



ORIGINAL ARTICLE

Long-term psychiatric disorders in families of severe COVID-19 patients

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Abstract

Aim: The present study aimed to describe in detail the changes to and assess the risk factors for poor long-term outcomes of psychiatric disorders in families of COVID-19 patients.

Methods: A single-center, retrospective study using questionnaires. Family members of patients admitted to the intensive care unit (ICU) with severe COVID-19 participated. Psychiatric disorders refer to the psychological distress such as anxiety, depression, and posttraumatic stress disorder (PTSD) experienced by the patient's family.

Results: Forty-six family members completed the survey and were analyzed. Anxiety, depression, and PTSD occurred in 24%, 33%, and 2% of family members, respectively, and psychiatric disorders occurred in 39%. On multivariable analysis, living in the same house with the patient was independently associated with a lower risk of psychiatric disorders in families of COVID-19 patients (OR, 0.180; 95% CI, 0.036–0.908; $p = 0.038$). Furthermore, four family members overcame psychiatric disorders, and six family members newly developed psychiatric disorders during the one-year follow-up period.

Conclusion: Approximately 40% of family members had long-term psychiatric disorders, and some of them overcame the psychiatric disorders, and some newly developed psychiatric disorders over the one-year follow-up. Living in the same house with the patient was possibly significantly associated with the reduction of long-term symptoms of psychiatric disorders, but this result must be interpreted with care. Further large studies are needed to examine the factors associated with the long-term mental status of family members.

KEY WORDS

coronavirus disease 2019, critical care, family, post-intensive care syndrome, resilience

INTRODUCTION

The COVID-19 pandemic increased intensive care unit (ICU) admissions of patients with severe respiratory failure.¹ Although the number of new severely ill patients

has decreased markedly due to the widespread use of vaccines,² some patients have continued to suffer from physical, mental, and cognitive dysfunction after ICU discharge, which is known as Post-Intensive Care Syndrome (PICS).^{3–5}

This work was performed at St. Luke's International Hospital, Tokyo, Japan.

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Long-term patient dysfunction leads to a burden on the families who are close to the patient and care for them, and it affects the daily lives and health of not only the patients but also their families.⁶ Whereas there have been several reports about long-term PICS associated with COVID-19, most of these reports have focused on the patients themselves,^{7,8} and the details of long-term psychiatric disorders of families associated with COVID-19 remain unknown. In our previous study of psychiatric disorders associated with COVID-19, 33% of families had symptoms of psychiatric disorders,⁹ but the median period from ICU discharge to the survey was only 138 days. Thus, it is not clear whether they overcame their psychiatric symptoms in the long term.

We hypothesized that some families of ICU-admitted COVID-19 patients develop new-onset psychiatric disorders during long-term follow-up, and there are certain protective factors. The purpose of this study was to describe the changes in mental status during one-year follow-up and examine the risk factors for psychiatric disorders in families of severe COVID-19 patients over the long term.

MATERIALS AND METHODS

Study design and participants

This was a retrospective analysis of prospectively collected data from the ICU of a single institution in central Tokyo, Japan. Short-term outcomes of psychiatric disorders (approximately 4.5 months after ICU discharge) were evaluated in the first survey.⁹ In the present study, long-term outcomes (1 year after the first survey) were evaluated in the second survey (Figure 1). COVID-19 patients admitted to the ICU between March 23, 2020, and September 30, 2021, and their

family members were eligible to participate in this study. Family members were identified as key persons who were first-degree relatives or other people who self-identified as significant to the patient, such as parents, spouses, significant others, children, and siblings. Only one family member included in the current study was the surrogate principal decision-maker as indicated in the patient's medical records. Inclusion and exclusion criteria of patients and family members, follow-up procedures, and the outcomes of the first survey have been described in the previous study.⁹

This study was approved by the institutional review board of St. Luke's International Hospital on September 16, 2022 (approval number 22-R071). The procedures were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975.

Current survey (second survey)

Eligible family members were contacted by telephone to participate in this study and asked if they could be sent a questionnaire for this study between October 30, 2022, and November 3, 2022. In the case of refusal, the questionnaire was not mailed. The survey booklet and informed consent documents were sent on November 4, 2022. Responses from family members with valid consent documents were used for assessment. In cases of no response, reminders were sent after 2 weeks.

