Relationship between grip strength during hospitalisation and mental disorders after discharge in critically ill patients: a post-hoc analysis of a prospective observational study

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ABSTRACT

Objectives Post-intensive care syndrome (PICS) is a recognised sequela after critical care. The development of an index that predicts PICS mental disorders will be of significance for the selection of subsequent interventions. The purpose of this study was to find factors associated with PICS mental disorders. We hypothesised that grip strength during hospitalisation may be associated with the PICS mental status after discharge.

Design A post-hoc analysis of a multicentre prospective observational study.

Setting Nine hospitals in Japan.

Participants Patients who were newly admitted to intensive care unit and stayed for at least 48 hours were included. Exclusion criteria were patients younger than 18 years, those who required assistance with ambulation prior to admission, those with concomitant central nervous system disorders and those with terminal conditions.

Primary and secondary outcome measures Psychiatric symptoms 3 months after discharge were assessed using the Hospital Anxiety and Depression Scale (HADS). The HADS total score (HADS-total) was assigned as the primary outcome.

Results 98 patients were included into this study. Grip strength at discharge negatively correlated with HADS-total 3 months after discharge (r = −0.37, p < 0.001, 95% CI −0.53 to −0.18). A multivariate analysis showed that grip strength was associated with anxiety (p = 0.025, 95% CI −0.21 to −0.015). Area under the curve for HADS anxiety score with grip strength at discharge was higher than that with Medical Research Council scores and the Barthel Index (0.71, 0.60, 0.61).

Conclusions Grip strength at discharge correlated with mental disorders 3 months after discharge. Therefore, it may be useful for predicting postdischarge mental disorders.

Trial registration number UMIN000036503.

INTRODUCTION

While the short-term prognosis of intensive care unit (ICU) patients has improved, long-term sequelae have become increasingly important and are recognised as post-intensive care syndrome (PICS). PICS includes cognitive impairment, physical disability and mental disability as well as psychological disability in the family members of a patient, which may persist for several months or more after discharge.

Mental disorders include symptoms of depression, anxiety and post-traumatic stress disorder, and the following risk factors have been identified: a history of mental disorders, female sex, a young age and the use of sedation during an ICU stay. While physical disabilities are the most apparent immediately after illness and abate over time, the mental disorders of PICS have a late onset and often worsen with time after discharge.

Therefore, mental disorders need to be evaluated for between 3 months and 1 year after discharge from hospital. The prediction during hospitalisation of mental disorders after discharge will be of significance for the selection of subsequent interventions.

STRENGTHS AND LIMITATIONS OF THIS STUDY

This study was a multicentre prospective study to evaluate both the physical functions at discharge and the mental status at 3 months after discharge.

A number of assessments for physical functions including grip strength were introduced simultaneously.

Anxiety and depression were discussed separately with an activity of daily living at discharge.

There were some drop-out patients in whom the questionnaire could not be collected.

We could not clarify the bidirectional relationship between grip strength and mental disorder.
A relationship between grip strength and mental disorders has been suggested in the elderly and chronically ill. In addition to the simple relationship between declines in activities of daily living (ADL) and mental disorders, the possibility of a significant effect of the mental state on grip strength has been considered. We previously demonstrated that grip strength correlated with mental disorders in PICS outpatients.

The purpose of this study was to find factors associated with PICS mental disorders. We hypothesised that grip strength during hospitalisation may also be related to the mental status of patients with PICS after discharge and would be associated with mental disorders compared with other measures of physical disability. Therefore, we conducted a post-hoc analysis of the EMPICS Study (Association between achievement of Early Mobilization and Psychiatric symptoms in Japanese Intensive Care Survivors), a multicentre prospective study to investigate the relationship between early mobilisation in ICU and psychiatric symptoms 3 months after discharge, and examined the relationship between grip strength and PICS mental disorders 3 months after discharge. In addition, to establish the relevance of declines in ADL, patients were divided into two groups according to the quality of ADL, and the relationship between grip strength and PICS mental disorders was analysed.

