



OPEN Factors affecting health-related quality of life in ICU survivors

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This multicenter prospective study investigated factors influencing mid-term health-related quality of life (HRQoL) among intensive care unit (ICU) survivors in Korea. Among 2,002 patients, 189 who completed follow-up assessments at 90 days post-discharge were included in the final analysis. HRQoL was measured using the five-level EuroQoL 5-Dimension (EQ-5D-5L) and Hospital Anxiety and Depression Scale (HADS) at 30 and 90 days after discharge. Multivariable regression identified older age, infection as the cause of ICU admission, higher clinical frailty scale (CFS), and baseline HADS scores as independent predictors of lower EQ-5D-5L scores at 90 days. Initial HADS and CFS were also significantly associated with persistent anxiety and depression symptoms. Specific domains of HRQoL, such as mobility, self-care, and usual activity, were particularly affected by these factors. The findings underscore the importance of early psychological and frailty assessments in ICU patients, as these measures can help identify individuals at risk for poor recovery trajectories. Routine evaluation and targeted interventions for patients with high anxiety, depression, or frailty at ICU admission may improve long-term outcomes and overall quality of life after critical illness.

Keywords Clinical frailty scale, Health-Related quality of life, ICU, Hospital anxiety and depression scale

Survivors of intensive care units (ICUs) frequently encounter enduring physical, psychological, and social challenges that markedly impair their health-related quality of life (HRQoL). Recent evidence indicates that, although the survival rates from severe illnesses have improved, the quality of life for these survivors often remains significantly compromised following discharge^{1–4}. Accordingly, HRQoL has emerged as a pivotal outcome measure for ICU survivors, transcending mere survival to encompass recovery, societal reintegration, and overall well-being.

The demographic and clinical profiles of ICU survivors are heterogeneous, encompassing a range of pre-existing health conditions and severity of the illnesses necessitating ICU admission. These individuals commonly face a complex interplay of ongoing physical disabilities, cognitive impairments, and emotional disturbances, a condition collectively recognized as post-intensive care syndrome (PICS)⁵. Factors that influence HRQoL among ICU survivors are manifold, including the presence of preexisting comorbidities, such as cardiovascular, hepatic, and respiratory diseases, severity of the initial illness, nature of medical interventions received during ICU stay, psychological factors, and a spectrum of social determinants, such as socioeconomic status^{3,6–8}.

Despite advances in empirical research, discerning the myriad factors that influence HRQoL continues to present significant challenges, largely due to variability among patient populations and therapeutic approaches. Therefore, a multicenter observational study that systematically and thoroughly assesses these factors across diverse settings is necessary. To address this gap, we have undertaken a multicenter prospective analysis aimed at elucidating the factors that affect HRQoL in ICU survivors.

Results

Baseline characteristics

A total of 2002 patients were screened during the study period. Of these, 1,763 were excluded (refusal to provide consent, $n = 1,525$; inability to communicate because of neurological status, $n = 238$). A total of 239 patients were

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included in this study, of whom 189 completed the EQ-5D-5L assessment on day 90 and were included in the final analysis (Fig. 1).

Baseline characteristics of the patients are shown in Table 1. The median age of the patients was 63.0 years (IQR, 53.0–71.0), 59.3% were male, 67 (35.4%) were retired, 63 (33.3%) were employed, and 134 (70.9%) had completed higher education. Most patients were admitted to the medical ICU (91.5%). The median length of stay in the ICU was 7 (4.0–12.0) days. The mean initial SAPS III score was 60.9 ± 16.0 , while the median sequential organ failure assessment (SOFA) score on day 1 was 6.0 (IQR, 3.0–9.0). Median scores for the CFS and CCI were 5.0 (IQR, 3.0–7.0) and 4.0 (IQR, 2.0–6.0), respectively. The median HADS score on day 1 was 13.0 (IQR, 7.0–18.0).

Factors associated with EQ-5D-5L scores at 90 days post-discharge

At 90 days post-discharge, several factors were significantly associated with decreased HRQoL among ICU survivors, as measured by the EQ-5D-5L questionnaire (Table 2). Older age was significantly associated with increased problems with mobility ($P=0.002$), self-care ($P<0.001$), and usual activities ($P=0.005$). Lower BMI was correlated with more severe issues in mobility ($P=0.005$), self-care ($P=0.010$), usual activities ($P=0.003$), and anxiety/depression ($P=0.002$). Longer ICU length of stay was associated with more severe problems in mobility ($P<0.001$), self-care ($P<0.001$), usual activities ($P=0.002$), and pain/discomfort ($P=0.013$). Higher severity of illness scores, such as SAPS III, were associated with poorer outcomes in mobility ($P=0.002$), self-care ($P=0.001$), and usual activities ($P=0.001$). Similarly, frailty, as measured by the CFS, was significantly associated with mobility ($P=0.001$), self-care ($P<0.001$), usual activities ($P<0.001$), and anxiety/depression ($P=0.049$). Opioid use in the ICU was significantly associated with increased problems in mobility ($P=0.006$) and self-care ($P=0.015$). Mechanical ventilation was also significantly associated with increased problems with mobility ($P=0.022$), self-care ($P=0.045$), and usual activities ($P=0.015$). Lower educational levels were linked to increased problems in mobility ($P=0.013$) and anxiety/depression ($P=0.042$). Vasopressor use in the ICU was associated with increased pain levels ($P=0.029$). Higher HADS scores on day 1 were significantly associated with increased problems in pain/discomfort ($P<0.001$) and anxiety/depression ($P=0.002$).

Table 3 shows the results for the multivariate analysis of factors influencing EQ-5D-5L dimensions at 90 days post-discharge. After adjusting for potential confounding factors, older age was significantly associated with poorer outcomes in multiple dimensions, including increased pain/discomfort ($P=0.004$), reduced ability to perform usual activities ($P<0.001$), diminished self-care capacity ($P<0.001$), and impaired mobility ($P<0.001$). Lower BMI was linked to difficulties in self-care ($P=0.002$), mobility ($P=0.006$), and anxiety/depression symptoms ($P=0.006$). Higher HADS scores on day 1 were strongly associated with increased pain/discomfort ($P<0.001$), anxiety/depression symptoms ($P=0.002$), and reduced ability to perform usual activities ($P<0.001$). Admission due to infection was a significant predictor of impairments in usual activities ($P=0.003$). CFS was consistently associated with poorer outcomes across multiple dimensions, including pain/discomfort ($P=0.042$), usual activities ($P<0.001$), self-care ($P<0.001$), and mobility ($P<0.001$). Socioeconomic factors also played a role: retired status was linked to worse outcomes in usual activities ($P=0.037$), self-care ($P=0.002$), and mobility ($P=0.007$). Higher education levels were associated with better outcomes in self-care ($P=0.019$) and mobility ($P=0.015$).

