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Original article

A novel scoring system to predict delirium and its relationship with the clinical course in patients with acute decompensated heart failure

Taiki Sakaguchi (MD)^a, Mayumi Watanabe (RN)^b, Chika Kawasaki (RN)^b,
Itomi Kuroda (RN)^b, Haruhiko Abe (MD)^{a,*}, Motoo Date (MD, PhD)^c,
Yasunori Ueda (MD, PhD, FJCC)^c, Yoshio Yasumura (MD, PhD, FJCC)^d,
Yukihiro Koretsune (MD, PhD, FJCC)^c

^aInstitute for Clinical Research, National Hospital Organization Osaka National Hospital, Osaka, Japan

^bCoronary Care Unit, National Hospital Organization Osaka National Hospital, Osaka, Japan

^cCardiovascular Division, National Hospital Organization Osaka National Hospital, Osaka, Japan

^dDepartment of Cardiology, Amagasaki Chuo Hospital, Amagasaki, Japan

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ABSTRACT

Background: Delirium is known to be a poor prognostic factor in patients with acute decompensated heart failure (ADHF). The purpose of this study was to determine predictors of delirium on admission of ADHF patients, and to establish a scoring formula to identify patients at high risk for delirium.

Methods and results: We recorded the Intensive Care Delirium Screening Checklist (ICDSC) score in 120 ADHF patients during their stay in the coronary care unit (CCU). Patients with a highest ICDSC score of 4 or more were diagnosed with delirium. We examined independent candidate predictors of delirium using multivariate logistic regression analysis and developed the following scoring formula, the delirium prediction score (DPS), using independent predictors of delirium and their regression coefficients: $DPS = \text{inferior vena cava diameter} + \text{C-reactive protein}$ (and additionally +10 for patients with a history of cerebral infarction). Receiver operating curve analysis indicated that evaluation using this scoring system at the time of admission was able to predict delirium with high accuracy (C-statistic: 0.885). In addition, the calculated scores had significantly positive correlations with duration of CCU stay and overall length of hospital stay.

Conclusions: We established a novel scoring system to predict on admission the likelihood of development of delirium in ADHF patients; this system also predicts prolongation of intensive care and hospital stay.

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Introduction

Delirium, defined as an acute onset of cognitive impairment [1], is a common symptom in patients admitted to the emergency department or intensive care unit and is reportedly associated with increased mortality and a longer hospital stay [2,3]. Delirium is also a common symptom in patients with acute decompensated heart failure (ADHF) that has been reported to have prognostic implications [4,5]. Although low performance in the 6-minute walk test [6], low left ventricular ejection fraction (LVEF) [7], high brain natriuretic peptide (BNP) levels [8], atrial fibrillation [9],

renal dysfunction [10], and hypotension [11] are reported as risk factors for cognitive impairment in chronic heart failure patients, their predictive ability for delirium in patients with ADHF are still unknown. Accurately assessing the risk of delirium at an early stage in ADHF may help to improve the prognosis. This study aimed to determine predictors of delirium at the time of admission in ADHF patients, and to establish a scoring formula to identify patients at a high risk for delirium.

Methods

Subjects

The study sample comprised 120 patients admitted to the coronary care unit (CCU) of Osaka National Hospital with a primary diagnosis of ADHF between February 2014 and August 2016. ADHF

* Corresponding author at: Institute for Clinical Research, National Hospital Organization Osaka National Hospital, 2-1-14 Hoenzaka, Chuo-ku, Osaka 540-0006, Japan.

E-mail address: abeh@onh.go.jp (H. Abe).

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was defined as new-onset decompensated heart failure or decompensation of chronic heart failure with symptoms that warrant hospitalization. All patients were admitted with clinical and radiographic evidence of congestion [12]. Patients who were previously diagnosed with dementia and who required primary angioplasty due to the complication of acute coronary syndrome were excluded from analysis. This study was approved by Osaka National Hospital Institutional Review Board #2 (Approval No. 16007).

Assessment of cognitive status

For all subjects, Intensive Care Delirium Screening Checklist (ICDSC) scores were evaluated by experienced nurses every 8 h throughout the period of their stay in the CCU. The ICDSC score is one of the most frequently employed tools to diagnose delirium in critically ill patients. The score evaluates the following 8 items: altered level of consciousness, inattention, disorientation, hallucinations or delusions, psychomotor agitation or retardation, inappropriate mood or speech, sleep/wake cycle disturbance, and symptom fluctuation. Subjects with an ICDSC score of 4 or more were diagnosed as being delirious [13]. The subjects were categorized based on the highest ICDSC score during their CCU stay, where $ICDSC \geq 4$ was the “delirium group” and $ICDSC \leq 3$ was the “non-delirium group”, respectively. The ICDSC scores of all subjects recovered to 0 before their discharge from the CCU.

