ORIGINAL CLINICAL REPORT

OPEN

Psychologic Distress and Quality of Life After ICU Treatment for Coronavirus Disease 2019: A Multicenter, Observational Cohort Study

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OBJECTIVES: To quantify short- and long-term psychologic distress, that is, symptoms of posttraumatic stress disorder, anxiety, and depression, and the health-related quality of life in coronavirus disease 2019 ICU survivors.

DESIGN: A prospective, observational cohort study.

SETTING: Postcoronavirus disease 2019 clinics of three hospitals in Rotterdam, the Netherlands.

PATIENTS: Adult patients admitted for coronavirus disease 2019 to the ICU, who visited the postcoronavirus disease 2019 follow-up clinic.

MEASURES AND MAIN RESULTS: The primary outcomes were psychologic distress and overall and mental health-related quality of life, assessed using the Impact of Event Scale-Revised, Hospital Anxiety and Depression Scale, Short-Form 36, and European Quality of Life 5D, 6 weeks, 3 months, and 6 months post hospital discharge. Second, we compared 3-month psychologic and mental health-related quality of life outcomes with a historical critical illness survivor cohort and overall and mental health-related quality of life with the Dutch population. We included 118 patients with a median age of 61 years (95% range, 36–77 yr) of whom 79 (68%) were male. At 6 weeks, 13 patients (23%) reported psychologic distress, copresence of probable psychiatric disorders was common, and no decline in psychologic distress was observed throughout follow-up. Coronavirus disease 2019 patients tend to suffer less from posttraumatic stress disorder and reported less severe symptoms of anxiety (Hospital Anxiety and Depression Scale Anxiety Score: 3 [0–17] vs 5 [0–16]; estimated mean difference 2.3 [95% CI, 0.0–4.7]; $p = 0.05$) and depression (Hospital Anxiety and Depression Scale Depression Score: 3 [0–15] vs 5 [0–16]; estimated mean difference 2.4 [95% CI, 0.1–2.4]; $p = 0.04$) than the historical critical illness cohort. Overall and mental health-related quality of life increased over time. Coronavirus disease 2019 ICU survivors reported better mental health-related quality of life than our historical cohort, but overall and mental health-related quality of life was still poorer than the Dutch population.

CONCLUSIONS: Psychologic distress was common in coronavirus disease 2019 ICU survivors and remained similar until 6 months after hospital discharge. Health-related quality of life increased over time and was higher than in a historical cohort, but was lower than in the Dutch population. Our findings highlight that coronavirus disease 2019 ICU survivors should be monitored after ICU treatment to detect possible psychologic distress.

KEY WORDS: coronavirus disease 2019; depression; intensive care unit; postintensive care syndrome; posttraumatic stress disorder; severe acute respiratory syndrome coronavirus 2

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has resulted in an unprecedented increase in ICU admissions all around the world, resulting in a growing population of coronavirus

DOI: 10.1097/CCE.0000000000000497

disease 2019 (COVID-19) ICU survivors. A substantial number of general ICU survivors suffer from a decreased health-related quality of life (HRQoL), mostly due to long-term sequelae of the postintensive care syndrome (PICS). PICS comprises new or worsening impairments in a patients' psychologic, cognitive, and physical health state, which frequently develop in critical illness survivors (1–3). The psychologic component of PICS consists of symptoms of posttraumatic stress disorder (PTSD), anxiety, and depression, and occurs in up to 60% of ICU survivors. These have been demonstrated to be the most important contributor to a decreased HRQoL, disabling patients to return to their former life (4).

Several risk factors for the development of psychologic sequelae of PICS have been elucidated and include severe illnesses, such as sepsis or acute respiratory distress syndrome, prolonged mechanical ventilation and prolonged ICU stay, fear of dying, and having memories of frightening delirium-related nightmarish and psychotic experiences (5–8). Most of these are common during COVID-19 ICU treatment. It has recently been demonstrated that episodes of dyspnea and limited patient- and family-centered care due to changing in-ICU circumstances during the pandemic might further increase this risk (9, 10). This may significantly increase the burden on healthcare resources across the care continuum and emphasizes the importance of determining the prevalence of psychologic PICS sequelae in COVID-19 ICU survivors.

In the current study, we aimed to quantify the psychologic burden and quality of life in COVID-19 ICU survivors and investigated how these developed until 6 months after hospital discharge. We compared these outcomes with a general historical cohort and with the general Dutch population.

METHODS

Study Design and Setting

This observational, prospective, multicenter study was conducted between May 5, 2020, and April 29, 2021, by the pulmonology and ICU departments of three hospitals in Rotterdam, the Netherlands; that is, the Erasmus Medical Center (Erasmus MC), a tertiary care, university hospital; the Franciscus Gasthuis & Vlietland Hospital; and Ikazia hospital, which are secondary care hospitals. Patients were invited to a post-COVID-19 follow-up clinic at the concurrent hospital at 6 weeks, 3 months, and 6 months after hospital discharge. This study is part of a larger study that was approved by the Medical Ethics Committee (MEC) of the Erasmus MC, which was found not to be subject to the Medical Research Involving Humans Act (MEC-2020-0511).