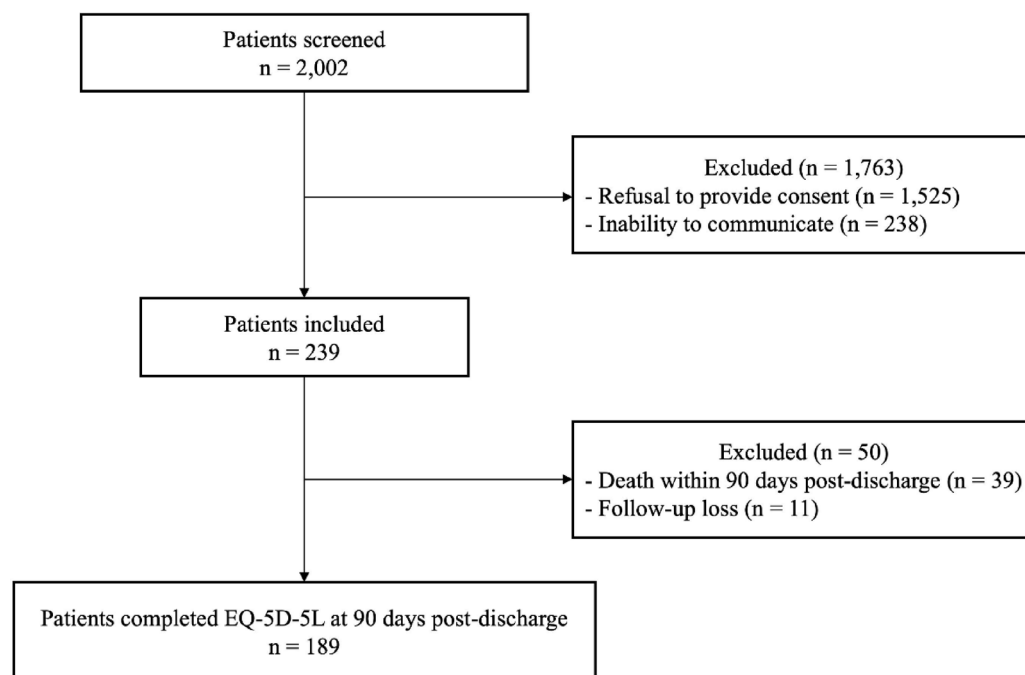


Fig. 1. Study flow diagram. EQ-5D-5L five-level version of EuroQoL 5-dimension.

Characteristic	N = 189
Age, years	63.0 (53.0–71.0)
Sex, male	112 (59.3)
BMI, kg/m ²	23.0 (20.9–26.8)
Smoking	
Never smoker	106 (56.1)
Current smoker	54 (28.6)
Ex-smoker	29 (15.3)
Living arrangement	
Living with others	157 (83.1)
Living alone	32 (16.9)
Employment status	
Employed	63 (33.3)
Seeking employment	13 (6.9)
Housework	16 (8.5)
Student	4 (2.1)
Retired	67 (35.4)
Others	26 (13.8)
Educational level	
Middle school or below	55 (29.1)
Higher education or above	134 (70.9)
ICU admission diagnosis	
Pulmonary disease	76 (40.2)
Gastrointestinal disease	28 (14.8)
Cardiovascular disease	17 (9.0)
Malignant disease	22 (11.6)
Renal disease	16 (8.5)
Neurologic disease	9 (4.8)
Postoperative care	2 (1.1)
Others	19 (10.1)
Infection as reason for admission	48 (25.4)
Transferred from ER to ICU	68 (36.0)
Medical ICU	173 (91.5)
SAPS III score	60.9 ± 16.0
SOFA score	6.0 (3.0–9.0)
Charlson comorbidity index	4.0 (2.0–6.0)
Clinical frailty scale	5.0 (3.0–7.0)
HADS score, Day 1	13.0 (7.0–18.0)
Visual analog scale	2.0 (0.0–6.0)
Opioid use in ICU	108 (57.1)
Sedative use in ICU	80 (42.3)
Vasopressor use in ICU	124 (65.6)
Ventilator use during ICU stay	96 (50.8)
RRT use during ICU stay	39 (20.6)
Delirium during ICU stay	41 (21.7)
ICU length of stay, days	7.0 (4.0–12.0)

Table 1. Baseline characteristics of the study population. Data are presented as number (percentage) or median (interquartile range). *BMI* body mass index, *ICU* intensive care unit, *SAPS* simplified acute physiology score, *SOFA* sequential organ failure assessment, *HADS* hospital anxiety and depression scale, *RRT* renal replacement therapy.

Table 4 presents the factors affecting EQ-5D-5L total scores at 90 days post-discharge. In the multivariate regression analysis, older age (coefficient = −0.002, 95% CI: −0.004 to −0.001, $P=0.001$), infection as the admission diagnosis (coefficient = −0.069, 95% CI: −0.116 to −0.022, $P=0.004$), higher CFS scores (coefficient = −0.016, 95% CI: −0.024 to −0.007, $P=0.001$), and higher baseline HADS total scores (coefficient = −0.005, 95% CI: −0.007 to −0.002, $P=0.001$) were significantly associated with lower EQ-5D-5L total scores.

