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Depression or anxiety and long-term mortality among adult survivors of intensive care unit: a population-based cohort study

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Abstract

Background Many patients who survive intensive care unit (ICU) stays experience persistent mental impairments. It is estimated that one-third of ICU survivors suffer from psychiatric disorders. However, research into how these disorders affect long-term outcomes in this population is scarce. Therefore, the aim of this study is to investigate the association between depression or anxiety and long-term mortality among ICU survivors.

Methods This population-based cohort study included patients admitted to the ICU between January 1, 2015 and December 31, 2019, who survived at least 1 year after ICU discharge. Exclusions were made for patients admitted for non-medical reasons and those who had been in the ICU in the previous 2 years, and 799,645 patients were included in the study. Follow-up data were obtained for up to 7 years. The primary outcome was long-term cumulative mortality. Mortality rates for patients with and without diagnoses of depression or anxiety were compared.

Results Of the 799,645 adult ICU survivors, 98,530 (12.3%) were newly diagnosed with depression or anxiety post-discharge, and 265,092 (33.2%) had been diagnosed prior to ICU admission. Multivariate Cox proportional hazards regression analysis revealed that the adjusted hazard ratio (HR) for long-term mortality was 1.17 (95% CI, 1.16–1.19) for those newly diagnosed with depression or anxiety, 1.28 (95% CI, 1.26–1.30) for depression alone, and 1.08 (95% CI, 1.06–1.11) for anxiety alone. For those with prior diagnoses, the adjusted HR was 1.08 (95% CI, 1.07–1.09) overall, 1.12 (95% CI, 1.11–1.14) for depression, and 1.04 (95% CI, 1.03–1.05) for anxiety.

Conclusions ICU survivors newly diagnosed with depression or anxiety exhibit higher long-term mortality rates compared to those without such diagnoses, including those diagnosed before ICU admission. Particularly, newly diagnosed depression is associated with an elevated mortality rate. These findings underscore the need for psychological interventions to enhance long-term survival among ICU survivors.

Keywords Intensive care unit, Depression, Anxiety, Mortality, Post-intensive care syndrome

Introduction

Owing to the increasing demand for critical care and decrease in short-term mortality after critical illnesses in the aging population, the importance of the long-term consequences of critical illness is growing [1]. Patients who survive prolonged stays in the intensive care unit (ICU) may experience long-term medical issues related to the unique ICU environment, regardless of the primary cause for admission [2]. Those discharged from

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the ICU often experience ongoing physical, cognitive, or mental impairments known as post-intensive care syndrome (PICS) [3]. The presence of PICS in ICU survivors is associated with a decrease in the overall quality of life, as well as a greater risk of mortality in the years following discharge [2]. A recent study reported that patients suffering from post-ICU mental impairments had lower health-related quality of life scores in both physical and mental aspects compared to those without symptoms [4]. Within the first year of discharge, approximately one-third of ICU survivors experience mental impairments, with depression and anxiety being the most common conditions [5].

Depression has been observed in approximately 29–34% of patients after ICU discharge [6], while symptoms of anxiety after a critical illness have been observed in 25–46% [7]. Previous studies have shown that a significant proportion of patients continue to experience symptoms of anxiety and depression even at the one-year follow-up [6, 7]. These psychological morbidities in intensive care patients are associated with stressful memories, psychiatric distress, and delusions [8, 9]. It is well-established that individuals with depression or anxiety have increased mortality compared to the general population [10, 11]. Furthermore, the risk of mortality for survivors of critical illnesses is higher than that of the general population [12, 13], and this increased risk persists for up to 4 years following ICU admission [13].

However, there is a lack of research regarding the association between depression or anxiety and long-term outcomes in ICU survivors. Therefore, this study aims to evaluate the association between depression or anxiety and long-term mortality in adult ICU survivors.

Methods

Data sources and setting

This is a population-based cohort study utilizing data from the Korean National Health Insurance Service (NHIS) database. The NHIS database contains inpatient and outpatient medical information, including patient demographics, diagnoses, procedures, drug prescriptions, type of patient insurance, and date of death. The hospital visits and associated diagnoses of each patient are recorded in the claims database, with the diagnoses classified according to the International Classification of Diseases, 10th Revision (ICD-10) codes [14, 15]. The NHIS operates as a nationwide single-insurer system in Republic of Korea. By law, the NHIS imposes compulsory contributions on insured individuals, making it mandatory for Republic of Korean citizens to pay insurance premiums, thereby covering almost the entire population of Republic of Korea [16].

Study design and population

This longitudinal cohort study analysed the long-term prognosis of patients admitted to the ICU between January 1, 2015 and December 31, 2019. Considering the extraordinary circumstances presented by the COVID-19 pandemic, this investigation included patients admitted to the ICU up to December 2019 [15]. To accommodate the data extraction capacity of the NHIS database, a five-year dataset spanning from 2015 was employed. Patients admitted to the ICU were identified by having submitted at least one reimbursement request using the health insurance claim codes AJ100–AJ390. These codes cover all ICUs. The study included only adult patients aged ≥ 18 years. Among all adult patients admitted to the ICU, those who survived for more than one year after hospital discharge, classified as ICU survivors, were eligible for inclusion in this study. Exclusions were made for ICU admissions due to traumatic or non-medical causes (ICD-10 S and T codes), such as burns, injuries, poisoning, asphyxiation, or anaphylaxis. In cases of non-medical aetiologies, there might be a potential for mental impairment attributable to factors beyond the unique environment of the ICU [17–20]. Considering the findings of a previous study that demonstrated variations in quality of life among subgroups categorised by the causes of ICU admission, these cases were excluded [21]. For patients admitted to the ICU more than once during the study period, the first episode was considered as the index date. Those with a history of ICU admission within 2 years prior to this episode were excluded as part of the washout period.

