611-1.
6. Guerin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med 2013;368(23):2159–2168. DOI: 10.1056/NEJMoa1214103.
7. Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, Wheeler A. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342(18):1301–1308. DOI: 10.1056/NEJM200005043421801.
8. Suchyta MR, Clemmer TP, Elliott CG, Orme JF Jr, Morris AH, Jacobson J, et al. Increased mortality of older patients with acute respiratory distress syndrome. Chest 1997;111(5):1334–1339. DOI: 10.1378/chest.111.5.1334.
9. Zilberberg MD, Epstein SK. Acute lung injury in the medical ICU: comorbid conditions, age, etiology, and hospital outcome. Am J Respir Crit Care Med 1998;157:1159–1164. DOI: 10.1164/ajrccm.157.4.9704088.
10. Sloane PJ, Gee MH, Gottlieb JE, Albertine KH, Peters SP, Burns JR, et al. A multicenter registry of patients with acute respiratory distress syndrome. Physiology and outcome. Am Rev Respir Dis 1992;146(2):419–426. DOI: 10.1164/ajrccm/146.2.419.
11. Brower RG, Lanken PN, MacIntyre N, Matthay MA, Morris A, Ancukiewicz M, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med 2004;351(4):327–336. DOI: 10.1056/NEJMoa032193.
12. Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, Hayden D, deBoisblanc B, et al. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 2006;354(24):2564–2575. DOI: 10.1056/NEJMoa062200.
13. Flaatten H, de Lange DW, Artigas A, Bin D, Moreno R, Christensen S, et al. The status of intensive care medicine research and a

future agenda for very old patients in the ICU. Intensive Care Med 2017;43(9):1319–1328. DOI: 10.1007/s00134-017-4718-z.
14. Boumendil A, Angus DC, Guitonneau AL, Menn AM, Ginsburg C, Takun K, et al. Variability of intensive care admission decisions for the very elderly. PLoS One 2012;7(4):e34387. DOI: 10.1371/journal.pone.0034387.
15. Gee MH, Gottlieb JE, Albertine KH, Kubis JM, Peters SP, Fish JE. Physiology of aging related to outcome in the adult respiratory distress syndrome. J Appl Physiol (1985) 1990;69(3):822–829. DOI: 10.1152/jappl.1990.69.3.822.
16. Guidet B, Leblanc G, Simon T, Woimant M, Quenot JP, Ganansia O, et al. Effect of systematic intensive care unit triage on long-term mortality among critically ill elderly patients in France: a randomized clinical trial. JAMA 2017;318(15):1450–1459. DOI: 10.1001/jama.2017.13889.
17. Muthu V, Dhooria S, Aggarwal AN, Behera D, Sehgal IS, Agarwal R. Acute respiratory distress syndrome due to tuberculosis in a respiratory ICU over a 16-year period. Crit Care Med 2017;45(10):e1087–e1090. DOI: 10.1097/CCM.0000000000002479.
18. Muthu V, Dhooria S, Agarwal R, Prasad KT, Aggarwal AN, Behera D, et al. Profile of patients with active tuberculosis admitted to a respiratory intensive care unit in a tertiary care center of North India. Indian J Crit Care Med 2018;22(2):63–66. DOI: 10.4103/ijccm.IJCCM_491_17.
19. Ferreira FL, Bota DP, Bross A, Melot C, Vincent JL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA 2001;286(14):1754–1758. DOI: 10.1001/jama.286.14.1754.
20. Sehgal IS, Agarwal R, Dhooria S, Prasad KT, Muthu V, Aggarwal AN. Risk stratification of acute respiratory distress syndrome using a $PaO_2$:$FiO_2$ threshold of 150 mm Hg: a retrospective analysis from an Indian intensive care unit. Lung India 2020;37(6):473–478. DOI: 10.4103/lungindia.lungindia_146_20.
21. Kao KC, Hsieh MJ, Lin SW, Chuang LP, Chang CH, Hu HC, et al. Survival predictors in elderly patients with acute respiratory distress syndrome: a prospective observational cohort study. Sci Rep 2018;8:13459. DOI: 10.1038/s41598-018-31811-w.
22. Eachempati SR, Hydo LJ, Shou J, Barie PS. Outcomes of acute respiratory distress syndrome (ARDS) in elderly patients. J Trauma 2007;63(2):344–350. DOI: 10.1097/TA.0b013e3180eea5a1.
23. Stupka JE, Mortensen EM, Anzueto A, Restrepo MI. Community-acquired pneumonia in elderly patients. Aging Health 2009;5(6):763–774. DOI: 10.2217/ahe.09.74.
24 . Laporte L, Hermetet C, Jouan Y, Gaborit C, Rouve E, Shea KM, et al. Ten-year trends in intensive care admissions for respiratory infections in the elderly. Ann Intensive Care 2018;8(1):84. DOI: 10.1186/s13613-018-0430-6.
25. Kothe H, Bauer T, Marre R, Suttorp N, Welte T, Dalhoff K. Outcome of community-acquired pneumonia: influence of age, residence status and antimicrobial treatment. Eur Respir J 2008;32(1):139–146. DOI: 10.1183/09031936.00092507.
26. Sehgal IS, Dhooria S, Behera D, Agarwal R. Acute respiratory distress syndrome: pulmonary and extrapulmonary not so similar. Indian J Crit Care Med 2016;20(3):194–197. DOI: 10.4103/0972-5229.178188.
27. Pelosi P, D'Onofrio D, Chiumello D, Paolo S, Chiara G, Capelozzi VL, et al. Pulmonary and extrapulmonary acute respiratory distress syndrome are different. Eur Respir J Suppl 2003;42:48s–56s. DOI: 10.1183/09031936.03.00420803.
28. Milberg JA, Davis DR, Steinberg KP, Hudson LD. Improved survival of patients with acute respiratory distress syndrome (ARDS): 1983-1993. JAMA 1995;273:306–309. PMID: 7815658.
29. Moreno R, Vincent JL, Matos R, Mendonca A, Cantraine F, Thijs L, et al. The use of maximum SOFA score to quantify organ dysfunction/failure in intensive care. Results of a prospective, multicentre study. Working Group on Sepsis related Problems of the ESICM. Intensive Care Med 1999;25(7):686–696. DOI: 10.1007/s001340050931.
30. Ando K, Doi T, Moody SY, Ohkuni Y, Sato S, Kaneko N. The effect of comorbidity on the prognosis of acute lung injury and acute respiratory distress syndrome. Intern Med 2012;51(14):1835–1840. DOI: 10.2169/internalmedicine.51.6434.
31. Finney SJ, Zekveld C, Elia A, Evans TW. Glucose control and mortality in critically ill patients. JAMA 2003;290(15):2041–2047. DOI: 10.1001/jama.290.15.2041.
32. Falciglia M, Freyberg RW, Almenoff PL, D'Alessio DA, Render ML. Hyperglycemia-related mortality in critically ill patients varies with admission diagnosis. Crit Care Med 2009;37(12):3001–3009. DOI: 10.1097/CCM.0b013e3181b083f7.
33. Boumendil A, Somme D, Garrouste-Orgeas M, Guidet B. Should elderly patients be admitted to the intensive care unit? Intensive Care Med 2007;33(7):1252. DOI: 10.1007/s00134-007-0621-3.