

# Long-term Survival and Quality of Life among Survivors Discharged from a Respiratory ICU in North India: A Prospective Study

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## ABSTRACT

**Background:** Advancements in the intensive care unit (ICU) have improved critically ill subjects' short-term outcomes. However, there is a need to understand the long-term outcomes of these subjects. Herein, we study the long-term outcomes and factors associated with poor outcomes in critically ill subjects with medical illnesses.

**Materials and methods:** All subjects ( $\geq 12$  years) discharged after an ICU stay of at least 48 hours were included. We evaluated the subjects at 3 and 6 months after ICU discharge. At each visit, subjects were administered the World Health Organization Quality of Life Instrument (WHO-QOL-BREF) questionnaire. The primary outcome was mortality at 6 months after ICU discharge. The key secondary outcome was quality of life (QOL) at 6 months.

**Results:** In total, 265 subjects were admitted to the ICU, of whom 53 subjects (20%) died in the ICU, and 54 were excluded. Finally, 158 subjects were included: 10 (6.3%) subjects were lost to follow-up. The mortality at 6 months was 17.7% (28/158). Most subjects [16.5% (26/158)] died within the initial 3 months after ICU discharge. Quality of life scores were low in all the domains of WHO-QOL-BREF. About 12% ( $n = 14$ ) of subjects could not perform the activity of daily living at 6 months. After adjusting for covariates, ICU-acquired weakness at the time of discharge (OR 15.12; 95% CI, 2.08–109.81,  $p < 0.01$ ) and requirement for home ventilation (OR 22; 95% CI, 3.1–155,  $p < 0.01$ ) were associated with mortality at 6 months.

**Conclusion:** Intensive care unit survivors have a high risk of death and a poor QOL during the initial 6 months following discharge.

**Keywords:** Acute respiratory distress syndrome, Neuromuscular weakness, Critical care, Critically ill, Critically ill patients, Domiciliary ventilation, Delirium.

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## HIGHLIGHTS

- Intensive care unit survivors not only have a high risk of death after discharge but also a poor QOL.
- Presence of neuromuscular weakness and need for respiratory support was independently associated with mortality post-ICU discharge.

## INTRODUCTION

Critical illness is a significant public health issue because of the high mortality rate and sizeable healthcare costs. The in-hospital mortality is 12% for patients who receive critical care but can be as high as 30% in those with sepsis.<sup>1</sup> In the intensive care unit (ICU), ICU and in-hospital mortality are commonly used as quality indicators. At the same time, long-term outcomes are often not studied due to patient attrition during follow-up. However, ICU survivors are at an increased risk of mortality.<sup>2</sup> Intensive care unit survivors could have long-term physical impairments, profound neuromuscular weakness, exercise limitation, neuropsychological issues, and poor quality of life (QOL) after hospital discharge.<sup>3</sup> Factors attributed to unfavorable long-term outcomes among ICU survivors include age, the severity of illness at admission, duration of mechanical ventilation, ICU and hospital length of stay (LOS), presence of comorbid illness, and acquisition of ICU-acquired neuromuscular weakness.<sup>2,4–7</sup>

The impact of critical illness on the patients extends beyond the commonly assessed physical parameters. Post-intensive care

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syndrome (PICS) is the persistence or appearance of cognitive, psychiatric, and physical disabilities even after recovery from the primary critical illness and discharge.<sup>8</sup> Though few studies have evaluated the presence of neuropsychological and cognitive dysfunction separately, only a few have evaluated various parameters of morbidity in the same cohort of subjects.<sup>9–11</sup> Further, studies have focused on long-term outcomes in specific subpopulations [subjects with acute respiratory distress syndrome (ARDS), sepsis, and others]<sup>10,12</sup> or specific interventions such as mechanical ventilation or the use of sedatives.<sup>13,14</sup> But knowledge of long-term morbidity and neurocognitive functions is limited in

critically ill subjects due to medical illness.<sup>15–18</sup> We hypothesized that ICU survivors would have an increased risk of death and a poor QOL after ICU discharge. We aimed to evaluate the mortality and the morbidity [assessed by QOL measurement, respiratory physiology (spirometry and six-minute walk test)] at 6 months after discharge from the ICU.

