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Long-Term Outcomes after Severe COVID-19 Infection: A Multicenter Cohort Study of Family Member Outcomes

To the Editor:

Early evidence suggests that survivors of severe coronavirus disease (COVID-19) experience long-term problems (1, 2). Less is known about the experience of family members of COVID-19 survivors. Previous research has described the emotional and social problems that family members of critical care survivors can experience in the months after hospital discharge (3–6). The experience of family members during the COVID-19 pandemic was different owing to restricted hospital visitation and altered modes of communication (7, 8). This study aimed to evaluate the long-term outcomes of family members of patients who had survived severe COVID-19 infection.

Methods

We undertook a multicenter, prospective observational cohort study across seven critical care units in five hospitals in Scotland. We report this observational cohort study, according to Strengthening the Reporting of Observational Studies in Epidemiology guidelines (9). Ethical approval was granted by The Liverpool Central Research Ethics Committee. All participants provided informed consent.

Patients who were admitted to critical care between March 2020 and May 2020 with a reverse transcriptase–polymerase chain reaction assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (or high clinical suspicion of SARS-CoV-2) were invited to a rehabilitation program. Details of this program—Intensive Care Syndrome: Promoting Independence and Return to Employment (InS:PIRE)—have been published previously (10–12). During the InS:PIRE consultation, patients and their family members have access to members of the multidisciplinary team including nurses, medical staff, pharmacists, and physiotherapists. Referral to other specialists such as clinical psychology and occupational therapy is available. In addition, social care organizations are available and can support issues with welfare benefits and employment. Because of hospital visiting

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restrictions, consultations took place virtually. Participants attended InS:PIRE between 3 and 7 months after hospital discharge.

Patients who attended InS:PIRE were offered the opportunity to take part in the research, as was the patient's closest family member. If family members agreed to participation during their virtual consultation, they were contacted by a member of the research team and consent and outcome measures were obtained. Data collection was undertaken via telephone or by postal completion of questionnaires after this initial InS:PIRE consultation. Study outcome measures were obtained before any referrals arising from the consultation took place (i.e., welfare benefit advice).

We collected family member demographics using a short questionnaire. Data collected included age, relationship to patient, sex, and employment status.

The primary outcome measure was anxiety. Anxiety and depression were measured using the Hospital Anxiety and Depression Scale. This includes 14 statements relating to mood: 7 questions relating to depression and 7 to anxiety (13). Cutoff points used to define anxiety and depression are shown in Table E1 in the online supplement. We used the Carer Strain Index, which measures strain related to care provision from the caregiver's perspective. It includes elements related to emotional adjustment, social issues, and physical and financial strain. Each question is given one point; a score of seven or greater is the cutoff point for high carer strain (14). Finally, the Insomnia Severity Index is a seven-question tool, validated for the screening of clinical insomnia (15). Participants rank sleep problems on a scale of zero to four and answer four other questions regarding satisfaction with sleep.

Results

Across the sites, 198 patients were invited to InS:PIRE after a critical care admission with COVID-19 pneumonia; 122 (61.6%) patients were reviewed and approached about research participation; and 93 patients and 47 family members consented to participate. Most (83%) family members were partners or spouses of the patient, six (12.8%) were children, and one (2.1%) was a parent. Thirty-four (72.3%) were female and the median age was 57 (interquartile range, 49–64) years (Table 1). The associated patient demographics for these 47 family members are also shown in Table 1.

Table 1. Patient and family member demographics

Demographic	Value (*n* = 47)
Family member demographics	
Age, yr, median (IQR)	57 (49–64)
Sex, female, *n* (%)	34 (72.3)
Relationship with patient, *n* (%)*	
Partner or spouse	39 (83)
Children	6 (12.8)
Parent	1 (2.1)
Patient demographics	
Age, yr, median (IQR)	60 (54–66)
Sex, male, *n* (%)	31 (66)
APACHE II (IQR)	16 (12.4–19)
Patient hospital length of stay, d, median (IQR)	25 (12.2–46.2)
Follow-up time, d, median (IQR)	113 (84–150)

Definition of abbreviations: APACHE = Acute Physiology and Chronic Health Evaluation; IQR = interquartile range.
*Data missing for one family member.

Nineteen (40.4%) family members described symptoms of anxiety; 12 (63.2%) had symptoms of moderate or severe anxiety. Symptoms of depression were noted in 10 (21.3%) family members. Problems with sleeping were reported in 20 (42.6%) family members via the Insomnia Severity Index (Table 2).

Twenty-one (44.7%) family members had a Carer Strain Index score of seven or greater, representing strain in their role. Thirteen (27.7%) described physical strain related to patient care and 14 (29.8%) described financial strain. The need for emotional adjustments (for example, because of severe arguments) was described by almost half (46.9%) the family members.

Employment data were available from 39 family members. Thirty-one (79.5%) were employed before the critical care admission, 1 (2.5%) was unemployed, and 7 (18%) were retired. At follow-up, 27 of the 31 (87.1%) family members working before critical care had returned to employment. Measured via the Carer Strain Index, 16 (34%) family members reported work adjustments in relation to care needs after hospital discharge (Table 2).