Participants

All consecutive adult (≥ 18 yr) patients admitted to the mixed medical-surgical ICU of one of the participating hospitals with a SARS-CoV-2 infection, proven by polymerase chain reaction, were eligible for participation. As part of regional standard of care, all post-ICU COVID-19 patients were invited to the institutional post–COVID-19 clinic at 6 weeks, 3 months, and 6 months after hospital discharge. Prior to these visits, patients were asked to fill out questionnaires to measure psychologic distress and HRQoL. Patients who completed these questionnaires were included. Patients consented online to use their data for medical research prior to filling out the questionnaires. Patients who were unable to understand the written Dutch language were excluded.

We compared patients who visited the post–COVID-19 clinic with a historical control cohort. This control cohort comprised 118 patients who had visited the post-ICU follow-up clinic between 2017 and 2020, prior to the SARS-CoV-2 outbreak. All of them were mechanically ventilated for a minimum of 24 hours.

Procedures

All COVID-19 ICU survivors were invited to a post–COVID-19 follow-up clinic at 6 weeks, 3 months, and 6 months after hospital discharge. Prior to each visit, patients were asked to fill out a set of questionnaires to obtain a measure of patients' health and psychologic status and to assess the HRQoL. Patients who did not fill out the questionnaires were contacted twice by telephone as a reminder by the Department of Pulmonology, after which they were excluded.

Patients treated in the ICU between 2017 and 2020, prior to the SARS-CoV-2 outbreak, who were mechanically ventilated, were routinely invited to a post-ICU follow-up clinic at 3 months after hospital discharge as part of standard care. Patients who responded to this invite were asked to fill out a set of questionnaires with

regard to their psychologic status and HRQoL. These data were used to form a historical cohort.

Outcomes

The primary outcomes were psychologic distress, that is, symptoms of PTSD, anxiety, and depression, and overall and mental HRQoL at 6 weeks, 3 months, and 6 months after hospital discharge. We compared 3-month psychologic outcomes and mental HRQoL with our historical cohort and both overall and mental HRQoL with the general Dutch population (11, 12).

Psychologic distress was expressed as symptoms of PTSD, anxiety, and/or depression. PTSD was assessed using the Impact of Event Scale-Revised (IES-R) in the COVID-19 cohort and using the Trauma Screening Questionnaire (TSQ) in the historical cohort (13, 14). Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) in both cohorts (15). The IES-R comprises 22 items and assesses subjective distress caused by a traumatic event; this scale has been previously validated in ICU survivors. The IES-R yields a total score (ranging from 0 to 88, with higher scores indicating more severe symptoms), and subscale scores can be calculated for symptoms of intrusion, avoidance, and hyperarousal. An IES-R sum score greater than or equal to 33 was considered as probable PTSD (16). The TSQ measures symptoms of PTSD and consists of 12 questions, which can be answered by "yes" or "no." Each question is based on the Diagnostic and Statistical Manual of Mental Disorders, 5th edition criteria and consists of a reexperiencing or arousal symptom of PTSD. A sum score higher than 10 is considered as probable PTSD (14). The HADS comprises 14 items, is commonly used to determine the levels of anxiety and depression that a patient is experiencing, and is validated in critical illness survivors (17). Seven of the items relate to anxiety, and seven relate to depression. A sum score above 8 on either the depression or anxiety subscale will be classified as probable depression and anxiety, respectively (15, 17).

HRQoL was assessed using the European Quality of Life 5D (EQ-5D) and Short-Form 36 (SF-36) questionnaires. The EQ-5D measures the HRQoL in five dimensions (mobility, self-care, usual activities, pain/discomforts, and anxiety/depression). By giving a weight to each answer option, a health state can be computed, the EQ-5D utility score, ranging from –0.446 (worst quality of life) to 1.000 (best quality of life) (11). Additionally, patients score their current subjective health using a Visual Analogue Scale (the European Quality of Life Visual Analogue Scale), ranging from 0 (worst health imaginable) to 100 (best health imaginable) (18, 19). The SF-36 is a 36-item, patient-reported survey of patient's health and quality of life. The SF-36 consists of eight scaled scores, which are the weighted sums of the questions in their section. The eight sections are vitality, physical functioning, bodily pain, general health perception, physical role functioning, emotional role functioning, social role functioning, and mental health (20). Additionally, the mental and physical component scale, that is, the Mental Component Scale-36 and Physical Component Scale-36, can be computed, assessing the mental and physical quality of life, respectively (21). These component scales are validated and normalized in a cohort of Dutch citizens to have a mean of 50 and a SD of 10 (12).

Statistical Analysis

Continuous data are presented as median (95% range), unless indicated otherwise. Discrete data are presented as absolute and relative frequency.

We used mixed-effects linear and logistic regression models to adjust for intergroup (i.e., time and study site) and intergroup differences (i.e., cohort and at-baseline-differing variables). To analyze the course of psychologic distress and HRQoL throughout follow-up, mixed-effects linear or logistic regression models were used, with a random intercept and/or slope for each individual and each study site, wherein time served as independent variable. To analyze the difference in continuous or categorical baseline variables between the COVID-19 and historical cohort, we used mixed-effects linear or logistic regression models, with a random intercept for each study site, wherein the cohort served as independent variable. To analyze differences in psychologic and HRQoL outcomes, mixed-effects linear and logistic regression models were used, wherein at-baseline-differing variables and the cohort served as independent variables. We used mixed-effects linear regression models for continuous outcomes, that is, the sum scores of the IES-R and HADS, the EQ-5D utility score and the SF-36 summary scales, and mixed-effects logistic regression models for discrete outcomes, that is, the proportion of patients suffering from either probable PTSD,

anxiety, or depression. We report the coefficient (95% CI), which implies the estimated mean difference, for linear models, and odds ratios (ORs), including its 95% CI, for logistic models. As only means and SDs of the EQ-5D utility score and the mental and physical component score from the general Dutch population were available, a standard Student's *t* test was used to analyze differences in HRQoL between the COVID-19 cohort and the general Dutch population.