## MATERIALS AND METHODS

The current study was a prospective observational study conducted between 1st August, 2016 and 30th June, 2017 in the respiratory intensive care unit (RICU) of our Institute. Respiratory intensive care unit is an eight-bedded unit with a patient-to-nurse ratio of 1:2–3 and two postdoctoral fellows round the clock. All subjects aged  $\geq 12$  years who were discharged from the ICU (ICU survivors) after an ICU stay of at least 48 hours were invited to participate in the current study. Patients admitted for observation after an intervention, immobile or had a tracheostomy at the time of ICU admission, had baseline neurocognitive impairment, were admitted at another ICU for  $\geq 48$  hours, had an active malignancy, and pregnant females were excluded from the current study.

The study was performed in-line with the principles of the Declaration of Helsinki. Written informed consent was obtained from all the study participants or next to kin to participate in the study. The study protocol was approved by the Institutional Ethics Committee (MK/2940/DM/1364). We have reported the study according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.<sup>19</sup>

### The Severity of Illness and Course during the Hospital Stay

We entered the daily patient data using a specifically designed computer software, as previously described.<sup>20,21</sup> Briefly, data were recorded at the time of RICU admission and after that every 24 hours. The worst value for each variable during the 24 hour was recorded. The time interval from RICU admission to 8:00 AM the next day was defined as day 0 (initial 24 hours). Values during the initial 24 hours were entered into a specifically designed software to calculate the baseline acute physiology and chronic health evaluation (APACHE II) scores and sequential organ-failure assessment (SOFA) scores. Subsequent calendar days were timed from 8:00 AM to 8:00 AM of the next day. Delta SOFA was calculated by subtracting the baseline SOFA score from the maximum SOFA score during the RICU stay.<sup>22</sup>

We also recorded the following information: (a) Baseline demographic profile; (b) Presence of comorbid illness and Charlson's Comorbidity Index (CCI);<sup>23</sup> (c) Indication for ICU admission; (d) Type of respiratory support (oxygen supplementation, positive-pressure ventilation); (e) Duration and dose of sedative and neuromuscular blocking agent used; (f) ICU and hospital LOS; (g) Requirement for renal-replacement therapy, vasopressor support, and tracheostomy during ICU stay; (h) Hospital-acquired infections; (i) The final diagnosis; and (j) The outcome (died, discharged with support [oxygen supplementation, home ventilation] or discharged without support). All patients received the standard care as per the ICU protocol, including enteral feeding, deep venous thrombosis, and stress ulcer prophylaxis.<sup>24–27</sup>

### Assessment at Discharge and Follow-up

The subjects were assessed at three monthly interval for 6 months after hospital discharge. All the subjects were telephonically contacted and requested for follow-up in the chest clinic. The

following information was obtained from those who agreed to follow-up:

**Neuromuscular weakness assessment:** It was assessed by clinical examination using the Medical Research Council (MRC) score. This score assigns a value between 0 (no contraction at all) and 5 (normal muscle strength) for each of the 12 muscle groups, including shoulder abductors, elbow flexors, wrist extensors, hip flexors, knee extensors, and dorsiflexors of the ankle; all scored bilaterally. The total score ranges between 0 and 60, and ICU-acquired weakness (ICUAW) was diagnosed if the total score was  $< 48$ .<sup>28</sup>

**Quality of life (QOL):** It was assessed by the World Health Organization Quality of Life Instrument (WHO-QOL-BREF), the Hindi version for those who visited the chest clinic at follow-up.<sup>29,30</sup> The WHO-QOL-BREF is an abbreviated version of the WHOQOL-100, which is a validated questionnaire and can be used in specific cultural settings to collect data suitable for subsequent comparison.<sup>29,31</sup> The questionnaire comprises 26 items that measure four domains (physical health, psychological health, social relationships, and environment).<sup>32</sup> It was administered to all the subjects at follow-up, and they were asked to fill out the questionnaire. It was assisted by the interviewer only if they could not read or write. The four domain scores denote an individual's perception of QOL in each domain. Domain scores are scaled in a positive direction (i.e., higher scores indicate good QOL while lower scores indicate poor QOL). The mean score of items within each domain was used to calculate the domain score. Mean scores were multiplied by 4 to obtain transformed scores and make them comparable with the scores used in the WHOQOL-100.

