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One-Year Outcomes of Postintensive Care Syndrome in Critically Ill Coronavirus Disease 2019 Patients: A Single Institutional Study

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IMPORTANCE: Postintensive care syndrome has a strong impact on coronavirus disease 2019 survivors.

OBJECTIVES: Assess the 1-year prevalence of postintensive care syndrome after coronavirus disease 2019.

DESIGN, SETTING, AND PARTICIPANTS: This was a single-center prospective cohort using questionnaires and telephone calls from 4 months to 1 year after ICU discharge. Patients who were treated for coronavirus disease 2019-related acute respiratory distress between March 19, 2020, and April 30, 2020, participated.

MAIN OUTCOMES AND MEASURES: Postintensive care syndrome was evaluated according to physical, mental, and cognitive domains. We surveyed the 8-item standardized Short Form questionnaire for assessing physical postintensive care syndrome; the Impact of Event Scale-Revised and the Hospital Anxiety and Depression Scale for assessing mental postintensive care syndrome; and Short-Memory Questionnaire for assessing cognitive postintensive care syndrome. The primary outcome was postintensive care syndrome occurrence of any domain at 1 year. Furthermore, the co-occurrence of the three postintensive care syndrome domains was assessed.

RESULTS: Eighteen patients consented to the study and completed the survey. The median age was 57.5 years, and 78% of the patients were male. Median Acute Physiology and Chronic Health Evaluation-II score was 18. During ICU stay, 78% received invasive mechanical ventilation, and 83% received systemic steroid administration. Early mobilization was implemented in 61%. Delirium occurred in 44%. The median days of ICU and hospital stay were 6 and 23.5, respectively. Overall postintensive care syndrome occurrence was 67%. Physical, mental, and cognitive postintensive care syndrome occurred in 56%, 50%, and 33% of patients, respectively. The co-occurrence of all three domains of postintensive care syndrome was 28%. Age and Acute Physiology and Chronic Health Evaluation-II scores were higher, and systemic steroids were more commonly used in the postintensive care syndrome groups compared with the nonpostintensive care syndrome groups. Chronic symptoms were more common in the postintensive care syndrome groups than the nonpostintensive care syndrome groups.

CONCLUSIONS AND RELEVANCE: Patients who suffered critical illness from coronavirus disease 2019 had a high frequency of postintensive care syndrome after 1 year. Long-term follow-up and care should be continuously offered.

KEY WORDS: 1 year; coronavirus disease 2019; critical care; intensive care unit; postintensive care syndrome; questionnaire

More than a year has passed since the World Health Organization declared the pandemic of coronavirus disease 2019 (COVID-19) on March 11, 2020 (1). While extensive research has focused on the acute

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phase of the disease, studies are increasingly published regarding the long-term effects of the disease (2–6).

With regard to ICU-treated patients, however, studied outcomes are limited to relatively early phases after discharge (2, 4–8). Only a few studies have evaluated long-term outcomes and the occurrence of postintensive care syndrome (PICS) defined as a new or worsening impairment in physical, mental, or cognitive health status arising and persisting after hospitalization for a critical illness (7–9). Not only has PICS become recognized, but it has also become the next target in the field of critical care medicine and may be increasingly impactful in the era of COVID-19 (10). However, little is known about the inpatient and outpatient strategies to prevent, screen, and follow-up PICS in COVID-19 survivors when interpersonal contact is restricted due to infection-containment measures. There is a need to evaluate the ICU treatment details, characteristics, and occurrence of long-term PICS in this population with respect to all three aspects of PICS.

This study aimed to thoroughly screen and follow-up critically ill COVID-19 survivors for PICS so that adequate outpatient care was provided promptly. We also sought to investigate the 1-year outcome and its full spectrum of PICS, including its physical, mental, and cognitive aspects, in COVID-19 survivors hospitalized at our single-center ICU.

METHODS

Study Design and Participants

This prospective study enrolled patients who were consecutively hospitalized in the ICU of a single institution in central Tokyo, Japan, for critically ill COVID-19 between March 19, 2020, and April 30, 2020. The hospital provided permission for the collection of data from electronic health records. This study was approved by the institutional review board of St. Luke's International Hospital (approval number 20-R102).

The inclusion criteria included ICU admission for acute respiratory distress and laboratory or radiological confirmation of COVID-19 (11). Patients who died during hospitalization were excluded. A laboratory diagnosis was based on a positive reverse transcriptase-polymerase chain reaction test results for the severe acute respiratory syndrome coronavirus 2 from samples, such as a nasal swab, pharyngeal swab, or sputum (12). A radiological diagnosis of COVID-19 was based on the presence of bilateral ground-glass opacities on chest CT (13).