All analyses were performed using R for Statistics (R Foundation for Statistical Computing, Vienna, Austria, 2015). A *p* value of less than 0.05 was considered statistically significant.

RESULTS

Figure 1 depicts the study's inclusion and follow-up. A total of 147 COVID-19 patients were eligible for inclusion and were invited to the post–COVID-19 follow-up clinic, of whom 118 (80%) filled out questionnaires prior to this visit and were finally included. Of these, 57 patients (48%) filled out questionnaires at 6 weeks, 107 (91%) filled out questionnaires at 3 months, and 80 (68%) filled out questionnaires at 6 months post hospital discharge.

Patients

Patients' baseline demographics and treatment-related characteristics are depicted in **Table 1**. Patients had a median age of 61 years (95% range, 36–77 yr), 79 (68%) were male, and the median body mass index was 27.8 (20.5–42.4). The median hospital length of stay was 22 days (1–67 d), and the median ICU length of stay was 13 days (0–49 d). Ninety-three patients (79%) were mechanically ventilated with a median duration of 284 hours (10–629 hr), of whom 59 were mechanically ventilated in prone position. Patients had a median Acute Physiology and Chronic Health Evaluation-IV score of 50 (26–96), Simplified Acute Physiology Score II score of 31 (18–57), and admission Sequential Organ Failure Assessment score of 2 (0–10). Ninety-four patients (80%) were treated with noradrenaline, 89 (75%) with midazolam, 95 (81%) with remifentanil, and 89 (75%) with sufentanyl.

COVID-19 ICU survivors were more frequently male (COVID-19, 79 [68%] vs historical cohort, 61 [51%]; OR, 1.7 [95% CI, 1.0–2.8]; $p = 0.04$) than survivors in the historical cohort. Although no differences were observed in the hospital or ICU length of stay, illness severity scores, or the proportion of patients being mechanically ventilated, COVID-19 ICU survivors were mechanically ventilated for a longer duration (median [95% range], COVID-19, 284 hr [10–629 hr] vs historical cohort, 89 hr [1–592 hr]; estimated mean difference –154 [95% CI, –217 to –87]; $p < 0.001$) and more often received mechanical ventilation in prone position (*n* [%], COVID-19, 55 [70%] vs historical, 3 [3%]; OR, 0.01 [95% CI, 0.00–0.14]; $p < 0.001$).

Psychologic Distress

At 6 weeks, 13 of 57 patients (23%) reported psychologic distress; the median IES-R sum score was 9 (95% range 1–40) with four patients (7%) reporting probable PTSD, the median HADS Anxiety Score was 4 (95% range 0–12) with nine patients (16%) reporting probable anxiety, and the median HADS Depression Score was 3 (95% range, 0–13) with eight patients (14%) reporting probable depression (**Fig. 2**). Copresence of probable PTSD, anxiety, and depression was reported by six of 13 affected patients (46%); two patients reported clinically relevant symptoms of PTSD and depression, two patients symptoms of anxiety and depression, and two patients symptoms of all three disorders (**Fig. 3*A***).

At 3 months, the proportion of patients reporting psychologic distress remained similar (*n* [%], 27/88 [25%]; OR, 0.73 [95% CI, 0.10–5.25]; $p = 0.75$), and no decline was observed in PTSD, anxiety, or depression outcomes (**Figs. 2** and **3*B***). COVID-19 ICU survivors tend to report probable PTSD less frequently than patients in the historical cohort (COVID-19, 12 [11%] vs historical cohort, 24 [20%]; OR, 4.1 [95% CI, 0.7–25.1]; $p = 0.13$). Furthermore, although COVID-19 ICU survivors did not more frequently report probable anxiety (OR, 2.4 [95% CI, 0.6–8.7]; $p = 0.20$) or probable depression (OR, 3.8 [95% CI, 0.9–15.4], $p = 0.06$), they reported less severe symptoms of anxiety (HADS Anxiety Score: 3 [0–17] vs 5 [0–16]; estimated mean difference 2.3 [95% CI, 0.0–4.7]; $p = 0.05$) and depression (HADS Depression Score: 3 [0–15] vs 5 [0–16]; estimated mean difference 2.4 [95% CI, 0.1–2.4]; $p = 0.04$) (Fig. 2).

At 6 months, 22 of 80 patients (28%) reported psychologic distress, which was similar as the proportion at 5–6 weeks post hospital discharge (OR, 1.15