**Respiratory physiology:** It was assessed by spirometric lung function tests [forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC)] and a six-minute walk test.<sup>33</sup>

We also assessed the patient's ability to ambulate and perform activities of daily living (ADL) without assistance.

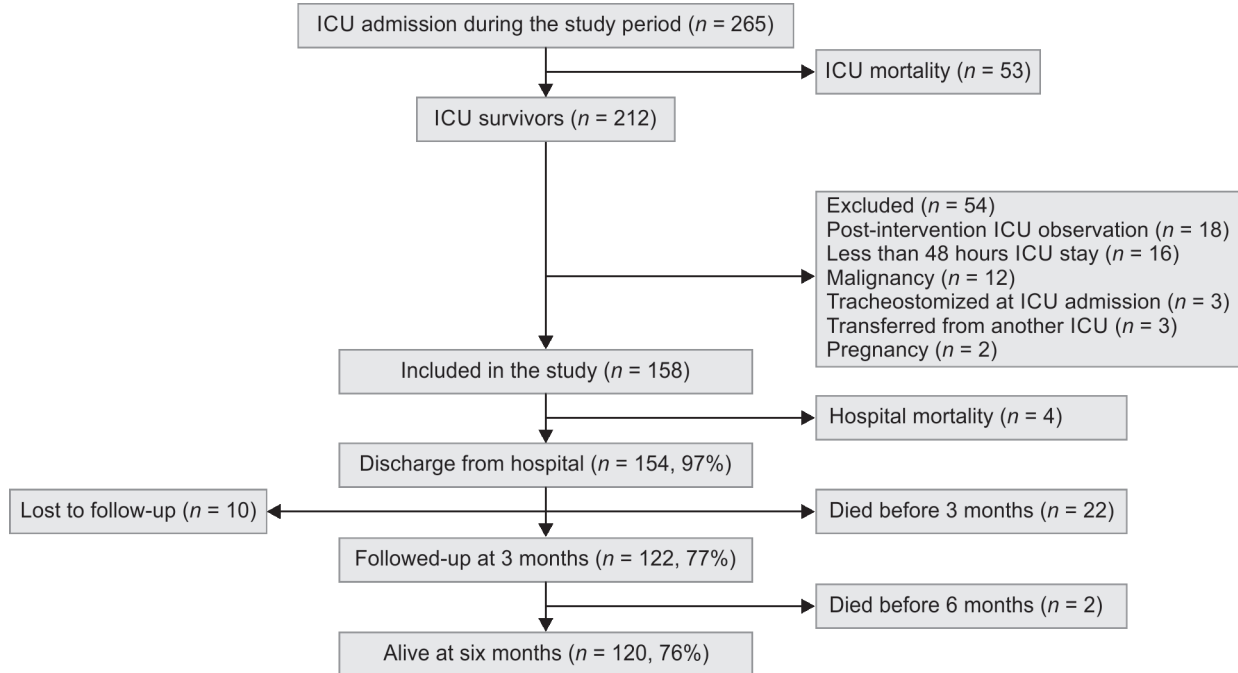
### Variables and Study Objective

The primary exposure was APACHE II at admission. Other markers of severity of critical illness were also tested in the univariate analysis: baseline SOFA score, delta SOFA score, and cause of ICU admission. The potential confounders were age, sex, major comorbidity (diabetes mellitus, hypertension, obesity, coronary artery disease, chronic kidney disease, chronic liver disease, or obstructive airway disease), a requirement of advanced respiratory support, need for renal-replacement therapy, duration of invasive mechanical ventilation, the dose of sedatives and neuromuscular blocking agents used, ICU and hospital LOS, and development of hospital-acquired infections. The primary objective was to study the mortality at 6 months after ICU discharge. The secondary outcomes were the QOL WHO-QOL-BREF the physical dysfunction, neuromuscular weakness (assessed by MRC), and the lung functions (spirometry) at 6 months after discharge from ICU. In addition, we studied the factors associated with mortality and poor QOL at 6 months after discharge.

