Postintensive care syndrome in mechanically ventilated patients secondary to respiratory disorders

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Background Patients admitted to ICU, especially those who are mechanically ventilated, are under the effects of many clinical, therapeutic, and emotional stress factors that usually lead to different physical, psychological, and cognitive disabilities. These acquired disabilities are called postintensive care syndrome (PICS).

Objective the aim was to detect any component of PICS in mechanically ventilated patients at respiratory ICU (RICU) after being discharged from ICU.

Patients and methods All recruited patients were assessed at three time points: first during admission to RICU, where all clinical and laboratory data were recorded; second following discharge from RICU, and third following 1 month of discharge from hospital. During the second and third points, cognitive, psychological, and physical components of PICS were assessed.

Results A total of 20 (50%) patients developed one or more component of PICS. There were highly significant differences between patients with and without PICS regarding age, duration of mechanical ventilation, duration of ICU admission, level P_aO_2, acute physiology and chronic health evaluation (APACHE) IV score, the presence of co-morbidities, and the process of weaning. There were highly significant positive correlations between age of patients, duration of mechanical ventilation and ICU stay, and the score of APACHE IV and the development of PICS, whereas there was a highly significant negative correlation regarding the level of P_aO_2.

Conclusion Patients with respiratory disorders admitted to the RICU should be evaluated and followed up for the detection of any components of PICS especially those who are old adult, have prolonged intubation or ICU stay, have co-morbidities, high APACHE IV score, and persistent hypoxemia.

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Introduction

Critical care medicine has been advancing with improved prognosis following ICU admissions, which has led to the discovery of different disabilities that ICU admitted patients experience. This discovery has led to research studies that are focused on the rapid healthy recovery and long-term prognosis for those patients [1]. Admitted patients at ICU in hospitals usually develop different disabilities, which include physical disorders, psychological alterations, or cognitive abnormalities. These disabilities are known as postintensive care syndrome (PICS) and occur after being discharged from hospitals [2]. The previous disabilities usually lead to difficulties in patients' daily lives following discharge from hospitals and affect their quality of life. Duration of ICU admission and also hospital stay are usually the causes [3]. PICS describes the remaining disabilities in patients who survive following ICU admission and includes the impairment of their physical power, psychological status, and cognitive abilities. Regarding families of patients admitted to ICU, the term 'post-intensive care syndrome-family (PICS-F)' includes the impairment of the psychological status of family members of the ICU survived patients [4,5].

The impairment of physical status includes the ICU-acquired generalized neuromuscular weakness, whereas the impairment of cognitive abilities includes the ICU-acquired deficiency in the process of thinking and judgment, and the impairment of psychological health includes mental health status affection developed after discharge from ICU [4,5]. PICS-F includes the acute and chronic psychological effects that are acquired by the family during ICU admission of their member, and also following their member discharge or even death. The incidence of PICS-F may reach 30% [6,7]. The incidence and prevalence of PICS are still unknown despite the well-known physical, psychological, and cognitive disabilities that occur during and following ICU stay [1]. PICS varies in presentation and can include one or combination of the previous mentioned disabilities. Moreover, the symptoms may occur during, just after discharge, or long periods following discharge from ICU. Beside

that symptoms may disappear rapidly or last for many years following discharge [8,9]. Easy fatigability, generalized muscle weakness, depression, anxiety, sleep pattern abnormalities, disturbed memory, slow process of thinking, and poor concentrations are the common symptoms of PICS [1].

Aim

The aim was to detect any component of PICS in mechanically ventilated patients at respiratory ICU after being discharged from ICU and 1 month following discharge from hospital.

Patients and methods

This study included 40 patients weaned off invasive mechanical ventilation (MV) secondary to a respiratory disorder. Patients were recruited from the Respiratory ICU (RICU), Menoufia University Hospitals, from November 2016 to April 2018. The study protocol was approved by the Ethics Committee of Menoufia University Hospitals, and before enrollment, an informed consent was obtained from the patients or patients' families.