Discussion

Consistent with previous research, family members of critical care survivors in this cohort experienced high levels of anxiety and depression in the post hospital discharge phase (3–6). Carer strain was higher in this cohort than in previously reported cohorts (16). Although the psychosocial burden of family members of patients with COVID-19 may appear similar to other family member cohorts after critical care, the symptom trajectory of this unique cohort remains poorly characterized. Previous research has shown that family members' psychosocial problems often improve over time (3). However, the COVID-19 family cohort is distinctive; not only did family members have less

Table 2. Family member outcomes

Outcome	Value (*n* = 47)
Hospital Anxiety and Depression Scale	
Anxiety, *n* (%)	
No anxiety	28 (59.6)
Mild anxiety	7 (14.9)
Moderate anxiety	8 (17)
Severe anxiety	4 (8.5)
Depression, *n* (%)	
No depression	37 (78.7)
Mild depression	4 (8.5)
Moderate depression	6 (12.8)
Severe depression	0 (0)
Carer Strain Index, *n* (%)	
Carer strain present (score of seven or greater on the scale)*	21 (44.7)
Financial strain present	14 (29.8)
Emotional adjustments	22 (46.9)
Physical strain	13 (27.7)
Work adjustments needed	16 (34)
Insomnia Severity Index, *n* (%)†	
No insomnia	25 (53.2)
Subthreshold insomnia	14 (29.8)
Moderate insomnia	4 (8.5)
Severe insomnia	2 (4.3)

*Breakdown from the Carer Strain Index.
†Data missing for two family members for the Insomnia Severity Index.

access while the patients were in hospital, but the usual support mechanisms, primarily other family and friends, have also been unavailable or inaccessible because of public health lockdowns and social restrictions. Future research should assess the symptom trajectory of this COVID-19 group, as their symptoms may not improve in the same manner as the non–COVID-19 cohort, or in tandem with patient-reported outcomes. Moreover, there is limited evidence describing effective interventions to support family members (17). This should be the focus of future research.

Limitations of this study are notable. We do not know if those included had preexisting mental health problems. Epidemiological studies have demonstrated a high level of anxiety at a population level because of the pandemic; this may have influenced the outcomes reported (18). We also do not know if the family members had COVID-19, which may have caused health-related anxiety not attributable to caregiving responsibilities. Finally, the outcomes reported in this study were measured after the initial InS:PIRE consultation. This initial review and the plan of care discussed may have alleviated some of the psychological burden that family members were experiencing. As such, the problems reported may be underestimating the psychological sequelae for informal caregivers.

This multicenter study has shown that family members of severe COVID-19 survivors often experience complex problems after hospital discharge. Further work is required to fully understand these issues. ■

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Diuretics in Patients with Obstructive Sleep Apnea and Concomitant Hypertension

To the Editor:

We read with great interest the original article from Giatti and colleagues (1) exploring the relationship between dietary sodium intake and severity of obstructive sleep apnea (OSA) (1). These findings suggest that the role of dietary sodium in the pathogenesis of OSA cannot be generalized but rather is limited to hypertensive patients (2). We agree with the authors about the fact that fluid redistribution from the legs to the neck during sleep (i.e., fluid shift) contributes to the severity of OSA in the restricted population of patients with hypertension and may constitute a specific endotype and a potential therapeutic target.

We have recently published a propensity score-matched analysis addressing this issue in a huge national real-life prospective observational cohort of patients with OSA (3). The 69,564 included patients with OSA had a median age of 56.9 years (interquartile range: 47.4–65.6), 67% were men, and the median apnea–hypopnea index (AHI) was 28 (14–43) events/h. Among them, 9,783 (14.1%) were treated with diuretics. Severe OSA was defined as an AHI $>$ 30 events/h, and the impact of diuretics on OSA severity was assessed by using a logistic regression model. We showed that diuretics reduce the severity of OSA only in patients with hypertension ($P < 0.01$) and particularly in patients with a body mass index (BMI) between 25 and 35 kg/m^2 ($P < 0.01$). No association was found between diuretics and OSA severity when we considered the entire population or subgroups suffering from heart failure (whatever their BMI), suggesting that this physiopathological trait is of lesser impact in this situation.

Many drugs have been investigated in randomized trials as candidate therapeutic agents for the management of OSA related to specific endotypes (e.g., poor upper airway muscle activity, high loop gain, low arousal threshold) (4). These research data do not currently translate into routine practice, and there are no clear recommendations for medications as primary therapy for OSA. The prevalence of hypertension in patients with OSA consistently reaches 50% across studies with a high rate of uncontrolled and resistant hypertension (5). According to our results, which are consistent with those of Giatti and colleagues, diuretics may have the potential to both reduce OSA severity and treat OSA-related hypertension.

For primary hypertension, the main drug classes recommended for treatment initiation in monotherapy in all international guidelines are thiazide diuretics, β-blockers, long-acting calcium channel blockers, and renin–angiotensin blockers. In the general population, each of these therapeutic classes is considered equally effective. In view of our analysis and the existing literature, diuretics might be the first choice medication for patients with OSA with concomitant hypertension.

In addition, interventions to reduce bodily fluid content (e.g., low sodium intake or diuretics) in men with severe OSA have been shown to slightly decrease AHI, suggesting that rostral fluid displacement is one among other mechanisms determining pharyngeal collapsibility (6) and in turn OSA severity. A major goal for personalized and precision medicine is to combine therapies appropriate for specific well-defined OSA endotypes and phenotypes. Combinations of therapies can include continuous positive airway pressure (the gold standard therapy for OSA), lifestyle interventions (weight loss, low-salt diet, and/or exercise), and pharmacological interventions targeting OSA-