Care in the ICU

Details of treatment strategies including medications, oxygen delivery, and other organ replacement therapy in the ICU are documented in our previously published study (11). Physiotherapy was provided by ICU exclusive physiotherapists and nurses. Programs such as range of motion and sitting position were introduced to the patients as early mobilization within 48 hours of ICU admission. Each patient had an ICU diary produced by nurses, which included photographs and notes of the patients' clinical course during ICU admission. Family members were not permitted to enter the ICU due to infection control restrictions, but the use of smartphones and tablets were allowed. We assisted calling family members upon the patients' request.

Patient Survey, Follow-Up, and Care Provided for PICS

A telephone call was made to each patient by a team of doctors, nurses, and a physical therapist, who were all ICU staff members between August 17, 2020, and August 21, 2020. First, the patient's ability to complete the mailed questionnaire was assessed. In the case of severe mental distress or patient refusal, the questionnaire was not mailed. The survey comprised the following items: the Post-COVID-19 Functional Status (PCFS) scale (14), modified Medical Research Council (mMRC) dyspnea scale (15), Hospital Anxiety and Depression Scale (HADS) (16), Impact of Event Scale-Revised (IES-R) (17), and the 8-item standardized Short Form (SF-8) questionnaire (18, 19). In addition, participants were asked about their living, marital, and working status and answered self-assessment questions regarding their abilities of concentration, memory, and forgetfulness (Supplemental Digital Content, **Text 1**, http://links.lww.com/CCX/A876). The survey booklet and an informed consent form were sent to patients' homes on August 21, 2020. Responses from patients with valid consent documents were used for assessment. Results of the questionnaire were assessed for study purposes and for providing proper care to patients with PICS. A telephone call was made promptly after confirmation of positive results to all the eligible patients regardless of whether they consented to the study. Patients who requested care regardless of the test results were also subject to a phone call. The study team member that had been most close to the patient during ICU admission was chosen to make the phone call. Patients were given the choices of consulting a physiotherapist or nurse psychotherapist. For patients who refused further counseling, the ICU office phone number was provided in case the patients changed their minds. At 6 months after discharge, a telephone call was made to all patients to ensure their well-being. Patients were again offered options of further consultation upon desire. A second survey including the same questions as the first survey in addition to the Short-Memory Questionnaire (SMQ) (20) was sent to all consenting patients on April 19, 2021. Patients were also asked if they had chronic symptoms that were present after 1 year from COVID-19 infection.

Data Collection

We collected data for baseline characteristics, comorbidities, illness severity, and mortality prediction scores at ICU admission (Sequential Organ Failure Assessment score, Acute Physiology and Chronic Health Evaluation [APACHE]-II), ICU therapies (systemic steroids, invasive mechanical ventilation, extracorporeal membrane oxygenation, renal replacement therapy, continuous benzodiazepine administration), and outcomes. Early mobilization programs performed within 48 hours of ICU admission were investigated. Information on delirium was collected from electronical ICU charts. ICU nurses performed routine assessments using the confusion assessment method for the ICU to determine delirium occurrence. Additionally, delirium was defined based on a positive Richmond Agitation-Sedation Scale score (16, 21) or bedside nurse's judgment of the presence of agitation, hallucination, or dangerous behavior. Furthermore, outcomes such as the duration of ICU stay, hospital stay, and place of discharge were investigated.

Study Endpoints

PICS was assessed according to three subgroups: physical PICS, mental PICS, and cognitive PICS. Physical and mental domains of PICS were evaluated based on the results of the 1-year questionnaire. Physical PICS was assessed using SF-8 Physical Component Scale (PCS). SF-8 is a comprehensive 8-item survey of health-related quality of life with two summary scales: PCS and Mental Component Scale (MCS). Scales were transformed to a normalized scale using norm-based scoring with 50 as the population mean. A PCS below 50 was defined as physical PICS (18, 19, 22). Mental PICS was assessed using HADS and IES-R scores (23). Patients with scores greater than or equal to 8 for anxiety and depression components of the HADS survey were considered to have anxiety and depression (16), and an average IES-R score greater than or equal to 1.6 or more indicated post-traumatic stress disorder (PTSD) (23). A composite endpoint of these score results was considered as mental PICS. Cognitive PICS was defined when the patient claimed to have deterioration of either concentration, memory, or forgetfulness throughout the follow-up period, along with a SMQ score of less than or equal to 39 at the 1-year assessment (21, 24). Diagnosis of PICS was made for patients with least one impairment in the three PICS domains. Care was offered to patients with positive results for any domain of PICS.