Exclusion criteria were as follows: (a) mechanically ventilated patients owing to nonrespiratory causes, (b) patients who only received noninvasive ventilation, (c) patients who did not complete the whole steps of the study, and (d) patients with past history of psychological disorders.

To be included in this study, all recruited patients were assessed at three time points:

(1) During invasive MV, where the following data were obtained:
  (a) Clinical and laboratory data, including sex, age, original disorder, comorbidities, duration of MV, duration of RICU admission, the weaning process, and arterial blood gases.
  (b) Acute physiology and chronic health evaluation (APACHE) IV score to assess the severity of critically ill patients was calculated for all recruited patients. The APACHE IV scoring system uses the worst physiological measurements on day 1 of ICU admission: pulse rate, respiratory rate, mean blood pressure, temperature, PaO_2, FiO_2, $PaCO_2$, sodium, bilirubin, blood urea nitrogen, creatinine, albumin, glucose, hematocrit, white blood cells, urine output, acid-base abnormalities, and neurologic

assessment by the Glasgow coma scale. Other variables used in the prediction model were source of ICU admission, chronic health status, reason for ICU admission, length of hospitalization before ICU admission, whether the patient received MV, or required emergency surgery or thrombolysis. The data for APACHE IV were calculated using the APACHE IV calculator [10].

(2) First day after discharge from RICU: criteria of PICS were assessed, which included the following:
  (a) Cognitive status: included delirium and dementia:
    (i) Delirium was assessed using Confusion assessment method, The Confusion assessment method includes four features found to have the greatest ability to distinguish delirium from other types of cognitive impairment [11].
    (ii) Dementia was assessed using the Mini Mental State Examination questionnaire for screening of dementia. For the illiterate people, the writing and reading parts of the Mini Mental State Examination were excluded, and the full score was calculated as 28 instead of 30 points [12].
  (b) Psychological status: includes depression and anxiety:
    (i) Depression was assessed using Hamilton depression rating scale [13] The Hamilton depression rating scale is designed to rate the severity of depression in patients. Although it contains 21 areas, it calculates the patient's score on the first 17 answers, where score 0–7: normal; 8–13 mild depression; 14–18: moderate depression; 19–22: severe depression; and score greater than or equal to 23: very severe depression [13].
    (ii) Anxiety was assessed using Hamilton anxiety rating scale. The scale consists of 14 items, each defined by a series of symptoms, and measures both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety). Each item is scored on a scale of 0 (not present) to 4 (severe), with a total score range of 0–56, where less than 17 indicates mild severity, 18–24 mild to moderate severity, and 25–30 moderate to severe [14].

(c) Physical status: includes neuromuscular status
   (i) It was made by bedside evaluation of the muscle strength with the use of the Medical Research Council (MRC) sum score. This score appoints a value between 0 (no contraction at all) and 5 (normal muscle strength) for each of 12 muscle groups, including shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension, and dorsiflexion of the ankle, all scored bilaterally. The sum score ranges between 0 and 60, and ICU-associated weakness (ICUAW) was diagnosed with a total less than 48 [15].

(3) One month after discharge from hospital: the three components of PICS (cognitive, psychological, and physical health status) were reassessed for all recruited 40 patients after 1 month of discharge from hospital [11–15].

Statistical analysis

Data were coded and analyzed using SPSS 17 (SPSS Inc., Chicago, Illinois, USA). Results are presented as mean value±SD or percentages. Standard t-test or χ^2-test was used for group comparisons. Correlations were done using Pearson's correlation. All these tests were used as tests of significance at P less than 0.05.

