

Psychological Symptoms in Relatives of Critically Ill Patients: A Longitudinal Cohort Study

OBJECTIVES: To explore the psychologic impact of an ICU stay on relatives and to determine patient and relative factors, including their pre-ICU mental health status, associated with psychologic symptoms 3 months after ICU admission.

DESIGN: A prospective, exploratory, longitudinal cohort study.

SETTING: A 12-bed ICU in a Dutch tertiary teaching hospital.

PATIENTS: The relatives of ICU patients admitted between March 2018 and December 2019.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Relatives completed the Hospital Anxiety and Depression Scale shortly after patients' ICU admission referring to the week before ICU admission and 3 months later, together with the Impact of Event Scale-Revised, assessing posttraumatic stress. A total of 387 were eligible of which 78 (20%) responded. Almost a quarter reported an increase of anxiety (23.1%) and depression (24.4%) between baseline and 3 months follow-up. One in six (17.9%) reported posttraumatic stress. Anxiety, depression, and posttraumatic stress at 3 months follow-up were significantly associated with preexisting anxiety and depression. Patients' factor associated with depression 3 months follow-up in relatives was length of ICU stay (odds ratio, 1.09; 95% CI, 1.02–1.16).

CONCLUSIONS: Relatives with preexisting psychologic symptoms before ICU admission are at risk to develop anxiety, depression, or posttraumatic stress shortly after ICU discharge of the patient. Screening and identification in an early stage enables early interventions to prevent relatives from worsening mental health during and after ICU admission.

KEY WORDS: anxiety; critical illness; depression; family; intensive care; posttraumatic stress

Increasingly more critically ill patients survive due to advanced ICU treatment, and almost 85% leave the hospital alive (1). ICU survivors pay a substantial price although by suffering from new or worsening impairments in physical, psychologic, and cognitive health status after critical illness that persist after the ICU treatment, defined as postintensive care syndrome (PICS) (2). Relatives are at high risk of developing mental health problems as well (3). They are witnessing their vulnerable loved ones in a critical situation surrounded by highly sophisticated and impressive equipment to keep them alive. At the same time, relatives play a key role as surrogate decision-maker, communicating with other relatives and healthcare professionals (4). Furthermore, after hospital discharge, more than half of the ICU survivors need informal care for at least 1 year, and in many cases, the relatives become the informal caregiver (5).

As a result, they are prone to develop depression, anxiety, acute stress syndrome, posttraumatic stress, or complicated grief for relatives of nonsurvivors, also defined as PICS-Family (PICS-F) (2, 6).

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To prevent relatives from suffering and to optimize their capability to support their beloved ones to regain active and fulfilling lives, early identification of relatives at risk is necessary (7).

The most important risk factor for adverse outcomes after ICU admission in ICU survivors is the health status before ICU admission (8). Although interventional trials do control for mental health illness-related medical care prior to ICU admission, the role of psychologic symptoms in the week before admission on the risk of developing PICS-F has never been studied before (9–11). Since relatives can have mental problems or be exposed to stressful events already before admission, it remains unclear what the role of the ICU admission is on post-ICU mental problems.

Therefore, the aim of the present study was to explore the psychologic impact of patients' ICU admission on relatives' mental health compared with mental health before ICU admission and to determine which patient and relative factors were associated with psychologic symptoms 3 months after ICU admission.

MATERIALS AND METHODS

Study Design, Setting, and Participants

A prospective, exploratory, longitudinal cohort study was performed in a 12-ICU-bed Dutch tertiary teaching hospital. Patient-related exclusion criteria were ICU readmissions, age under 18 years, and ICU stay shorter than 12 hours. Exclusion criterion was not being able to understand the Dutch language. We enrolled the primary contact, regardless whether the patient survived or died during the study period. The relatives provided written informed consent to participate, and the ICU patients provided written informed consent in order to extract data from their electronic health record (EHR). The study was approved by the Medical Ethical Review Board of Twente (registration number K18-01).

Data Collection

Enrollment took place between March 2018 and December 2019. Relatives received the baseline questionnaire between 12 and 72 hours after ICU admission, as soon as the peak of the "shock and disbelief" was over, and the relative was ready to receive information according to the nurses judgment. Relatives received the follow-up questionnaire 3 months after

ICU admission. The baseline questionnaire contained questions on sociodemographic characteristics, for example, age, gender, education, religion, and nationality. The history of psychopathology of the relative was investigated by adding a question about pre-existent psychologic problems in the year prior to the ICU admission. Relatives were also asked to complete the clinical frailty score of the patient on a nine-point scale using the Dutch translation of the validated of the Clinical Frailty Scale (13). Medical patient data were retrieved from the EHR, including ICU length of stay (LOS), admission type (urgent or elective), mechanical ventilation (MV), and the Acute Physiology And Chronic Health Evaluation-IV score.