Statistical Analyses

The results of each questionnaire were analyzed and compared according to the study period of 4 months and 1 year. Patients with PICS were compared with patients without PICS, and the group of patients with impairments in all three domains of PICS was compared with patients with none of the three domains. In addition, each subgroup of PICS patients was compared the corresponding non-PICS group. For example, physical PICS group was compared with the nonphysical PICS group. In addition to the survey results, variables such as baseline demographics, comorbidities, living and marital status, illness severity and mortality prediction scores, ICU treatments, the occurrence of delirium, and outcomes were compared.

Continuous variables are presented as median and interquartile ranges (IQRs). Categorical variables are reported as the number and percentages. The groups were compared using Kruskal-Wallis test or Mann-Whitney *U* test, and categorical comparisons were drawn using the Fisher exact test or chi-square test, as deemed appropriate. Wilcoxon signed rank test was used for paired data. Statistical analyses were performed using the JMP Version 12 statistical software (SAS Institute, Cary, NC). A two-sided p value of less than 0.05 was considered statistically significant for all analyses. Missing data were not replaced or estimated.

RESULTS

Among 27 eligible patients, 18 patients responded to both 4-month and 1-year assessments with a valid consent form and were included in the study (**Fig. 1**).

Baseline Characteristics

Baseline and demographic characteristics are shown in **Table 1**. All patients were of Japanese ethnicity. Median age was 57.5 (IQR, 49.5–71.8), 78% were male, and 83% had comorbidities of any kind. Seventy-eight percent were employed or self-employed at the time of hospital admission and the remaining 22% were unemployed or retired. None of the patients lived in nursing homes or long-term care facilities before hospitalization. All patients were physically independent in daily life activities, and none were receiving social services. No patients were previously diagnosed with mental diseases or cognitive impairments.

Results of the Questionnaire

Major results of the questionnaire of 4 months and 1 year after ICU discharge are demonstrated in Supplemental Digital Content (**Supplemental Table 1**, http://links.lww.com/CCX/A865). Patients answered the surveys at a median of 130 days (IQR, 111–134 d) and 365 days (IQR, 345–375 d), respectively. Seventy-two percent of patients had a PCS below 50 at 4 months post-ICU discharge, compared with 56% at 1-year assessment, but there was no statistical difference between the study periods. Similarly, there were no differences between the results of the two study periods in PCFS, mMRC, IES-R, HADS anxiety and depression, or MCS of SF-8. At 4-month evaluation, 50%, 44%, and 39% claimed to have deterioration of concentration, memory, and forgetfulness, respectively, since COVID-19 infection. At 1-year evaluation, 12%, 18%, and 18% claimed to have deterioration of concentration, memory, and forgetfulness, respectively, since the first survey. One patient claimed that all abilities improved from the 4-month survey to the 1-year survey.

Occurrence of Each PICS Domain

Figure 2 shows the distribution of patients based on each PICS subgroup. Physical, mental, and cognitive PICS occurred in 10 (56%), 9 (50%), and 6 (33%) patients, respectively. In the mental PICS domain, four patients presented impairments in all anxiety, depression, and PTSD components and are illustrated as the overlapping colors. Among the six patients with cognitive PICS, all patients had an SMQ score lower than 39; five claimed to have deterioration in concentration, memory, and forgetfulness at the 4-month evaluation, whereas one denied deterioration at 4 months but claimed decreasing ability at 1-year evaluation.