Definition and main variables

Follow-up data were obtained for up to 7 years, until December 31, 2022, with the primary outcome being long-term cumulative mortality. Diagnoses of depression and anxiety were identified using the ICD-10 codes (Depression: F32.x, F33.x, F34.1; Anxiety: F41.x) from the NHIS data. ICU survivors were classified into three groups as follows: (1) Pre-ICU depression or anxiety group: patients diagnosed with anxiety or depression before ICU admission; (2) Post-ICU depression or anxiety group: patients with no prior history of these conditions, newly diagnosed within one year of hospital discharge; and (3) Control group: patients not diagnosed with depression or anxiety before or after ICU admission. Depression and anxiety were also analysed separately.

Covariates

Patient-related confounders were extracted from the NHIS claims database. Demographic factors such as age, sex, type of insurance, income, and place of residence

were obtained at the time of ICU admission. Economic status was divided into five groups. Medicaid beneficiaries were classified as the lowest economic group. The Medicaid program is a public assistance program for the most vulnerable individuals, who are recipients of the National Basic Livelihood Security System as part of social welfare programs. Excluding Medicaid beneficiaries, income levels were categorized into quartiles (Q1: lowest; Q2; Q3; Q4: highest). To examine the comorbid status, the Charlson Comorbidity Index (CCI) was calculated. To reflect disease severity, the use of vasopressors or inotropic drugs, endotracheal intubation, mechanical ventilation, renal replacement therapy, and extracorporeal membrane oxygenation (ECMO) during ICU treatment were included as confounders. The use of vasopressors and inotropic drugs was identified using the anatomical therapeutic chemical classification system [22]. Hospitals were categorized as tertiary, general, or other, according to classifications defined by healthcare law in Republic of Korea.

Statistical analysis

Descriptive statistics were used to analyse the baseline characteristics of the patients. Categorical variables are presented as frequencies and percentages, and continuous variables as means with standard deviations. The ANOVA test was used for comparisons of continuous variables, and the Chi-square test for categorical variables.

To conduct a balanced analysis, we employed inverse probability of treatment weighting (IPTW), including factors such as age, sex, economic status, and conditions listed in the CCI in the IPTW calculations. Standardized mean differences (SMD) were calculated to assess the balance quality after IPTW.

The Kaplan–Meier method was used to estimate survival curves, and the log-rank test was employed to compare the groups. A Cox proportional hazards model was used to identify the impact of anxiety or depression on long-term mortality, with results presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Covariates included the use of vasopressors or inotropic drugs, mechanical ventilation, renal replacement therapy, ECMO, length of ICU stay, and number of ICU admissions. Furthermore, we incorporated the year of ICU admission, type of hospital, and place of residence as variables to adjust for the effects of healthcare resource efficiency, based on previous studies [23, 24]. Differences were considered statistically significant at a p-value of <0.05 with two-sided, unpaired testing. Statistical analysis for this study was conducted using the SAS Enterprise Guide version 7.1 (SAS Institute Inc., Cary, North Carolina, USA).

Results

Study population

Between January 2015 and December 2019, 1,375,640 adult patients were admitted to the ICU. Of these, 1,032,319 (75.0%) survived for more than one year after discharge. Patients admitted for non-medical reasons (155,825) and those with a history of ICU admission within the previous 2 years (76,849) were excluded. Ultimately, 799,645 ICU survivors were included in the analysis (Fig. 1). The median follow-up period was 3.80 years (IQR, 2.51–5.24), with a maximum of 7.00 years. The baseline characteristics of the study population are summarized in Table 1. Among the ICU survivors, 98,530 (12.3%) were newly diagnosed with depression or anxiety, while 265,092 (33.2%) had been diagnosed with these conditions prior to their ICU admission. After IPTW, the groups were balanced for the included covariates, with an absolute SMD <0.05 (Table 2).

Long-term mortality according to the diagnosis of depression or anxiety

The Kaplan–Meier survival curves indicated that depression or anxiety was associated with an increased risk of mortality (log-rank test, $p<0.001$) (Fig. 2). Both the pre-ICU and post-ICU depression or anxiety groups exhibited higher mortality rates compared to the control group, with the post-ICU group displaying the highest rates. The results of the Cox regression analysis are presented in Fig. 3. The HR for long-term mortality was 1.10 (95% CI: 1.09–1.11) in the pre-ICU depression or anxiety group and 1.22 (95% CI: 1.20–1.23) in the post-ICU group. After adjusting for confounding factors, the adjusted hazard ratio (aHR) for long-term mortality was 1.08 (95% CI: 1.07–1.09) for the pre-ICU group and 1.17 (95% CI: 1.16–1.19) for the post-ICU group.

Subgroup analyses

Of the 799,645 ICU survivors, 52,742 were newly diagnosed with depression and 45,788 with anxiety. The baseline characteristics of groups diagnosed and not diagnosed with depression, and those diagnosed and not diagnosed with anxiety, are summarized in Supplementary Tables 1 and 2.

The cumulative mortality rate was highest in the post-ICU depression group (Supplementary Fig. 1). The cumulative mortality rates for patients diagnosed and not diagnosed with depression, as well as for those diagnosed and not diagnosed with anxiety, are presented in Supplementary Fig. 2.