	Mobility				Self-care				Usual activity			
	None (n = 89)	Moderate (n = 87)	Severe (n = 13)	P	None (n = 114)	Moderate (n = 66)	Severe (n = 9)	P	None (n = 79)	Moderate (n = 95)	Severe (n = 15)	P
Male	56 (62.9)	50 (57.5)	6 (46.2)	0.464	75 (65.8)	34 (51.5)	3 (33.3)	0.046	48 (60.8)	57 (50.0)	7 (46.7)	0.583
Age	58.0 (48.0–69.0)	65.0 (59.5–74.0)	64.0 (61.0–79.0)	0.002	59.5 (47.0–69.0)	66.0 (61.0–77.0)	72.0 (61.0–79.0)	<0.001	59.0 (45.5–69.0)	63.0 (57.0–74.0)	64.0 (61.0–79.0)	0.005
Living alone	10 (11.2)	18 (20.7)	4 (30.8)	0.096	18 (15.8)	10 (15.2)	4 (44.4)	0.078	12 (15.2)	16 (16.8)	4 (26.7)	0.554
Employed	36 (40.4)	25 (28.7)	2 (15.4)	0.204	48 (42.1)	15 (22.7)	0 (0.0)	0.048	32 (40.5)	30 (31.6)	1 (6.7)	0.334
Middle school or below	17 (19.1)	32 (36.8)	6 (46.2)	0.013	27 (23.7)	23 (34.8)	5 (55.6)	0.057	19 (24.1)	28 (29.5)	8 (53.3)	0.072
BMI	24.4 (22.1–28.1)	22.2 (19.8–25.3)	21.7 (20.8–26.5)	0.005	24.2 (21.3–27.4)	22.3 (19.8–25.2)	21.1 (18.5–21.9)	0.010	24.4 (22.0–28.3)	22.5 (20.3–25.5)	21.2 (19.7–23.7)	0.003
ICU LOS	5.0 (3.0–8.0)	8.0 (4.0–14.5)	13.0 (8.0–22.0)	<0.001	5.0 (3.0–9.0)	9.0 (5.0–18.0)	13.0 (8.0–19.0)	<0.001	5.0 (3.0–10.0)	7.0 (4.0–13.0)	12.0 (8.0–20.0)	0.002
Opioid use in ICU	41 (46.1)	56 (64.4)	11 (84.6)	0.006	59 (51.8)	40 (60.6)	9 (100.0)	0.015	43 (54.4)	51 (53.7)	14 (93.3)	0.013
Sedative use in ICU	33 (37.1)	39 (44.8)	8 (61.5)	0.203	48 (42.1)	26 (39.4)	6 (66.7)	0.298	32 (40.5)	37 (38.9)	11 (73.3)	0.040
Vasopressor use in ICU	55 (61.8)	59 (67.8)	10 (76.9)	0.473	71 (62.3)	46 (69.7)	7 (77.8)	0.441	46 (58.2)	67 (70.5)	11 (73.3)	0.190
SAPS III	58.4 ± 14.0	61.3 ± 17.0	75.2 ± 15.6	0.002	58.4 ± 14.4	62.6 ± 16.9	78.3 ± 17.4	0.001	60.5 ± 14.1	58.8 ± 16.7	75.6 ± 14.4	0.001
SOFA	5.0 (3.0–8.0)	6.0 (3.0–10.0)	9.0 (5.0–11.0)	0.013	6.0 (3.0–9.0)	5.5 (4.0–11.0)	10.0 (7.0–11.0)	0.040	6.0 (3.0–9.0)	5.0 (3.0–10.0)	9.0 (6.0–11.5)	0.100
CCI	3.0 (2.0–6.0)	4.0 (3.0–6.0)	4.0 (3.0–5.0)	0.010	3.5 (2.0–6.0)	5.0 (3.0–6.0)	5.0 (4.0–8.0)	0.007	4.0 (2.0–6.0)	4.0 (3.0–6.0)	5.0 (3.5–6.0)	0.045
CFS	4.0 (2.0–7.0)	5.0 (3.0–7.0)	8.0 (7.0–8.0)	0.001	4.0 (2.0–7.0)	5.0 (3.0–8.0)	8.0 (7.0–8.0)	<0.001	5.0 (2.0–7.0)	4.0 (3.0–6.5)	8.0 (7.0–8.0)	<0.001
Ventilator	37 (41.6)	49 (56.3)	10 (76.9)	0.022	53 (46.5)	35 (53.0)	8 (88.9)	0.045	38 (48.1)	45 (47.4)	13 (86.7)	0.015
RRT	17 (19.1)	19 (21.8)	3 (23.1)	0.882	23 (20.2)	14 (21.2)	2 (22.2)	0.979	17 (21.5)	17 (17.9)	5 (33.3)	0.377
Delirium	18 (20.2)	19 (21.8)	4 (30.8)	0.689	21 (18.4)	18 (27.3)	2 (22.2)	0.381	18 (22.8)	19 (20.0)	4 (26.7)	0.805
VAS	3.0 (0.0–7.0)	2.0 (0.0–6.0)	3.0 (1.0–5.0)	0.851	2.0 (0.0–7.0)	2.0 (0.0–5.0)	5.0 (1.0–7.0)	0.729	2.0 (0.0–6.0)	2.0 (0.0–6.0)	3.0 (1.0–6.5)	0.698
HADS, Day 1	11.0 (5.0–17.0)	14.0 (9.0–20.0)	13.0 (9.0–15.0)	0.020	13.0 (6.0–18.0)	13.0 (8.0–22.0)	13.0 (9.0–22.0)	0.207	12.0 (5.0–17.0)	14.0 (8.0–20.5)	13.0 (8.0–23.0)	0.024