Overall Occurrence of PICS

The proportion of patients with physical, mental, and

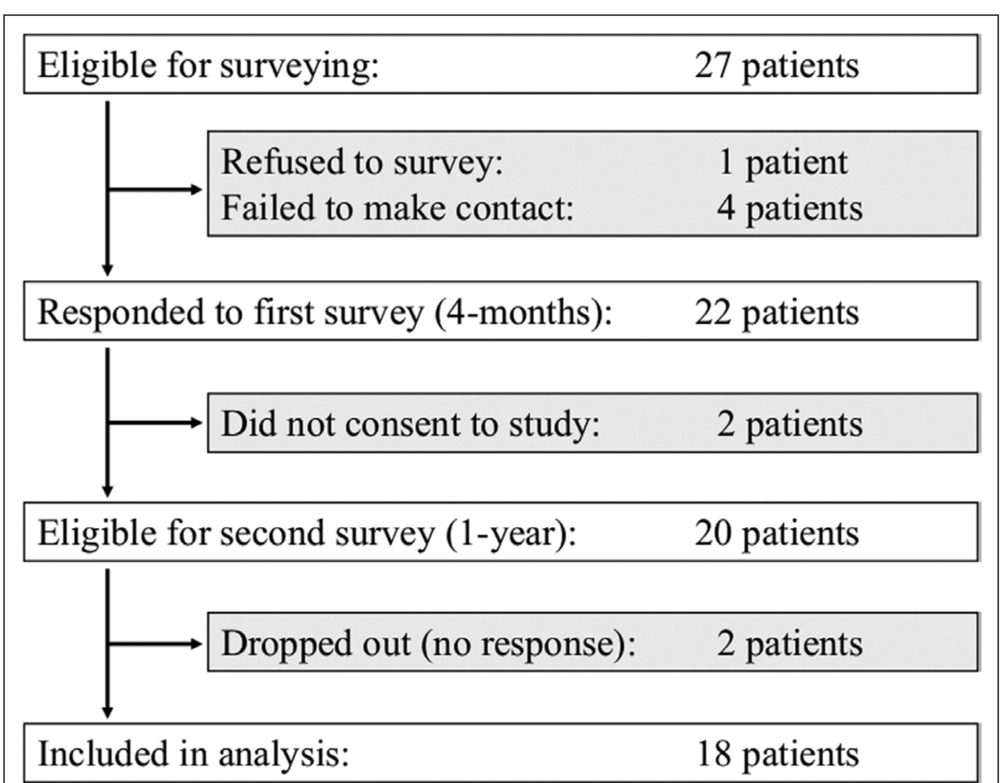

Figure 1. Flow chart of patient selection and exclusion. Eighteen patients completed the study and were enrolled in the analysis.

TABLE 1.
Baseline and Demographic on Hospital Admission

Variable	Total ($n = 18$)
Age, yr	57.5 (49.5–71.8)
Male	14 (78)
BMI, kg/m^2	24.4 (22.0–28.6)
Overweight (25 ≤ BMI < 35),	6 (33)
Obese (35 ≤ BMI)	1 (6)
Comorbidities	
Hypertension	8 (44)
Diabetes	7 (39)
Coronary artery disease	1 (6)
Asthma	5 (3)
Chronic obstructive pulmonary disease	2 (11)
Cancer[a]	1 (6)
Current or former smoker	12 (67)
Habitual or occasional alcohol consumption	9 (50)
Marital status	
Married	9 (50)
Separated or divorced	0 (0)
Widowed	2 (11)
Unmarried	6 (33)
Unknown	1 (6)
Living status	
Alone	9 (50)
With family	9 (50)

BMI = body mass index.
[a]Includes untreated or simultaneously treated neoplasms.
Data are expressed as numbers (percentage) or median (interquartile range).

cognitive PICS is shown in **Figure 3**. There were 12 patients (67%) who had at least one type of PICS. All six patients who had cognitive PICS had mental PICS. Five patients (28%) applied to all domains of PICS.

Comparison of PICS Versus Non-PICS

The comparison of PICS versus non-PICS and patients of all three PICS domains versus patients without all three domains is shown in **Table 2**. The PICS group had higher APACHE-II scores (PICS vs non-PICS: 19.0 [IQR, 17.8–22.0] vs 12.0 [IQR, 10.3–13.0]; $p = 0.014$) and higher usage rates of systemic steroids (PICS vs non-PICS: 100% vs 50%; $p = 0.025$). Patients with all three domains were older than the patients none of the three domains (patients with all three domains vs patients none of the three domains: 72.0 [IQR, 61.0–77.0] vs 56.0 [IQR, 48.0–62.0]; $p = 0.043$). Eleven patients (61%) received early mobilization therapy, including 10 (56%) that accomplished sitting position. There were no differences in early mobilization implementation rates among the groups that were compared.