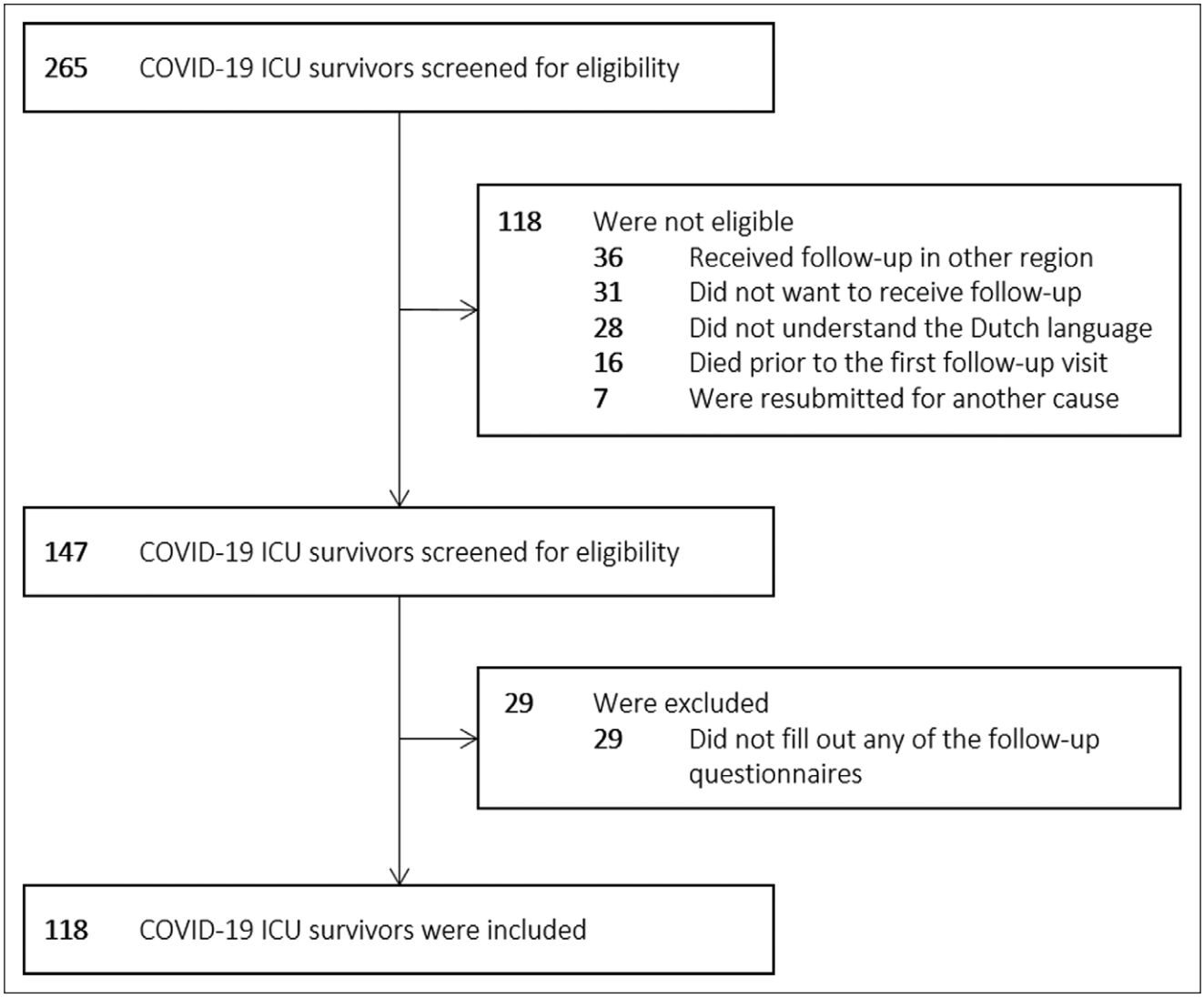

Figure 1. Flowchart of the study's inclusion and follow-up. COVID-19 = coronavirus disease 2019.

[0.21–5.91]; $p = 0.90$) and at 3 months (OR, 1.86 [95% CI, 0.43–8.12]; $p = 0.41$) (**Figs. 2*A*** and **3*C***). Although the severity of PTSD decreased during follow-up (estimated mean difference between 6 wk and 3 mo: −3.29 [95% CI, −5.71 to −0.87]; $p < 0.01$ and estimated mean difference between 3 mo and 6 mo: −2.43 [95% CI, −4.32 to −0.53]; $p = 0.01$), the severity of anxiety and depression symptoms and the proportion of patients reporting probable PTSD, anxiety, and depression remained similar (**Fig. 2*B***).

Mental and Overall HRQoL

Six weeks after hospital discharge, the overall HRQoL was 0.69 (mean EQ-5D utility score, SD 0.24). The overall HRQoL remained similar until 3 months (estimated mean difference 0.03 [95% CI, −0.02 to 0.07]; $p = 0.28$) but improved at 6 months (estimated mean difference between 6 wk and 6 mo: 0.10 [95% CI, 0.05–0.15]; $p < 0.001$ and estimated mean difference between 3 and 6 mo: 0.07 [95% CI, 0.03–0.07]; $p < 0.001$) (**Fig. 4*A***). Throughout follow-up, the overall HRQoL was lower than in the general Dutch population (6 wk: estimated mean difference 0.16 [95% CI, 0.10–0.22]; $p < 0.001$ and 3 mo: 0.15 [0.10–0.20]; $p < 0.001$ and 6 mo: 0.08 [95% CI, 0.03–0.77]; $p < 0.001$).