	Pain			Anxiety/depression			P	Severe (n = 4)	Moderate (n = 80)	None (n = 105)	Severe (n = 7)	Moderate (n = 126)	None (n = 56)
	None (n = 56)	Moderate (n = 126)	Severe (n = 7)	P	None (n = 105)	Moderate (n = 80)							
Male	37 (66.1)	72 (57.1)	3 (42.9)	0.352	64 (61.0)	46 (57.5)		2 (50.0)					
Age	63.5 (48.0–69.0)	63.0 (54.0–73.0)	64.0 (62.0–66.0)	0.370	62.0 (49.0–69.0)	63.0 (57.0–75.0)		65.5 (47.5–74.5)					
Living alone	9 (15.1)	22 (17.5)	1 (14.3)	0.956	15 (14.3)	17 (21.2)		0 (0.0)					
Employed	22 (39.3)	38 (30.2)	3 (42.9)	0.097	38 (36.2)	24 (30.0)		1 (25.0)					
Middle school or below	13 (23.2)	40 (31.7)	2 (28.6)	0.504	34 (32.4)	18 (22.5)		3 (75.0)					
BMI	24.3 (21.2–28.2)	22.6 (20.8–26.5)	21.8 (21.3–24.2)	0.202	24.3 (21.6–27.2)	22.0 (19.4–25.2)		20.7 (17.8–25.0)					
ICU LOS	4.5 (3.0–9.5)	7.0 (4.0–13.0)	10.0 (8.5–16.5)	0.013	6.0 (4.0–11.0)	6.0 (4.0–13.0)		9.0 (7.5–11.0)					
Opioid use in ICU	28 (50.0)	75 (59.5)	5 (71.4)	0.360	60 (57.1)	45 (56.2)		3 (75.0)					
Sedative use in ICU	23 (41.1)	52 (41.3)	5 (71.4)	0.283	43 (41.0)	34 (42.5)		3 (75.0)					
Vasopressor use in ICU	34 (60.7)	85 (67.5)	5 (71.4)	0.640	61 (58.1)	59 (73.8)		4 (100.0)					
SAPS III	61.0 ± 16.5	60.3 ± 15.3	69.1 ± 23.6	0.369	60.1 ± 14.1	60.3 ± 18.2		68.5 ± 19.3					
SOFA	7.0 (4.0–10.0)	5.5 (3.0–9.0)	7.0 (3.0–11.0)	0.648	6.0 (3.0–9.0)	5.0 (3.0–9.6)		9.5 (5.0–12.5)					
CCI	4.0 (2.0–6.0)	4.0 (2.0–6.0)	4.0 (4.0–5.5)	0.663	4.0 (2.0–6.0)	4.0 (2.5–6.0)		5.0 (3.5–7.0)					
CFS	4.0 (2.0–7.0)	5.0 (3.0–7.0)	8.0 (4.0–8.0)	0.226	4.0 (3.0–7.0)	5.5 (3.5–8.0)		4.0 (2.5–6.5)					
Ventilator	28 (50.0)	63 (50.0)	5 (71.4)	0.538	56 (53.3)	36 (45.0)		4 (100.0)					
RRT	13 (23.2)	25 (19.8)	1 (14.3)	0.799	22 (21.0)	16 (20.0)		1 (25.0)					
Delirium	14 (25.0)	25 (19.8)	2 (28.6)	0.667	23 (21.9)	16 (20.0)		2 (50.0)					
VAS	2.0 (0.0–5.5)	3.0 (1.0–6.0)	5.0 (1.0–6.5)	0.308	3.0 (0.0–6.0)	2.0 (0.0–6.0)		4.5 (1.5–7.0)					
HADS, Day 1	8.5 (4.0–15.5)	14.0 (8.0–19.0)	17.0 (12.0–22.0)	<0.001	11.0 (5.0–17.0)	14.5 (9.0–21.5)		19.5 (9.0–26.5)					

Table 2. EQ-5D-5L problems at 90 days post-discharge by ICU variables, background data, and current health State. Data are presented as number (percentage) or median (interquartile range). EQ-5D-5L, five-level version of EuroQoL 5-dimension. *BMI* body mass index, *ICU* intensive care unit, *LOS* length of stay, *SAPS* simplified acute physiology score, *SOFA* sequential organ failure assessment, *CCI* Charlson comorbidity index, *CFS* clinical frailty scale, *RRT* renal replacement therapy, *VAS* visual analog scale, *HADS* hospital anxiety and depression Scale.

Factors associated with HADS scores at 90 days post-discharge

Multivariate regression analysis identified significant predictors of anxiety and depression symptoms 90 days post-discharge, as measured by the HADS (Table 5). For the anxiety subscale, higher CFS scores (coefficient = 0.308, 95% CI: 0.132 to 0.484, $P = 0.001$) and higher baseline HADS total scores (coefficient = 0.189, 95% CI: 0.135 to 0.243, $P < 0.001$) were significantly associated with increased anxiety symptoms. For the depression subscale, older age (coefficient = 0.075, 95% CI: 0.038 to 0.112, $P < 0.001$) and higher baseline HADS total scores (coefficient = 0.215, 95% CI: 0.142 to 0.289, $P < 0.001$) were significant predictors of higher depression scores. For the total HADS score, higher CFS scores (coefficient = 0.529, 95% CI: 0.150 to 0.909, $P = 0.007$) and higher baseline HADS total scores (coefficient = 0.385, 95% CI: 0.268 to 0.501, $P < 0.001$) were significantly associated with increased overall anxiety and depression symptoms (Table 6).

Relationship between initial HADS, CFS, and outcomes at 90 days post-discharge

Figure 2 illustrates the relationships between initial HADS scores, CFS, and outcomes at 90 days, specifically follow-up HADS scores and EQ-5D-5L total scores.

The associations between day 1 HADS scores and 90-day outcomes are depicted in Fig. 2A. A positive correlation was observed between day 1 HADS scores and 90-day follow-up HADS scores (correlation: 0.435, $P < 0.001$), suggesting that higher anxiety and depression levels at ICU admission are associated with persistent psychological distress at 90 days. Additionally, a negative correlation was noted between day 1 HADS scores and 90-day EQ-5D-5L total scores (correlation: -0.192 , $P = 0.008$), indicating that greater baseline anxiety and depression are linked to poorer HRQoL at 90 days. Figure 2B shows the association between CFS scores and 90-day outcomes. A positive correlation between CFS and 90-day follow-up HADS scores (correlation: 0.205, $P < 0.001$) indicates that higher frailty levels are associated with increased psychological distress. Conversely, a negative correlation between CFS and 90-day EQ-5D-5L total scores (correlation: -0.298 , $P = 0.008$) suggests that greater frailty is linked to poorer HRQoL at 90 days. These findings highlight the combined impact of psychological distress and frailty on long-term patient outcomes.

Changes in EQ-5D-5L domain scores over time

Changes in each of the five EQ-5D-5L domains between day 30 and day 90 post-discharge were also analyzed separately from the total EQ-5D-5L scores (Table S1). Significant improvements were observed in the domains of mobility (mean score: 2.04 to 1.84, $P < 0.01$), self-care (1.78 to 1.61, $P < 0.01$), and usual activities (2.12 to 1.90, $P < 0.01$). The total EQ-5D-5L index score also increased significantly from 0.73 ± 0.18 at day 30 to 0.76 ± 0.16 at day 90 ($P < 0.01$). In contrast, no statistically significant changes were noted in the pain/discomfort and anxiety/depression domains. These findings suggest that physical function domains tend to improve more clearly over time than psychological or emotional dimensions.