Each subgroup of PICS versus the corresponding non-PICS group is compared and demonstrated in Supplemental Digital Content (**Supplemental Table 2**, http://links.lww.com/CCX/A866). There was a difference in APACHE-II scores of the mental PICS group and the nonmental PICS group (mental PICS vs nonmental PICS: 19.0 [IQR, 18.0–22.0] vs 13.0 [IQR, 10.0–18.0]; $p = 0.024$). Although there were no statistical differences, physical PICS patients tended to have a higher APACHE-II score (physical PICS vs nonphysical PICS: 19.0 [IQR, 18.0–21.5] vs 13.0 [10.8–17.3]; $p = 0.090$), and a higher usage rate of systemic steroids (physical PICS vs nonphysical PICS: 100% vs 63%; $p = 0.069$). In addition, patients tended to be older in the mental PICS group (mental PICS vs nonmental PICS: 61.0 [IQR, 57.0–77.0] vs 49.0 [IQR, 47.0–62.0]; $p = 0.070$) and the cognitive PICS group (cognitive PICS vs noncognitive PICS: 66.5 [IQR, 58.8–75.8] vs 53.5 [IQR, 47.8–64.3]; $p = 0.061$). Details of systemic steroid dose and duration of administration according to each PICS groups are illustrated in Supplemental Digital Content (**Supplemental Table 3**, http://links.lww.com/CCX/A867).

The results of the questionnaire at 4 months and 1 year according to groups of PICS versus non-PICS, and patients with all three domains versus patients without all three domains, are displayed in Supplemental Digital Content (**Supplemental Table 4**, http://links.lww.com/CCX/A868). There were no differences between the results of the 4 months and 1-year surveys for any subgroup.

Chronic Symptoms at 1-Year Evaluation

Chronic symptoms that were present at 1-year evaluation are shown in Supplemental Digital Content (**Supplemental Table 5**, http://links.lww.com/CCX/A869). Sleep difficulty was the most common

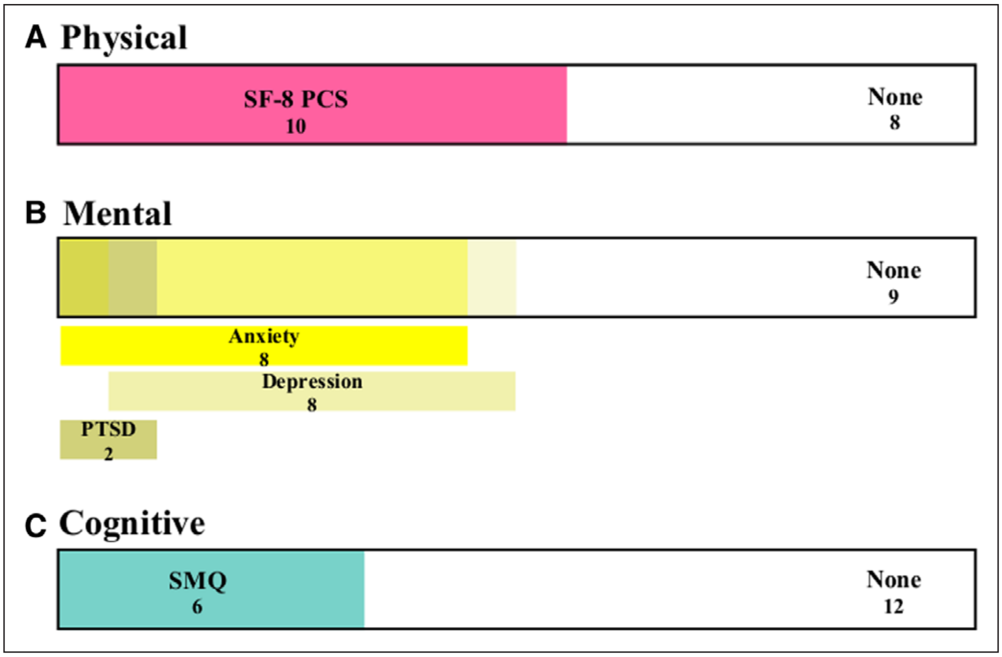

Figure 2. The occurrence of physical, mental, and cognitive postintensive care syndrome (PICS). The *colored bars* show the proportion of patients who were applicable for each domain. Mental PICS was a composite endpoint of anxiety, depression, and post-traumatic stress disorder (PTSD). One patient displayed all three symptoms, and one patient had depression only. PCS = Physical Component Scale, SF-8 = 8-item standardized Short Form, SMQ = Short-Memory Questionnaire.

