Postintensive Care Syndrome-Family Associated With COVID-19 Infection

OBJECTIVES: To assess the prevalence of and risk factors for postintensive care syndrome in family (PICS-F) in the COVID-19 era.

DESIGN: A single-center retrospective study using questionnaires and telephone calls.

SETTING: An ICU at St. Luke’s International Hospital.

PATIENTS: Patients who were treated for COVID-19–related acute respiratory distress syndrome between March 23, 2020, and September 30, 2021, and their family members participated.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: PICS-F refers to the psychologic distress such as anxiety, depression, and posttraumatic stress disorder (PTSD) experienced by the patient’s family. The primary outcome was PICS-F occurrence. Furthermore, factors related to PICS-F development were identified using statistical analysis. Of 85 patients with COVID-19 who were admitted to the ICU, 57 family members consented to the study and completed the survey, and 54 family members’ data were analyzed. The median age of family members was 53.5 years, 68.5% were female, and 46.3% were spouses. The median age of patients was 55.5 years, and 83.3% were male. During their ICU stay, 68.5% received invasive mechanical ventilation, 11.1% received venovenous extracorporeal membrane oxygenation, and 11.1% underwent tracheostomy. The median ICU and hospital stays were 7 and 22 days, respectively. Overall PICS-F occurred in 33%. Anxiety, depression, and PTSD occurred in 24%, 26%, and 4% of family members, respectively. The prevalence of all three components of PICS-F was 4%. Multivariable analysis showed that Family Satisfaction with the ICU Survey (FS-ICU) scores were independently associated with PICS-F development (odds ratio, 0.941; 95% CI, 0.891–0.983; \( p = 0.005 \)).

CONCLUSIONS: One-third of family members of COVID-19 patients admitted to the ICU had symptoms of PICS-F. These results suggest that measurement of FS-ICU may be helpful as a predictor of PICS-F development. In addition, increasing the level of ICU care satisfaction of the family members may prevent PICS-F.

KEY WORDS: COVID-19; critical care; family; intensive care unit; postintensive care syndrome; questionnaire

Postintensive care syndrome (PICS) is a collective concept that refers to physical, mental, and cognitive dysfunctions that develop in patients and their families after the patient is discharged from the ICU (1). Family members of ICU survivors can also suffer from similar symptoms, such as anxiety, depression, and posttraumatic stress disorder (PTSD), and these symptoms have been called “postintensive care syndrome-family (PICS-F),” with a prevalence of 20–40% (2).

The COVID-19 pandemic increased ICU admissions of patients with severe respiratory failure (3), and PICS-F is expected to have increased. Whereas
PICS associated with COVID-19 has attracted more and more attention, most of these reports have focused on the patients themselves (4, 5). Although the mental status of family members of severe COVID-19 patients has been reported narratively, PICS-F associated with COVID-19 infection has not been comprehensively examined (6, 7).

The purpose of this study was to examine the clinical characteristics, frequency rate, and risk factors of PICS-F associated with COVID-19 infection and to provide new approaches to prevent PICS-F during this pandemic.

**MATERIALS AND METHODS**

**Study Design and Participants**

This was a retrospective study conducted at the ICU of a single institution in central Tokyo, Japan. This study was approved by the institutional review board of St. Luke’s International Hospital on October 28, 2021 (approval number 21-R123). Those procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975.

COVID-19 was confirmed by RNA detection of severe acute respiratory syndrome coronavirus 2 using real-time polymerase chain reaction of oropharyngeal or nasopharyngeal swabs (8). 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. The inclusion criteria of patients were a diagnosis of COVID-19 and an ICU stay of at least 24 hours. On the other hand, the patient exclusion criterion was a lack of family members or any other significant person. 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, spouse, 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. Family members listed in their medical records who could not be contacted and those who were unable to complete the consent process and questionnaires were excluded (Supplemental Table 1, http://links.lww.com/CCX/B21).