Results

This prospective cohort observational analytical study included 40 weaned mechanically ventilated patients secondary to a respiratory disorder cause. This study included 26 males and 14 females, with a mean age of 57.85±16.67 years. Of the 40 patients, 11 had chronic obstructive airway disease, seven had interstitial lung disease, six had obstructive sleep apnea, four had bronchial asthma, three patients had pneumonia, and two of the remaining four patients had adult respiratory distress syndrome (ARDS) and two had bronchiectasis. Regarding the weaning process, 25 patients were weaned easily. The mean MV duration was 6.025 days, whereas the mean ICU stay was 8.852 days. A total of 20 patients developed one element or more of PICS either rapidly following weaning or lately following 1 month from weaning. (Table 1) Regarding the onset of elements of PICS, there were 15 cases that developed delirium at day 1 following discharge from RICU, eight cases of them continued for 1 month, and in seven cases, the delirium disappeared. Moreover, there were three cases that developed dementia at day 1, two of the improved at 1 month, whereas four new cases developed a new-onset dementia at 1 month.

Table 1 General characteristics of the studied groups

Age (mean±SD)	57.85±16.67
Sex	
Male	26
Female	14
MV duration (mean) (days)	6.025
ICU duration (mean) (days)	8.852
APACHE IV score (mean)	52.45
PaO_2 (mean) (mmHg)	46.15
$PaCO_2$ (mean) (mmHg)	62.475
pH	7.33
Original disease (N)	
COPD	11
Overlap	5
OSA	6
Pneumonia	3
Bronchiectasis	2
ILD	7
ARDS	2
BA	4
Comorbidity (N)	
Present	24
Absent	16
Normal	27
Weaning (N)	
Prolonged	15
Easy	25
PICS (N)	
Present	20
Absent	20

APACHE, acute physiology and chronic health evaluation; ARDS, adult respiratory distress syndrome; BA, bronchial asthma; COPD, chronic obstructive airway diseases; ILD, interstitial lung diseases; MV, mechanical ventilation; OSA, obstructive sleep apnea; $PaCO_2$, arterial carbon dioxide tension; PaO_2, arterial oxygen tension; PICS, postintensive care syndrome.

Regarding depression, of the seven cases that developed depression at day 1, only two cases improved at 1 month, whereas five new cases developed a new-onset depression at 1 month. All the nine cases that developed anxiety at day 1 improved with no newly developed cases at 1 month. Nine of the 16 cases that developed physical affection at day 1, had suffered from it at 1 month, with no newly developed new cases. (Table 2) Comparing the patients who developed and those who did not developed PICS, there were highly significant differences between both groups regarding age, duration of MV, duration of ICU admission, level PaO_2, APACHE IV score, the presence of co-morbidities, and the process of weaning, whereas there were nonsignificant differences between both groups regarding sex, original disease, level of $PaCO_2$, and level of PH. (Table 3) Regarding the correlation between different studied parameters and the group of patients who developed any element of PICS, there were highly significant positive

Table 2 Timing of postintensive care syndrome

PICS	Day 1 (*N*)	1 month		
		Disappeared	Continued from day 1	Newly developed
Delirium	15	7	8	0
Dementia	3	2	1	4
Depression	7	2	5	5
Anxiety	9	9	0	0
Physical affection	16	7	9	0

PICS, postintensive care syndrome.

Table 3 Comparison between patients with and without postintensive care syndrome

Groups	With PICS (*n*=20)	Without PICS (*n*=20)	*t*-Test	*P* value
Age	62.55	53.15	3.219	0.003**
MV duration	7.95	4.1	6.614	0.000**
ICU duration	11.4	6.25	6.76	0.000**
APACHE	65.75	39.15	6.386	0.000**
PaO_2	44.65	47.65	2.85	0.007**
$PaCO_2$	65.7	59.25	0.764	0.449
pH	7.32	7.34	0.357	0.723
Group	Positive	Negative	χ^2	*P* value
Original disease				
COPD	5	6	11.9	0.104
Overlap	5	0		
OSA	2	4		
Pneumonia	0	3		
Bronchiectasis	1	1		
ILD	4	3		
ARDS	2	0		
BA	1	3		
Comorbidity				
Present	16	8	6.667	0.01**
Absent	4	12		
Normal	7	20		
Weaning				
Prolonged	15	0	24	0.000**
Easy	5	20		
Sex				
Male	15	11	1.578	0.32
Female	5	9		