The validated and recommended Hospital Anxiety and Depression Scale (HADS) was used (14) to identify anxiety and depression among patients in non-psychiatric hospital clinics. A cut off score of greater than or equal to 8 on a scale from 0 to 21 was used for both HADS anxiety and HADS depression (14, 15). Relatives were asked to assess themselves in the week prior to the ICU admission of the patient.

The Impact of Event Scale-Revised (IES-R) was used to assess posttraumatic stress at 3 months follow-up. The mean score on the IES-R of greater than 26 points was considered as severe posttraumatic stress, as was used in former studies in relatives of critically ill (16, 17). Participants were instructed to keep the patients' ICU stay in mind while they completed the questionnaire.

Statistical Analysis

Descriptive analysis was performed. Continuous variables are reported as mean with SD for normally distributed variables and as median with first and third interquartile range (IQR) for variables with a skewed distribution. The outcome measures of the HADS anxiety, HADS depression, and the IES-R were dichotomized using the cut off scores (HADS \geq 8, IES-R \geq 26). Missing values were replaced by the mean of the not missing values with a maximum of five missing values on the IES-R records. The Wilcoxon signed-rank test was used to compare individual differences of the median scores of anxiety and depression between baseline and follow-up. The associations with the psychologic symptoms at follow-up were analyzed using univariate logistic regression analysis. Multicollinearity was tested for the included factors, for which MV was

dichotomized, and showed that none of the factors were correlated. All analyses were performed using the software IBM Statistical Package for the Social Sciences, Version 24. For all analyses, we applied a significance level of alpha less than or equal to 0.05 (two sided).

RESULTS

Relative and Patient Characteristics

In total, 1,058 adult ICU patients were admitted of whom 1,005 (96%) were eligible for inclusion. In 78 cases (20%), both the baseline and the 3 months follow-up questionnaire were completed. The enrollment process is reported in **Figure 1**. The relative and patient characteristics including the relatives' psychological symptoms in the week before ICU admission are presented in **Table 1**.

Psychologic Symptoms 3 Months After ICU Admission

The median score on anxiety dropped from 6 (4.0–10.3) to 2 (1.0–6.0), and the median score of depression

dropped from 5 (2.0–7.3) to 3 (0.0–5.0) (**Table 2**). At 3 months, anxiety and depression were present in 12 (15.4%) and eight (10.3%), respectively. Posttraumatic stress were present in 14 (17.9%) (**Table 2**). Almost a quarter deteriorated on the HADS anxiety score (23.1%) or remained stable (5.1%). On the HADS depression score, 24.4% deteriorated or remained stable (25.6%) (**Table 3**).

Factors Associated With Psychologic Symptoms in Relatives 3 Months After Patients' ICU Admission

Anxiety after 3 months was associated with anxiety at baseline (odds ratio [OR], 1.39; 95% CI, 1.14–1.71) and depression at baseline (OR, 1.31; 95% CI, 1.082–1.58). Factors associated with depression after 3 months were anxiety at baseline (OR, 1.34; 95% CI, 1.09–1.68), depression at baseline (OR, 1.61; 95% CI, 1.91–2.18), and ICU LOS (OR, 1.09; 95% CI, 1.02–1.16). Posttraumatic stress at 3 months follow-up was associated with anxiety at baseline (OR, 1.21; 95% CI, 1.04–1.41) and depression at baseline (OR, 1.19; 95% CI, 1.02–1.39). No other statistically significant associations were found (**Table 4**).