The mental HRQoL was 43.7 (mean MSC-36, SD 12.2) at 6 weeks, improved at 3 months (estimated mean difference between 6 wk and 3 mo: 3.24 [95% CI, 1.04–5.43]; $p < 0.01$), but remained similar between 6 months and at 3 months (estimated mean difference 0.71 [95% CI, −1.15 to 2.56]; $p = 0.46$) (**Fig. 4*B***). COVID-19 ICU survivors reported a better mental HRQoL at

TABLE 1.
Baseline Demographics and Treatment-Related Characteristics of the Study Population

Characteristics	Coronavirus Disease 2019 Cohort, *N* = 118	Historical Cohort, *N* = 120	*p*
Baseline demographics			
Age, median (95% range)	61 (36–77)	63 (26–83)	0.96
Gender, male, *n* (%)	79 (68)	61 (51)	0.01
Body mass index, kg/m^2, median (95% range)	27.8 (20.5–42.4)	26.0 (20.5–35.7)	0.19
Treatment-related characteristics			
Hospital length of stay, d, median (95% range)	22 (1–67)	21 (4–73)	0.98
ICU length of stay, d, median (95% range)	13 (0–49)	7 (1–58)	0.31
MV			
Received MV, *n* (%)	92 (80)	120 (100)	0.99
Duration of MV, hr, median (95% range)	284 (10–629)	87 (24–537)	< 0.001
Lowest F_{IO_2}	28.0 (19.9–48.0)	21.0 (21–34)	0.30
Lowest Pa_{O_2}/F_{IO_2} rate	0.11 (0.07–1.87)	1.26 (0.38–3.25)	0.63
Prone positioning, *n* (%)	55 (70)	3 (3)	< 0.001
Illness Severity Scores			
Acute Physiology and Chronic Health Evaluation-IV score	49 (26–97)	46 (0–96)	0.47
Simplified Acute Physiology Score II score	31 (18–57)	34 (6–55)	0.62
Admission Sequential Organ Failure Assessment score	2 (0–10)	3 (0–11)	0.95

MV = mechanical ventilation.
Baseline demographics and treatment-related characteristics, as obtained through digital patient dossiers. No medication-related data from the historical cohort were available.

3 months post hospital discharge than patients in the historical cohort (COVID-19, 45.9 [SD 13.4] vs historical cohort, 40.2 [SD 12.3]; estimated mean difference −8.37 [95% CI, −16.09 to −0.65]; $p = 0.04$) (Fig. 4*B*), with higher physical functioning (estimated mean difference −15.18 [95% CI, −29.53 to −0.83]; $p = 0.04$), bodily pain (estimated mean difference −14.92 [−29.55 to −0.30]; $p = 0.05$), emotional role functioning (estimated mean difference −31.19 [−54.43 to −7.96]; $p < 0.01$), and mental health (estimated mean difference −12.63 [−23.20 to −2.06]; $p = 0.02$) subscales (**Fig. S1, *A*** and ***B***, http://links.lww.com/CCX/A735). In contrast, the mental HRQoL was poorer than in the general Dutch population at each follow-up timepoint.

DISCUSSION

Our results demonstrate that approximately one fourth of COVID-19 ICU survivors experience substantial psychologic distress up to 6 months after hospital discharge. Mental and overall HRQoL were lower in COVID-19 ICU survivors than in the general Dutch population, but mental HRQoL was higher in the COVID-19 cohort than in our historical cohort of critical illness survivors. Although no decline in psychologic distress was observed over time, both overall and mental HRQoL improved during follow-up.

The altered circumstances surrounding an ICU admission for COVID-19, including nonstop media attention emphasizing mortality and ICU admission rates and limited family support, have emphasized the need for post–COVID-19 ICU follow-up (22–24). Previous studies reporting the prevalence of psychologic distress following previous coronavirus epidemics, that is, the Severe Acute Respiratory Syndrome coronavirus and Middle East Respiratory Syndrome coronavirus, have underscored this need (25, 26). During these epidemics, increased psychologic distress was observed in terms of

