



Research Article

Intensive Care Unit and 12-month Mortality of Patients with Acute Respiratory Failure Admitted to the Intensive Care Unit: What is the Role of Comorbidities?

 Huriye Berk Takir,  Zuhale Karakurt,  Nezihe Ciftaslan Goksenoglu,  Cuneyt Salturk,  Ozlem Yazicioglu Mocin,  Aysem Askim Oztin,  Nalan Adiguzel,  Gokay Gungor

Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey

Abstract

Objectives: There are limited data regarding the effect of comorbidities in the intensive care unit (ICU) and 12-month mortality rates of patients with acute respiratory failure (ARF) who are admitted to the ICU. The present investigation was designed to determine the effect of comorbidities and identify long-term mortality predictors in this patient group.

Methods: A retrospective observational cohort study was performed in a 22-bed, tertiary ICU in a teaching and research hospital. All patients who were admitted to the ICU during 2012 were included in the study. Demographics, comorbidities, ICU data at the time of admission, and the last control were recorded. ICU mortality and 12-month mortality after ICU discharge were analyzed by Cox regression and Kaplan–Meier survival analysis.

Results: During the study period, 1022 patients (362 females) were admitted to the ICU, and the ICU mortality was 20.8%. Older age, non-invasive mechanical ventilation failure, more invasive mechanical ventilation days, tachycardia, Acute Physiological and Chronic Health Evaluation (APACHE II) score at the time of admission, low albumin, and the ratio of partial arterial oxygen pressure to inspired fractionated oxygen were associated with increased mortality. Interestingly, the presence of chronic obstructive pulmonary disease (COPD) was associated with decreased mortality. The 12-month mortality rate of the 809 patients who were discharged from the ICU was 51.9% (n = 420). Half of these patients died within the first 2 months after discharge. Cancer, low albumin, and higher APACHE II score at the time of discharge were identified as mortality risk factors.

Conclusion: Patients with ARF who are admitted to the ICU have a higher rate of mortality, and only half survive >1 year after discharge. COPD is a comorbid disease associated with an increased likelihood of long-term survival, whereas malignancy is associated with poor prognosis after ICU discharge.

Keywords: Comorbidity, intensive care unit, mortality

Cite This Article: Berk Takir H, Karakurt Z, Ciftaslan Goksenoglu N, Salturk C, Yazicioglu Mocin O, Oztin AA, Adiguzel N, Gungor G. Intensive Care Unit and 12-month Mortality of Patients with Acute Respiratory Failure Admitted to the Intensive Care Unit: What is the Role of Comorbidities?. EJMO 2019;3(1):49–58.

Acute respiratory failure (ARF) is a leading cause of intensive care unit (ICU) admission and both short- and long-term mortalities.^[1] Despite significant advances in treatment strategies for critically ill patients in the ICU, the mortality rate of ARF remains high.^[2] Specific diseases or conditions affecting ICU outcomes are well studied, i.e., solid or hematological malignancies, neurological diseases,

obesity, septic shock, and renal failure,^[3–5] and chronic obstructive pulmonary disease (COPD) is known to account for the majority of ICU admissions and mortality due to ARF. Cardiovascular diseases, hypertension, osteoporosis, depression, diabetes mellitus (DM), and lung cancer are reported as COPD-related comorbidities.^[6] A recent study investigated COPD as a cause of ICU admission and a co-

Address for correspondence: Huriye Berk Takir, MD. Sureyyapasa Gogus Hastaliklari ve Gogus Cerrahisi Egitim ve Arastirma Hastanesi, Istanbul, Turkey

Phone: +90 505 774 59 88 **E-mail:** huriyebek@yahoo.com

Submitted Date: August 14, 2018 **Accepted Date:** November 30, 2018 **Available Online Date:** January 04, 2019

©Copyright 2019 by Eurasian Journal of Medicine and Oncology - Available online at www.ejmo.org



morbid condition and concluded that COPD is an independent risk factor for increased morbidity and mortality.^[7] Although the need for ICU admission due to ARF is increasing, there are limited data regarding comorbidities and their effects on long-term mortality after ICU discharge. In the present study, we aimed to investigate the effect of comorbidities and identify long-term mortality predictors of acute problems.

Methods

This retrospective, observational, cohort study was conducted in a 22-bed, level III ICU of a tertiary teaching hospital for chest diseases and thoracic surgery over a 12-month period between January and December 2012, approved by the local Ethics Committee of Istanbul Medeniyet University School of Medicine in Istanbul, Turkey. It was conducted in accordance with the ethical principles stated in the Declaration of Helsinki.^[8] Informed consent could not be obtained due to the retrospective design.

Patients

All patients who admitted to the respiratory ICU due to ARF during the study period were included in the study. The patients were divided into two groups according to mortality during and after their time in the ICU, and patients were further subdivided into two groups based on 12-month mortality. The data were compared as survivor and non-survivor groups.

Data

Patient demographics; diseases underlying ARF; and comorbidities such as COPD, DM, hypertension, coronary artery disease, malignancy, cerebrovascular event, and renal failure were recorded from the patients' ICU files. We determined the patients' pre-ICU condition and where they were admitted from (home, emergency department, or ward). The lengths of stay (LOS) in the hospital and ICU, long-term oxygen therapy (LTOT), and long-term non-invasive mechanical ventilation (NIMV) or invasive mechanical ventilation (IMV) through tracheostomy at home were recorded. The Acute Physiological and Chronic Health Evaluation (APACHE II) score was calculated as an ICU severity index.^[9] Arterial blood gas (ABG) values, serum biochemical values, complete blood counts, C-reactive protein (CRP) level, and presence of infection as sepsis and septic shock were noted. Mortality after ICU discharge was recorded from the online deceased declaration system.