Data collection

Baseline patient characteristics, including age, sex, treatment, clinical data, such as durations of ICU stay and

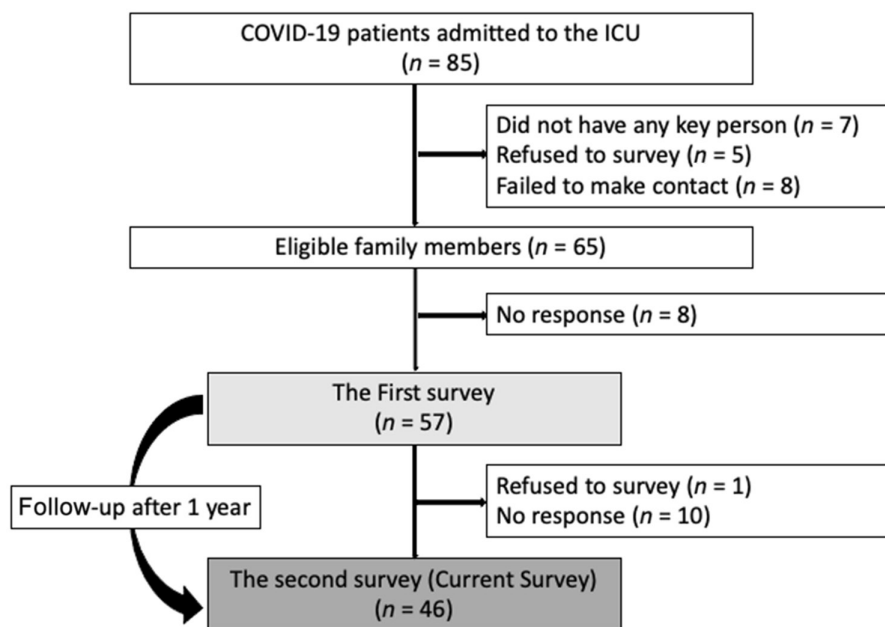


FIGURE 1 Flow chart of family members' selection and exclusion. Forty-six families completed the study and were enrolled in the analysis.

hospital stay, and outcomes were retrieved from the patients' electronic health records. Family members' characteristics such as age, sex, living with the patient or not, relationship to the patient, working status, educational level, the Hospital Anxiety and Depression Scale (HADS),¹⁰ the Impact of Event Scale-Revised (IES-R),¹¹ and the Connor-Davidson Resilience Scale-25 (CD-RISC-25) score¹² were addressed in the questionnaire. Family members with scores ≥ 8 for the anxiety and depression components of the HADS survey were considered to have anxiety and depression, respectively.¹³ An average IES-R score ≥ 1.6 indicated PTSD.¹⁴ The CD-RISC-25 score was originally developed by Connor and Davidson, and the form translated into Japanese was obtained for this study. This form consisted of 25 questions, each rated on a 5-point scale (0–4); higher scores on this scale were associated with higher levels of psychological resilience in family members. The abbreviated item contents presented by Connor and Davidson are presented in [Table S1](#) because publication of detailed descriptions of each item is not allowed due to strict regulation by the developer (Supplemental Digital Content, [Table S1](#)). In addition, participants were asked about the changes in their lives over the previous year, and they answered self-assessment questions regarding their complaints after leaving the hospital.

Study endpoints

The primary endpoint was to examine the risk factors for psychiatric disorders in families of severe COVID-19 patients in the long term associated with COVID-19. A diagnosis of psychiatric disorders was made for family members with impairment in at least one of the three elements: anxiety, depression, and PTSD.^{10,11} The secondary endpoint was to describe the changes in mental status in families over the past year.

Statistical analyses

Data were anonymized and analyzed statistically. Continuous variables are presented as medians and interquartile range, and the Wilcoxon rank-sum test was used to compare family members with and without psychiatric disorders. Categorical variables are presented as proportions, and Pearson's chi-squared test was used to compare family members with and without psychiatric disorders. Fisher's exact test was used as appropriate. Statistical analyses were performed using JMP Version 17 statistical software (SAS Institute, Cary, NC). Univariate and multivariable logistic regression analyses were performed to assess the primary endpoint. On multivariable analysis, adjustment of potential confounders, such as length of hospital stay, CD-RISC-25 score, and living in the same house with the patient, was performed. CD-RISC-25 and living in the same house with the patient were selected

because they were significant on univariate analysis, and length of hospital stay was selected as an indicator of patient severity. Sankey visualization was used to describe the changes in mental status from the first survey to the current survey. A two-sided p -value of less than 0.05 was considered significant for all analyses. Missing data were not replaced or estimated.