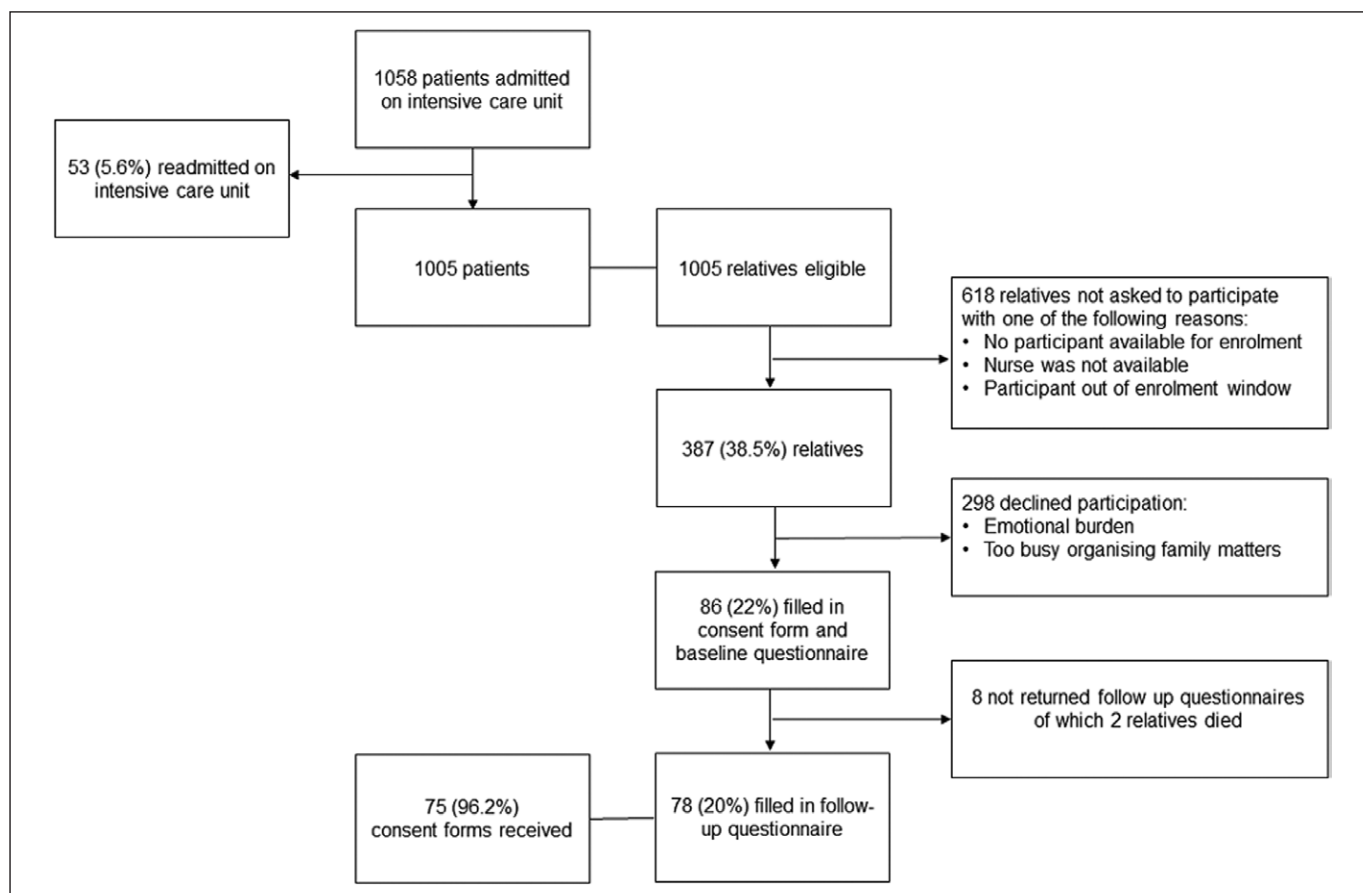


Figure 1. Flow chart of relative and patient participation.

TABLE 1.
Baseline Characteristics of the Study Population

Characteristics From Questionnaire	Relatives, N = 86	Patients, N = 86
Age (yr), median (IQR)	58 (50.0–69.3)	69 (57.5–75.0)
Male, n (%)	39 (45.3)	49 (57.0)
Religious/spiritual, n (%)	32 (37.2)	
Dutch nationality, n (%)	84 (97.7)	
Education, n (%)		
Low	15 (17.4)	
Middle/high	71 (82.6)	
Relative is patients'		
Spouse, n (%)	54 (72.8)	
Other, n (%)	32 (37.2)	
Psychologic problems in the year prior to the ICU admission, n (%)	8 (9.3)	
HADS anxiety at baseline, n (%)		
Normal (0–7)	50 (58.1)	
Mild (8–10)	15 (17.4)	
Severe (11–21)	21 (24.4)	
HADS depression at baseline, n (%)		
Normal (0–7)	65 (75.6)	
Mild (8–10)	12 (14.0)	
Severe (11–21)	9 (10.5)	
Clinical Frailty Scale, median (IQR)		3 (2.0–4.0)
Died, n (%)		15 (19.0)
In ICU		2 (2.6)
In hospital after ICU discharge		7 (9.0)
After hospital discharge		6 (8.0)
Patients' characteristics, N = 75		
Elective ICU admissions, n (%)		21 (28.0)
Acute Physiology And Chronic Health Evaluation-IV, median (IQR)		58 (42–82)
Mechanical ventilated, n (%)		30 (40)
Mechanical ventilation (d), median (IQR)		2.0 (1.0–5.6)
Length of ICU stay (d), median (IQR)		3 (2.0–5.0)

HADS = Hospital Anxiety and Depression Scale, IQR = interquartile range.