Cox regression analyses were conducted separately for groups diagnosed with depression and those not diagnosed, as well as for groups diagnosed with anxiety

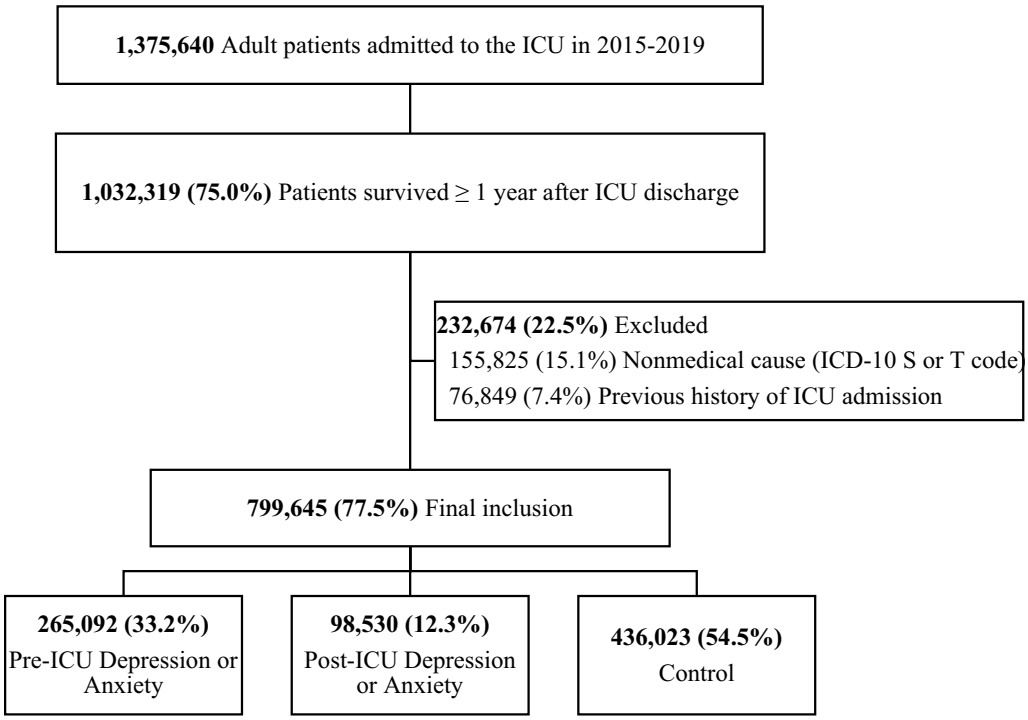

Fig. 1 Flow diagram of study population. ICU; Intensive care unit

and those not diagnosed. The results of these subgroup Cox regression analyses are presented in Fig. 4. The aHR for long-term mortality in the pre-ICU and post-ICU depression groups was 1.12 (95% CI: 1.11–1.14) and 1.28 (95% CI: 1.26–1.30), respectively. The aHR for long-term mortality in the pre-ICU and post-ICU anxiety groups was 1.04 (95% CI: 1.03–1.05) and 1.08 (95% CI: 1.06–1.11), respectively.

Discussion

To the best of our knowledge, this is the first nationwide population-based study to investigate the association between long-term mortality and psychiatric disorders among ICU patients. The association between long-term mortality and depression or anxiety was more pronounced in patients newly diagnosed after ICU discharge than in those diagnosed before admission. Specifically, patients newly diagnosed with depression or anxiety after ICU discharge had a 1.17-fold increased risk of long-term mortality compared to those without these psychiatric disorders. Notably, those newly diagnosed with depression after ICU discharge faced a 1.28-fold higher risk of long-term mortality compared to patients without this diagnosis.

A significant finding of this study is the differential association between long-term mortality and depression or anxiety among patients diagnosed before versus after ICU admission. A post-ICU diagnosis of depression or anxiety within 1 year of discharge may be indicative of sequelae from ICU care. The observation that ICU survivors newly diagnosed with depression or anxiety exhibit a higher risk of long-term mortality post-discharge, compared to those with pre-existing psychiatric disorders, underscores the importance of addressing the psychiatric domain of PICS.

The Society of Critical Care Medicine proposed the concept of PICS in 2010. (1) PICS is a complex condition that affects three domains of function—psychiatric, cognitive, and physical—following critical illness. (3) While research into PICS has expanded, the psychiatric domain—which includes newly developed psychiatric conditions following critical illness—remains relatively underexplored [25]. Psychiatric disorders following critical illness pose significant concerns, as depression has been linked to an increased risk of adverse medical outcomes and higher healthcare costs [26]. The prevalence of psychiatric disorders within the PICS framework has been reported to range from 13 to 25% [25]. In this study, the prevalence of newly diagnosed psychiatric disorders within 1 year after ICU discharge was 12.3% (98,530 out of 799,645). It is crucial to acknowledge that previous studies have struggled to determine whether the psychiatric conditions observed after critical illness are newly developed or pre-existing