### Statistical Analysis

It was performed using a statistical software package (IBM SPSS for Windows, version 23.0; Armonk, NY, United States). Descriptive frequencies were expressed using the mean [standard deviation (SD)] and the median [interquartile range (IQR)]. Differences between the categorical and continuous variables were compared

**Flowchart 1:** Flow diagram depicting the flow of subjects during the study



using the Chi-square test and the *t*-test (or Mann–Whitney *U* test), respectively. A multivariate logistic regression analysis was performed to assess the factors associated with mortality at 6 months after discharge from the hospital. We entered clinically relevant variables for the multivariate regression analysis (gender, presence of delirium, baseline APACHE II score, delta SOFA, CCI, need for IMV, presence of HAI, hospital LOS, presence of ICUAW, and the need for home ventilation). We performed univariate and multivariate linear regression analysis to determine the factors affecting the different domains of WHOQOL-BREF as described previously.<sup>10,34</sup> The dependent variable was the domain of WHOQOL-BREF at 3 or 6 months and the independent variables were gender, delta SOFA, days in hospital, and others. A *p*-value of less than 0.05 was considered statistically significant.

## RESULTS

During the study period, 265 patients were admitted to the ICU. Fifty three (20%) died during the ICU stay. Of the 212 subjects transferred out of the ICU, 54 were excluded, and 158 were enrolled in the current study (Flowchart 1). Four subjects died in hospital after discharge from ICU. In total, 154 subjects were finally discharged from the hospital. The mean (SD) age of the study population [73 (46.2%) males] was 47.9 (19.8) years (Table 1). The most common indication for admission to ICU was acute respiratory failure (*n* = 126, 79.7%), followed by sepsis and altered mentation (Table 1). The baseline acute physiology and chronic health evaluation II (APACHE II) score was 14.3 (6.7), with predicted hospital mortality of 25%. The median (IQR) CCI was 2 (0–3); 59.5% (*n* = 94) of subjects had at least one comorbid illness that included chronic respiratory disease, chronic kidney disease, chronic heart disease, diabetes mellitus, or immunosuppressive therapy (Table 1).

Most subjects required assisted ventilation [invasive, 109 (69%); noninvasive, 40 (25.3%)] with a median (IQR) duration of 116 (64–219) hours. Vasopressor requiring shock and renal failure requiring renal-replacement therapy were present in 58 (36.7%) and 13 (8.2%) subjects, respectively. The median (IQR) ICU and hospital LOS were 6 (4–10) and 12 (7–19) days, respectively. Tracheostomy was performed in 15 (9.5%) patients. ICUAW [MRC <48; mean (SD), 40.4 (7)] was seen in 40.5% (64/158) at the time of discharge. Twenty-five subjects (13 with tracheostomy) were discharged with support [oxygen supplementation or home NIV (*n* = 23)].

### Mortality at Six Months Follow-up of ICU Survivors

Ten patients were lost to follow-up at 3 months, while 26 (out of 148, 17.6%) died at 3 months. At 6-month follow-up, two subjects died additionally [6 months mortality of 18.9%, (28/148)]. Assuming the worst-case scenario for those lost to follow-up, the mortality at 6 months for ICU survivors would have been 24% (38/158). The overall mortality at 6 months (including those who died in hospital) was 30.5% (81/265). The overall mortality at 6 months after including 10 subjects lost to follow-up and assuming the worst-case (all died) scenario would be 34.3% (91/265).