**PICS-F Care in St. Luke’s International Hospital**

As for family-centered care for PICS-F, the Society of Critical Care Medicine has published “Guidelines for Family-Centered Care in the Neonatal, Pediatric, and Adult ICU” (9). According to this guideline, relaxing visitation restrictions is effective in preventing PICS-F. However, family members’ visits to the ICU were restricted to avoid the spread of infection during the pandemic. In the ICU, patients were not allowed to use cell phones, and many of them were intubated and could not talk. Their families could do nothing but waited for a call from the doctors. An attempt was made to conduct visits through a screen using a tablet device, but it was not very useful because the family members could not enter the hospital if they had close contact with COVID-19 patients, and patients were often unable to talk due to sedative medications.

During peaks in the waves of the pandemic, medical teams had very little time to make telephone calls to families. Therefore, doctors tended to contact families only when a patient’s medical condition changed (i.e., need for intubation). For sedated and intubated patients, an ICU diary was written every day by a nurse and given to patients when leaving the ICU. Before the COVID-19 era, nurses were able to explain the ICU diary to family members when they came to the hospital for visits, but with restricted visiting, they had less opportunity to provide these explanations.

**Survey**

First, all eligible patients were contacted by telephone by the attending physicians for participation in this study between November 5, 2021, and November 8, 2021. Patients were also asked if they agreed to have family members contacted for participation. Only one family member could participate per patient. Second, family members were contacted by telephone to participate in this study between November 10, 2021, and November 13, 2021, and asked for their address to ensure that they received the questionnaire. In the case of severe mental distress or refusal, the questionnaire was not mailed. The survey booklet and informed consent documents were sent on November 14, 2021. Responses from patients with valid consent documents were sent on November 14, 2021. Responses from patients with valid consent documents were used for assessment. In the cases of no response, reminders were sent after 2 weeks.
The survey comprised the following items: the Hospital Anxiety and Depression Scale (HADS) (10), the Impact of Event Scale-Revised (IES-R) (11), and the Family Satisfaction with the ICU Survey (FS-ICU) (12, 13). Family members with scores greater than or equal to 8 for the anxiety and depression components of the HADS survey were considered to have anxiety and depression (14). An average IES-R score greater than or equal to 1.6 or more indicated PTSD (15). The FS-ICU is designed to measure satisfaction during hospitalization, but because of the COVID-19 visitation restrictions, items not applicable to the FS-ICU, such as questions about “The Atmosphere in the ICU Waiting Room was?,” were uniformly marked as “not applicable” and excluded from the questionnaire. In addition, participants were asked about their living and working statuses and educational level, and they answered self-assessment questions regarding their complaints during hospitalization.

Data Collection

Baseline patient characteristics, including age, sex, and clinical data, such as durations of ICU stay and hospital stay and severity, were retrieved from the patients' electronic health records. Family members' characteristics such as age, sex, relationship to patient, working status, educational level, HADS, IES-R, and FS-ICU were addressed in the questionnaire. Data were anonymized and analyzed statistically.

Study End Points

The primary end point was the incidence rate of PICS-F associated with COVID-19 infection. PICS-F is composed of three elements: anxiety, depression, and PTSD. A diagnosis of PICS-F was made for family members with impairment in at least one of the three PICS-F elements (16, 17). The secondary end point was to identify the factors related to PICS-F development.

Statistical Analyses

Continuous variables are presented as medians and interquartile range (IQR), and the Wilcoxon rank-sum test was used to compare family members with and without PICS-F. Categorical variables are presented as proportions, and Pearson chi-square test was used to compare family members with and without PICS-F. Fisher exact test was used when appropriate. Statistical analyses were performed using the JMP Version 12 statistical software (SAS Institute, Cary, NC). Univariate and multivariate logistic regression analyses were performed to assess the primary end point. On multivariate analysis, potential confounders, such as patient age, relationship with patients, and FS-ICU, were adjusted. A two-sided p value of less than 0.05 was considered significant for all analyses. Missing data were not replaced or estimated.