Table 1 Baseline characteristics of study populations

	Total	Control	Pre depression or anxiety	Post depression or Anxiety	*p* value
Number of patients	799,645	436,023	265,092	98,530	
Age	64.4 ± 14.6	62.2 ± 14.8	68.4 ± 13.6	63.8 ± 14.3	< .0001
Age group					< .0001
18–29	15,575 (2.0)	10,993 (2.5)	2,982 (1.1)	1,600 (1.6)	
30–39	30,080 (3.8)	20,213 (4.6)	5,990 (2.3)	3,877 (3.9)	
40–49	77,743 (9.7)	50,538 (11.6)	16,621 (6.3)	10,584 (10.7)	
50–59	159,344 (19.9)	99,047 (22.7)	39,250 (14.8)	21,047 (21.4)	
60–69	192,054 (24.0)	108,962 (25.0)	59,223 (22.3)	23,869 (24.2)	
70–79	200,233 (25.0)	93,235 (21.4)	83,293 (31.4)	23,705 (24.1)	
≥ 80	124,616 (15.6)	53,035 (12.2)	57,733 (21.8)	13,848 (14.1)	
Sex					< .0001
Male	455,787 (57.0)	278,975 (64.0)	120,703 (45.5)	56,109 (57.0)	
Female	343,858 (43.0)	157,048 (36.0)	144,389 (54.5)	42,421 (43.1)	
Income					< .0001
Medicaid	71,509 (8.9)	26,737 (6.1)	36,752 (13.9)	8,020 (8.1)	
Quartile 1 (Lowest)	148,323 (18.6)	83,515 (19.2)	45,496 (17.2)	19,312 (19.6)	
Quartile 2	139,003 (17.4)	81,174 (18.6)	39,956 (15.1)	17,873 (18.1)	
Quartile 3	177,248 (22.2)	101,855 (23.4)	53,360 (20.1)	22,033 (22.4)	
Quartile 4 (Highest)	263,562 (33.0)	142,742 (32.7)	89,528 (33.8)	31,292 (31.8)	
Comorbidities					
CCI score	3.7 ± 2.4	3.3 ± 2.2	4.5 ± 2.5	3.7 ± 2.3	< .0001
Hypertension	563,569 (70.5)	288,420 (66.2)	205,534 (77.5)	69,615 (70.7)	< .0001
Dyslipidaemia	587,572 (73.5)	302,660 (69.4)	214,687 (81.0)	70,225 (71.3)	< .0001
Acute myocardial infarction	113,900 (14.2)	71,165 (16.3)	31,945 (12.1)	10,790 (11.0)	< .0001
Congestive heart failure	162,696 (20.4)	79,483 (18.2)	65,453 (24.7)	17,760 (18.0)	< .0001
Peripheral vascular disease	165,899 (20.8)	68,910 (15.8)	78,563 (29.6)	18,426 (18.7)	< .0001
Cerebral vascular accident	312,101 (39.0)	137,275 (31.5)	126,620 (47.8)	48,206 (48.9)	< .0001
Dementia	83,037 (10.4)	22,996 (5.3)	51,449 (19.4)	8,592 (8.7)	< .0001
Pulmonary disease	429,986 (53.8)	205,746 (47.2)	171,916 (64.9)	52,324 (53.1)	< .0001
Connective tissue disorder	45,460 (5.7)	17,582 (4.0)	22,746 (8.6)	5,132 (5.2)	< .0001
Peptic ulcer	346,925 (43.4)	161,816 (37.1)	145,327 (54.8)	39,782 (40.4)	< .0001
Liver disease	76,175 (9.5)	36,612 (8.4)	30,476 (11.5)	9,087 (9.2)	< .0001
Diabetes	382,306 (47.8)	188,958 (43.3)	147,275 (55.6)	46,073 (46.8)	< .0001
Diabetes complications	104,629 (13.1)	45,705 (10.5)	47,282 (17.8)	11,642 (11.8)	< .0001
Paraplegia	50,130 (6.3)	20,720 (4.8)	18,363 (6.9)	11,047 (11.2)	< .0001
Renal disease	74,199 (9.3)	35,301 (8.1)	30,734 (11.6)	8,164 (8.3)	< .0001
Tumour	148,270 (18.5)	83,605 (19.2)	47,693 (18.0)	16,972 (17.2)	< .0001
Lymphoma	3,521 (0.4)	1,756 (0.4)	1,278 (0.5)	487 (0.5)	< .0001
Leukaemia	1,614 (0.2)	874 (0.2)	507 (0.2)	233 (0.2)	0.025
Metastatic cancer	23,786 (3.0)	13,639 (3.1)	7,070 (2.7)	3,077 (3.1)	< .0001
Severe liver disease	12,107 (1.5)	5,838 (1.3)	4,864 (1.8)	1,405 (1.4)	< .0001
HIV	572 (0.1)	339 (0.1)	179 (0.1)	54 (0.1)	0.033
Intervention					
Mechanical ventilation	137,730 (17.2)	76,226 (17.5)	41,536 (15.7)	19,968 (20.3)	< .0001
Renal replacement	16,480 (2.1)	8,614 (2.0)	5,710 (2.2)	2,156 (2.2)	< .0001
Vasopressor or inotropic drugs	340,504 (42.6)	189,364 (43.4)	110,217 (41.6)	40,923 (41.5)	< .0001
ECMO	3,245 (0.4)	2,071 (0.5)	706 (0.3)	468 (0.5)	< .0001
Length of ICU stay, days	14.0 ± 13.5	13.1 ± 13.0	14.3 ± 13.4	16.9 ± 15.8	< .0001
Length of hospital stay, days	17.9 ± 25.8	16.2 ± 23.1	18.2 ± 25.6	24.2 ± 34.9	< .0001

Table 1 (continued)