Discussion

This multicenter prospective study provides important insights into the factors influencing HRQoL and psychological outcomes among ICU survivors 90 days post-discharge, emphasizing the impact of initial psychological states and clinical characteristics. The findings contribute to the limited body of research on mid-term HRQoL predictors in critically ill patients, with a focus on anxiety, depression, and functional recovery.

Previous evidence indicates varied outcomes for ICU survivors, with a general decline in HRQoL, particularly in physical functioning³. This decline is more pronounced in patients who suffer from severe conditions, such as acute respiratory distress syndrome or sepsis^{9,10}. Most studies utilized the SF-36 and EQ-5D scores, which are well-recognized measures of HRQoL^{2,3,11–13}. Factors associated with HRQoL include frailty status, length of ICU stay, mechanical ventilation duration, and sedation duration. Additionally, PICS, unemployment, low income, and advanced age are significantly associated with declines in mental and functional health^{3,4,14,15}.

Clinical frailty, as measured by the CFS, is a significant determinant of both HRQoL and psychological outcomes among ICU survivors¹⁶. Frailty, a critical marker of resilience and recovery capacity, was strongly associated with worse mobility, reduced self-care ability, and heightened psychological distress at 90 days post-discharge. Frail patients demonstrated diminished independence, impaired physical function, and increased anxiety and depression, highlighting the interplay between physical and mental health during recovery. These findings emphasize the importance of assessing frailty at ICU admission to guide individualized rehabilitation strategies and post-ICU care. This observation aligns with previous studies linking frailty to poor recovery trajectories, underscoring its predictive value for long-term outcomes and its role in optimizing post-ICU interventions.

The HADS was developed to assist in identifying anxiety disorders and depression in patients hospitalized due to various illnesses¹⁷. Comprising a total of 14 items, this questionnaire is known to be more useful and appropriate for evaluating and supporting the mental health of hospitalized patients than diagnosing and treating psychiatric patients¹⁸. Since its development in 1983, the HADS has been validated in numerous countries worldwide. In South Korea, a systematic translation process led to the creation of the Korean version of HADS, which has demonstrated reliability and validity¹⁹. Evidence indicates that a score of 8 or above on both the HADS-Anxiety (HADS-A) and HADS-Depression (HADS-D) subscales offers the optimal sensitivity and specificity for case definition²⁰.

Our results indicate that initial HADS scores significantly influence both mid-term HADS and EQ-5D-5L scores among ICU survivors, consistent with previous research indicating that early psychological distress can adversely affect long-term HRQoL. For instance, Davydow et al. demonstrated that higher baseline anxiety and depression levels are associated with poorer HRQoL outcomes in ICU survivors⁴. Similarly, Needham et al. highlighted the importance of early psychological assessments in predicting post-ICU recovery trajectories²¹. The current results expand on such findings by demonstrating the important association between initial HADS

	Univariable analysis		Multivariable analysis	
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
Factors influencing pain domain				
Age	0.005 (0.000 to 0.010)	0.031	0.007 (0.002 to 0.012)	0.004
C-reactive protein	−0.001 (−0.002 to 0.000)	0.022		
HADS, Day 1	0.019 (0.010 to 0.029)	<0.001	0.021 (0.012 to 0.030)	<0.001
Factors influencing usual activities domain				
Age	0.011 (0.005 to 0.017)	<0.001	0.012 (0.006 to 0.017)	<0.001
BMI	−0.032 (−0.051 to −0.013)	0.001		
ICU length of stay	0.012 (0.002 to 0.021)	0.014		
Albumin	−0.183 (−0.329 to −0.036)	0.015		
Infection as reason for admission	0.314 (0.114 to 0.514)	0.002	0.2854 (0.097 to 0.474)	0.003
Charlson Comorbidity Index	0.040 (0.006 to 0.075)	0.021		
Clinical Frailty Scale	0.052 (0.014 to 0.089)	0.008		
Retired	0.047 (0.003 to 0.092)	0.037		
Higher education or above	−0.196 (−0.390 to −0.001)	0.049		
HADS, Day 1	0.017 (0.005 to 0.028)	0.004	0.021 (0.010 to 0.032)	<0.001
Factors influencing self-care domain				
Female sex	0.214 (0.045 to 0.383)	0.013	0.269 (0.123 to 0.416)	0.002
Age	0.013 (0.008 to 0.018)	<0.001	0.013 (0.009 to 0.018)	<0.001
BMI	−0.027 (−0.045 to −0.009)	0.003	−0.025 (−0.040 to −0.009)	0.002
ICU length of stay	0.019 (0.011 to 0.028)	<0.001	0.019 (0.011 to 0.026)	<0.001
Albumin	−0.162 (−0.300 to −0.023)	0.022		
Opioid use in ICU	0.216 (0.048 to 0.384)	0.012		
Infection as reason for admission	0.298 (0.109 to 0.487)	0.002		
SAPS III	0.009 (0.004 to 0.014)	0.001		
SOFA	0.028 (0.006 to 0.049)	0.011		
Charlson Comorbidity Index	0.048 (0.016 to 0.080)	0.004		
Clinical Frailty Scale	0.069 (0.034 to 0.104)	<0.001		
Ventilator use in ICU	0.176 (0.010 to 0.343)	0.038		
Retired	0.066 (0.024 to 0.108)	0.002		
Higher education or above	−0.219 (−0.402 to −0.036)	0.019		
HADS, Day 1	0.011 (0.000 to 0.022)	0.046		
Factors influencing movement domain				
Age	0.018 (0.009 to 0.028)	<0.001	0.018 (0.009 to 0.027)	<0.001
BMI	−0.046 (−0.078 to −0.015)	0.004	−0.041 (−0.070 to −0.012)	0.006
ICU length of stay	0.036 (0.021 to 0.051)	<0.001	0.034 (0.020 to 0.049)	<0.001
Sedative use in ICU	0.319 (0.021 to 0.616)	0.036		
Opioid use in ICU	0.478 (0.186 to 0.771)	0.001		
Infection as reason for admission	0.548 (0.215 to 0.881)	0.001		
SAPS III	0.017 (0.008 to 0.026)	<0.001		
SOFA	0.038 (0.000 to 0.076)	0.048		
Charlson Comorbidity Index	0.063 (0.005 to 0.120)	0.033		
Clinical Frailty Scale	0.134 (0.072 to 0.195)	<0.001		
Ventilator use in ICU	0.450 (0.159 to 0.74)	0.003		
Living with others	−0.417 (−0.809 to −0.024)	0.037		
Retired	0.102 (0.028 to 0.176)	0.007		
Higher education or above	−0.403 (−0.726 to −0.081)	0.015		
HADS, Day 1	0.022 (0.002 to 0.041)	0.028		
Continued				