Definitions

ARF was classified as hypoxemic (ratio of partial arterial oxygen pressure to inspired fractionated oxygen [$\text{PaO}_2/\text{FiO}_2$] <300 and partial arterial carbon dioxide pressure

[PaCO_2] <45 mmHg). Hypercapnic/hypoxemic ARF was defined as $\text{PaCO}_2 >45$ mmHg and $\text{PaO}_2/\text{FiO}_2 <300$, and hypercapnic ARF was $\text{PaCO}_2 >45$ mmHg and $\text{PaO}_2/\text{FiO}_2 >300$.^[10,11] Sepsis was defined as the presence of infection together with systemic inflammatory response syndrome, and septic shock was diagnosed in patients who were unresponsive to fluid resuscitation and required vasopressor agents.^[12,13]

COPD was defined as the presence of dyspnea, chronic cough, sputum associated with exposure to organic or inorganic dust, chemicals, or cigarette smoking, and airway obstruction on spirometry (forced expiratory volume in 1 s [FEV1] $<70\%$).^[6]

Mechanical Ventilation

NIMV was initially applied to all patients with ARF if there were no contraindications and they were hemodynamically stable, cooperative, had no organ failure other than respiratory failure; their ABG analysis revealed $\text{pH}=7.28-7.34$, $\text{PaCO}_2=45-90$ mmHg, and $\text{PaO}_2/\text{FiO}_2 >200$, and their Glasgow coma scale was >3 due to hypercapnic confusion. NIMV was applied by a specialized ICU team including nurse and seven pulmonologists. NIMV absolute and relative contraindications were as follows: (1) Respiratory arrest and unable to fit mask and (2) Medically unstable (hypotensive shock, uncontrolled cardiac ischemia or arrhythmia, and uncontrolled copious upper gastrointestinal bleeding), agitation, uncooperativeness, inability to protect airway, impaired swallowing, excessive secretions not managed by secretion clearance techniques, multiple (two or more) organ failure, or recent upper airway or upper gastrointestinal surgery.^[10,11,14] NIMV was provided in pressure assist-control mode with ICU mechanical ventilators through a double-tube circuit with a full-face or oronasal mask. Pressure support (PS) was initially set at 8–10 cm H_2O and gradually increased to a maximum of 30 cm H_2O until the exhaled tidal volume was 5–7 mL/kg and guided by patient tolerance. Positive end-expiratory pressure (PEEP) was set at 5 cm H_2O and raised or lowered gradually to treat hypoxemia or enhance patient compliance. FiO_2 was adjusted to maintain oxygen saturation (SaO_2) at 90%. NIMV was applied intermittently for 1–4 h, and initial ABG samples were obtained at the end of the 1st h. The duration of each session was determined by ABG value improvement, consciousness level, and patient compliance. The definition of NIMV failure in hypercapnic patients was no pH improvement, no change or a rise in breathing frequency after 1–2 h, and lack of cooperation. For hypoxic patients, failure was considered as no or a minimal rise in $\text{PaO}_2/\text{FiO}_2$ after 1–2 h (<200).^[10]

IMV was applied in the presence of absolute or relative contraindications for NIMV, as mentioned above. IMV was ap-

plied by assist control ventilation in pressure control mode. Inspiratory pressure was set for a target tidal volume of 5–7 mL/kg ideal body weight (airway plateau pressure <30 cm H₂O) under a sedation protocol. The Richmond Agitation-Sedation Scale was used for infusion and assessment of the daily need for sedation.^[15] When patients met the previously described criteria for weaning, the PS ventilation mode was used and gradually decreased (1–2 cm H₂O every 1–2 h).^[16] When the PS reached 8–10 cm H₂O and PEEP was 0 or <5 cm H₂O, the patient progressed to spontaneous breathing trials using a T-piece with oxygen support (trial duration of 30 min). NIMV was applied in cases of moderate respiratory distress after extubation if there was no contraindication.

Glucose level was measured with an Accu-Chek device (Roche/Hitachi, Basel, Switzerland). Hypoglycemia was defined as glucose ≤70 mg/dL, hyperglycemia ≥100 mg/dL, and normoglycemia 70–100 mg/dL. DM was defined as fasting blood glucose ≥126 mg/dl. The glucose level in critically ill patients was targeted between 140 and 180 mg/dL.

Statistical Analysis

Descriptive analyses were performed to compare demographic and ICU data. Groups were compared with Mann–Whitney U-tests for non-parametric continuous variables and Student's t-tests for parametric and continuous variables. Chi-square tests were employed for dichotomous variables. The median with interquartile range or mean±standard deviation is reported for non-parametric continuous or parametric continuous variables, respectively. Count and percentage were used when applicable. Kaplan–Meier survival analyses were carried out to predict long-term mortality after ICU discharge. Cox regression analyses were performed to predict long-term mortality risk factors. We included variables that were statistically significant following univariate analyses of survival and non-survival in patients following ICU discharge. P<0.05 was considered as statistically significant. Data were analyzed using Statistical Package for the Social Sciences software (SPSS version 20.0; IBM, Armonk, NY, USA).

Results

Patients' Characteristics and Comorbidities

A total of 1022 patients were admitted to the ICU with ARF during the study period, and 809 patients (291 females) survived and were discharged (Fig. 1). The overall ICU mortality rate was 20.8%, and the 12-month mortality rate was 51.9%. COPD was the most frequent comorbidity in both the survivors and non-survivor groups (50.6% vs. 38.0%), but the prevalence of COPD in the survivors group was 75% higher than that in the non-survivors group (Table 1). Among patients who died in the ICU, malignancy was the second most

common comorbidity after COPD. The frequency of malignancy was nearly three-fold in the non-survivor group (28.2% vs. 10.6%). The percentage of patients who were previously using home devices (LTOT and NIMV) was significantly higher in the survivor group (46.1% vs. 34.9%, p=0.004, and 23.8% vs. 12.0%, p<0.001 respectively) (Table 1).