	Total	Control	Pre depression or anxiety	Post depression or Anxiety	*p* value
Number of ICU admission	1.3 ± 0.8	1.2 ± 0.7	1.4 ± 0.9	1.4 ± 0.9	< .0001
Year of ICU admission					< .0001
2015	157,366 (19.7)	84,842 (19.5)	52,499 (19.8)	20,025 (20.3)	
2016	163,648 (20.5)	88,831 (20.4)	54,730 (20.7)	20,087 (20.4)	
2017	161,844 (20.2)	88,287 (20.3)	53,406 (20.2)	20,151 (20.5)	
2018	156,348 (19.6)	85,424 (19.6)	51,792 (19.5)	19,132 (19.4)	
2019	160,439 (20.1)	88,639 (20.3)	52,665 (19.9)	19,135 (19.4)	
Type of hospital					< .0001
Tertiary	356,440 (44.6)	208,615 (47.8)	106,856 (40.3)	40,969 (41.6)	
General	435,818 (54.5)	224,133 (51.4)	155,133 (58.5)	56,552 (57.4)	
Other	7,387 (0.9)	3,275 (0.8)	3,103 (1.2)	1,009 (1.0)	
Residence at admission to ICU					< .0001
Capital city (Seoul)	428,149 (53.5)	247,221 (56.7)	130,069 (49.1)	50,859 (51.6)	
Other metropolitan city	172,310 (21.6)	89,718 (20.6)	60,694 (22.9)	21,898 (22.2)	
Other area	199,186 (24.9)	99,084 (22.7)	74,329 (28.0)	25,773 (26.2)	
Long-term death	193,877 (24.3)	86,927 (19.9)	80,825 (30.5)	26,125 (26.5)	< .0001

CCI charlson comorbidity index, HIV human immunodeficiency virus, ECMO extracorporeal membrane oxygenation, ICU intensive care unit

[9, 25, 27]. Marra et al. noted that while the prevalence of physical impairments decreased from 23 to 17% between 3 and 12 months post-ICU, the reduction in psychiatric impairments was insignificant, remaining at 13% [28]. Numerous strategies have been proposed to prevent PICS; however, the interventions implemented during hospitalization have proven insufficient for its effective prevention [29]. Therefore, successful management of PICS necessitates long-term follow-up, such as establishing a PICS follow-up system involving a multidisciplinary team [30]. According to a systematic review and meta-analysis, interventions at PICS follow-up clinics have been shown to improve depression and mental health-related quality of life [31].

This study found that newly diagnosed depression among ICU survivors was associated with a higher mortality risk compared to newly diagnosed anxiety (HR: 1.33 vs. HR: 1.13, respectively). This association persisted even after adjusting for several confounding factors (aHR: 1.28 vs. aHR: 1.08, respectively). Depression has been linked to higher mortality rates from common medical conditions such as cardiovascular, cerebrovascular, and respiratory diseases, hypertension, and diabetes mellitus [32]. Hatch et al. reported an association between symptoms of depression and increased mortality within 2 years following ICU discharge [33]. However, this study did not previously demonstrate an association between newly diagnosed anxiety and an increased mortality rate after ICU discharge. The observed link between depression and mortality in patients who have received ICU care could partly be explained by the severity of chronic medical conditions both before and after discharge [34, 35]. Nonetheless, it remains unclear whether there is a biological association between chronic diseases and depression. Moreover, the mortality risk was higher in patients newly diagnosed with depression or anxiety after ICU discharge compared to those diagnosed before ICU admission. These findings highlight the importance of addressing newly developed psychiatric disorders in ICU survivors.

Previous studies on risk factors for ICU-related depression and anxiety have identified several contributors, including ICU length of stay, duration of mechanical ventilation, and the use of anxiolytic or sedating medications during hospitalization as increasing the risk of anxiety associated with critical illness [25, 36–38]. In this study, the proportion of patients who received mechanical ventilation was higher in the group newly diagnosed with depression or anxiety after ICU discharge (20.3%) compared to the group diagnosed before ICU admission (15.7%) and the control group (17.5%). Additionally, the ICU length of stay was longer in the post-ICU depression or anxiety group (16.8 ± 15.6 days) compared to the pre-ICU group (14.2 ± 13.3 days) and the control group (13.1 ± 12.7 days). While this study did not focus on investigating the risk factors for the development of psychiatric complications, it observed trends consistent with those from previous research. Given the limited