ARDS, adult respiratory distress syndrome; APACHE, acute physiology and chronic health evaluation; BA, bronchial asthma; COPD, chronic obstructive airway disease; ILD, interstitial lung disease; MV, mechanical ventilation; OSA, obstructive sleep apnea; PICS, postintensive care syndrome. *Significant. **Highly significant.

correlations regarding age of patients, duration of MV and ICU stay, and the score of APACHE IV. However, there was a highly significant negative correlation regarding the level of PaO_2. (Table 4) Regarding the correlation between different studied parameters and the timing of each element of PICS, (a) regarding delirium, early and late incidences were correlated with the same parameters typically; (b) regarding dementia, early incidence was affected with ages of the patients (highly significant) than late incidence (nonsignificant), whereas late incidence was affected with the duration of ICU stay (highly significant) than early incidence (significant); (c) regarding depression, late incidence was affected

with ages of the patients (highly significant) than early incidence (nonsignificant); (d) regarding anxiety, there were no detected events of PICS at 1 month following discharge from RICU, whereas the early incidence was affected mainly with the duration of both MV and RICU stay; (e) and finally, regarding physical affection, there were no differences between early and late factors correlated with this affection (Table 5).

Discussion

Follow-up of mechanically ventilated patients owing to any respiratory disorder following both weaning and discharging from the respiratory ICU usually lacks the

care of their cognitive, psychological, and general physical conditions (PICS), which may be affected during the period of RICU admission. So the aim of this work was to detect any component of PICS in mechanically ventilated patients at respiratory ICU after being weaned just before ICU discharge and 1 month following hospital discharge. In this work, patients with older age, longer duration of MV and RICU stay, lower levels of PaO_2, higher APACHE IV score, who had co-morbidities, and who experienced prolonged weaning process developed PICS, unlike patients without these findings. Moreover, there were highly significant positive correlations regarding age of patients, duration of MV and RICU stay, and the score of APACHE IV and the development of element(s) of PICS, whereas there was a highly significant negative correlation regarding the level of PaO_2. Many studies have assessed the neurocognitive disorders after the discharge from the ICU; they differed from the present study in that they studied either all ICU admitted patients with different system disorders and not just respiratory causes or studied specific diseases in ICU admitted patients such as ARDS and septicemia [16]. Moreover, they followed up patients for longer durations (mostly 1–2 years) than that found in the present work [16]. In this study, the risks of developing PICS were multifactorial, included older ages, duration of MV and RICU

admission, the presence of co-morbidities, severity of the conditions (higher APACHE IV score), and degree of hypoxemia. In this work, different factors either related to admitted patients or RICU related were studied. The mechanism and the process of pathophysiology of cognitive disabilities in patients discharged from critical care units is still poorly understood. Moreover, these disabilities were usually explained with complex multifactorial elements that interact with different risk factors that are either genetic or acquired such as comorbidities [16]. Many studies [17–22] stated that arterial blood hypoxemia (and the duration of this hypoxemia), the presence of hypotension, and blood glucose levels abnormalities, besides the process of cytokine activation following inflammation, are the mean mechanisms involved in the process of cognitive impairment following ICU admission. One of the important factors was the age. The mean ages in the group of this study that developed PICS was 62.55 years compared with 53.15 for those without PICS, with a highly significant difference. The finding in the present work was supported by Singh-Manoux et al. [23] who stated the cognitive disabilities could occur in 43–49 year olds, with marked deterioration of it at older ages (ages 65–70 years). Moreover, Ehlenbach et al. [24] studied older adults admitted to intensive care units and critical care hospitals and found that their studied patients had a marked decline in cognitive abilities than a matched group that was not hospitalized. Besides the similar related factors studied in the present work like age, PaO_2, blood pressure, and blood glucose levels, they [24] studied other factors such as effects of sedatives and analgesics, and effect of systemic inflammations, which were not studied in the present work. In the present work, 20 of 40 cases (50%) developed one or more component of PICS. These findings agree with of Torres et al. [25] who followed up patients admitted to ICU for more than 2 days for 3 months. They found that more than