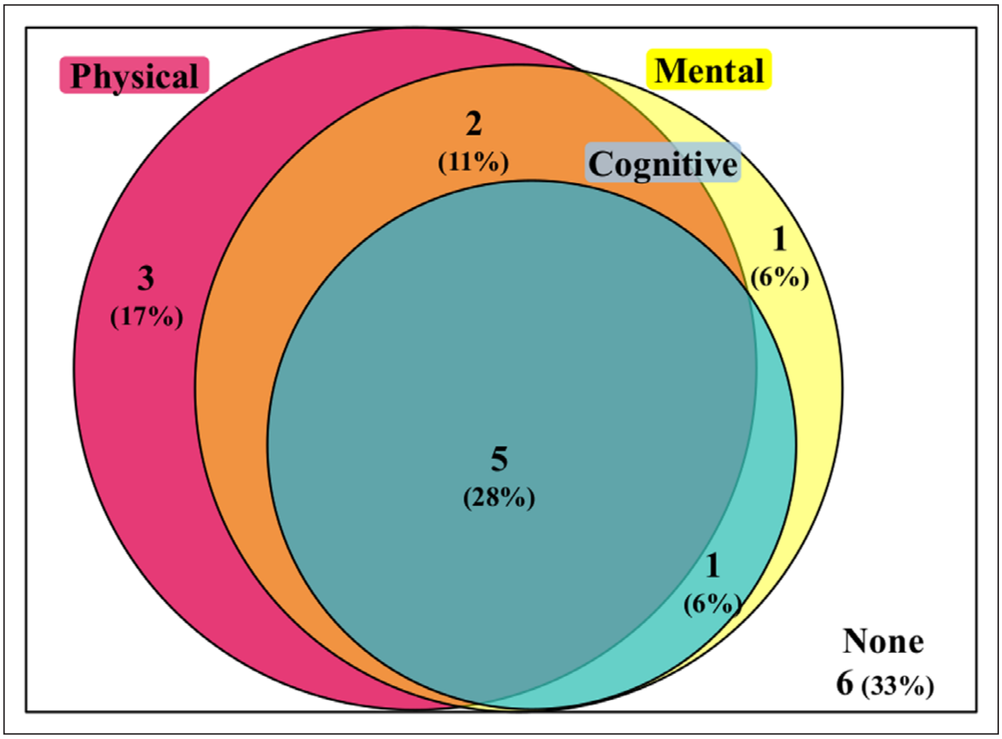

Figure 3. Overlapping of each subgroup of postintensive care syndrome (PICS). Physical, mental, and cognitive PICS are displayed by the *pink*, *yellow*, and *blue circles*, respectively. The overlap of the *circles* represents the co-occurrence of the impairments.

symptom among all patients (6 [33%]) and was more common in the group of patients with all three domains (patients with all three domains vs patients without all three domains: 80% vs 15%; $p = 0.022$), the mental PICS group (mental PICS vs nonmental PICS: 67% vs 0%; $p = 0.009$), and the cognitive PICS group (cognitive PICS vs noncognitive PICS: 83% vs 8%; $p = 0.004$). Fatigue was also more commonly observed in the mental (mental PICS vs nonmental PICS: 56% vs 0%; $p = 0.029$) and cognitive PICS groups (cognitive PICS vs noncognitive PICS: 67% vs 8%; $p = 0.022$).

DISCUSSION

This study investigated the 1-year outcomes of PICS in 18 patients who were hospitalized for critical illness due to COVID-19. The rates of physical, mental, and cognitive PICS were 56%, 50%, and 33%, respectively. Sixty-seven percent of patients had at least one type of impairment, whereas the co-occurrence rate of all three domains was 28%.

There are several strengths of this study. First, we were able to provide adequate inpatient care such as a high implementation rate of early mobilization and ICU diaries during ICU hospitalization. Although this study was a

TABLE 2.

Comparison of Postintensive Care Syndrome Versus Nonpostintensive Care Syndrome and Patients With Three Domains Versus Patients Without Three Domains