There was no difference in sex ratio or mean body mass index between the two groups. Except COPD and malignancy, there were similar ICU mortality rates with regard to comorbidities. Patients who had previously used home ventilation devices (LTOT and NIMV) were predominantly in the survivor group (46.1% vs. 34.9%, p<0.01, and 23.8% vs. 12.0%,

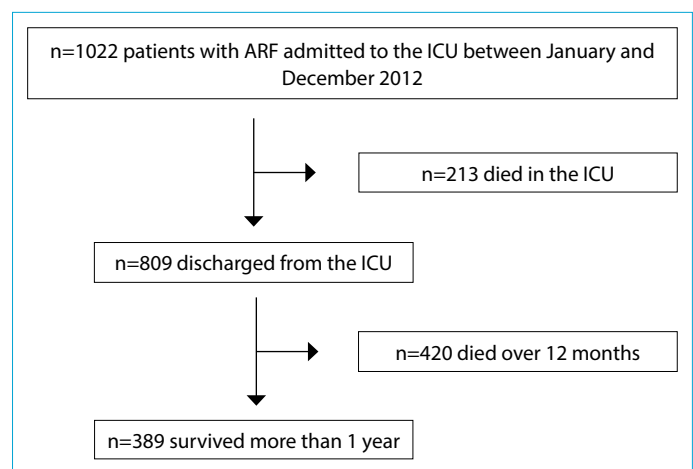


Figure 1. Patient outcome flowchart.

Table 1. Comparison of patient characteristics and comorbidities in groups stratified by ICU mortality

	ICU		p
	Survivors n=809	Nonsurvivors n=213	
Female, %	35.9%	33.3%	0.47
Age	66.01±13.97	69.04±13.09	0.004
Body mass index, kg/m ²	25±7.42	24.59±7.34	0.032
Comorbidities, n (%)			
COPD	409 (50.6)	81 (38.0)	0.001
Hypertension	289 (35.7)	55 (38.0)	0.007
DM	169 (20.9)	38 (17.8)	0.32
Coronary artery disease	128 (15.8)	35 (16.4)	0.83
Malignancy	86 (10.6)	60 (28.2)	0.001
Cerebrovascular event	47 (5.8)	10 (4.7)	0.52
Chronic renal failure	44 (5.4)	6 (2.8)	0.11
LTOT at home, n (%)	365 (46.1)	73 (34.9)	0.004
NIMV at home, n (%)	188 (23.8)	25 (12.0)	0.001
Hospitalization in the previous year	1.62±2.10	1.63±2.93	0.95

COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; ICU: intensive care unit; LTOT: long-term oxygen therapy; NIMV: non-invasive mechanical ventilation.

$p < 0.001$, respectively) (Table 1). Frequent ICU admissions in the previous year were higher in the non-survivor group.

ICU Data

Non-survivors had significantly higher APACHE II scores and were more likely to be invasively ventilated than survivors (Table 2). Patients who survived were mostly treated with NIMV (67.1%). LOS in the ICU was similar in the two groups, and there were no differences in ABG values (Table 2). Among the hematological and biochemical parameters, CRP, white blood cell, blood urine nitrogen, serum creatinine, aspartate transaminase, and alanine transaminase were significantly higher in the non-survivor group, but albumin was significantly lower (Table 2).

On ICU admission, the mean APACHE II scores in the COPD and non-COPD patients were 19 ± 7 and 19 ± 6 , respectively. Among patients who did not survive, the mean APACHE II scores on ICU admission were 27 ± 7 and 30 ± 9 in the COPD and non-COPD patients, respectively.

Long-term Mortality

Mortality was significantly higher among older patients ($p < 0.001$, Table 3). Among the comorbidities assessed, malignancy was 3 times higher in the non-survivor group (15.7% vs. 5.1%, $p < 0.001$). Nearly half of the patients in this group previously had a LTOT device at home (52.3%). Patients more frequently admitted to ward and ICU had worse outcome (Table 3). Patients in both the groups spent the same mean number of days in the ICU. Except protein and albumin levels, all serum biochemical and hematological values were similar.

Kaplan–Meier curves were generated to assess 2-year survival after ICU discharge, and nearly half of the deaths occurred within 5 months (Fig. 2). Patients with COPD had a better prognosis (Fig. 3), whereas those with malignancy lived significantly shorter after ICU discharge (Fig. 4).

The Cox regression analysis results of mortality after discharge from ICU are shown in Table 4. Malignancy was

Table 2. ICU data of patients with acute respiratory failure grouped according to mortality in the ICU