METHODS

This was a post-hoc analysis of the EMPICS Study, a multicentre prospective cohort study. Informed consent was obtained from all patients. Strengthening the Reporting of Observational Studies in Epidemiology guidelines were followed for reporting. Patients who were newly admitted to ICU in nine facilities nationwide between June and December 2019 and stayed for at least 48 hours (up to 25 consecutive registrations in each hospital) were included. Exclusion criteria were patients younger than 18 years, those who required assistance with ambulation prior to admission, those with concomitant central nervous system disorders and those with terminal conditions. We also excluded patients with a history of psychiatric disorders. Psychiatric symptoms 3 months after discharge were evaluated using the Hospital Anxiety and Depression Scale (HADS) by mail questionnaire. HADS is a self-assessment test consisting of seven questions each on anxiety and depression. A score of between 8 and 10 for both anxiety and depression indicates suspected, while a score of 11 or higher indicates confirmed. The HADS total score (HADS-total), HADS anxiety score (HADS-A) and HADS depression score (HADS-D) were extracted for analyses.

At the time of ICU admission, the following basic information on patients was recorded: age, sex, body mass index (BMI), the Acute Physiology and Chronic Health Evaluation (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, Charlson Comorbidity Index, the Barthel Index (BI) before admission and the diagnosed disease.

During the ICU stay, we collected information on the use of a ventilator, sedatives, analgesics, vasopressors, muscle relaxants and dialysis. In addition, grip strength, Medical Research Council (MRC) scores and BI were measured at the time of discharge.

Grip strength was assessed in patients with a minimum MRC score of 3 points for both right and left wrist dorsiflexion and elbow flexion. Grip strength was measured using a hydraulic handgrip dynamometer (Jamar Hand dynamometer, NIHON MEDIX, MG-4005NC) three times on both sides alternating left–right. Care was taken to perform measurements with the elbow at 90° flexion. Patients were allowed at least 6 s to generate maximum peak force, with a minimum of 60 s rest in between each test. Observers supported the device manually during measurements. The maximum value on each side was the subject of analysis.

RESULTS

A total of 1014 patients were admitted to the ICU, 203 remained after the removal of patients according to the exclusion criteria and 98 were ultimately included following the further removal of 28 patients who died in hospital, 74 who did not respond to the 90-day questionnaire, 2 with an untested grip strength at discharge and 1 who voluntarily discharged. The questionnaire collection rate was 57% (Figure 1). Table 1 shows the baseline clinical data of patients: mean age was 70.5 years; 63% men;

Patient and public involvement

Patients and family members were given consent for the study on admission to the ICU. It was also explained that the study would be published.

Statistical analysis

HADS-total 3 months after hospital discharge was the primary endpoint, and HADS-A and HADS-D were the secondary endpoints. Pearson’s correlation coefficients were calculated to clarify the relationship between HADS-total and grip strength at hospital discharge. Pearson’s correlation coefficients were also calculated for BI and HADS-total as well as MRC scores and HADS-total. Receiver operating characteristic (ROC) curves for HADS and grip strength were created and the area under the curve (AUC) was calculated.

Multivariate analyses were also performed using multiple regression analyses of age, sex, BMI, APACHE II and grip strength at discharge as explanatory variables. The same multivariate analyses were performed by changing grip strength at discharge to BI or MRC scores. Since the median value of BI was 100, we divided patients into two groups: one with BI=100 (52 patients) and the other with BI<100 (46 patients), and examined the relationships between grip strength and HADS-A and HADS-D in the high and low ADL groups.

All statistical analyses were conducted with R Studio (V.4.1.0). A p value<0.05 indicated a significant difference.
BMI 23 kg/m²; ICU stay 4.7 days; hospital stay 23.5 days; APACHE II score 18 points; SOFA score 7 points at ICU admission; BI 100 points before admission; MRC score 58 points at ICU discharge; background diseases were cardiac diseases in 49% and gastrointestinal diseases in 15.3%. The number of people with HADS-A and HADS-D scores of 8 or higher was 26 and 16, respectively.