Table 4 Correlations between different parameters and the presence of postintensive care syndrome

Parameters	r	P value
Age	0.463	0.003**
MV duration	0.732	0.000**
ICU duration	0.739	0.000**
APACHE	0.719	0.000**
PO_2	−0.42	0.007**
PCO_2	0.123	0.449
pH	−0.058	0.723

APACHE, acute physiology and chronic health evaluation; MV, mechanical ventilation. **Highly significant.

Table 5 Correlation between different parameters and timing of postintensive care syndrome

	Age		MV duration		ICU duration		APACHE		PO_2		PCO_2		pH	
	r	P	r	P	r	P	r	P	r	P	r	P	r	P
Delirium D1	0.561	0.000**	0.679	0.000**	0.661	0.000**	0.686	0.000**	−0.495	0.001**	0.167	0.302	0.154	0.342
Delirium M1	0.617	0.000**	0.637	0.000**	0.599	0.000**	0.63	0.000**	−0.388	0.01**	0.33	0.038	0.288	0.071
Dementia D1	0.416	0.008**	0.466	0.002**	0.45	0.04*	0.43	0.006**	−0.065	0.69	0.285	0.075	0.272	0.089
Dementia M1	0.289	0.071	0.456	0.003**	0.453	0.003**	0.432	0.005**	−0.079	0.627	0.137	0.398	0.132	0.418
Depression D1	0.305	0.056	0.521	0.001**	0.514	0.001**	0.562	0.000**	−0.24	0.135	0.245	0.127	0.207	0.201
Depression M1	0.407	0.009**	0.587	0.000**	0.599	0.000**	0.648	0.000**	−0.283	0.077	0.223	0.167	0.157	0.334
Anxiety D1	0.138	0.397	0.45	0.001**	0.518	0.01**	0.272	0.09	−0.257	0.109	0.14	0.389	0.144	0.377
Physical D1	0.53	0.000**	0.807	0.000**	0.817	0.000**	0.781	0.000**	−0.191	0.237	0.316	0.087	0.256	0.111
Physical M1	0.497	0.001**	0.632	0.000**	0.628	0.000**	0.605	0.000**	−0.307	0.054	0.319	0.045*	0.326	0.04*

APACHE, acute physiology and chronic health evaluation; D1, day 1; M1, 1 month. *Significant. **Highly significant.

50% of their patients developed one or more component of PICS. Moreover, regarding the risk factors related to the development of PICS, the results of this study are in agreement with their study [25] in recoding the same risk factors such as duration of ICU admission, duration of MV, and severity of the disease. However, unlike us they recorded the effect of sedation. In this study, at 1-month follow-up, depression was recorded in 10 cases (five new and five cases continued from day 1), and it was the most predominant symptom, which is in agreement with that of Torres *et al.* [25] who found that psychological components of PICS predominated in their patients at 3 months following discharge. Hopkins *et al.* [26] in their study that included 55 mechanically ventilated patients secondary to ARDS found that 100% of the cases developed on discharge one or more of the following: poor concentration, memory problems, impaired attention, and impaired speed of mental process. Beside the previous abnormalities, their patients developed abnormalities in physical status that affect their quality of life. They [26] reassessed their patients after one year of discharge and found that cognitive, psychological, and physical abnormalities were present. They explained their findings owing to mainly the presence of severe inflammations, persistent hypoxemia, or drug induced. The difference between the incidence in the present study and that of Hopkins *et al.* [26] may be owing to the difference of the inclusion criteria, as we used different respiratory disorders with different mostly reversible ratios of hypoxemia, unlike that of their study, which used cases of ARDS that were characterized by resistant hypoxemia, which is always mentioned as a risk factor for developing PICS. The negative correlations between the levels of arterial oxygen tension and the development of different components with the PICS that were found in the present study are also supported by Mikkelsen *et al.* [18] who studied and followed up neurological and psychological changes in patients with ARDS and concluded that hypoxemia was the main factor in developing these changes. Different studies [27–31] have reported that diseases that are associated with hypoxia such as chronic obstructive airway disease and obstructive sleep apnea, following cardiac or respiratory arrest, result in cognitive abnormalities owing to neuropathological effects. In the present work, there was a highly significant negative correlation between levels of PaO_2 and development of PICS. This result agrees with that of Findley *et al.* [30] who found that the degree of hypoxemia was significantly correlated with cognitive abnormalities in patients with obstructive sleep apnea syndrome.