RESULTS

Of the 57 family members in the first survey, one family member was excluded because she refused to join this survey. Of the 56 eligible family members, 46 (82%) responded, and 46 family members were included in the current analysis ([Figure 1](#)).

Baseline characteristics of families and patients

The characteristics of the families and patients are shown in [Table 1](#). The median family member's age was 54 [interquartile range (IQR), 48–66] years, 31 (67.4%) were female, and 20 (48.8%) were living in the same house with the patient. Twenty-one (45.7%) were spouses including partners, 17 (37%) were parents or children, and 8 (17.4%) were other family members such as siblings. About half of the family members had at least a college degree, and 32 (71.1%) had jobs. Family members answered the surveys at a median of 486 [IQR, 443–645] days from ICU discharge. Overall, the median patient age was 55 [IQR, 49–73] years, and 39 (84.8%) were male. Thirty-three (69.6%) patients were intubated, 5 (10.9%) were managed with venovenous extracorporeal membrane oxygenation (VV-ECMO), and 5 (10.9%) underwent tracheostomy. The median length of hospital stay was 22 [IQR 12.8–41] days, of which 7 [IQR 4–14.3] days were in the ICU. Overall, 33 (71.7%) patients were discharged home, and 3 (6.5%) died.

Overall occurrence of psychiatric disorders

The numbers of families who suffered from anxiety, depression, and PTSD were 11 (24%), 15 (33%), and one (2%), respectively ([Figure 2](#)). Those who met all or any two of the components are shown by overlapping colors ([Figure 2](#)). There were 18 (39%) family members who had at least one of the psychiatric disorders. In addition, one (2%) family member had all three components of psychiatric disorders.

Comparison of clinical characteristics between families with psychiatric disorders and non-psychiatric disorders

The comparison of the families with and without psychiatric disorders is shown in [Table 1](#). The number of families who were

TABLE 1 Baseline characteristics and Comparison of the families with psychiatric disorders versus non-psychiatric disorders.

Variable	Total (n=46)	Psychiatric disorders group (n=18)	Non-psychiatric disorders group (n=28)	p-Value
Family members				
Age (y)	54 [48–66]	55 [49–66]	53 [46–67]	0.735
Sex (female)	31 (67.4)	13 (72.2)	18 (64.3)	0.575
Living in the same house with the patient (Yes)	20 (48.8)	4 (25.0)	16 (64.0)	0.015
Relationship with the patient				
Spouse	21 (45.7)	6 (33.3)	15 (53.6)	0.241
Child or parent	17 (37.0)	7 (38.9)	10 (35.7)	
Other family member	8 (17.4)	5 (27.8)	3 (10.7)	
Number of days from ICU discharge to completion of questionnaire	486 [443–645]	460 [437–582]	509 [444–648]	0.399
Employed part or full-time	32 (71.1)	13 (72.2)	19 (70.4)	1.000
Highest level of education				
High school or less	23 (50.0)	9 (50.0)	14 (50.0)	1.000
University	23 (50.0)	9 (50.0)	14 (50.0)	
CD-RISC-25 (total score)	63.0 [52.5–74.5]	58.5 [30.8–67.3]	72.0 [61.0–77.0]	0.024
Patients				
Age (y)	55 [49–73]	58 [50–74]	52 [46–73]	0.290
Sex (male)	39 (84.8)	14 (77.8)	25 (89.3)	0.289
Treatment				
Intubation	32 (69.6)	13 (72.2)	19 (67.9)	0.754
VV-ECMO	5 (10.9)	2 (11.1)	3 (10.7)	0.966
Tracheostomy	5 (10.9)	1 (5.6)	4 (14.3)	0.353
Length of hospital stay (days)	22 [12.8–41]	29.5 [14.8–49.5]	19 [11–37.5]	0.107
Duration of ICU stay (days)	7 [4–14.3]	7.5 [4–16.3]	7 [4.3–12.3]	0.973
Left hospital by oneself	33 (71.7)	12 (66.7)	21 (75.0)	0.511
Patient death	3 (6.5)	1 (5.6)	2 (7.1)	0.932

Note: Data are presented as medians [interquartile range] for continuous variables and as N (percentage) for categorical variables.

Abbreviations: CD-RISC-25, Connor-Davidson Resilience Scale-25; ICU, intensive care unit; VV-ECMO, venovenous extracorporeal membrane oxygenation.