### Quality of Life (QOL)

The in-person follow-up rate at 3 and 6 months was 73.8% (90/122) and 55.8% (67/120), respectively. The details of QOL scores are shown in Table 2. All four domains were less than the normal cutoff in the general population.<sup>35</sup> The most severely affected domains were the physical, psychological, and social. All the domains showed an improving trend at 6 months, however, they were still lower than the general norms of the individual domains (Table 3).<sup>35</sup> Factors affecting the individual components of the QOL are described in supplemental tables 1–4. The physical domain was affected by age, duration of mechanical ventilation, use of



**Table 1:** Baseline characteristics of the study cohort (n = 158)

Variables	N (%)
Age in years, mean (SD)	47.9 (19.8)
Male gender	73 (46.2)
<i>Indications for ICU admission</i>	
Respiratory failure	126 (79.7)
Sepsis and multiorgan dysfunction	30 (19)
Coma	2 (1.3)
<i>Diagnosis</i>	
AECOPD/Bronchial asthma	41 (26)
Acute febrile illness	33 (20.9)
Community-acquired pneumonia	19 (12)
Acute decompensated heart failure	9 (5.7)
Pulmonary tuberculosis	9 (5.7)
Obesity hypoventilation syndrome	7 (4.4)
Urosepsis	5 (3.2)
Neuromuscular weakness (LGBS, MG, CIDP)	5 (3.2)
Poisoning	5 (3.2)
Neuroparalytic snake envenomation	5 (3.2)
Others (PTE, bronchiectasis, ILD, SLE)	20 (12.6)
<i>Severity of illness at admission, mean (SD)</i>	
Baseline APACHE II score	14.3 (6.71)
Baseline SOFA	5.5 (3.05)
<i>Comorbid illness</i>	
Chronic respiratory disease	69 (43.7)
Chronic kidney disease	9 (5.7)
Congestive cardiac failure	25 (15.8)
Diabetes mellitus	30 (19)
Connective tissue disease	6 (3.8)
Charlson's comorbidity index, median (IQR)	2 (0–3)
<i>Type of respiratory support</i>	
Oxygen supplementation	9 (5.7)
Noninvasive ventilation	40 (25.3)
Invasive mechanical ventilation	109 (69)
Duration of IMV in hours, median (IQR)	116 (64–219)
<i>Intensity of care</i>	
Shock requiring vasopressors for at least 1 hr	58 (36.7)
Central venous catheter	80 (50.6)
Renal-replacement therapy	13 (8.2)
Tracheostomy	15 (9.5)
<i>Dosage of sedatives</i>	
Midazolam in mg, mean (SD)	108 (226.5)
Fentanyl in µg, mean (SD)	272.3 (627.4)
<i>Dosage of neuromuscular blocking agents</i>	
Vecuronium in mg, mean (SD)	11.1 (37.8)
Atracurium in mg mean (SD)	32.4 (283.2)
<i>Outcome</i>	
ICU LOS days, median (IQR)	6 (4–10)
Hospital LOS days, median (IQR)	12 (7–19)
Discharge on home ventilation	23 (14.5)

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; APACHE, acute physiology and chronic health evaluation; CIDP, chronic inflammatory demyelinating polyneuropathy; ICU, intensive care unit; IQR, interquartile range; ILD, interstitial lung disease; IMV, invasive mechanical ventilation; LGBS, Landry Guillain–Barre syndrome; LOS, length of stay; MG, myasthenia gravis; PTE, pulmonary thromboembolism; SD, standard deviation; SLE, systemic lupus erythematosus; SOFA, Sequential Organ Failure Assessment

**Table 2:** Survival, quality of life, lung functions, and six-minute walk distance of subjects at 3 and 6 months follow-up