In this work, older age, longer duration of MV and RICU stay, higher APACHE IV score, and the presence of co-morbidities, had highly significant positive correlations with the development of PICS. The previous findings disagreed with that of Davydow *et al.* [32] who stated that depression was common in patients admitted to ICU and affect their quality of life and stated that age, sex, and severity of the illness were not risk factors. They found that early post-ICU depressive symptoms were a strong risk factor for subsequent post-ICU depressive symptoms. In the present study, 16 (40%) patients developed generalized muscle weakness, which is in agreement with that of Nordon-Craft *et al.* [33], and Bednařík *et al.* [34] who stated that the incidence of ICU-associated muscle weakness ranged between 25 and 100%. Different studies reported different risk factors, such as systemic inflammations, sepsis, comorbidities, hyperglycemia, and steroids, as a risk factor for muscle weakness [33,34]. The durations of ICU and hospital stays, which were found to have highly significant positive correlations with the development of ICUAW in this work, were supported by different studies [35–40] which also recorded that ICU-acquired physical problems such as muscle paresis and weakness, easy fatigability, and polyneuropathy are some of the most influencing factors. Moreover, the previous disabilities related to the duration of MV and ICU stay. In the present study, there was no role of sex in the development of any components of PICS which disagrees with Nordon-Craft *et al.* [33] who recorded fourfolds increase of incidence of ICU-acquired weakness in women as in men, with no clear explanation. In the present study, delirium was diagnosed in 15 patients (37.5% of whole studied patients and 75% of patients who developed PICS). Moreover, the present work showed highly significant positive correlations between MV and hospital stay and the development of delirium. Studies considered delirium beside it is a component of PICS. It is also a risk factor for the development of other components of the PICS. Those who experience delirium while hospitalized in the ICU are at an increased risk of developing a long-term cognitive dysfunction after discharge [41,42]. Ely *et al.* [43] studied 275 patients admitted to ICU due to medical causes and found that patients who developed delirium stayed 10 days longer than patients without delirium. Moreover, Lat *et al.* [44] during their study on 134 admitted patients to ICU due to surgical and traumatic causes recorded longer period of ICU stay and longer period of MV in patients with delirium than those without. In their study about the psychological disturbances in patients admitted to ICU, Saeed *et al.* [45] found

that only hallucinations (*P*=0.0001) and feeling neglected (*P*=0.019) appeared to be significantly and directly correlated with the duration of MV. Other psychological disturbances including fear, loneliness, feeling bored, depression, isolation, feeling insecure, lack of acceptance of the situation as well as lack of self-confidence did not show a significant correlation with the duration of MV. However, they studied both surgical and medical patients during ICU stay only.

Conclusion

Patients with respiratory disorders admitted to the RICU should be evaluated and followed up for detection of any components of PICS especially those who are old adult, with prolonged intubation or ICU stay, have co-morbidities, with high APACHE IV score, and with persistent hypoxemia.

Recommendations

It is recommended to follow up RICU survivors following discharge for longer duration than 1 month. M, it is important to study PICS in a specific respiratory disorder, and in those non-intubated, RICU-admitted patients. The effects of PICS on patients' quality of life should be studied.

Limitations of the study

This study did not include patients admitted to RICU without MV. The effect of drugs such as sedatives and neuromuscular blockers was not involved in this work.

Conflicts of interest

There are no conflicts of interest.

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