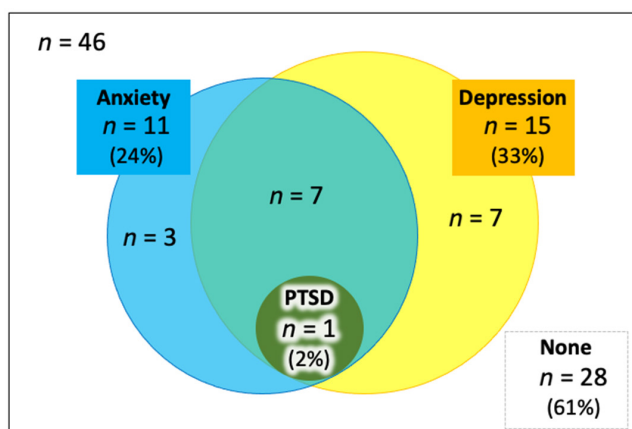


FIGURE 2 Overlapping of each component of psychiatric disorders. The overlap of the circles represents the co-occurrence of the components.

living in the same house with a patient was significantly lower in the psychiatric disorders group than in the non-psychiatric disorders group (25.0% vs. 64.0%, $p=0.015$). The CD-RISC-25

score was significantly lower in the psychiatric disorders group than in the non-psychiatric disorders group (median 58.5 [IQR, 30.8–67.3] vs. 72 [IQR, 61–77], $p=0.024$). No other significant differences were observed between the two groups (Table 1).

Factors related to long-term psychiatric disorders of families

On multivariable analysis, living in the same house with the patient was significantly associated with a lower risk of psychiatric disorders of the families (OR, 0.180; 95% CI, 0.036–0.908; $p=0.038$) (Table 2).

Changes in mental status from the first survey to the current survey

In the 46 families included in the analysis of the current study, changes in mental status from 1 year earlier (first

TABLE 2 Risk factors for long-term psychiatric disorders.

Variable	Adjusted OR	95% CI	p-Value
Length of hospital stay (days)	1.000	0.970–1.033	0.955
CD-RISC-25 score (total score)	0.975	0.944–1.007	0.118
Living in the same house with the patient (Yes)	0.180	0.036–0.908	0.038

Abbreviations: CD-RISC-25, Connor-Davidson Resilience Scale-25; CI, Confidence interval; OR, Odds ratio.

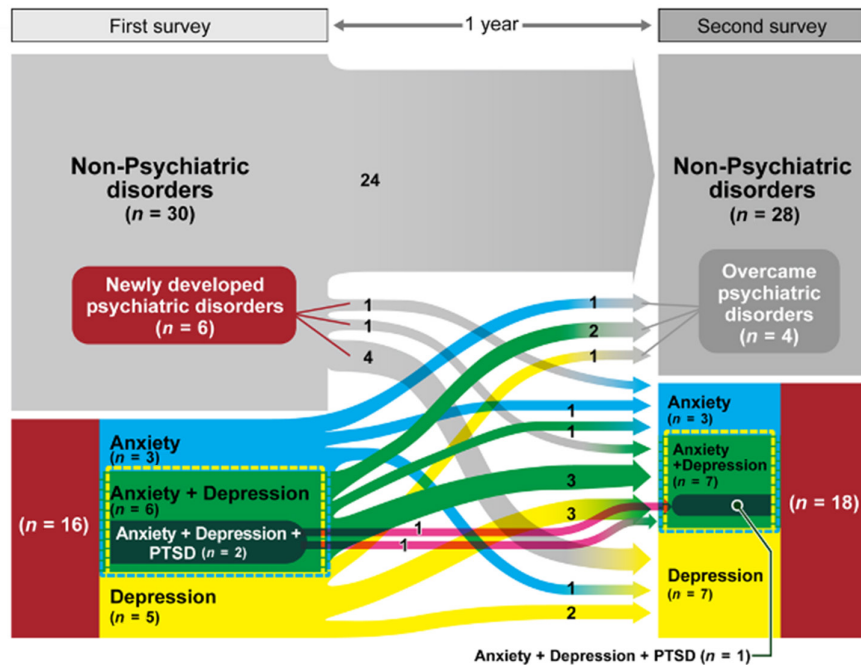


FIGURE 3 Changes in mental status from the first survey to the current survey. Whereas four families overcame psychiatric disorders, six families newly developed psychiatric disorders.

survey) were compared (Figure 3). Of the 46 families included in the current survey, 16 had symptoms of psychiatric disorders in the first survey, and 18 had symptoms of psychiatric disorders in the current survey. Of the 30 families who had no psychiatric disorders in the first survey, 24 also had no psychiatric disorders in the current survey, whereas the remaining 6 developed psychiatric disorders over the preceding year. On the other hand, of the 16 families who had at least one of the components of psychiatric disorders in the first survey, 12 still had some components of psychiatric disorders in the current survey, but the remaining 4 had overcome psychiatric disorders over the preceding year.