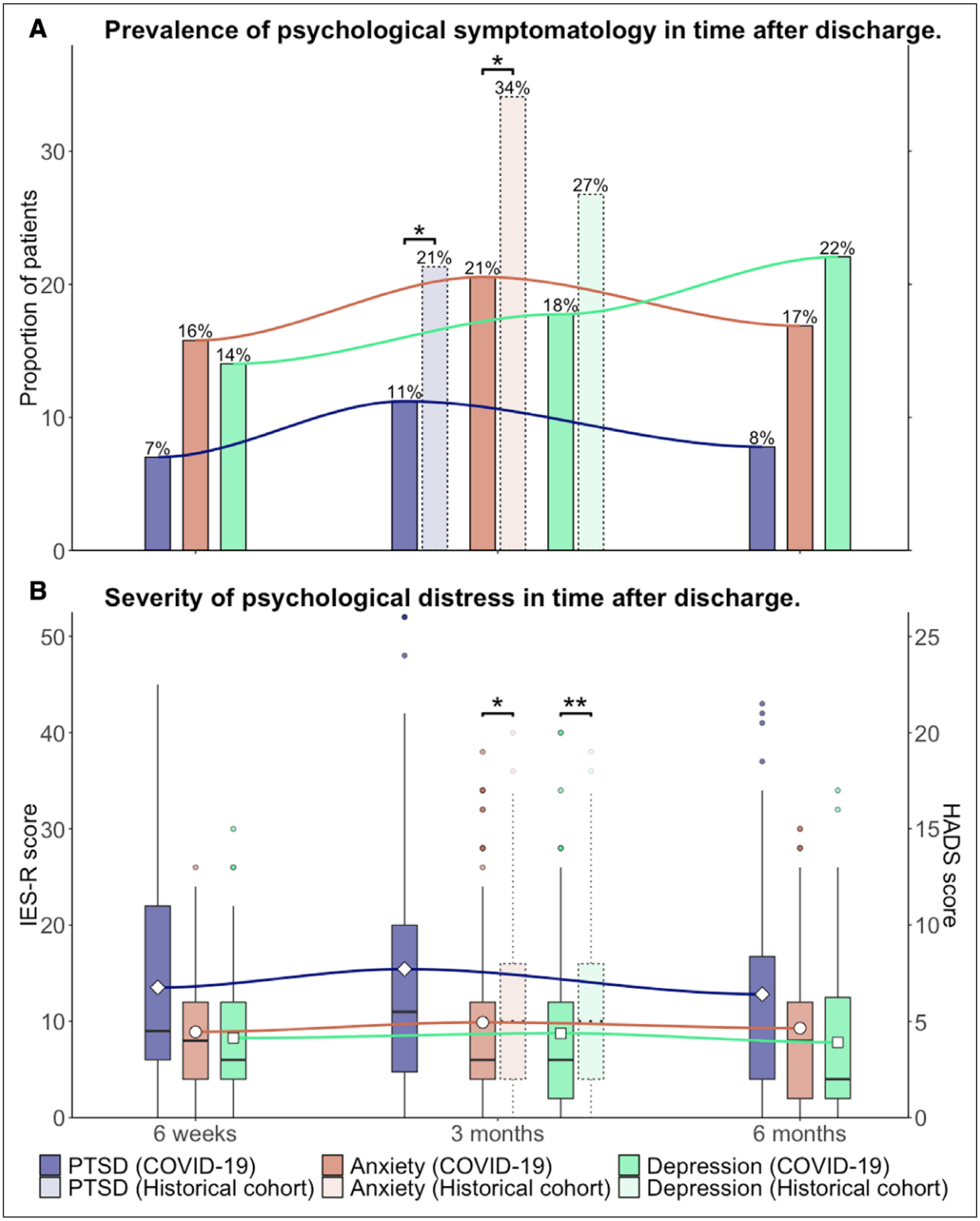

Figure 2. Prevalence and severity of psychologic distress in time after discharge. **A**, *Bar plots* of the prevalence of probable posttraumatic stress disorder (PTSD), anxiety, and depression in time after discharge; (**B**) *boxplots* of the severity of PTSD-, anxiety-, and depression-related symptoms in time after discharge. PTSD was measured using the Impact of Event Scale-Revised (IES-R), and a sum score greater than or equal to 33 was considered as probable PTSD; anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS) and a score greater than or equal to 8 on either the anxiety or depression scale was considered as probable anxiety and depression, respectively. The *diamonds*, *circles*, and *squares* in the *boxplots* represent the mean values of the IES-R sum score, HADS Anxiety Score, and HADS Depression Score at each follow-up time point, respectively. At 3 mo, the severity of anxiety and depression and prevalence of probable PTSD, anxiety, and depression were compared with the severity of anxiety and depression and prevalence of probable PTSD, anxiety, and depression in a historical critical illness survivor cohort. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$. COVID-19 = coronavirus disease 2019.

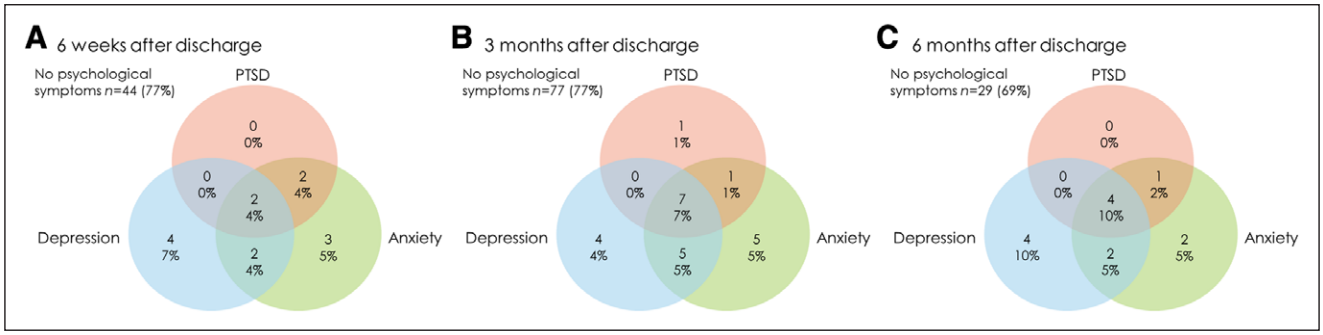

Figure 3. Copresence of probable posttraumatic stress disorder (PTSD), anxiety, and depression. Venn diagram of the copresence of probable PTSD, anxiety, and depression at 6 wk (**A**), 3 mo (**B**), and 6 mo (**C**) after hospital discharge. PTSD was measured using the Impact of Event Scale-Revised, and a sum score greater than or equal to 33 was considered as probable PTSD; anxiety and depression were measured using the Hospital Anxiety and Depression Scale, and a score greater than or equal to 8 on either the anxiety or depression scale was considered as probable anxiety and depression, respectively.