Clinical profiles of patients

Care was provided to each patient under the direction of the treating physician in accordance with Japanese ADHF treatment guidelines. Baseline characteristics, such as comorbidities [hypertension, diabetes mellitus, atrial fibrillation, and old cerebral infarction (OCI)], blood pressure, heart rate, plasma BNP concentration, serum bilirubin, alkaline phosphatase (ALP), urea nitrogen (BUN), creatinine, glucose, sodium, potassium, C-reactive protein (CRP) concentration, white blood cell count (WBC), and hemoglobin concentration were recorded on admission. LVEF, tricuspid regurgitation pressure gradient (TRPG), and maximum diameter of the inferior vena cava (IVCd) were also determined using echocardiography on admission. Duration of stay in the CCU and overall duration of hospitalization were assessed as surrogate indicators of the degree of treatment difficulty. Patients were discharged after the treating physician confirmed restoration of clinical stability.

Statistical analysis

The various measurements are expressed as mean values with standard deviations. Statistical significance was set at $p < 0.05$. Comparisons of parameters between the delirium and non-delirium groups were performed using the Student's *t*-test. Univariate and multivariate logistic regression analyses were used to determine independent relationships between patient characteristics on admission and the occurrence of delirium. We included all the factors assessed by univariate analyses into the first model of multivariate analysis using a forward stepwise variable selection method (significance levels for entering and removing variables were both set at $p < 0.05$). The association of each variable with the occurrence of delirium was expressed as the odds ratio (OR) with 95% confidence intervals (CIs). After identifying the independent predictors using the aforementioned multivariate logistic regression analyses, we developed a scoring formula using these predictors and their proportionally weighted regression coefficients. Further, the optimal cut-off value of this scoring formula for predicting the development of delirium was determined based on the Youden index of receiver operating characteristic (ROC) curve analysis. Finally, we tested the viability

of this score by assessing its correlations with duration of CCU stay, and overall duration of hospitalization using univariate linear regression analysis and Pearson's correlation coefficients. Statistical analyses were performed using MedCalc for Windows, version 13.1.2.0 (MedCalc Software, Ostend, Belgium).

Results

Subject characteristics

Among the study subjects, a total of 38 (31.7%) delirium events were diagnosed on the basis of ICDSC scores of 4 or more during their CCU stay. The clinical characteristics on admission and the initial treatment and medication for the two groups of subjects with and without delirium are shown in Table 1. Subjects with delirium had a significantly higher incidence of OCI, higher TRPG and IVC diameter, worse renal function, and more severe inflammatory response. In our study, there was no significant difference in the age of patients in the two groups.

Clinical course during hospitalization

The clinical indices that indicate the degree of treatment difficulty and the medications used to treat delirium are shown in Table 2. Subjects with delirium had significantly longer durations of CCU and overall hospital stay, and a lower incidence of discharge to home. In-hospital death and admission to a sanatorium or nursing home were more common in patients with delirium.

Predictors of delirium on admission

As shown in Table 3, multivariate logistic regression analysis showed the following factors to be independent predictors of delirium: history of OCI (OR: 7.95, 95% CI: 2.34–27.0, $p < 0.001$), IVCd (OR: 1.29, 95% CI: 1.11–1.50, $p < 0.001$), and CRP (OR: 1.25, 95% CI: 1.10–1.42, $p < 0.001$). Using these predictors, we developed the following scoring formula, designated the Delirium Prediction Score (DPS), by proportionally weighting each of their regression coefficients:

$$DPS = IVCd + CRP(+10 \text{ in patients with a history of OCI})$$

As shown in Fig. 1, receiver operating curve analysis indicated that the DPS on admission was able to predict delirium with high accuracy (C-statistic: 0.885). When using a cut-off value of 26 in the Youden index, its sensitivity and specificity to predict delirium were 82.9% and 83.1%, respectively. In addition, the DPS had significant positive correlations with duration of CCU stay ($r = 0.507$, $p < 0.001$) and overall duration of hospitalization ($r = 0.466$, $p < 0.001$) (Fig. 2).

Determinants of the duration of delirium

In the delirium group, none of the treatments for delirium shown in Table 2 shortened the duration of delirium (with and without dexmedetomidine, 6.5 ± 11.4 days vs. 6.5 ± 10.6 days, respectively, $p = 0.993$; intravenous haloperidol, 4.5 ± 4.6 days vs. 7.5 ± 12.5 days, respectively, $p = 0.274$; and oral major tranquilizer, 7.1 ± 13.0 days vs. 6.1 ± 8.6 days, respectively, $p = 0.835$). On the other hand, the duration of delirium was found to have a significant negative correlation with the rate of IVCd reduction within 3 days after admission ($r = 0.720$, $p < 0.001$) (Fig. 3), but not with the CRP reduction rate in the same period ($p = 0.627$).

Discussion

In this study, we established a novel scoring system that enables prediction at the time of admission of both delirium and

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