RESULTS

A total of 85 patients diagnosed with COVID-19 were admitted to the ICU during this study period. Twenty patients were excluded because they did not have a key person or could not make contact or refused to join this survey. Of 65 eligible family members, 57 (88%) responded. Three patients were excluded because they had a history of mental disease before this survey (Fig. 1).

Baseline Characteristics

The characteristics of the patients and family members are given in Table 1. All patients and families were of Japanese ethnicity. The median family member's age was 53.5 years (IQR, 46.8–64.3 yr), 68.5% were female, and about half of them lived with the patients; 46.3% were spouses including partners, 33.3% were parents or children, and...
20.4% were other family members such as siblings. About half of the family members had at least a college degree, and more than half had jobs. Family members answered the surveys at a median of 138 days (IQR, 85–285 d) from ICU discharge.

Overall, the median patient age was 55.5 years (IQR, 49–74.5 yr), and 83.3% were male, 68.5% of patients were intubated, 11.1% were managed with VV-ECMO, and 11.1% underwent tracheostomy. The median length of hospital stay was 22 days (IQR, 12–40.3 d), of which 7 days (IQR, 4–13.3 d) were in the ICU. Overall, 66.7% of patients could be discharged home, and 5.6% died.

**Overall Occurrence of PICS-F**

The proportions of anxiety, depression, and PTSD are shown in Figure 2. The percentages of family members who suffered from anxiety, depression, and PTSD were 24%, 26%, and 4%, respectively. Those who met all or any two of the components are shown by overlapping colors (Fig. 2). There were 18 family members (33%) who had at least one of the PICS-F components. In

| Variable                                                                 | Total (n = 54) | PICS-F (n = 18) | Non-PICS-F (n = 36) | p    |
|--------------------------------------------------------------------------|----------------|----------------|---------------------|------|
| **Family members**                                                       |                |                |                     |      |
| Age (yr)                                                                 | 53.5 (46.8–64.3) | 53.5 (46.8–58.5) | 54 (46.3–65.8)       | 0.532|
| Sex (female)                                                             | 37 (68.5)      | 13 (72.2)      | 24 (66.7)            | 0.764|
| Lived with patient                                                       | 26 (53.1)      | 9 (50.0)       | 17 (54.8)            | 0.775|
| Relationship with the patient                                           |                |                |                     |      |
| Spouses                                                                  | 25 (46.3)      | 10 (55.6)      | 15 (41.7)            | 0.176|
| Children or parents                                                      | 18 (33.3)      | 3 (16.7)       | 15 (41.7)            |      |
| Other family members                                                     | 11 (20.4)      | 5 (27.8)       | 6 (16.7)             |      |
| Number of days from ICU discharge to completion of questionnaire         | 138 (85–285)   | 129 (85–205)   | 138 (84–292)         | 0.557|
| Employed part or full time                                              | 37 (68.5)      | 13 (72.2)      | 24 (66.7)            | 0.764|
| Highest level of education                                               |                |                |                     |      |
| High school or less                                                      | 26 (48.1)      | 11 (61.1)      | 15 (41.7)            | 0.250|
| University                                                               | 28 (51.9)      | 7 (38.9)       | 21 (58.3)            |      |
| Family satisfaction with the ICU Survey (total score)                    | 62 (50.8–68.3) | 53.5 (35.5–63.3) | 65.5 (57–70)         | 0.0041|
| **Patients**                                                             |                |                |                     |      |
| Age                                                                      | 55.5 (49–74.5) | 53 (48.5–60.3) | 56.5 (49.3–77)       | 0.229|
| Sex (male)                                                               | 45 (83.3)      | 15 (83.3)      | 30 (83.3)            | 1.000|
| Treatment                                                                |                |                |                     |      |
| Intubation                                                               | 37 (68.5)      | 13 (72.2)      | 24 (66.7)            | 0.764|
| Venovenous extracorporeal membrane oxygenation                          | 6 (11.1)       | 3 (16.7)       | 3 (8.3)              | 0.388|
| Tracheostomy                                                             | 6 (11.1)       | 1 (5.6)        | 5 (13.9)             | 0.651|
| Length of hospital stay, d                                               | 22 (12–40.3)   | 24 (12.8–40.3) | 21.5 (12–42.5)       | 0.890|
| Duration of ICU stay, d                                                  | 7 (4–13.3)     | 6 (4–13)       | 7.5 (4–13.8)         | 0.692|
| Left hospital by oneself                                                | 36 (66.7)      | 14 (77.8)      | 22 (66.7)            | 0.527|
| Patient death                                                            | 3 (5.6)        | 0 (0)          | 3 (8.3)              | 0.543|