Table 2 Baseline characteristics of study populations before and after IPTW

	Before IPTW					After IPTW			
	Total	**Control**	**Pre Depression or Anxiety**	**Post Depression or Anxiety**	**SMD**	**Control**	**Pre Depression or Anxiety**	**Post Depression or Anxiety**	**SMD**
Number of patients	799,645	436,023	265,092	98,530		439,688	262,698	98,843	
Age	64.4 ± 14.6	62.2 ± 14.8	68.4 ± 13.6	63.8 ± 14.3	0.288	64.7 ± 14.8	64.7 ± 14.6	64.7 ± 14.6	0.004
Age group					0.299				0.011
18–29	15,575 (2.0)	10,993 (2.5)	2,982 (1.1)	1,600 (1.6)		8,511 (1.9)	5,352 (2.0)	1,876 (1.9)	
30–39	30,080 (3.8)	20,213 (4.6)	5,990 (2.3)	3,877 (3.9)		16,345 (3.7)	9,897 (3.8)	3,613 (3.7)	
40–49	77,743 (9.7)	50,538 (11.6)	16,621 (6.3)	10,584 (10.7)		42,102 (9.6)	24,972 (9.5)	9,318 (9.4)	
50–59	159,344 (19.9)	99,047 (22.7)	39,250 (14.8)	21,047 (21.4)		86,248 (19.6)	51,064 (19.4)	19,220 (19.4)	
60–69	192,054 (24.0)	108,962 (25.0)	59,223 (22.3)	23,869 (24.2)		104,220 (23.7)	62,565 (23.8)	23,609 (23.9)	
70–79	200,233 (25.0)	93,235 (21.4)	83,293 (31.4)	23,705 (24.1)		110,663 (25.2)	66,601 (25.4)	25,191 (25.5)	
≥ 80	124,616 (15.6)	53,035 (12.2)	57,733 (21.8)	13,848 (14.1)		71,599 (16.3)	42,247 (16.1)	16,016 (16.2)	
Sex					0.250				0.005
Male	455,787 (57.0)	278,975 (64.0)	120,703 (45.5)	56,109 (56.9)		247,389 (56.3)	147,549 (56.2)	55,873 (56.5)	
Female	343,858 (43.0)	157,048 (36.0)	144,389 (54.5)	42,421 (43.1)		192,299 (43.7)	115,149 (43.8)	42,970 (43.5)	
Economic status					0.188				0.007
Medicaid	71,509 (8.9)	26,737 (6.1)	36,752 (13.9)	8,020 (8.1)		42,540 (9.7)	24,953 (9.5)	9,391 (9.5)	
Quartile 1 (Lowest)	148,323 (18.6)	83,515 (19.2)	45,496 (17.2)	19,312 (19.6)		81,302 (18.5)	48,810 (18.6)	18,220 (18.4)	
Quartile 2	139,003 (17.4)	81,174 (18.6)	39,956 (15.1)	17,873 (18.1)		75,842 (17.2)	45,270 (17.2)	16,970 (17.2)	
Quartile 3	177,248 (22.2)	101,855 (23.4)	53,360 (20.1)	22,033 (22.4)		96,532 (22.0)	57,474 (21.9)	21,736 (22.0)	
Quartile 4 (Highest)	263,562 (33.0)	142,742 (32.7)	89,528 (33.8)	31,292 (31.8)		143,472 (32.6)	86,191 (32.8)	32,526 (32.9)	
Comorbidities									
CCI score	3.7 ± 2.4	3.3 ± 2.2	4.5 ± 2.5	3.7 ± 2.3	0.356	3.8 ± 2.4	3.8 ± 2.4	3.8 ± 2.4	0.011
Hypertension	563,569 (70.5)	288,420 (66.2)	205,534 (77.5)	69,615 (70.7)	0.170	311,028 (70.7)	185,561 (70.6)	69,862 (70.7)	0.001
Dyslipidemia	587,572 (73.5)	302,660 (69.4)	214,687 (81.0)	70,225 (71.3)	0.180	323,206 (73.5)	192,607 (73.3)	73,165 (74.0)	0.011
Acute myocardial infarction	113,900 (14.2)	71,165 (16.3)	31,945 (12.1)	10,790 (11.0)	0.105	61,334 (14.0)	35,321 (13.5)	14,405 (14.6)	0.022
Congestive heart failure	162,696 (20.4)	79,483 (18.2)	65,453 (24.7)	17,760 (18.0)	0.109	89,721 (20.4)	53,368 (20.3)	20,667 (20.9)	0.010
Peripheral vascular disease	165,899 (20.8)	68,910 (15.8)	78,563 (29.6)	18,426 (18.7)	0.223	92,138 (21.0)	55,079 (21.0)	21,074 (21.3)	0.006
Cerebral vascular disease	312,101 (39.0)	137,275 (31.5)	126,620 (47.8)	48,206 (48.9)	0.241	173,856 (39.5)	101,747 (38.7)	38,082 (38.5)	0.014
Dementia	83,037 (10.4)	22,996 (5.3)	51,449 (19.4)	8,592 (8.7)	0.296	49,146 (11.2)	27,939 (10.6)	10,600 (10.7)	0.012
Pulmonary disease	429,986 (53.8)	205,746 (47.2)	171,916 (64.9)	52,324 (53.1)	0.240	237,472 (54.0)	141,990 (54.1)	53,738 (54.4)	0.005
Connective tissue disorder	45,460 (5.7)	17,582 (4.0)	22,746 (8.6)	5,132 (5.2)	0.126	25,418 (5.8)	15,159 (5.8)	5,796 (5.9)	0.003
Peptic ulcer	346,925 (43.4)	161,816 (37.1)	145,327 (54.8)	39,782 (40.4)	0.240	191,545 (43.6)	114,418 (43.6)	43,558 (44.1)	0.007
Liver disease	76,175 (9.5)	36,612 (8.4)	30,476 (11.5)	9,087 (9.2)	0.069	42,449 (9.7)	25,642 (9.8)	9,557 (9.7)	0.002
Diabetes	382,306 (47.8)	188,958 (43.3)	147,275 (55.6)	46,073 (46.8)	0.164	211,313 (48.1)	126,145 (48.0)	47,719 (48.3)	0.003
Diabetes complications	104,629 (13.1)	45,705 (10.5)	47,282 (17.8)	11,642 (11.8)	0.142	58,178 (13.2)	34,902 (13.3)	13,330 (13.5)	0.005
Paraplegia	50,130 (6.3)	20,720 (4.8)	18,363 (6.9)	11,047 (11.2)	0.161	28,467 (6.5)	16,269 (6.2)	5,983 (6.1)	0.012

Table 2 (continued)