	Survivors n=809	Nonsurvivors n=213	p
APACHE II score at the time of ICU admission	19.2±6.7	28.8±8.3	0.001
IMV, n (%)	256 (31.6)	146 (68.5)	0.001
IMV day	2 (1-5)	3 (1-8)	0.006
NIMV, n (%)	543 (67.1)	119 (55.9)	0.002
NIMV, day	4 (2-7)	3 (2-7)	0.11
Length of ICU stay, day	6 (3-8)	5 (1-10)	0.038
ABG values at the time of ICU admission, mean±SD			
pH	7.30±0.46	7.08±1.21	0.009
PaCO ₂ , mmHg	62.8±24.4	59.8±28.8	0.16
PaO ₂ /FiO ₂	205±113	165±103	0.001
HCO ₃ ⁻ , mmol	32.2±22.6	27.7±10.5	0.006
Hematologic and biochemical blood values at the time of admission			
CRP, mg/dL, median (25%-75%)	43.3 (14.9-110.0)	105.0 (38.8-158.0)	0.001
WBC×10 ⁹ /L, mean±SD	11.8±5.8	15.1±9.2	0.001
Hb, mean±SD	12.1±2.2	11.0±2.8	0.001
PLT×10 ⁹ /L, median (25%-75%)	238 (181-311)	226 (149-337)	0.15
Glucose, mg/dL, median (25%-75%)	140 (110-184)	142 (109-198)	0.60
BUN, mg/dL, median (25%-75%)	23 (16-34)	35 (24-53)	0.001
Serum creatinine, mg/dL, median (25%-75%)	0.80 (0.66-1.19)	1.1 (30.74-1.60)	0.001
Protein, g/dL, mean±SD	6.5±1.1	6.1±2.0	0.024
Albumin, g/dL, mean±SD	3.0±0.07	2.5±0.7	0.001
AST, U/L, median (25%-75%)	22 (16-35)	31 (21-60)	0.001
ALT, U/L, median (25%-75%)	20 (13-34)	26 (15-61)	0.001
Sodium, mmol/L, mean±SD	138±6	139±8	0.07
Potassium, mmol/L, mean±SD	4.5±0.7	4.6±0.9	0.049

ABG: arterial blood gases; ALT: alanine transaminase; APACHE II: Acute Physiological and Chronic Health Evaluation; AST: aspartate transaminase; BUN: blood urine nitrogen; CRP: C-reactive protein; Hb: hemoglobin; IMV: invasive mechanical ventilation; NIMV: noninvasive mechanical ventilation; PLT: platelet; WBC: white blood cell.

Table 3. Mortality after discharge from the ICU

	Long-term mortality		
	Survivors n=389	Nonsurvivors n=420	p
Female, %	40.1%	32.1%	0.018
Age, years	64±14	68±13	0.001
Comorbidities, n (%)			
COPD	203 (52.2)	206 (49.0)	0.37
Hypertension	149 (38.3)	140 (33.3)	0.14
DM	92 (23.7)	77 (18.3)	0.06
Coronary artery disease	62 (15.9)	66 (15.7)	0.93
Malignancy	20 (5.1)	66 (15.7)	0.001
Cerebrovascular event	17 (4.4)	30 (7.1)	0.92
Chronic renal failure	13 (3.3)	31 (7.4)	0.011
LTOT at home, n (%)	150 (39.4)	215 (52.3)	0.001
NIMV at home, n (%)	76 (20.0)	112 (27.3)	0.017
Hospitalization in the previous year, mean±SD	1.4±1.9	1.8±2.3	0.001
ICU admission in the previous year, mean±SD	0.4±0.7	0.6±1.0	0.001
ICU data			
APACHE II score at the time of discharge from the ICU	10.6±3.5	12.8±4.1	0.001
Length of stay in the ICU, days	6 (3-8)	6 (3-8)	0.95
IMV, n (%)	256 (31.6)	146 (68.5)	0.001
IMV day	2 (1-5)	3 (1-8)	0.006
NIMV, n (%)	543 (67.1)	119 (55.9)	0.002
NIMV, days	4 (2-7)	3 (2-7)	0.11
Length of ICU stay, days	6 (3-8)	5 (1-10)	0.038
ABG at the time of discharge			
pH	7.46±0.07	7.46±0.07	0.38
PaCO ₂ , mmHg	46.9±11.0	46.9±11.9	0.95
PaO ₂ /FiO ₂	264±138	238±146	0.007
HCO ₃ , mmol	34.9±21.3	32.7±8.6	0.052
Hematologic and biochemical blood values at the time of discharge			
CRP, mg/dL, median (25%-75%)	24 (14-64)	36 (17-73)	0.018
WBC×10 ⁹ /L, mean±SD	8.5±4.0	9.2±5.1	0.032
Hb (mean±SD)	11.3±3.2	10.6±3.2	0.02
PLT×10 ⁹ /L, median (25%-75%)	249±107	249±109	0.99
Glucose, mg/dL, median (25%-75%)	108±39	104±37	0.12
BUN, mg/dL, median (25%-75%)	28±14	31±18	0.002
Serum creatinine, mg/dL, median (25%-75%)	0.72 (0.59-0.91)	0.71 (0.58-1.0)	0.48
Protein, g/dL, mean±SD	6.4±0.7	6.0±0.8	0.001
Albumin, g/dL, mean±SD	2.6±0.6	2.4±0.6	0.001
AST, U/L, median (25%-75%)	22 (15-31)	20 (15-30)	0.37
ALT, U/L, median (25%-75%)	20 (13-33)	19 (12-34)	0.25
Sodium, mmol/L, mean±SD	138±4	138±5	0.11
Potassium, mmol/L, mean±SD	4.4±0.5	4.5±0.6	0.28

ABG: arterial blood gases; ALT: alanine transaminase; APACHE II: Acute Physiological and Chronic Health Evaluation; AST: aspartate transaminase; BUN: Blood urine nitrogen; CRP: C-reactive protein; DM: diabetes mellitus; Hb: hemoglobin; ICU: intensive care unit; IMV: invasive mechanical ventilation; NIMV: noninvasive mechanical ventilation; PLT: Platelet; WBC: white blood cell.