Details of families who overcame psychiatric disorders and who newly developed psychiatric disorders

Four family members overcame psychiatric disorders over the preceding year. Of the 4 family members who overcame psychiatric disorders, 3 were men, 2 were living with the patient, and 2 were spouses. All of them had a full-time job. On

the other hand, of the 6 family members who newly developed psychiatric disorders, 4 were women, and all were not living in the same house with the patient (Table 3).

DISCUSSION

This study investigated long-term psychiatric disorders in 46 families of COVID-19 patients admitted to the ICU. The rates of anxiety, depression, and PTSD were 24%, 33%, and 2%, respectively; 39% of families had at least one and, therefore, had symptoms of psychiatric disorders. On multivariable analysis, living in the same house with the patient was independently associated with a lower risk of psychiatric disorders. Furthermore, compared to 1 year earlier, four families overcame psychiatric disorders, and six families newly developed psychiatric disorders during the preceding year.

Other than cases associated with severe COVID-19, several reports have assessed psychiatric disorders of families over time with a range of follow-up from 1 to 12 months. Anderson et al. performed a prospective, longitudinal, cohort study of 50 families of ICU patients

TABLE 3 Details of families who overcame/ newly developed psychiatric disorders.

Case	Age (y)	Sex	Lived with patient	Relationship with the patient	Treatment	Outcome at hospital discharge	CD-RISC Score-25	First survey			Second survey		
								Anxiety	Depression	PTSD	Anxiety	Depression	PTSD
Overcame psychiatric disorders													
1	36	F	Yes	Spouse	Intubation	Left hospital by oneself	73	Yes	Yes	No	No	No	No
2	48	M	No	Child	Intubation	Left hospital by oneself	75	No	Yes	No	No	No	No
3	42	M	Yes	Spouse	Intubation	Left hospital by oneself	77	Yes	No	No	No	No	No
4	48	M	No	Sibling	VV-ECMO	Hospital transfer	82	No	Yes	Yes	No	No	No
Newly developed psychiatric disorders													
5	65	F	No	Child	Oxygenation	Left hospital by oneself	62	No	No	No	No	Yes	No
6	75	M	Patient death	Sibling	Intubation	Hospital transfer	68	No	No	No	No	Yes	No
7	54	F	No	Sibling	Intubation	Left hospital by oneself	80	No	No	No	No	Yes	No
8	33	M	No	Child	Intubation	Left hospital by oneself	61	No	No	No	No	Yes	No
9	64	F	No	Spouse	VV-ECMO	Hospital transfer	91	No	No	No	No	Yes	No
10	52	F	No	Sibling	Intubation	Hospital transfer	39	No	No	No	No	Yes	No

during hospitalization, 1 month after, and 6 months after; they found that anxiety and depression improved over the follow-up period.¹⁵ The psychiatric symptoms of families have improved over time in most studies,^{16,17} whereas two studies^{18,19} showed that the prevalence of psychiatric symptoms increased after 1 year, even though it decreased over a six-month period (Supplemental Digital Content, Table S2). These results suggest that families who had psychiatric symptoms for longer than 1 year might continue to have such symptoms for a long time. In addition, those studies only compared the total number of cases of psychiatric symptoms, and the trends in the same individuals were unknown. The present study differs from previous studies in that it examined the changes in mental status of individuals 1 year later. Of the 46 families in the current study, 16 had symptoms of psychiatric disorders in the first survey, and 18 had symptoms of psychiatric disorders in the second survey 1 year later. The total number of families with psychiatric disorders was almost unchanged, but focusing on individuals, it was a result of the addition of those who had overcome psychiatric disorders and those who had newly developed psychiatric disorders. However, regarding the six families who developed psychiatric disorders during the 1-year follow-up period, it was not possible to show an association between the patient's admission to the ICU and the onset of psychiatric disorder in the families. Therefore, the psychiatric disorder in these six families cannot be defined PICS-F. This could be a limitation of the present study; therefore, more prospective, observational studies are needed in the future.