Variable	Total (*n* = 18)	PICS (*n* = 12)	Non-PICS (*n* = 6)	*p*	Patients With Three Domains (*n* = 5)	Patients Without Three Domains (*n* = 13)	*p*
Age, yr	57.5 (49.5–71.8)	59.5 (54.8–77.0)	52.5 (48.3–60.5)	0.241	72.0 (61.0–77.0)	56.0 (48.0–62.0)	0.043
Male	14 (78)	8 (67)	6 (100)	0.245	4 (80)	10 (77)	1.000
Body mass index, kg/m^2	24.4 (22.0–28.6)	24.6 (22.1–30.7)	23.4 (21.5–25.9)	0.640	22.3 (22.0–24.3)	24.9 (22.1–30.3)	0.183
Comorbidities							
Respiratory comorbidities[a]	6 (33)	5 (42)	1 (17)	0.600	1 (20)	5 (38)	0.615
Current or former smoker	12 (67)	7 (58)	5 (83)	0.600	2 (40)	10 (77)	0.538
Lifestyle comorbidities[b]	12 (67)	8 (67)	4 (67)	1.000	2 (40)	10 (77)	0.268
Living alone	9 (50)	7 (58)	2 (33)	0.620	1 (20)	8 (62)	0.294
Married	9 (50)	6 (50)	3 (50)	1.000	4 (80)	5 (38)	0.294
Sequential Organ Failure Assessment	6.0 (3.3–7.8)	6.0 (3.8–7.3)	5.5 (2.8–7.5)	0.571	6.0 (4.0–7.0)	6.0 (3.0–8.0)	0.619
Acute Physiology and Chronic Health Evaluation-II	18.0 (13.0–19.8)	19.0 (17.8–22.0)	12.0 (10.3–13.0)	0.014	20.0 (18.0–22.0)	17.0 (11.0–19.0)	0.137
Invasive mechanical ventilation	14 (78)	9 (75)	5 (83)	1.000	4 (80)	10 (77)	1.000
Days of invasive mechanical ventilation, d	5.5 (4.3–10.8)	5.0 (4.0–12.0)	6.0 (5.0–7.0)	0.737	8.5 (4.5–19.0)	5.5 (4.3–7.0)	0.722
Extracorporeal membrane oxygenation	1 (6)	0 (0)	1 (17)	0.333	0 (0)	1 (8)	1.000
Tracheostomy	3 (17)	2 (17)	1 (17)	1.000	1 (20)	2 (15)	1.000
Renal replacement therapy	1 (6)	1 (8)	0 (0)	1.000	0 (0)	1 (8)	1.000
Systemic steroids	15 (83)	12 (100)	3 (50)	0.025	5 (100)	10 (77)	0.522
Continuous benzodiazepine	4 (22)	3 (25)	1 (17)	1.000	1 (20)	3 (23)	1.000
Range of motion within 48 hr of ICU admission	11 (61)[c]	6 (50)	5 (83)	0.316	3 (60)	8 (62)	1.000
Sitting position within 48 hr of ICU admission	10 (56)[c]	6 (50)	4 (67)	0.638	3 (60)	7 (54)	1.000
Occurrence of delirium	8 (44)	5 (42)	3 (50)	1.000	3 (60)	5 (38)	0.608

(*Continued*)

TABLE 2. (*Continued*).
Comparison of Postintensive Care Syndrome Versus Nonpostintensive Care Syndrome and Patients With Three Domains Versus Patients Without Three Domains

Variable	Total (n = 18)	PICS (n = 12)	Non-PICS (n = 6)	p	Patients With Three Domains (n = 5)	Patients Without Three Domains (n = 13)	p
ICU stay, d	6.0 (5.0–12.5)	6.5 (4.5–13.5)	6.0 (5.3–8.3)	0.962	7.0 (5.0–13.0)	6.0 (5.0–11.0)	0.921
Hospital stay, d	23.5 (18.0–39.5)	28.0 (17.8–44.3)	21.5 (18.3–25.5)	0.779	23.0 (18.0–33.0)	24.0 (18.0–41.0)	0.921
Discharged to other hospital or recovery hotel[d]	4 (22)	3 (25)	1 (17)	1.000	2 (40)	2 (15)	0.533

PICS = postintensive care syndrome.

[a]Includes chronic respiratory disease and asthma.

[b]Includes hypertension, diabetes mellitus, dyslipidemia, and obesity.

[c]All patients who accomplished sitting position had also carried out range of motion.

[d]Patients who had repeated positive reverse transcriptase-polymerase chain reaction tests required isolation at an observatory hotel before discharge.

Data are expressed as numbers (percentage) or median (interquartile range).

two-point evaluation study, we continuously followed-up our patients via telephone and provided further care if necessary. The details of 1-year outcomes and PICS occurrence in critically ill COVID-19 survivors are described in the full spectrum of physical, mental, and cognitive domains. Finally, our findings propose that PICS is detectable at 4 months, but follow-up should not be halted because patients may continue to suffer from PICS or long-term COVID-19 manifestations.