PICS-F = Postintensive Care Syndrome in Family.

Data are presented as medians (interquartile range) for continuous variables and as n (%) for categorical variables.
addition, two family members (4%) had all three components of PICS-F.

Comparison of PICS-F Versus Non-PICS-F

The comparison of PICS-F versus non-PICS-F is shown in Table 1. The PICS-F group had lower FS-ICU scores than the non-PICS-F group (53.5 [IQR, 35.5–63.3] vs 65.5 [IQR, 57.0–70.0]; \( p = 0.004 \)). No significant differences were observed between the two groups except for FS-ICU.

Independent Factors related to PICS-F

Multivariable analysis showed that FS-ICU was independently associated with PICS-F development (odds ratio, 0.941; 95% CI, 0.891–0.983; \( p = 0.005 \)) (Table 2).

Comparison of Details of FS-ICU Between the PICS-F and Non-PICS-F Groups

Scores for family needs, respect and compassion for family members, and ease of getting information were significantly lower in the PICS-F group than in the Non-PICS-F group (Supplemental Fig. 1, http://links.lww.com/CCX/B21).

DISCUSSION

This study investigated PICS-F outcomes in 54 family members of COVID-19 patients admitted to the ICU. The rates of anxiety, depression, and PTSD were 24%, 26%, and 4%, respectively; 33% of family members had at least one and, therefore, had symptoms of PICS-F.

The present study also demonstrated that FS-ICU scores were significantly associated with PICS-F.

Only a few studies have examined the prevalence of PICS-F in families of patients admitted to the ICU with COVID-19. McPeake et al (18) investigated family members of COVID-19 patients admitted to the ICU between 3 and 7 months after hospital discharge and observed that 40.4% of family members developed symptoms of anxiety, and 21.3% of family members described symptoms of depression. Jin et al (19) investigated 57 family members of COVID-19 patients admitted to the ICU between 3 and 4 months after hospital discharge and observed that 56.1% of family members described symptoms of anxiety, 26.3% of family members developed symptoms of depression, and 57.9% of family members described symptoms of PTSD. The present results showed a lower prevalence of PICS-F than previous studies, and there are several possible reasons for this.

First, the differences in PICS-F occurrence rates may be due to the differences in evaluation methods, such as diagnostic criteria, and the timing of evaluation. Jin et al (19) conducted their study 3–4 months after hospital discharge, earlier than the present study. This may have contributed to the difference in results, since symptoms of PICS-F have been reported to decrease over time. Second, the background characteristics of the participants (age, sex, severity of the patient, etc.) may have differed in each study. Risk factors for PICS-F include a female family member (20), a younger family member (21), a younger patient (22), a spouse (23), or death of the patient in the ICU (24). Although McPeake et al (18) reported the same diagnostic criteria for anxiety and depression using the HADS as in the present study, the prevalence of PICS-F may have been higher than the present results because most of the participants were partners or spouses of the patients. Less than 50% of family members in the present study were spouses or partners. In the present study, three patients died in the ICU. Moreover, when asked for consent to participate by phone, some family members did not agree to participate because recollection of the hospitalization period was painful. These family members may have had PICS-F, but the actual results could be underestimated because these individuals were excluded from the study. Differences in the research design may have contributed to the differences in the results. We consider that a uniform scale
for evaluating PICS-F is necessary to improve understanding of PICS-F in families of COVID-19 patients.