	3 months	6 months
Number alive	122	120
No. on tracheostomy	1 (0.8)	1 (0.8)
Proportion of subjects not able to perform ADL, n (%)	16 (13.3)	14 (11.7)
MRC score	58.3 (4.6)	59.1 (3.4)
QOL domains (WHOQOL BREF) at 3 months (n = 90) and 6 months (n = 67)		
Overall perception of QOL	79.6 (17.4)	76.6 (18.1)
Overall perception of health	74.4 (22.8)	75.2 (19.9)
Physical health	59.8 (17.1)	63 (17.5)
Psychological health	64.1 (16.9)	64.9 (16)
Social relationships	68.9 (22.4)	69.4 (21.)
Environment	63.5 (15.6)	65.1 (16.7)
Spirometry variables at 3 months (n = 74) and 6 months (n = 63)		
FVC, in liters	2.4 (0.8)	2.6 (0.8)
FEV1, in liters	1.8 (0.9)	2 (0.9)
FVC, % predicted	74.9 (20.4)	81.9 (21.6)
FEV1, % predicted	72 (30.1)	79.7 (31.2)
PEFR, in liters	293.3 (127.7)	316.2 (119.6)
FEF 25–75, in liters	134.7 (98.2)	142.1 (92.2)
Six-minute walk distance (6MWD) at 3 months (n = 79) and 6 months (n = 65)		
6MWD, in meters	407.3 (119)	424.5 (98.4)
6MWD, % predicted	77.2 (19.7)	79.6 (16)
Desaturation <88%, n (%)	9 (11.3%)	5 (7.6%)

Values are provided as mean (SD) unless otherwise specified; QOL, quality of life; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; PEFR, peak expiratory flow rate; FEF 25–75, forced mid-expiratory flow, ADL, activities of daily living; MRC, Medical Research Council

**Table 3:** Proportion of subjects with a good (score ≥70) quality of life at 3 and 6 months follow-up

Domain	3 months (n = 90)	6 months (n = 67)
Physical	24 (26.7)	25 (37.3)
Psychological	41 (45.6)	31 (46.3)
Social	50 (56.2)	37 (56.1)
Environment	33 (36.7)	29 (43.3)

Values are provided as number (percentage)

neuromuscular blocking agents, and the MRC score at the time of ICU discharge. The psychological and the social domains were affected by age and neuromuscular blocking agents, respectively. The environmental domain was affected by age and the MRC score at ICU discharge.

### Spirometric Lung Function

Spirometry could be performed by 74 and 63 patients at 3 and 6 months, respectively (Table 2). The mean (SD) percentage of predicted FVC at 3 months was 74.9% (20.4%), and the mean (SD) percentage of predicted FEV1 at 3 months was 72% (30.1%). These

**Table 4:** Comparison of demographics, comorbidity, and ICU variables amongst survivors and nonsurvivors at 6 months

	Survivors (n = 120)	Nonsurvivors (n = 28)	p-value	aOR (95% CI)
<i>Demographics</i>				
Age in years	45.6 (18.8)	61.36 (20.3)	<0.01	
Male sex, n (%)	53 (44)	13 (46)	0.82	1.30 (0.26–6.62)
<i>Organ failure at ICU admission</i>				
ARDS, n (%)	30 (25)	3 (11)	0.10	
Acute kidney injury, n (%)	33 (27.5)	13 (46.4)	0.051	
Shock, n (%)	41 (34)	15 (53.5)	0.057	
Renal replacement therapy, n (%)	5 (0.4)	7 (25)	<0.01	
Delirium, n (%)	28 (23.3)	18 (64.2)	<0.01	1.88 (0.41–8.71)
Baseline APACHE II score	13.3 (6.3)	19.1 (6.12)	<0.01	1.1 (0.9–1.3)
Delta SOFA	1.8 (2.4)	3.1 (3.2)	0.02	1.1 (0.8–1.5)
Charlson's comorbidity index	1.7 (1.8)	3.5 (2.4)	<0.01	1.4 (0.9–2.2)
<i>Mechanical ventilation</i>				
Invasive MV, n (%)	79 (65.8)	21 (75)	0.717	1.38 (0.24–7.97)
Hours of IMV	130.7 (108.6)	502.1 (427.7)	<0.01	
No. of days on sedation	1.2 (2)	1.7 (2.6)	0.30	
Subjects who received sedation, n (%)	58 (48)	17 (61)	0.29	1.2 (0.2–8.3)
No. of days on NMBs	0.3 (1.2)	0.5 (0.1)	0.36	
Subjects who received NMBs, n (%)	26 (22)	2 (7)	0.10	
Midazolam in mg, mean (SD)	184.7 (225.9)	316.2 (439.5)	0.01	
Fentanyl in µg, mean (SD)	460.8 (687.1)	376.5 (755)	0.68	
Vecuronium mg, mean (SD)	42.6 (72.9)	126 (93.3)	0.65	
Atracurium mg, mean (SD)	170.8 (687.1)	87.5 (123.7)	0.65	
<i>Course during hospital stay</i>				
ICU LOS	7.1 (5.7)	21.0 (17.3)	<0.01	
Hospital LOS	13.1 (9.2)	35.5 (31.1)	<0.01	1 (0.96–1.1)
HAI in ICU, n (%)	8 (6.7)	10 (35.7)	0.560	1.5 (0.2–14.6)
Ventilator-associated pneumonia, n (%)	5 (4)	9 (32)	<0.01	
Tracheostomized in ICU, n (%)	1 (0.1)	14 (50)	<0.01	
MRC score	52.4 (10)	36.7 (8.2)	<0.01	0.9 (0.8–0.9)
ICUAW, n (%)	41 (34.1)	23 (82)	<0.01	15.12 (2.08–109.81)*
Home ventilation, n (%)	7 (5.8)	16 (57)	<0.01	22 (3.1–155)*