DISCUSSION

In this prospective cohort study, we found that in almost half of the relatives (42%) and a quarter of the relatives (24%), mild to severe symptoms of anxiety and depression were present in the week prior to the

ICU admission. At 3 months, anxiety and depression were present in 15% and 10%, respectively, and 18% reported posttraumatic stress. Factors associated with psychologic symptoms 3 months after admission were anxiety and depression at baseline. Patients' ICU LOS was associated with depression at 3 months follow-up.

TABLE 2.
Psychologic Symptoms in Relatives of ICU Patients 3 Months After Admission

Outcomes	Before ICU Admission (N = 86)	3 mo Follow-Up (N = 78)
HADS anxiety, median (IQR)	6 (4.0–10.3)	2 (1.0–6.0)
Score ≥ 8, n (%)	36 (41.9)	12 (15.4)
HADS depression, median (IQR)	5 (2.0–7.3)	3 (0.0–5.0)
Score ≥ 8, n (%)	21 (24.4)	8 (10.3)
Impact of Event Scale-Revised, median (IQR)	Not applicable	6 (2–16.3)
Score > 26, n (%)		14 (17.9)

HADS = Hospital Anxiety and Depression Scale, IQR = interquartile range.

TABLE 3.
Course of Psychologic Symptoms Over 3 Months Follow-Up

	Improved	Stable	Deteriorated	z	p
HADS anxiety, n (%)	56 (71.8)	4 (5.1)	18 (23.1)	−5.27	< 0.0001*
HADS depression, n (%)	39 (50.0)	20 (25.6)	19 (24.4)	−3.21	< 0.001*

HADS = Hospital Anxiety and Depression Scale.

*Level of significance is smaller or equal 0.05.

The reduction of symptoms of anxiety and depression might be the result of the relief relatives felt knowing their loved ones survived and have come home to recover. These findings are in line with literature showing that the prevalence of psychologic symptoms in informal caregivers of ICU survivors is highest during and shortly after the ICU admittance (18). Our results suggest though that the prevalence of psychologic symptoms is already high in the week prior to admission. This might imply that relatives are exposed to stressful events already before the ICU admission like worsening of the patients' medical condition. It is common that critical illness often does not arise suddenly but emerges as a complication of multiple chronic comorbidities and their treatments.

Despite the decrease of relatives with mental problems 3 months follow-up, still one in six of the relatives report symptoms of anxiety or posttraumatic stress and one in 10 symptoms of depression. Also, a quarter of the relatives deteriorated on the anxiety and depression scales at 3-month follow-up. Besides preexisting anxiety and depression as risk factors for psychologic symptoms, we found that ICU LOS was positively associated with depression at 3 months follow-up. The longer period of exposure to ICU stressors like uncertainty about

the course of patients' medical condition, sleep deprivation, and surrogate decision making might result in a higher risk for psychologic symptoms among relatives 3 months after admission. After hospital discharge, many relatives find themselves in the role as informal caregiver, so the depressive symptoms 3 months after admission could also relate to caring for patients who had longer ICU lengths of stay. A study showed that 36% of the relatives of ICU survivors experience caregiver burden 2 months after ICU discharge (19). A recent Dutch study found that relatives of former ICU patients had a higher number of new episodes of primary care 2–5 years after ICU discharge, but not in the first year. They suggested that relatives might prioritize the health of the former ICU patient over their own in the first year after ICU discharge and develop a broad range of symptoms and diseases including psychologic morbidity more than 1 year after discharge (20).