	Univariable analysis		Multivariable analysis	
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
Factors influencing anxiety/depression Domain				
BMI	−0.029 (−0.045 to −0.013)	0.001	−0.023 (−0.039 to −0.007)	0.006
Vasopressor use in ICU	0.217 (0.056 to 0.378)	0.008		
Clinical Frailty Scale	0.034 (0.001 to 0.068)	0.042		
HADS, Day 1	0.019 (0.009 to 0.029)	<0.001	0.016 (0.006 to 0.026)	0.002

Table 3. Multivariable logistic regression analysis for factors influencing each domain of EQ-5D-5L at 90 days*. * Each domain of EQ-5D-5L is scored on a 5-point scale, where 1 indicates no problems and 5 indicates extreme problems. *EQ-5D-5L* five-level version of EuroQoL 5-dimension, *BMI* body mass index, *ICU* intensive care unit, *SAPS* simplified acute physiology score, *SOFA* sequential organ failure assessment, *HADS* hospital anxiety and depression scale.

	Univariable analysis		Multivariable analysis	
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
Age	− 0.003 (− 0.004 to − 0.001)	<0.001	− 0.002 (− 0.004 to − 0.001)	0.001
BMI	0.007 (0.002 to 0.012)	0.004		
ICU length of stay	− 0.004 (− 0.006 to − 0.001)	0.002		
Sedative use in ICU	− 0.051 (− 0.096 to − 0.006)	0.027		
Opioid use in ICU	− 0.065 (− 0.109 to − 0.020)	0.005		
Infection as reason for admission	− 0.082 (− 0.133 to − 0.032)	0.002	− 0.069 (− 0.116 to − 0.022)	0.004
SAPS III	− 0.002 (− 0.004 to − 0.001)	0.001		
Charlson Comorbidity Index	− 0.009 (− 0.018 to − 0.000)	0.039		
Clinical Frailty Scale	− 0.020 (− 0.029 to − 0.011)	<0.001	− 0.016 (− 0.024 to − 0.007)	0.001
Ventilator use in ICU	− 0.063 (− 0.107 to − 0.018)	0.006		
Retired	− 0.014 (− 0.025 to − 0.002)	0.019		
Higher education or above	0.053 (0.003 to 0.102)	0.036		
HADS, Day 1	− 0.004 (− 0.007 to − 0.001)	0.008	− 0.005 (− 0.007 to − 0.002)	0.001

Table 4. Multivariable logistic regression analysis for factors influencing the total score of EQ-5D-5L at 90 days*. *Total score is the sum of responses across all domains, where lower scores indicate poorer quality of life. *EQ-5D-5L* five-level version of EuroQoL 5-dimension, *BMI* body mass index, *ICU* intensive care unit, *SAPS* simplified acute physiology score, *HADS* hospital anxiety and depression scale.

Anxiety	Univariable analysis		Multivariable analysis	
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
BMI	− 0.156 (− 0.255 to − 0.057)	0.002		
Vasopressor use in ICU	1.281 (0.308 to 2.255)	0.010		
Sedative use in ICU	1.485 (0.557 to 2.413)	0.002		
Opioid use in ICU	1.840 (0.926 to 2.753)	<0.001		
Clinical Frailty Scale	0.347 (0.151 to 0.544)	0.001	0.308 (0.132 to 0.484)	0.001
Use of ventilator in ICU	1.186 (0.260 to 2.111)	0.012		
Visual analog scale, Initial	0.267 (0.133 to 0.400)	<0.001		
HADS, Day 1	0.195 (0.140 to 0.250)	<0.001	0.189 (0.135 to 0.243)	<0.001
Depression				
Age	0.059 (0.019 to 0.099)	0.004	0.075 (0.038 to 0.112)	<0.001
BMI	− 0.147 (− 0.277 to − 0.017)	0.027		
Opioid use in ICU	1.701 (0.493 to 2.908)	0.006		
HADS, Day 1	0.193 (0.118 to 0.269)	<0.001	0.215 (0.142 to 0.289)	<0.001

Table 5. Multivariable logistic regression analysis for factors influencing each domain of HADS at 90 days. *BMI* body mass index, *ICU* intensive care unit, *HADS* Hospital Anxiety and Depression Scale.

	Univariable analysis		Multivariable analysis	
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
BMI	− 0.297 (− 0.507 to − 0.087)	0.006		
Vasopressor use in ICU	2.248 (0.182 to 4.313)	0.033		
Sedative use in ICU	2.390 (0.409 to 4.370)	0.018		
Opioid use in ICU	3.586 (1.647 to 5.526)	< 0.001		
Clinical frailty scale	0.608 (0.189 to 1.027)	0.005	0.529 (0.150 to 0.909)	0.007
Ventilator use in ICU	1.992 (0.026 to 3.958)	0.047		
Visual analog scale, initial	0.396 (0.108 to 0.684)	0.007		
HADS, Day 1	0.395 (0.277 to 0.513)	< 0.001	0.385 (0.268 to 0.501)	< 0.001

Table 6. Multivariable logistic regression analysis for factors influencing total score of HADS at 90 days. *BMI* body mass index, *ICU* intensive care unit, *HADS* hospital anxiety and depression scale.

scores on multiple EQ-5D-5L domains, including mobility, self-care, pain/discomfort, and anxiety/depression, underscoring the interconnectedness of psychological and physical recovery.