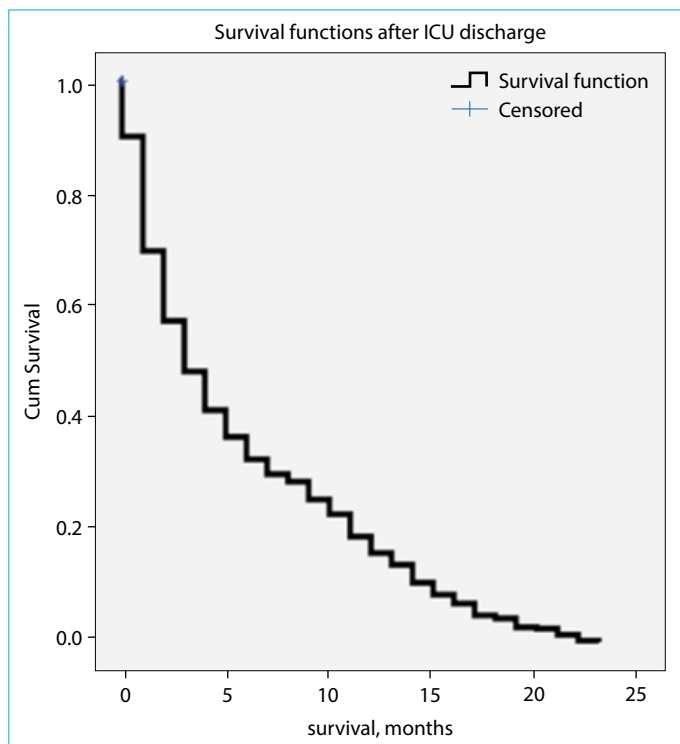


Figure 2. Kaplan–Meier plot showing the survival of patients with acute respiratory failure after intensive care unit discharge.

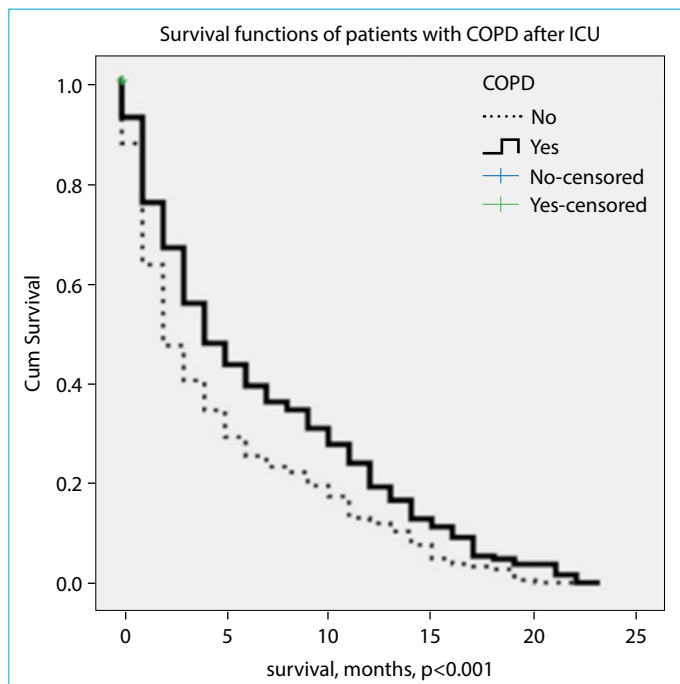


Figure 3. Kaplan–Meier plot showing the survival of patients with chronic obstructive pulmonary disease after intensive care unit discharge.

found to be a significant risk factor for long-term mortality. Similar to malignancy, older age also found to be associated with worse outcome. COPD was a protective factor for short-term mortality.

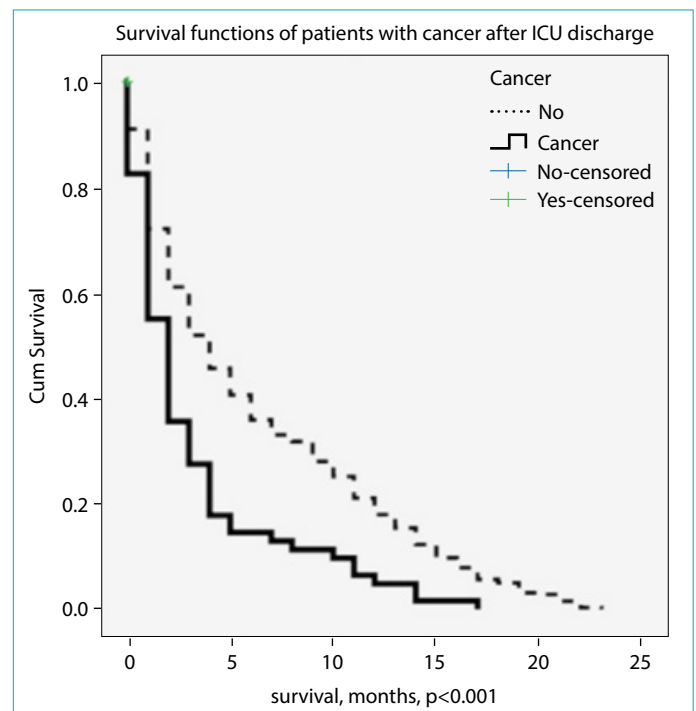


Figure 4. Kaplan–Meier plot showing the survival of patients with malignancy after intensive care unit discharge.

Table 4. Cox regression analysis of mortality risk factors after discharge from ICU

	OR	95% CI	p
Malignancy	1.81	1.36-2.41	0.001
COPD	0.70	0.57-0.87	0.001
Age	1.01	1.01-1.02	0.006
DM	0.95	0.72-1.24	0.69
Hypertension	0.89	0.72-1.11	0.32
Cerebrovascular disease	0.90	0.60-1.35	0.60
Chronic renal failure	1.03	0.68-1.56	0.89
Coronary artery disease	0.90	0.60-1.35	0.89
Use LTOT at home	1.05	0.82-1.35	0.69
Use NIMV at home	0.99	0.75-1.31	0.94

CI: confidence interval; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; LTOT: long-term oxygen therapy; NIMV: non-invasive mechanical ventilation; OR: odds ratio.