	Before IPTW					After IPTW			
	Total	Control	Pre Depression or Anxiety	Post Depression or Anxiety	SMD	Control	Pre Depression or Anxiety	Post Depression or Anxiety	SMD
Renal disease	74,199 (9.3)	35,301 (8.1)	30,734 (11.6)	8,164 (8.3)	0.078	41,255 (9.4)	24,857 (9.5)	9,537 (9.7)	0.006
Tumor	148,270 (18.5)	83,605 (19.2)	47,693 (18.0)	16,972 (17.2)	0.034	80,952 (18.4)	48,752 (18.6)	18,668 (18.9)	0.008
Lymphoma	3,521 (0.4)	1,756 (0.4)	1,278 (0.5)	487 (0.5)	0.009	1,973 (0.5)	1,200 (0.5)	442 (0.5)	0.001
Leukemia	1,614 (0.2)	874 (0.2)	507 (0.2)	233 (0.2)	0.007	894 (0.2)	537 (0.2)	203 (0.2)	0.001
Metastatic cancer	23,786 (3.0)	13,639 (3.1)	7,070 (2.7)	3,077 (3.1)	0.018	13,055 (3.0)	7,961 (3.0)	2,996 (3.0)	0.002
Severe liver disease	12,107 (1.5)	5,838 (1.3)	4,864 (1.8)	1,405 (1.4)	0.026	6,757 (1.5)	4,108 (1.6)	1,528 (1.6)	0.001
HIV	572 (0.1)	339 (0.1)	179 (0.1)	54 (0.1)	0.006	314 (0.1)	198 (0.1)	69 (0.1)	0.001

IPTW inverse probability treatment weighting, SMD standardized mean difference, CCI charlson Comorbidity Index, HIV human immunodeficiency virus

number of studies investigating risk factors within the psychiatric domain of PICS, it is crucial to identify these factors and implement strategies to manage patients at high risk of developing such complications.

The present investigation was constrained by the unavailability of post-ICU discharge data on health-related quality of life, physical function, and cognitive function. This limitation precludes the incorporation of these factors into our analytical framework. Consequently, the study's capacity to ascertain the independent impact of mental health conditions, such as depression and anxiety, on long-term mortality following ICU discharge was restricted. Given that two or more PICS impairments can coexist, evaluating the isolated association between a single PICS impairment and mortality may be challenging [39]. Nonetheless, our finding that long-term mortality is elevated in patients with depression or anxiety underscores the significance of addressing interventions for psychiatric disorders in post-ICU multidisciplinary follow-up clinics. Interestingly, a study conducted in France reported that multidisciplinary post-ICU consultations had unexpected detrimental effects on depression and anxiety [40]. This contrasts with previous research

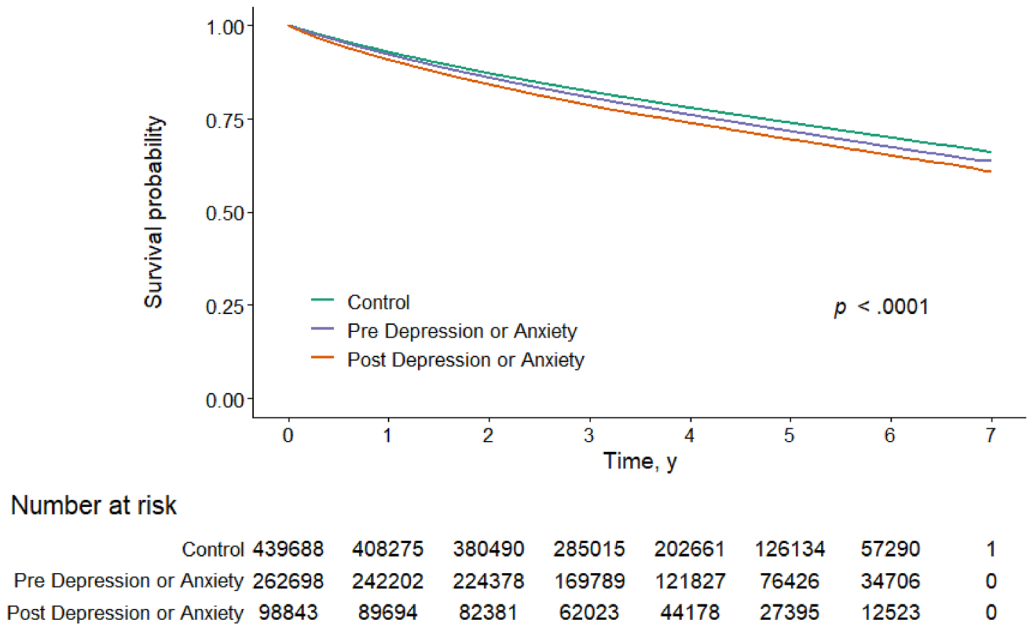

Fig. 2 Long-term mortality among ICU survivors with and without depression of anxiety

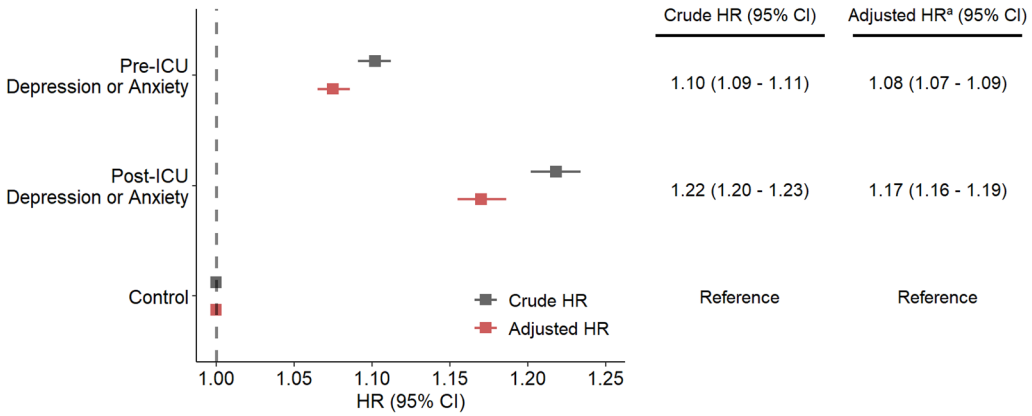

Fig. 3 Forest plot of Cox regression analysis identifying the association between depression or anxiety and long-term mortality in ICU survivors. [a]Adjusted for intervention, length of ICU stay, number of ICU admission, year of ICU admission, type of hospital, residence at admission to ICU. ICU; Intensive care unit, HR; Hazard ratio