PTSD, anxiety, and depression (27–31). These studies however mostly described small samples and assessed psychologic symptomatology early after, or even during, hospitalization. Contrastingly, studies involving larger samples and assessing psychologic distress beyond 1 month reported a prevalence rate that match our findings (26, 32, 33). A French study by Valent et al (34) reported similar poor outcome regarding quality of life in post–COVID-19 ICU patients. We add to the literature by showing that the the psychological well-being and HRQoL are better than in a historical cohort, but worse than in the general Dutch population. A recent large Chinese study found that anxiety and/or depression are important psychologic complications in a large non-ICU post-COVID population (33). Although only 4% of 1,733 patients were admitted to the ICU, this study confirms our findings and underscores the importance of post–COVID-19 syndrome. Because cultural and healthcare system differences may affect the observed prevalence of psychological trauma and findings are limited by small sample sizes and low data quality, future studies should elaborate on these findings and are as such needed (35, 36).

Compared with the occurrence of psychologic distress of general ICU survivors, we observed a lower prevalence of PTSD (22% vs 11%), anxiety (46% vs 21%), and depression (41% vs 18%) at 3 months than a recent, nationwide study in the United Kingdom that included non–COVID-19 patients who received at least 24 hours of ICU treatment (37) and lower prevalence rates than previous studies in survivors of other severe coronaviruses, survivors of acute lung injury and acute respiratory distress syndrome, and a Dutch cohort of critical illness survivors (3, 26, 38–41). These findings are in line with previously published studies, which reported a limited prevalence of PTSD, anxiety, and depression (36, 42, 43). As risk factors were highly prevalent, and episodes of dyspnea appear to increase the risk of the development of psychologic disorders, this is remarkable (9). It can be hypothesized that COVID-19 ICU patients are, in general, younger and more frequently male than "general" ICU survivors, possibly making them less prone for developing psychologic distress (5–7). The lack of predisposing factors (such as preexisting cognitive impairment) could possibly explain the low prevalence of PTSD and depression (44–46). It can also be hypothesized that the deep sedation strategy, mostly by benzodiazepines, used to maintain comfort during mechanical ventilation in prone position has prevented them from developing memories of frightening, delirium-related nightmarish, and psychotic memories, which are important contributors for the development of psychologic distress (47–49).

COVID-19 patients reported a better HRQoL than patients in our historical cohort. Garrigues et al (50) also demonstrated that HRQoL in their cohort of COVID-19 survivors was quite satisfactory, although they both included patients who were admitted to the ICU as those who were not, and the HRQoL outcomes reported by Valent et al (34) and Taboada et al (51) were comparable with our outcomes. This increased HRQoL compared with general ICU survivors could be due to the low incidence of psychologic distress, as it is known that psychologic distress is the most important contributor to a declined HRQoL (4). Nevertheless, a quarter of our cohort still reported