Discussion

The results of the present study demonstrate that nearly half of patients with COPD survived >12 months after discharge from the ICU. COPD was associated with better survival than other comorbidities. Half of all mortality occurred in the first 5 months after discharge, and patients with malignancies had worse prognoses. DM, hypertension, coronary artery disease, cerebrovascular event, and chronic renal failure did not affect short- or long-term mortality.

Comorbidities

COPD Mortality in the ICU

Studies investigating hospital mortality of COPD patients have reported a wide range of mortality rates from 11% up to 48%.^[17, 18] Williams et al. performed a prospective cohort study of 19,921 patients who were followed for 15 years and demonstrated that age, comorbidity, and critical illness type all influenced long-term survival after ICU discharge.^[19] Funk et al.^[7] investigated the long-term mortality (10 years) rate of patients with and without COPD after ICU stays. They compared patients in whom COPD was either a comorbid disease or the reason underlying ARF and determined that COPD was an independent risk factor for mortality. In the 1st month after ICU admission, the probabilities of mortality were 22%, 19%, and 12% in patients who were admitted with ARF due to COPD, those with comorbid COPD, and those without COPD, respectively.^[7] The present study showed that patients who survived were more likely to have COPD as a comorbid disease compared to non-survivors. Our results also demonstrated that survivors were predominantly using home ventilation devices; therefore, it is possible that the longer survival of COPD patients was associated with NIMV and LTOT use at home. The overall ICU mortality of COPD patients was 16.5%, which is consistent with the lower end of results reported by other groups. Alaithan et al.^[20] reported a low ICU mortality rate of 6%, but their patient population had lower APACHE II scores (mean of 17). In the present study, the median APACHE II scores in the survivor and non-survivor groups were 19 and 27, respectively. Still, our survival rates were higher than those reported by Raurich et al. and Ai-Ping et al. (26% and 24%, respectively). IMV was the most used ventilation type among non-surviving COPD patients in those studies.^[17, 21] In our patient population, NIMV was predominantly implemented for respiratory support management, and it is possible that this was associated with increased survival.

COPD short- and Long-term Mortality After ICU Discharge

Previous studies have shown that NIMV increases short-term survival in COPD patients with ARF.^[22, 23] Similarly, previous utilization of LTOT and NIMV was approximately 76% and 52% higher, respectively, in ICU survivors in the short term. Williams et al.^[19] assessed a large series of survivors after ICU admission and found that the risk of death was highest in the first 12 months, and it was greater than the general population for 14 years (although it stabilized after the first 12 months). A Spanish population-based study of 20,571 participants carried out by Garcia-Aymerich et al.^[24] revealed that hospitalizations for COPD increased a

subsequent mortality for the median 10-year follow-up period, regardless of the level of lung function impairment. A Danish study reported a 36% 12-month mortality, and an American multicenter study described a 43% rate in the same time period, with roughly half of the patients being readmitted within 6 months.^[25, 26] In the present study, the 12-month mortality rate was 51.9% and half of all deaths occurred in the first 2 months following ICU discharge.

DM

Diabetic patients are more likely to develop complications in the ICU, but their mortality risk is not increased.^[27] Despite a variable range of blood glucose cutoff values in different studies, the mortality rates of ICU patients with DM were lower compared to non-diabetic patients in the higher mean glucose range.^[28-31] Moreover, some authors concluded that high glucose variability in non-diabetic ICU patients is more harmful than diabetes itself.^[32, 33] This could be because high blood glucose levels for reasons other than diabetes, for example, sepsis are associated with poor ICU prognosis. According to the 2008 worldwide Surviving Sepsis Campaign, sepsis management protocols achieved tight blood glucose levels, and the normoglycemia in intensive care evaluation-survival using glucose algorithm regulation study showed that safe blood glucose levels were <180 mg/dL.^[34, 35] In a recent trial, Sechterberger et al. retrospectively analyzed data from 10,320 patients and found that DM affects the association between three of four measures of glycemic control and ICU mortality. They also identified associations between ICU mortality and mean glucose and high glucose variability in the non-DM cohort but not the DM cohort, whereas hypoglycemia (≤ 2.2 mmol/L) was associated with ICU mortality in both.^[36] In the present study, DM was not associated with a higher long-term mortality rate.

Cardiovascular Diseases

There are limited data regarding the long-term mortality of patients with ARF with comorbid cardiovascular conditions including hypertension, coronary artery disease, or arrhythmias. In the present study, neither hypertension nor coronary artery disease was significantly associated with ICU or long-term mortality. This is likely related to advances in the treatment of cardiovascular diseases. However, patients with chronic respiratory failure who use LTOT and NIMV may have additional cardiovascular diseases. Arrhythmias deteriorate with the presence of chronic hypoxemia, and this can negatively affect long-term survival.

Malignancy

Previous studies reported a range of in-hospital mortality

rates between 22% and 85% in patients with lung cancer.^[37–43] Nearly 1% of hospitalized patients with solid organ tumors experience ARF.^[44] Roques et al.^[42] reported ICU, hospital, and 6-month mortality rates of 43%, 54%, and 73%, respectively. The authors found that the presence of respiratory failure and poor performance status increased 6-month mortality by nearly 3.5 fold, including the need for mechanical ventilation. In the present study, patients with malignancies had a higher mortality rate in the 12 months after ICU discharge (77%), with nearly half dying within 2 months and 90% dying within 5 months.

In our study, patients using NIMV and LTOT were more likely to survive than those who did not in short term. The reasons for ICU admission among those patients were underlying chronic respiratory diseases, and the mortality rates of these diseases are not high. However, patients using NIMV and LTOT for long periods of time (12-month) had significantly shorter survival times. This is expected because NIMV and LTOT are prescribed for end-stage chronic respiratory failure diseases including bronchiectasis, restrictive lung diseases, COPD, and lung cancer on the purpose of palliative care.