The present study differs from previous studies in that the factors associated with PICS-F development in the COVID-19 era were analyzed statistically. As far as we could find, there were no similar studies limited to patients with COVID-19. Azoulay et al (25) performed univariate linear regression analysis to identify factors associated with the IES-R score and HADS of family members 90 days after ICU discharge or death of their relative. They concluded that information provided by ICU physicians perceived as being inadequate and involvement in end-of-life decisions were independent risk factors for PICS-F. Although that study was not limited to COVID-19, the result was consistent with the present study finding that FS-ICU was an independent factor related to PICS-F. It may be helpful to administer the FS-ICU to family members at the time of discharge to predict the onset of PICS-F, and improvement of the FS-ICU items may prevent the onset of PICS-F. Beck et al (7) examined psychologic distress in COVID-19 patients, 15% of whom were admitted to the ICU, and their relatives 30 days after hospital discharge. Resilience, defined as a person’s emotional and mental capacities to adapt well when experiencing critical life events, was negatively associated with psychologic distress in this study. Thus, interventions to foster resilience in family members may also improve FS-ICU (7).

In the present study, significant differences were observed in three items of FS-ICU, including ease of obtaining information, mental support for family members, and whether the healthcare providers were willing to respond to their needs. Before the COVID-19 era, family members could come to the hospital and ask about the patient’s condition when they wanted to know, but due to pandemic-related restrictions on visitation, they had no choice but to wait for a phone call from the doctor. We believe that the family members may be able to better understand the patient’s condition by setting a date and time in advance for the doctor to call to explain the condition. We also suggest that the ICU diary be used not only for the patient but also for the family. ICU diaries in which nurses record what happened to the patient every day are supposed to help patients recover their mental functions by bridging the gap between their delusional memories of their ICU stay and reality (26). If family members can view the ICU diary in real time, it may not only make it easier for them to understand the patient’s condition but it may also help reduce family dissatisfaction and prevent the development of PICS-F. An ICU diary may also foster resilience in family members and contribute to the prevention of PICS-F.

Some limitations remain to be addressed in this study. First, the sample size was small (n = 54), and family members were only selected from a single hospital in Japan. There will likely be variations across racial and geographic populations, and caution is required when interpreting the results. Second, there was a wide range of days between discharge from the hospital and the time the questionnaire was administered, and this study relied on self-reporting, which might not be reliable. Third, the family’s mental state before the patient was admitted could not be assessed. Finally, although this study involved one key person per patient, he or she might not represent the feelings of all family members.

### TABLE 2.
Prognostic Factors for the Development of Postintensive Care Syndrome in Family

| Variable                                | Adjusted OR (95% CI) | p      |
|-----------------------------------------|----------------------|--------|
| Patient’s age                           | 0.963 (0.910–1.009)  | 0.117  |
| Relationship with the patient           |                      |        |
| Spouses                                 | Reference            | –      |
| Children or parents                     | 0.370 (0.063–1.743)  | 0.212  |
| Other family members                    | 1.085 (0.216–5.277)  | 0.919  |
| Family satisfaction with the ICU Survey | 0.941 (0.891–0.983)  | 0.005  |

OR = odds ratio.

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CONCLUSIONS

One-third of family members of COVID-19 patients admitted to the ICU had symptoms of PICS-F. Measurement of FS-ICU may be helpful as a predictor of PICS-F development. In addition, increasing the level of ICU care satisfaction of the family members may help prevent PICS-F.

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