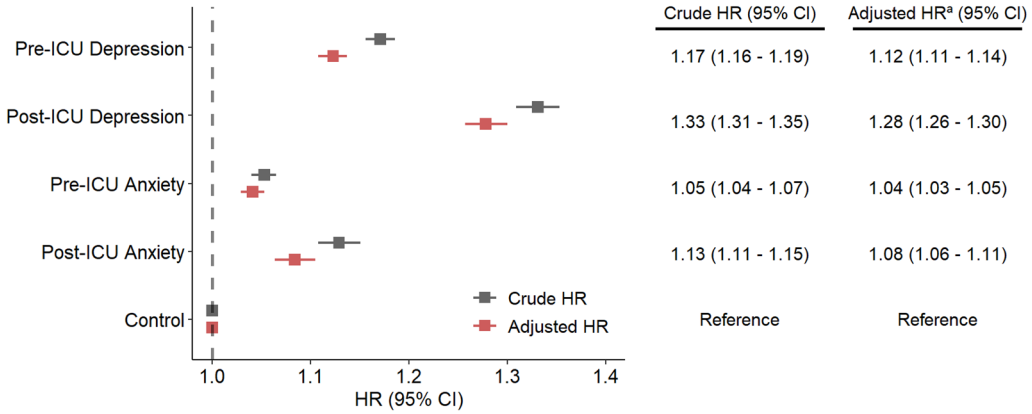

Fig. 4 Forest plot of Cox regression analysis identifying the association between psychiatric disorders and long-term mortality in ICU survivors. [a]Adjusted for intervention, length of ICU stay, number of ICU admission, year of ICU admission, type of hospital, residence at admission to ICU. ICU; Intensive care unit, HR; Hazard ratio

indicating that post-discharge rehabilitation enhances physical recovery and reduces mortality rate [41, 42]. Although multidisciplinary follow-up care may offer potential advantages in ameliorating PICS, current evidence regarding its efficacy remains inconclusive [43]. Consequently, the findings of this study, which demonstrate an association between newly diagnosed depression or anxiety and long-term mortality, underscore the need to develop effective post-ICU strategies to ameliorate depression and anxiety.

This study should be interpreted with the following limitations in mind. First, we were unable to adjust for severity using ICU mortality scores, such as the Acute Physiology and Chronic Health Evaluation score or the Sequential Organ Failure Assessment score, because the NHIS database only provides information on prescribed medications, procedures, and registered ICD-10 diagnostic codes. To account for severity, we extracted data on the use of mechanical ventilation, renal replacement therapy, vasopressor or inotropic drugs, and ECMO. Second, the diagnosis of depression and anxiety was defined using ICD-10 codes, and the validity of our findings depends on the accurate coding of outcomes. These diagnostic codes were recorded by clinicians; however, the possibility of diagnostic inaccuracies cannot be ruled out. Additionally, as the study relied on ICD-10 codes rather than instruments such as the Hospital Anxiety and Depression Scale or EuroQol, it is possible that cases of depression or anxiety in patients who did not seek medical care may have been omitted. Patients requiring medical attention due to a higher disease burden may have been diagnosed more thoroughly, potentially leading to a detection bias. Nonetheless, the nationwide scale of this study, combined with its relatively large patient population, may have mitigated this limitation. Third, we were unable to adjust for all

potential confounding factors, such as levels of physical activity, appetite, lifestyle patterns, newly developed medical conditions, and new medications. Fourth, due to the retrospective nature of the study design, selection bias may have occurred.

Conclusions

Both pre-ICU and post-ICU depression or anxiety were associated with increased long-term mortality rates. The risk of long-term mortality was greater in the post-ICU depression or anxiety group compared to the pre-ICU group. Additionally, patients newly diagnosed with depression after ICU discharge faced a higher risk of long-term mortality than those newly diagnosed with anxiety.

List of abbreviations

ICU	Intensive care unit
PICS	Post-intensive care syndrome
NHIS	Korean National Health Insurance Service
ICD-10	International Classification of Diseases, 10th Revision
CCI	Charlson Comorbidity Index
ECMO	Extracorporeal membrane oxygenation
IPTW	Inverse probability of treatment weighting
SMD	Standardized mean differences
HRs	Hazard ratios
CIs	Confidence intervals

Supplementary Information

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Additional file1 (DOCX 1473 KB)

Additional file2 (DOCX 241 KB)

Additional file3 (DOCX 30 KB)

Additional file4 (DOCX 19 KB)

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Author contributions

K.H.Y.: Conceptualization, Methodology, Writing – Original Draft, Writing – Review & Editing. J.L.: Project administration, Supervision, Writing – Review & Editing. J.O.: Project administration, Writing – Review & Editing. N.C.: Methodology, Formal analysis, Data Curation. T.H.L., H.K., B.S.K., Y.C.: Writing – Review & Editing. All authors reviewed the manuscript.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study design was approved by the Institutional Review Board of Hanyang University Hospital (HYUH 2023–04-049) and the Health Insurance Review and Assessment Service (NHIS-2024–1-315). Informed consent was waived because the data analyses were conducted retrospectively using anonymized data. This data was prepared by an independent technician at the NHIS centre, who was not affiliated with this study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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