Limitations

There are several limitations of the present study. First, it was a retrospective analysis conducted in a single center. However, we included a large number of patients who were followed 24 h a day by an ICU team that included seven pulmonologists. Second, our findings cannot be generalized to all other ICU patients since the study was carried out in a respiratory-based medical ICU. Still, the results of this study are useful for providing information about respiratory-originating ICU patients. Third, comorbidities were recorded from patients' files and during follow-up, so it is possible that additional comorbidities were underdiagnosed.

The strength of this study is that the mortality rates were determined using data from an electronically controlled system. As such, there was no case loss in the follow-up period.

Conclusion

The most remarkable finding of this study was that half of patients died within 12 months and half of the deaths occurred in the first 5 months after discharge. This could be valuable information for both physicians and patients' family members. In this respect, respiratory ICU patients should be followed up closely after discharge due to the high risk of mortality. We found that the presence of malignancy was associated with worse long-term outcome after ICU discharge. Interestingly, COPD predicted better ICU survival than other comorbidities including DM, hy-

pertension, coronary artery disease, cerebrovascular event, and chronic renal failure, which did not affect short- or long-term survival. Although the present results cannot be generalized to other types of ICU patients, future studies should investigate long-term survival predictors in medical, surgical, and obstetrical ICU patients.

Competing Interests

All authors contributed in the study do not have any industry relationships for the past 2 years and do not have any conflicts of interest. Manuscript has been read and approved by all the authors and each author believes that the manuscript represents honest work.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – Z.K.; Design – H.B.T., Z.K., C.S., O.M., N.A., G.G., N.Ç.G.; Supervision – Z.K., H.B.T.; Materials – H.B.T.; Data collection &/or processing – H.B.T., Z.K., C.S., O.M., N.A., G.G., N.Ç.G.; Analysis and/or interpretation – H.B.T., Z.K., G.G., N.Ç.G.; Literature search – H.B.T., A.A.Ö.G.; Writing – H.B.T., Z.K.; Critical review – H.B.T., Z.K.

References

1. Vasilyev S, Schaap RN, Mortensen JD. Hospital survival rates of patients with acute respiratory failure in modern respiratory intensive care units. An international, multicenter, prospective survey. *Chest* 1995;107:1083–8. [\[CrossRef\]](#)
2. Luhr OR, Antonsen K, Karlsson M, Aardal S, Thorsteinsson A, Frostell CG, et al. Incidence and mortality after acute respiratory failure and acute respiratory distress syndrome in Sweden, Denmark, and Iceland. The ARF study group. *Am J Respir Crit Care Med* 1999;159:1849–61. [\[CrossRef\]](#)
3. Belenguer-Muncharaz A, Albert-Rodrigo L, Ferrandiz-Selless A, Cebrián-Graullera G. Ten-year evolution of mechanical ventilation in acute respiratory failure in the hematological patient admitted to the intensive care unit. *Med Intensiva* 2013;37:452–60. [\[CrossRef\]](#)
4. Duarte AG, Justino E, Bigler T, Grady J. Outcomes of morbidly obese patients requiring mechanical ventilation for acute respiratory failure. *Crit Care Med* 2007;35:732–7. [\[CrossRef\]](#)
5. Azoulay E, Soares M, Darmon M, Benoit D, Pastores S, Afessa B, et al. Intensive care of the cancer patient: Recent achievements and remaining challenges. *Ann Intensive Care* 2011;1:5.
6. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease, Updated 2014. Avail-