Uniquely, these findings establish initial HADS scores as a central predictor, not only of persistent psychological distress but also of mid-term functional outcomes, emphasizing the necessity for routine psychological assessment during ICU admission. Early identification of patients with high anxiety and depression scores could enable targeted interventions, such as psychological counseling or structured post-discharge follow-ups, to mitigate the long-term effects. Furthermore, the results support the development of multidisciplinary recovery programs, integrating mental health support to address the sustained challenges faced by ICU survivors. These findings highlight the importance of proactive mental health management to optimize recovery and improve overall HRQoL in this vulnerable population.

This study has several strengths. First, it is the first large-scale prospective observational study conducted in Korea to explore factors affecting the HRQoL of ICU survivors. Second, by including all ICU patients rather than focusing on a specific disease group, this study identified influential factors that are broadly applicable to any patient admitted to the ICU. This comprehensive approach enhances the clinical utility of the findings, as they can inform strategies for a wide range of critically ill patients, regardless of their underlying conditions.

Despite its strengths, this study has limitations. First, the sample was relatively small compared to the number of patients initially screened, which may limit the generalizability of the findings. The high rate of refusal to provide consent among eligible patients could have introduced selection bias. Previous studies suggest that cultural factors, including stigma and reluctance to disclose psychological distress, can affect research participation, particularly in studies involving mental health assessments^{22,23}. Second, the study population was confined to patients in South Korean tertiary medical centers, and cultural or healthcare system differences may impact the applicability of these results to other settings. Third, the reliance on telephone interviews for HRQoL assessments may have introduced reporting bias, limited the ability to capture subtle psychological or functional impairments, and excluded patients with communication barriers. Fourth, we did not evaluate skeletal muscle loss or strength, which are known to significantly affect post-ICU physical recovery²⁴. Fifth, subgroup analyses based on categorical divisions of HRQoL scores, such as severe impairment categories, involved relatively small samples, and the results should, therefore, be interpreted with caution. Lastly, although multivariate regression was employed to adjust for a wide range of variables, we cannot exclude the influence of unmeasured confounders, such as pre-ICU functional status and post-discharge social support, which may have affected the outcomes.

Conclusion

Through this large-scale prospective observational study, we demonstrated that initial HADS scores and clinical frailty are significant predictors of mid-term HRQoL outcomes in ICU survivors, influencing both psychological well-being and functional recovery. Frailty, a critical marker of resilience and recovery capacity, was consistently associated with worse outcomes across multiple dimensions, including mobility, self-care, and psychological distress. This finding highlights the importance of systematically assessing both HADS scores and frailty at the onset of ICU admission or as early as possible during the ICU stay. Early identification of patients with high anxiety or depression levels and those with significant frailty enables targeted interventions, such as psychological support, tailored physical rehabilitation, and structured follow-ups, to mitigate long-term impairments in HRQoL. Additionally, the results underscore the need for a multidisciplinary approach to ICU recovery, integrating mental health management alongside individualized rehabilitation strategies to optimize outcomes. These findings provide critical evidence to guide clinical practice and improve overall quality of care for this vulnerable population.

Methods

Study design and participants

This multicenter prospective cohort study was conducted at four tertiary/academic medical centers in South Korea from June 2021 to September 2022. From day 1 to ICU discharge, the researchers assessed patients for delirium using the 4 A's test (4AT) and Confusion Assessment Method for the ICU (CAM-ICU), documenting its presence throughout the ICU stay.