The results of univariate analyses are shown in figure 2. Negative correlations were observed between grip strength at discharge and HADS-total, HADS-A and HADS-D 3 months after discharge (figure 2A: r=−0.37, p<0.001, 95% CI −0.53 to −0.18; figure 2B: r=−0.37, p<0.001, 95% CI −0.53 to −0.19; figure 2C: r=−0.30, p=0.0026, 95% CI −0.47 to −0.11, respectively). In the analysis of the relationships between HADS and other physical function assessment tools, BI and MRC scores both correlated with HADS-total (figure 3A: r=−0.22, p=0.029, 95% CI −0.40 to −0.023; figure 3B: r=−0.25, p=0.014, 95% CI −0.43 to −0.052, respectively). All physical function assessment tools at the time of discharge were associated with HADS 3 months after discharge; however, since BI and MRC scores were based on a point system, many patients had perfect scores and, thus, the distribution of patients was skewed. On the other hand, grip strength was a continuous variable with a normal distribution.

Regarding HADS-A and HADS-D, 8 points or more was considered to be positive, and an ROC curve for grip strength at discharge was created. AUC was 0.71 for HADS-A (figure 4A) and 0.56 for HADS-D (figure 4B). We also created an ROC curve with BI and MRC scores for HADS-A and HADS-D. AUC with BI were 0.60 (figure 4C) for HADS-A and 0.58 for HADS-D (figure 4D), while AUC with MRC scores were 0.61 for HADS-A (figure 4E) and 0.44 for HADS-D (figure 4F).

The results of multivariate analyses are shown in online supplemental table 1. HADS-A correlated with grip strength at discharge (p=0.025, 95% CI −0.21 to −0.015), whereas HADS-total and HADS-D did not
(p=0.063, 95% CI −0.36 to 0.007; p=0.23, 95% CI −0.17 to 0.04). When grip strength at discharge was changed to other physical disability indices (MRC scores and BI) and HADS-A was used as an outcome in multivariate analyses, correlations were observed for MRC scores, but not for BI (p=0.038, 95% CI −0.26 to −0.009; p=0.16, 95% CI −0.07−0.01) (online supplemental table 2).

Figure 5A–D shows the results of the analysis of the relationship between grip strength and anxiety/depression after 3 months in the two ADL groups. When anxiety was the outcome, the correlation coefficient with grip strength was small in the low ADL group (figure 5A: BI=100: r=−0.40, p=0.0035, 95% CI −0.60 to −0.14; figure 5B: BI<100: r=−0.24, p=0.10, 95% CI −0.50 to 0.050). On the other hand, when depression was the outcome, it correlated with grip strength in the low ADL group (figure 5C: BI=100: r=−0.11, p=0.45, 95% CI −0.37 to 0.17; figure 5D: BI<100: r=−0.41, p=0.0043, 95% CI −0.63 to −0.14).

DISCUSSION
The results of univariate analyses revealed a correlation between grip strength at discharge and anxiety and

...depression 3 months after discharge. MRC scores and BI also correlated with HADS, whereas grip strength at discharge had a higher correlation coefficient. In multivariate analyses, a relationship was detected between grip strength at discharge and anxiety, but not depression. The AUC with grip strength was not high, but was better than that with BI and MRC scores.

Figure 4  Receiver operating characteristic curves for HADS (HADS-A and HADS-D) 3 months after hospital discharge with physical strength. Receiver operating characteristic curves for each HADS score with physical strength are shown. (A) Grip strength and HADS-A (AUC 0.71), (B) grip strength and HADS-D (AUC 0.56), (C) BI and HADS-A (AUC 0.60), (D) BI and HADS-D (AUC 0.58), (E) MRC scores and HADS-A (AUC 0.61) and (F) MRC scores and HADS-D (AUC 0.44). AUC, area under the curve; BI, the Barthel Index; HADS, Hospital Anxiety and Depression Scale; HADS-A, HADS anxiety score; HADS-D, HADS depression score; MRC, Medical Research Council.