Up to date, there have been several reports regarding PICS in COVID-19 patients. Martillo et al (7) investigated COVID-19 survivors of the ICU at 1 month from hospital discharge and observed a 91% prevalence of overall PICS, which was higher than our study. Prével et al (25) examined mental dysfunctions in 18 to 19 patients at 6 months after ICU discharge and revealed that depression, anxiety, and PTSD were seen in 11%, 22%, and 6%, respectively. Another report studying COVID-19 survivors following extracorporeal membrane oxygenation use at 1 year found depression in 40%, anxiety in 60%, and PTSD in 40% (26). In our study, the prevalence of depression, anxiety, and PTSD was 44%, 44%, and 11%, respectively. Meanwhile, three previous studies have investigated all three PICS domains in a non-COVID population after at least 3 months of discharge (21, 27, 28). The occurrence rate of overall PICS at 3 to 6 months postdischarge ranged from 64% to 84%; furthermore, the rates of having all three PICS domains were 2%, 6%, and 33% in each study. Marra et al (27) additionally reported a prevalence of overall PICS (56%) and overlapping PICS (4%) at 12 months evaluation, which is lower than that of our study. The differences in PICS occurrence rates may be because the methods and timings of evaluation were unique to each study and also did not target a specific disease such as critically ill COVID-19. Thus, our findings suggest that PICS caused by critical illness due to COVID-19 may be more frequent than PICS caused by other etiologies, and long-term follow-up and care should be provided, as the prevalence remains high 1-year after discharge.

Our results suggest that a higher APACHE-II score and the use of systemic steroids are associated with PICS, and older age is associated with developing all three domains of PICS. Higher disease severity and steroids are known risk factors for physical PICS (29, 30). Likewise, older age is significantly associated with cognitive PICS (29, 31). Our results demonstrated a tendency of association between APACHE-II, systemic steroids, and physical PICS and between age and cognitive PICS, which is consistent with previous observations (29–31). Furthermore, because physical PICS was the most prevalent among the three domains, these results were most reflected in the overall PICS group. In contrast, because cognitive PICS was the least prevalent among the three domains, it was reflected most kin the group with all three PICS domains. In our study, the overall rate of early mobilization was 61%, which was higher than a previous prevalence study targeting ICU-treated COVID-19 patients in June 2020 and July 2020 (32). However, the physical PICS group tended to have a lower rate than the nonphysical PICS group (4 [40%] vs 7 [88%]; $p = 0.067$). Our results may suggest that early mobilization plays an important role in preventing physical PICS in COVID-19 survivors. Taken together, risk factors that may contribute to PICS development after critical illness due to COVID-19 are likely to be no different from PICS development from other etiologies. Furthermore, our patients were not only victims of a new and obscure disease but also a phenomenal pandemic. Media influence such as COVID-19–related deaths of celebrities may have triggered predominately mental impairments in our patients (33). In addition, because COVID-19 is associated with long-term consequences, there may be an underlying pathophysiology that is unique to the development of PICS (2, 5, 6). Larger scale studies and multivariate analysis are necessary to identify the exact risk factors of PICS in COVID-19 survivors.

The rate of PICS occurring after COVID-19 was relatively high, and our results support that postacute follow-up is crucial for ICU-treated patients. It was evident that our patients had a variety of long-term consequences; therefore, evaluating all three domains is necessary for comprehensive care. Furthermore, the comparison between 4 months and 1-year evaluation was proven to be no different in the overall study population or in each PICS subgroup. This may indicate that most long-term impairments are detectible by at least 4 months after acute illness. Rightfully, previous studies have mostly focused on 3 to 6 months of follow-up for the evaluation of PICS (21, 27, 28). However, many of our patients suffered chronic symptoms persisting for over a year after acute COVID-19 illness. In accordance, increasing studies have highlighted the long-term aftereffects of COVID-19 after a year (5, 6). We suggest that follow-up should not be halted, and care should be provided for our patients in need.

We must address some limitations. The number of patients included in the study was small, and this was a single-center study. This study was conducted by ICU working staff members, so 1 month or 3 months post-ICU evaluation was not possible due to the heavy workload that was persistent throughout the pandemic. In addition, comparison with patients' baseline status was not possible. Selection bias may have occurred because this was a mailed survey that required the participants to respond. It is likely that patients who were severely impaired or ill were not capable of consenting to or returning the survey. We were also unable to perform a comparison of non-COVID-19 ICU survivors with our patients. Finally, the definition of PICS has not yet gained consensus, and our methods of evaluation were limited to questionnaires that were available in Japanese and answerable via postal mail.

CONCLUSIONS

Two-thirds of the survivors of critically ill COVID-19 presented with at least 1 impairment of PICS, and 28% had overlapping impairments of all three domains. These findings suggest that PICS related to COVID-19 is frequent, and many patients are in need of long-term evaluation. More than a year has passed since the outbreak of COVID-19. One-year evaluation may not be the final goal but is a key milestone in the evaluation of PICS. We suggest it is ideal to continue to care for these patients because the 1-year data may be beneficial for the comparison of extended long-term outcomes. Treatment or care should not only target the improvement of early but also the chronic outcomes as its impact will continue.

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