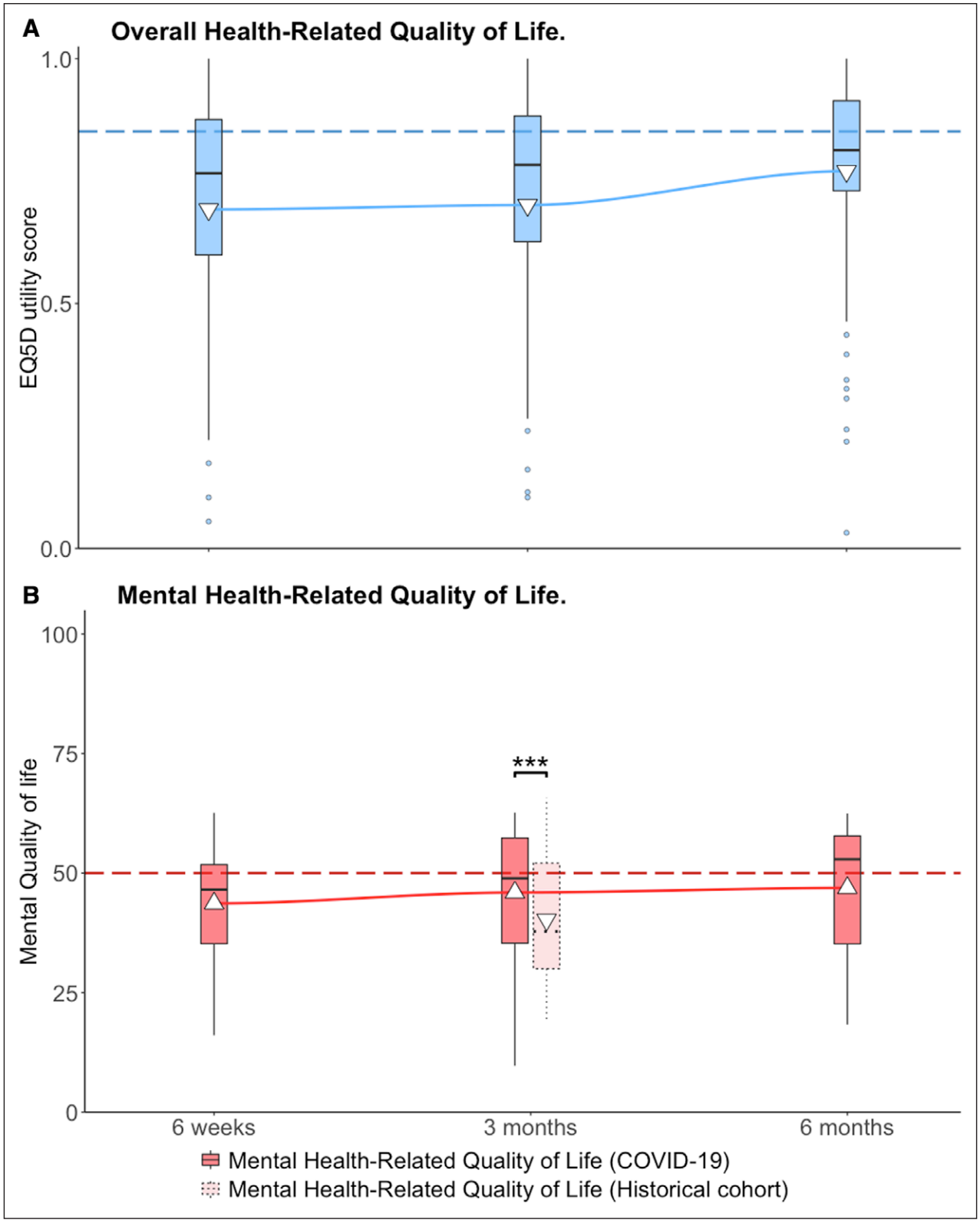

Figure 4. Overall and mental health-related quality of life (HRQoL) in time after discharge. *Boxplots* of the overall (**A**) and mental (**B**) HRQoL throughout follow-up. Overall HRQoL was expressed as the European Quality of Life 5D (EQ-5D) utility score; mental HRQoL as the Mental Component Scale (MCS) 36 of the Short-Form 36. The *inverted triangles* and *triangles* represent the mean EQ-5D utility and MCS-36 score at each follow-up time point, respectively. At 3 mo, the mental HRQoL was compared with the mental HRQoL in a historical critical illness survivors cohort. The *blue* and *red dotted lines* represent the overall and mental HRQoL of the general Dutch population, adjusted for age, respectively. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$. COVID-19 = coronavirus disease 2019.

psychologic distress 6 months after hospital discharge, and HRQoL was poorer than the Dutch population, illustrating the importance of long-term post discharge health management in COVID-19 critical illness survivors. Considering this still substantial proportion of COVID-19 ICU survivors that suffer from psychologic sequelae and poor HRQoL, together with the anticipated surge of post-ICU care caused by the current pandemic, the prevention and treatment of PICS are a major objective to achieve a sustained improvement in the quality of ICU care in future decades (52, 53). Despite several interventions, such as ICU diaries and ICU follow-up clinics, have been explored in the last years, all have yielded unsatisfactory and ambiguous results. As such, no robustly effective treatment strategy is available. We recently demonstrated that innovative techniques such as an ICU-specific virtual reality intervention might improve outcomes (54). We are currently studying the effects on a larger scale (55).

This is, to the best of our knowledge, the first study assessing psychologic distress and HRQoL in COVID-19 ICU survivors beyond 4 months post discharge, and our results suggest the need for awareness of long-term psychologic distress and for longitudinal follow-up care after COVID-19. Some limitations should however be acknowledged. First, our patients were treated in three ICUs in a restricted area in the Netherlands, possibly limiting generalizability. Second, we used self-reports to assess psychologic distress and HRQoL. Although commonly used and validated, formal assessment of psychologic disorders requires consultation with a psychologist or psychiatrist, and usage of self-reports may result in an overestimation of psychologic distress. Also, in the historical critical illness survivors cohort, we assessed PTSD using the TSQ, in contrast to the IES-R which was used for COVID-19 patients, disabling us to compare the severity of PTSD symptoms between the COVID-19 and historical cohort. Third, only patients who visited our post–COVID-19 follow-up clinic and completed the follow-up assessments were included. This may have resulted in some extent of selection bias. This however accounts for all prospective ICU follow-up clinic studies that are eventually subject to enrolment bias, which may confound results and reduce external validity. To tackle these limitations, the most appropriate method of patient follow-up and rehabilitation has yet to be established and could be dependent of cultural differences. It must also be noted that only 11% of our population declined to visit the follow-up clinic, suggesting a limited influence of selection bias (56). Last, we observed a difference in follow-up rates between timepoints. Under the assumption that data were missing at random, the mixed-effects regression models account for this. We can however not be entirely sure that the data were indeed missing at random. As such, any decline or increase in score could also be attributed to the difference in patients' response.

In conclusion, psychologic distress was common and remained prevalent until 6 months post hospital discharge. HRQoL increased over time and was higher than a historical general ICU cohort but was lower than in the general Dutch population. Our findings highlight that COVID-19 ICU survivors should be closely monitored after discharge but appear not to be more affected by psychologic distress than a general ICU population.

ACKNOWLEDGMENTS

We sincerely thank Tim IM Korevaar, MD, PhD, for his statistical expertise and extensive help during the revision of the article.

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccejournal).

All authors assisted in the study design. Mr. Vlake, Dr. Hellemons, and Mr. Van Bavel conducted the study, recruited patients, and collected the data. Mr. Vlake, Mr. Van Bavel, and Dr. van Genderen independently verified the data. Mr. Vlake and Dr. van Genderen performed the data analysis. Dr. Van Bommel was the principle investigator in the Erasmus MC. Dr. Wils was the principle investigator of the Franciscus Gasthuis & Vlietland. Dr. Schut was the principle investigator of the Ikazia hospital. Mr. Vlake and Dr. van Genderen wrote the first draft of the article. Drs. Van Bommel, Wils, Bienvenu, Klijn, and Gommers helped to draft the final version of the article. All authors reviewed and approved the final article.

Supported, in part, by BeterKeten (foundation) and ZonMw (foundation).

The authors have disclosed that they do not have any conflicts of interest.

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

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