As this is the first study in which relatives assessed anxiety and depression in the week prior to the ICU admission, it helps us to place the mental health problems of relatives in a broader time perspective. Anxiety and depression do not arise abruptly as a result from the ICU admission but are already present before

TABLE 4.
Univariate Logistic Regression Analysis for Dichotomized Psychologic Symptoms

Relative and Patient Factors	HADS Anxiety ≥ 8			HADS Depression ≥ 8			Impact of Event Scale-Revised > 26		
	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>
Relative variables (<i>n</i> = 78)									
Age	1.01	0.97–1.06	0.59	1.06	0.99–1.14	0.11	0.99	0.94–1.03	0.45
Male	0.60	0.16–2.19	0.44	0.40	0.75–2.10	0.28	8.33	0.27–2.26	0.76
No religion/spirituality	3.92	0.78–19.30	0.09	2.12	0.40–11.26	0.38	1.23	0.37–4.10	0.73
Education low	1.87	0.43–8.12	0.41	3.60	0.74–17.48	0.12	2.44	0.63–9.50	0.20
Patient is spouse	1.30	0.36–4.67	0.69	1.05	0.23–4.74	0.95	0.56	0.18–1.80	0.33
History of psychopathology	6.40	0.81–50.73	0.08	Not applicable			1.43	1.38–14.78	0.77
HADS anxiety at baseline	1.39	1.14–1.71	0.001	1.34	1.08–1.68	0.01	1.21	1.04–1.41	0.02
HADS depression at baseline	1.31	1.08–1.58	0.006	1.61	1.91–2.18	0.00	1.19	1.02–1.39	0.03
Patient variables from questionnaire (<i>n</i> = 86)									
Age	0.99	0.95–1.03	0.61	0.99	0.92–1.03	0.44	1.00	0.98–1.02	0.78
Male	1.47	0.40–5.38	0.56	1.18	0.26–5.33	0.83	0.91	28–2.94	0.88
Died	0.82	0.16–4.18	0.81	2.90	0.61–13.81	0.18	3.00	0.83–10.84	0.09
Clinical Frailty Score	1.01	0.68–1.51	0.95	1.39	0.87–2.24	0.17	1.15	0.80–1.65	0.46
Patient variables from medical file (<i>n</i> = 72)									
Elective ICU admission	0.79	0.18–3.53	0.76	2.16	0.24–19.75	0.50	0.67	0.17–2.59	0.56
Acute Physiology And Chronic Health Evaluation-IV	0.99	0.96–1.02	0.44	0.98	0.95–1.02	0.34	1.01	0.99–1.03	0.46
Mechanical ventilation	1.19	1.02–1.39	0.02	1.13	0.99–1.29	0.07	1.11	0.98–1.25	0.10
Length of ICU stay (d)	1.06	0.99–1.13	0.08	1.09	1.02–1.16	0.02	1.06	1.00–1.13	0.06

HADS = Hospital Anxiety and Depression Scale, OR = odds ratio.

admission and might be prolonged by new stressors during admission. Symptoms of anxiety or depression short before admission make relatives vulnerable for mental disorders in the long term. From this perspective, the decrease of symptoms on the short term in this study could be a temporary state of relief and hope in the first weeks after returning home.

Several limitations need to be addressed. First, the low response rate is an important limitation, which was mostly due to the fact that nurses gave a short explanation to the family while they handed out the information letter. They had no time for a more personal and extensive guidance. Second, anxiety and depression at baseline were assessed in retrospective shortly after the

ICU admission. Relatives completed the baseline questionnaire while having their loved one in the ICU. This sets a major methodological limitation to the baseline scores and could have biased our findings. Also, it could explain the gap with the number of relatives reporting mental health problems in the year prior to the admission. Third, the selection process might have missed relatives with severe psychologic symptoms who did not feel capable to participate, which might have led to underreporting of the results. On the other hand, we realize that relatives with no psychologic symptoms might also not be motivated to participate. Fourth, considering the finding that relatives tend to efface their own symptoms in the first year after ICU discharge

and the results of former studies indicating an increase of posttraumatic stress in relatives over time (21, 22), a 3-month follow-up might be too short a period to monitor the course of the psychologic symptoms.

An ICU admission has serious mental impact on both the patients and their relatives who in many cases already experience high levels of stress before the admission, resulting in anxiety and depression which makes them vulnerable for psychologic morbidity on the long term. Relatives at risk can already be identified in an informal way with a HADS screening prior to or shortly after ICU admission and profit from early interventions like psychoeducation or the recommendation to consult their general practitioner, to lower the chronic stress levels, and to protect them from worsening mental health during and after ICU admission.

CONCLUSIONS

In this exploratory single-center study, we found that one in four of the relatives reported an increase of anxiety and depression symptoms in the 3 months following the ICU admission and a significant group of relatives of ICU patients at risk for anxiety, depression, and post-traumatic stress in the long term, already report symptoms in the week before the ICU admission. Screening and identification of relatives at risk in an early stage enables early interventions targeting stressors during and after the ICU admission and could prevent these relatives from developing psychologic morbidity and other health-related problems on the long term.

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