This was a study of families of patients admitted to the ICU with COVID-19. There have been several reports of psychiatric disorders in families of COVID-19 patients. Amass et al. examined the mental status of 330 families of patients admitted to the ICU with COVID-19 approximately 3 and 6 months after ICU admission, and they observed that 63.6% of families developed symptoms of PTSD at 3 months and 48.4% of families developed symptoms of PTSD at 6 months.²⁰ They reported that family visitation restrictions in the COVID-19 era and fractured communication with healthcare practitioners might have played roles in increasing stress-related disorders in families. Moreover, many severe COVID-19 patients have had long-term severe sequelae.²¹ Although long-term psychiatric disorders in families of severe COVID-19 patients have not been reported and have remained unclear, we suggest that families could be burdened as caregivers for a long time, which increases the long-term prevalence of psychiatric disorders.

In the present study, more families in the non-psychiatric disorders group were living in the same house with the patient. Fonseca et al. examined the factors associated with the prevalence of anxiety and depression in families of patients admitted to an ICU and concluded that living with the patient was associated with the presence of anxiety symptoms in the families.²² The reason that the present finding differed from their results might be the difference in the timing of the assessment of mental status. Fonseca et al. examined

the mental status of families on days 3–5 of ICU admission. Living with the patient might be associated with early psychiatric disorder development, but in the long term, living with the patient might contribute to a reduction of psychiatric disorders. In addition, one of the factors preventing PICS is family involvement, and it is possible that cohabitation improves outcomes of not only patients, but also has a long-term positive effect on the patient's family's psychiatric symptoms.^{23,24} However, long-term cohabitation with a patient after discharge from the ICU might include other factors, such as the patient surviving and not having severe sequelae, that would make it difficult to live at home. Moreover, the present study had an inadequate sample size for comprehensive statistical analysis. Thus, further larger studies will be needed to examine this hypothesis.

Resilience is a protective factor that helps individuals recover from difficulties, stressful situations, and so on.²⁵ Families with a high CD-RISC score are considered resilient families. Peter et al. examined the associations between resilience and symptoms of depression, anxiety, and acute stress in families of critically ill patients.²⁶ They concluded that resilient families had significantly fewer psychological symptoms. Although a significant difference was not observed in multivariable analysis in the present study, the association between resilience and psychiatric symptoms of families is beginning to attract attention in the field of PICS-F. However, resilience was assessed only at the time of the second survey (median 486 days from ICU discharge). Thus, as the initial value of family resilience at the time of ICU admission was not measured, the association between changes in family resilience and psychiatric symptoms remains unclear. Future prospective observational studies that include initial values of family resilience and mental status should be conducted to clarify the association between the transition of family mental disorders and resilience.

The present study had several limitations. First, we performed a multivariate analysis, but the sample size was small ($n=46$) and may not have been sufficiently adjusted for confounding factors. Second, family members were only selected from a single hospital in Japan. Different countries have different religions, medical insurance systems, and social security systems after hospital discharge, so the actual financial stress and feelings about the loss of family members may be different, limiting the generalizability of the present results. Third, there was a wide range of days between discharge from the hospital and the time the questionnaire was administered, and the present study relied on self-reporting, which might not be reliable. Fourth, it was not possible to assess the mental status of the families before the patients were admitted; therefore, the mental status before the patient's admission to the ICU might have contributed to the diagnosis of psychiatric disorder. Fifth, because the CD-RISC-25 score was not obtained at the first survey, the change in the CD-RISC-25 score between the first and second surveys could not be addressed. Sixth, six families newly developed anxiety and/or depression during the one-year follow-up period, but it was not known whether they developed PICS-F in the

present study. Finally, although this study involved one key person per patient, he or she might not have been representative of all family members. Due to these important limitations, the results of this study are limited and should be interpreted with caution.

CONCLUSIONS

Approximately 40% of families had long-term psychiatric disorders after the patients were discharged from the hospital; some of them overcame the psychiatric disorders, but some newly developed psychiatric disorders compared to 1 year earlier. Living in the same house with the patient was possibly significantly associated with the reduction of long-term psychiatric disorders, but this result was based on too limited a sample and must be interpreted with care. Further large studies to examine the factors associated with the long-term mental status of families are needed.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

Approval of the research protocol: This study was approved by the institutional review board of St. Luke's International Hospital on September 16, 2022 (approval number 22-R071).

Informed Consent: Written informed consent was obtained from participants.

Registry and the Registration No. of the study/Trial: N/A.

Animal Studies: N/A.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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