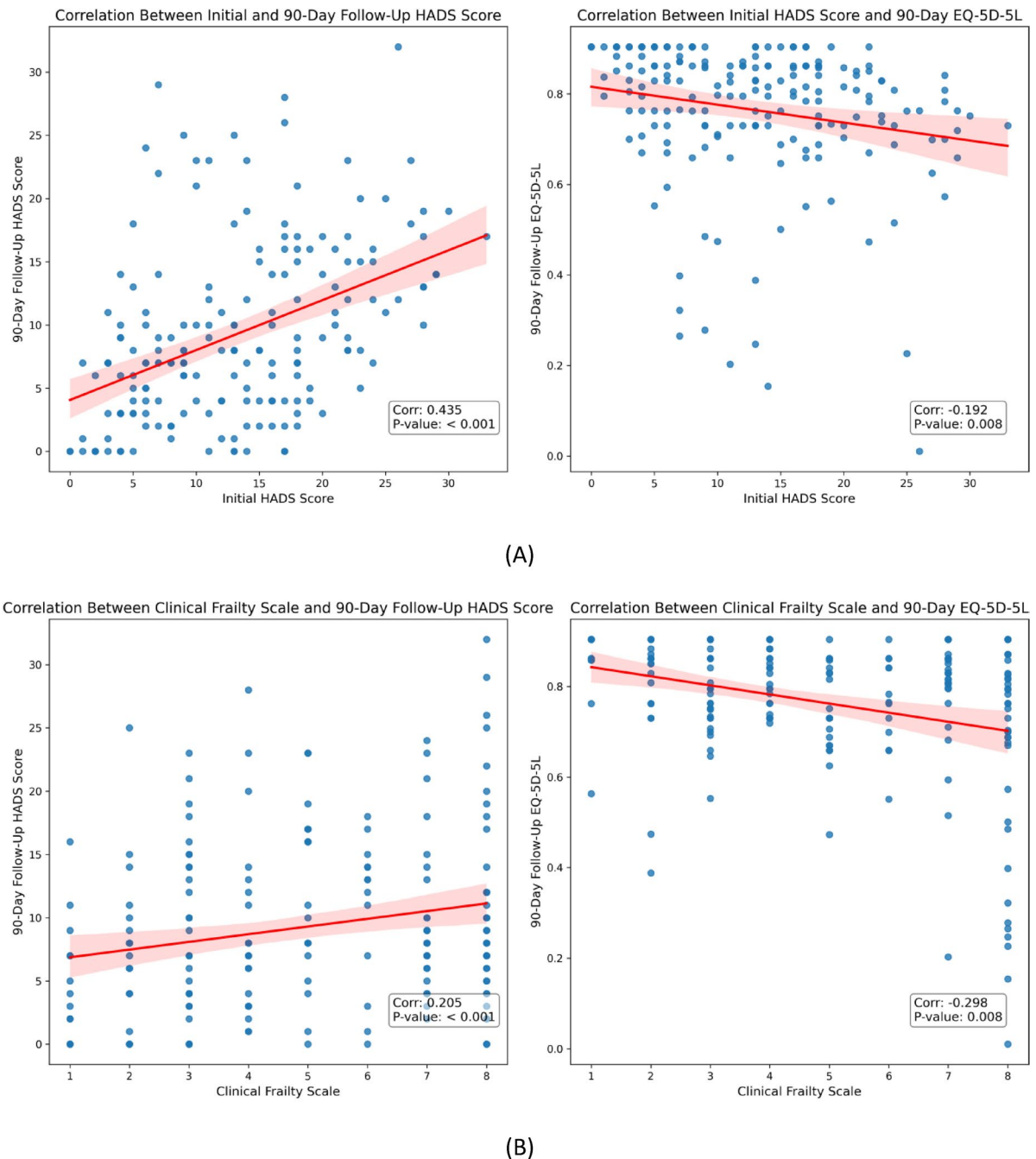


Fig. 2. Correlation among initial HADS, CFS, and outcomes 90 days post-discharge. **(A)** Correlation between initial HADS scores and 90-day outcomes. **(B)** Correlation between clinical frailty scale and 90-day outcomes. HADS hospital anxiety and depression scale, EQ-5D-5L five-level version of EuroQoL 5-Dimension.

On day 1, defined as the day of admission to the ICU, baseline characteristics, including sex, age, living arrangement, employment status, education level, smoking history, alcohol history, and body mass index (BMI), were collected. Additionally, psychological and subjective assessments, such as the Hospital Anxiety and Depression Scale (HADS) and Visual Analog Scale (VAS), were measured. Key laboratory data, including protein and albumin levels, were also recorded at ICU admission. During the ICU stay, the researchers documented key clinical variables, including ICU length of stay (LOS), presence of infection as the reason for admission, previous history of delirium, Simplified Acute Physiology (SAPS) III score, SOFA score, Charlson Comorbidity Index (CCI), Clinical Frailty Scale (CFS), and the use of vasopressors, sedatives, opioids, mechanical ventilation, and renal replacement therapy (RRT).

Inclusion criteria were adults aged 20 and over, admitted to the ICU for more than 24 h, and with no cognitive dysfunction before ICU admission. Exclusion criteria were failure to provide informed consent, inability to

communicate due to a history of psychiatric problems, Parkinson's disease, or stroke, or inability to participate in the HRQoL assessment interview 90 days post-discharge.

HRQoL measurement

HRQoL was assessed through telephone interviews conducted 30- and 90-days post-discharge. HRQoL assessments included the new five-level version of EuroQoL 5-Dimension (EQ-5D-5L) and Hospital Anxiety and Depression Scale (HADS). All research nurses and intensivists involved in this study were trained to properly administer these questionnaires. The HADS was measured on day 1 and 30 and 90 days after discharge, while the EQ-5D-5L was assessed 30- and 90-days post-discharge. Post-discharge interviews were conducted via telephone. The EQ-5D-5L, developed by the EuroQoL Group, is a standardized tool used to evaluate a patient's health status across five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each rated on a five-level scale ranging from 1 (no problems) to 5 (extreme problems)²⁵. The total EQ-5D-5L score is calculated by summing responses across all domains, with lower scores indicating poorer quality of life and higher scores indicating better quality of life. The HADS score is employed to evaluate the patient's levels of anxiety and depression, comprising 14 items split into two subscales assessing anxiety and depression, each item scored from 0 (no symptoms) to 3 (severe symptoms), with higher scores indicating more severe anxiety or depression⁶.

Statistical analysis

Continuous variables are reported as means with standard deviations or medians with interquartile ranges, depending on their distribution. Categorical variables are presented as numbers (%). Differences between groups were analyzed using the independent t-test or Mann–Whitney U test for continuous variables, and the chi-squared or Fisher's exact test for categorical variables, as appropriate. Prior to analysis, an a priori power calculation was performed to estimate the minimum required sample size for multivariable regression. Using conventional parameters ($\alpha = 0.05$, power = 0.80, and medium effect size $f^2 = 0.15$) and assuming 10 explanatory variables, the estimated, minimum sample size was approximately 50 patients. Multivariate logistic regression analyses with stepwise selection were performed to identify significant predictors of 90-day HRQoL outcomes. To assess potential multicollinearity among independent variables included in the regression models, variance inflation factors (VIFs) were calculated. All VIF values were below commonly accepted thresholds ($VIF < 5$), indicating no significant collinearity. Detailed results are presented in Table S2. In addition to initial HADS scores, the model included clinically meaningful variables: demographic factors (sex, age, living arrangement, employment status, education level, smoking history, alcohol history, BMI), ICU-related variables (ICU LOS, use of vasopressors, sedatives, opioids, mechanical ventilation, RRT), clinical factors at ICU admission (protein level, albumin level, infection as the reason for admission, SAPS III, SOFA, CCI, CFS, VAS), and delirium incidence and prior history (presence of delirium, previous history of delirium). Clinical parameters with a P value of 0.05 in the univariate logistic regression were included in the multivariate logistic regression. To evaluate the goodness-of-fit of the logistic regression model, we used the Hosmer–Lemeshow test²⁶. The test results indicated an adequate fit between the model and the observed data. The goodness-of-fit was computed to assess the relevance of the logistic regression model. Odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) were calculated. Longitudinal changes in HRQoL from Day 30 to Day 90 were analyzed using repeated-measures approaches, and correlations between initial HADS scores, CFS, and 90-day HRQoL were assessed with linear regression. All tests were two-sided, and P -values < 0.05 were considered statistically significant. Statistical analyses were conducted using Python software version 3.13.0 (Python Software Foundation, Beaverton, Oregon, United States).

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions

KHK and JL analyzed and interpreted the patient data and drafted the manuscript. JML, YSL, KSC, and CRC made substantial contributions to the study conception. YSL, KSC, CRC, and JL designed the study, interpreted the data, and substantively revised the manuscript. All authors read and approved the final manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics statement

This study was conducted in accordance with the relevant legislation and approved by the Ethics Committee of Seoul St. Mary's Hospital (KC21ONDI0504). The study complied with the Declaration of Helsinki and Good Clinical Practice Guidelines, and all patients provided informed consent for inclusion in the study.

Additional information

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1038/s41598-025-11431-x>.

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