- able at: <http://www.goldcopd.org>. Accessed Feb 05, 2104.
7. Funk GC, Bauer P, Burghuber OC, Fazekas A, Hartl S, Hochrieser H, et al. Prevalence and prognosis of COPD in critically ill patients between 1998 and 2008. *Eur Respir J* 2013;41:792–9.
 8. M PN. World medical association publishes the revised declaration of helsinki. *Natl Med J India* 2014;27:56.
 9. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: A severity of disease classification system. *Crit Care Med* 1985;13:818–29. [CrossRef]
 10. Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet* 2009;374:250–9. [CrossRef]
 11. Ambrosino N, Vaghegghini G. Noninvasive positive pressure ventilation in the acute care setting: Where are we? *Eur Respir J* 2008;31:874–86. [CrossRef]
 12. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al 2001 SCCM/ESICM/ACCP/ATS/SIS international sepsis definitions conference. *Intensive Care Med* 2003;29:530–8.
 13. Spoelstra-de Man AM, Girbes AR. Comment on surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2008 by Dellinger et al. *Intensive Care Med* 2008;34:1160–2. [CrossRef]
 14. Ambrosino N, Vaghegghini G. Non-invasive ventilation in exacerbations of COPD. *Int J Chron Obstruct Pulmon Dis* 2007;2:471–6.
 15. Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, et al. The richmond agitation-sedation scale: Validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 2002;166:1338–44. [CrossRef]
 16. Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, et al. Weaning from mechanical ventilation. *Eur Respir J* 2007;29:1033–56. [CrossRef]
 17. Ai-Ping C, Lee KH, Lim TK. In-hospital and 5-year mortality of patients treated in the ICU for acute exacerbation of COPD: A retrospective study. *Chest* 2005;128:518–24. [CrossRef]
 18. Knaus WA. Prognosis with mechanical ventilation: The influence of disease, severity of disease, age, and chronic health status on survival from an acute illness. *Am Rev Respir Dis* 1989;140:58–13. [CrossRef]
 19. Williams TA, Dobb GJ, Finn JC, Knuiman MW, Geelhoed E, Lee KY, et al. Determinants of long-term survival after intensive care. *Crit Care Med* 2008;36:1523–30. [CrossRef]
 20. Alaithan AM, Memon JI, Rehmani RS, Qureshi AA, Salam A. Chronic obstructive pulmonary disease: Hospital and intensive care unit outcomes in the kingdom of saudi arabia. *Int J Chron Obstruct Pulmon Dis* 2012;7:819–23. [CrossRef]
 21. Raurich JM, Pérez J, Ibáñez J, Roig S, Batle S. In-hospital and 2-year survival of patients treated with mechanical ventilation for acute exacerbation of COPD. *Arch Bronconeumol* 2004;40:295–300. [CrossRef]
 22. Celikel T, Sungur M, Ceyhan B, Karakurt S. Comparison of noninvasive positive pressure ventilation with standard medical therapy in hypercapnic acute respiratory failure. *Chest* 1998;114:1636–42. [CrossRef]
 23. Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: A multicentre randomised controlled trial. *Lancet* 2000;355:1931–5. [CrossRef]
 24. Garcia-Aymerich J, Serra Pons I, Mannino DM, Maas AK, Miller DP, Davis KJ, et al. Lung function impairment, COPD hospitalisations and subsequent mortality. *Thorax* 2011;66:585–90.
 25. Connors AF Jr, Dawson NV, Thomas C, Harrell FE Jr, Desbiens N, Fulkerson WJ, et al. Outcomes following acute exacerbation of severe chronic obstructive lung disease. The SUPPORT investigators (Study to understand prognoses and preferences for outcomes and risks of treatments) *Am J Respir Crit Care Med* 1996;154:959–67. [CrossRef]
 26. Eriksen N, Hansen EF, Munch EP, Rasmussen FV, Vestbo J. Chronic obstructive pulmonary disease. Admission, course and prognosis. *Ugeskr Laeger* 2003;165:3499–502.
 27. Siegelaa SE, Hoekstra JB, DeVries JH. Special considerations for the diabetic patient in the ICU; targets for treatment and risks of hypoglycaemia. *Best Pract Res Clin Endocrinol Metab* 2011;25:825–34. [CrossRef]
 28. Egi M, Bellomo R, Stachowski E, French CJ, Hart GK, Hegarty C, et al. Blood glucose concentration and outcome of critical illness: The impact of diabetes. *Crit Care Med* 2008;36:2249–55.
 29. Falciiglia 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;37:3001–9. [CrossRef]
 30. Graham BB, Keniston A, Gajic O, Trillo Alvarez CA, Medvedev S, Douglas IS, et al. Diabetes mellitus does not adversely affect outcomes from a critical illness. *Crit Care Med* 2010;38:16–24.
 31. Rady MY, Johnson DJ, Patel BM, Larson JS, Helmers RA. Influence of individual characteristics on outcome of glycemic control in intensive care unit patients with or without diabetes mellitus. *Mayo Clin Proc* 2005;80:1558–67. [CrossRef]
 32. Egi M, Bellomo R, Stachowski E, French CJ, Hart G. Variability of blood glucose concentration and short-term mortality in critically ill patients. *Anesthesiology* 2006;105:244–52.
 33. Krinsley JS. Glycemic variability and mortality in critically ill patients: The impact of diabetes. *J Diabetes Sci Technol* 2009;3:1292–301. [CrossRef]
 34. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, et al. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2008. *Intensive Care Med* 2008;34:17–60. [CrossRef]
 35. Jacob S, Nitschmann S. Intensive or conventional glucose control in critically ill patients: NICE-SUGAR (The normoglycemia in intensive care evaluation-survival using glucose algorithm regulation study). *Internist (Berl)* 2010;51:670, 672–3.
 36. Sechterberger MK, Bosman RJ, Oudemans-van Straaten HM,

- Siegelaar SE, Hermanides J, Hoekstra JB, et al. The effect of diabetes mellitus on the association between measures of glycaemic control and ICU mortality: A retrospective cohort study. *Crit Care* 2013;17:R52. [\[CrossRef\]](#)
37. Boussat S, El'rini T, Dubiez A, Depierre A, Barale F, Capellier G, et al. Predictive factors of death in primary lung cancer patients on admission to the intensive care unit. *Intensive Care Med* 2000;26:1811–6. [\[CrossRef\]](#)
38. Lin YC, Tsai YH, Huang CC, Hsu KH, Wang SW, Tsao TC, et al. Outcome of lung cancer patients with acute respiratory failure requiring mechanical ventilation. *Respir Med* 2004;98:43–51. [\[CrossRef\]](#)
39. Reichner CA, Thompson JA, O'Brien S, Kuru T, Anderson ED. Outcome and code status of lung cancer patients admitted to the medical ICU. *Chest* 2006;130:719–23. [\[CrossRef\]](#)
40. Soares M, Darmon M, Salluh JIF, Ferreira CG, Thiéry G, Schlemmer B, et al. Prognosis of lung cancer patients with life-threatening complications. *Chest* 2007;131:840–6. [\[CrossRef\]](#)
41. Adam AK, Soubani AO. Outcome and prognostic factors of lung cancer patients admitted to the medical intensive care unit. *Eur Respir J* 2008;31:47–53. [\[CrossRef\]](#)
42. Roques S, Parrot A, Lavole A, Ancel PY, Gounant V, Djibre M, et al. Six-month prognosis of patients with lung cancer admitted to the intensive care unit. *Intensive Care Med* 2009;35:2044–50. [\[CrossRef\]](#)
43. Toffart AC, Minet C, Raynard B, Schwebel C, Hamidfar-Roy R, Diab S, et al. Use of intensive care in patients with nonresectable lung cancer. *Chest* 2011;139:101–8. [\[CrossRef\]](#)
44. Azoulay E, Thiéry G, Chevret S, Moreau D, Darmon M, Bergeron A, et al. The prognosis of acute respiratory failure in critically ill cancer patients. *Medicine (Baltimore)* 2004;83:360–70.