The relationships between grip strength and depressive and anxiety symptoms at the same time point in outpatients have already been reported; however, to the best of our knowledge, this is the first study to demonstrate a relationship between grip strength at discharge and postdischarge mental disorders. Measurements of grip strength at discharge may predict PICS mental disorders.
3 months after discharge. The results of multivariate analyses showed that grip strength was associated with anxiety among PICS mental disorders. A previous study found that grip strength was significantly lower in women with depression or anxiety disorders than in normal subjects,9 while another reported that depressive symptoms negatively correlated with grip strength in adults older than 50 years.6 This is consistent with the present results on ICU patients. Patients with physical dysfunction often have mental disorders. It has also been reported that patients with mental disorders are often unable to output physical strength, especially grip strength.6 9 It is possible that some systemic or neurological injury leading to physical dysfunction may have occurred in patients who presented with mental disorders after critical care.10 Because of the bidirectional relationship between mental and physical disability, the relationship between grip strength and mental disability was also observed in this study, but the detailed mechanism remains unclear.

When patients were divided into two groups according to ADL, grip strength was associated with depression in the low ADL group, and grip strength was associated with anxiety in the high ADL group. Patients with low ADL had greater physical disability than those with high ADL, which was reflected in grip strength, and it is possible that low ADL decreased quality of life and led to depression. Patients in the high ADL group did not have major physical disabilities and did not develop depression, but those with high anxiety may have had this reflected in their physical functioning, resulting in lower grip strength. However, as mentioned above, the mechanism of the relationship between mental disorders and physical disorders cannot be mentioned from this study and is unknown, so further research with a prospective study is desirable.

**Figure 5** Relationships between grip strength and HADS scores in two groups divided by activities of daily living, following the division of patients into two groups with BI=100 and BI<100. Pearson’s correlation coefficient was calculated to clarify the relationship between HADS and grip strength. (A) Scatter plot of HADS-A and grip strength in the group with BI=100 (r=−0.40, p=0.0035). (B) Scatter plot of HADS-A and grip strength in the group with BI<100 (r=−0.24, p=0.10). (C) Scatter plot of HADS-D and grip strength in the group with BI=100 (r=−0.11, p=0.45). (D) Scatter plot of HADS-D and grip strength in the group with BI<100 (r=−0.41, p=0.0043). BI, the Barthel Index; HADS, Hospital Anxiety and Depression Scale; HADS-A, HADS anxiety score; HADS-D, HADS depression score.
Grip strength may be easily measured in any facility. Although BI and MRC scores are the most common tools for assessing physical disability, grip strength reflects the condition of a patient in more detail and correlates well with mental disorders, suggesting its potential as a useful indicator. Another tool that has been recommended for the assessment of physical function in PICS is the 6-min walk test.4 This test assesses motor performance by measuring the total distance walked as fast as possible in 6 min, but it cannot be performed for patients who have difficulty walking. Therefore, a simple assessment tool that may be used for all patients is desired, and grip strength has potential for this purpose.

Although we were unable to precisely predict post-discharge PICS mental disorders using grip strength at discharge, it may facilitate the identification of patients at high risk of PICS mental disorders, even in facilities that do not have PICS outpatient services or follow-ups. Although all ICU patients may develop PICS, it is difficult to follow-up all patients from the standpoint of cost and continuity. Patients with PICS mental disorders require individualised treatment (including medication, psychotherapy and cognitive-behavioural therapy), and referral to a psychiatrist needs to be considered.11 If high-risk patients are identified, a limited number of patients may be followed up and referred to a psychiatrist if necessary, which may be more cost-effective.

The present study had several limitations. It was a non-randomised trial. Deaths and uncontrolled cases may have had a large impact on the results obtained. In addition, there were some confounding factors that were not adjusted for, such as educational history and frailty. Furthermore, the questionnaire response rate was low at 57%. Although patients with a history of mental disorder prior to admission were excluded, the detailed mental status of the subject patients prior to admission was not assessed, which may have affected the results. Since we were unable to follow-up patients beyond 3 months after discharge, long-term outcomes remain unknown. Mental disorders may change with a longer time course after discharge.

CONCLUSIONS
In patients who had been in the ICU for more than 48 hours, grip strength at discharge correlated with depression and anxiety 3 months after discharge. Grip strength measurements at discharge may be a more accurate indicator of postdischarge mental disorders than BI and MRC scores.

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