\*p-value <0.05. Values are provided as mean (SD) unless otherwise specified

aOR, adjusted Odds ratio; APACHE, acute physiology and chronic health evaluation; ARDS, acute respiratory distress syndrome; CI, confidence interval; ICU, intensive care unit; HAI, hospital-acquired infection; ICUAW, ICU-acquired weakness; IMV, invasive mechanical ventilation; IQR, interquartile range; LOS, lengths of stay; MRC, medical research council; SOFA, Sequential Organ Failure Assessment; NMBs, neuromuscular blockade agents

values of FVC and FEV1 improved at 6-month visit to 81.9% (21.6%) and 79.7% (31.2%), respectively. The mean values of other variables at 3 and 6 months are shown in Table 2.

### Physical Activity

Six-minute walk test could be performed in 79 and 65 patients at 3 and 6 months, respectively (Table 2). Eleven and two subjects at 3- and 6-months, respectively, could not perform a six-minute walk test as they used a wheelchair. The mean (SD) walk distance at 3 and 6 months was 407.3 (119) meters and 424.5 (98.4) meters, respectively. The mean (SD) percentage-predicted walk distance was 77.2% (19.7%) and 79.6% (16%) at 3 and 6 months, respectively. Nine (11%) and 5 (8%) at 3 and 6 months, respectively, experienced desaturation (SpO<sub>2</sub> <88% on pulse oximetry) during the six-minute walk test.

Among 120 survivors who were followed up either through OPD visit or telephonically, 14 (11.7%) were still unable to walk

independently and required assistance to carry out activities of daily living. Twenty (16.7%) subjects had not resumed their occupation. The median (IQR) time to recovery of routine activity was 30 (30–60) days.

### Comparison of Survivors with Non-survivors at 6 Months

Information from 148 subjects was available (10 subjects lost to follow-up) for this analysis. Subjects who died at 6 months were significantly older, had a higher APACHE-II score, delta SOFA score, and higher CCI score than the survivors (Table 4). The nonsurvivors also had a significantly longer duration of MV, longer ICU, and hospital LOS. A higher proportion of nonsurvivors had suffered from ventilator-associated pneumonia, delirium, and ICUAW during their ICU stay. The presence of ARDS, shock, or acute kidney injury at the time of ICU admission was not different between survivors and nonsurvivors. On multivariate logistic regression analysis,



the presence of ICU-acquired weakness at discharge (OR 15.12; 95% CI, 2.08–109.81,  $p < 0.01$ ) and the need for home MV (OR 22; 95% CI, 3.1–155,  $p < 0.01$ ) were associated with mortality at 6 months (Table 4).

## DISCUSSION

The results of our study suggest that 19% of the subjects discharged from the ICU die within 6 months. Notably, 12% of those who survived still required assistance in daily living activities, and a majority had a poor QOL. The physical and psychosocial domains were the most affected domains of QOL, mainly due to the persistence of muscle weakness. After adjusting for the covariates, neuromuscular weakness at the time of discharge and the need for home mechanical ventilation were associated independently with post-ICU mortality.

Intensive care unit mortality is one of the most used primary outcomes in studies involving critically ill subjects. However, location-based mortality (ICU and hospital mortality) alone has the risk of underestimating the mortality and primarily depends on case mix, the severity of illness, discharge bias, and others.<sup>36,37</sup> The duration-dependent mortality rates (30- or 90-day mortality) are likely to capture the consequence of critical illness on survival.<sup>36,37</sup> This was highlighted in the current study, where 90- and 180-day mortality was higher than the ICU mortality like previous studies.<sup>38,39</sup> The results of the current study are also similar to a recent multicenter study from Japan.<sup>40</sup> In our cohort, the presence of ICUAW at the time of discharge was an independent predictor of mortality at 6 months after ICU discharge, similar to previous studies.<sup>41</sup> Another factor associated with higher 6-month mortality was the need for home ventilation.<sup>42–44</sup> The common indications for home ventilation were difficult weaning and persistent weakness, suggesting the consequence of critical illness rather than the comorbid illness responsible for mortality after hospital discharge.

Survival alone, however, is an inadequate measure of patient-centered outcomes.<sup>15</sup> Apart from the risk of higher mortality, critically ill subjects who survive are known to have a poor QOL than the general population.<sup>45,46</sup> The QOL tends to improve with time, but this improvement is not uniform across domains.<sup>46</sup> In our study, we found that all the ICU survivors had a poor QOL score in all four domains (physical, psychological, social relationship, and environmental). The physical domain was mainly affected due to the presence of muscle weakness and nonspecific pains. The psychological domain was primarily affected by negative feelings and low self-esteem. The environmental domain was mainly affected by the financial burden due to the inability to return to work, this suggests that most subjects continue to have a poor QOL after critical illness. We do not know how long it takes for full recovery as the follow-up was limited to 6 months. Previous studies have shown that the QOL among ICU survivors had a complete recovery after adjusting for the coexisting conditions.<sup>47,48</sup> The presence of comorbid illness did not affect the QOL in our cohort on a multivariate regression analysis. This could be due to the difference in the case-mix and indication for ICU admission.

The mean FVC and FEV1 of survivors and 6MWD at follow-up were lower than 80% of predicted values and tended to normalize by 6 months, similar to previous studies.<sup>10,49,50</sup> However, unlike previous studies that included only subjects with ARDS, about 40% of the subjects in the current study had a chronic respiratory disease.

Also, some of our patients were unable to perform spirometry due to tracheostomy, the persistence of muscle weakness, and other factors.

Our study has a few limitations, the major limitation being the lack of baseline QOL measurement and muscle weakness, hence, it is difficult to determine whether QOL decrements and weakness at follow-up reflect the impact of critical illness or simply a lower baseline value, especially in those with underlying diseases. We have not assessed the cognitive function of subjects at follow-up. Moreover, follow-up of 6 months may be too short, though an ideal time of follow-up is not yet determined. The data are limited to medically ill patients and cannot be extrapolated to all ICU populations. About 40% of the subjects did not consent to in-person follow-up, however, this is a real-world scenario where many patients do not come for follow-up after discharge. Also, we assumed a worst-case scenario for those lost to follow-up. Finally, we did not record the details of treatment received by individual patients after discharge. It is likely that the clinical outcomes may be better in those who underwent physical rehabilitation and physiotherapy compared with those who did not receive physical rehabilitation. The strength of the study is the assessment of critically ill subjects both by objective measures (spirometry, 6-minute walk test, MMRC) and the use of a more holistic measure of QOL (WHO-QOL), unlike previous studies that have used other QOL measures (SF-36, EQ-5D, and others) that may not capture all the domains of QOL.<sup>40,51</sup>

## CONCLUSION

In conclusion, critically ill subjects in our cohort had high mortality and poor QOL after discharge from the hospital. The presence of neuromuscular weakness and the need for respiratory support independently predict mortality post-ICU discharge.

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## SUPPLEMENTARY MATERIAL

All the supplementary material from Supplementary 1 to 4 tables is available online on the website of [www.IJCCM.org](http://www.IJCCM.org)

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