Electrocardiographic Abnormalities Predict Adverse Clinical Outcomes in Patients with Subarachnoid Hemorrhage

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Background: We conducted a retrospective cohort study of a large sample to assess whether electrocardiographic (ECG) abnormalities are independently associated with the occurrence of neurogenic pulmonary edema (NPE), delayed cerebral ischemia (DCI), and in-hospital death after nontraumatic subarachnoid hemorrhage (SAH). *Methods:* In this retrospective observational study, patients who were admitted within 72 hours of SAH symptom onset between 2013 and 2015 were enrolled. Twelve-lead ECG findings obtained within 72 hours after SAH and the presence of NPE, DCI, and in-hospital death were collected based on the results reported in the medical records. *Results:* We included 834 patients. NPE occurred in 192 patients (23%). The median delay from SAH onset to NPE was 3 days (interquartile range [IQR]: 5 days). DCI occurred in 223 patients (27%; median delay to DCI, 4 days; IQR: 5 days). In total, 141 patients (17%) died in the hospital (median time to death, 12 days; IQR: 18 days). The frequency of ECG abnormalities for all enrolled patients was 65%. Corrected QT prolongation had an adjusted risk ratio (RR) of 1.5 (1.1-2.2) for NPE and 1.8 (1.3-2.4) for DCI. ST depression had an adjusted RR of 3.0 (1.2-7.5) for in-hospital death. NSSTTCs (nonspecific ST- or T-wave changes) had an adjusted RR of 2.7 (1.8-4.2) for NPE, 2.8 (1.9-4.3) for DCI, and 2.2 (1.3-3.5) for in-hospital death. All RRs were adjusted for age and Hunt–Hess scores. *Conclusions:* ECG abnormalities assessed within 72 hours after SAH using a standard 12-lead ECG are independently associated with an increased risk of adverse clinical outcomes in patients with nontraumatic SAH. **Key Words:** Subarachnoid hemorrhage—neurogenic pulmonary edema—delayed cerebral ischemia—in-hospital death—electrocardiographic abnormalities.

Introduction

Electrocardiography (ECG) often reveals abnormalities such as prolongation of the corrected QT (QTc) interval and changes in the ST segment and T-wave morphology in patients with subarachnoid hemorrhage (SAH) in the absence of known organic heart disease.[1-6] The mechanisms of these abnormalities are not completely understood, but they are thought to be related to the sympathetic overactivity induced by SAH.[7-9] ECG abnormalities are associated with an increased risk of poor outcome after SAH.[10] However, whether this association is independent of known clinical risk factors for poor outcomes is unclear.

Neurogenic pulmonary edema (NPE)[11-15] and delayed cerebral ischemia (DCI) are 2 important outcome predictors.[16] With an incidence of approximately 25%, NPE is a well-recognized phenomenon in SAH.[11,12,17] NPE can lead to acute cardiopulmonary failure with consequent global hypoperfusion and hypoxia, and these effects can cause severe secondary ischemic brain damage and have

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been reported to be associated with worse clinical outcomes.[11-15] DCI is a clinical syndrome of focal neurological deficits, cognitive deficits, or both that occurs unpredictably in 30% of patients 3-14 days after the initial hemorrhage.[18] DCI remains the single most important cause of mortality and morbidity in patients who survive to definitive aneurysm treatment.[19] Because cerebral autoregulation is disturbed after SAH,[20] impaired cardiac performance may lead to reduced cerebral blood flow and contribute to the development of DCI.[21]

We conducted a retrospective cohort study of a large sample to assess whether ECG abnormalities are independently associated with the occurrence of NPE, DCI, and in-hospital death after SAH.

Methods

Study Population

This retrospective cohort study was approved by the hospital. We reviewed the hospital records of all patients with nontraumatic SAH admitted to the neurosurgical intensive care unit (ICU) from January 2013 to December 2015. The diagnosis of SAH was established by computed tomography (CT) scan or xanthochromia of the cerebrospinal fluid if the CT scan was nondiagnostic. The exclusion criteria included SAH resulting from tumor, arteriovenous malformation, or recent head/neck operation for a reason other than SAH; admission delay more than 72 hours; age less than 18 years; coronary artery disease; pneumonia; chronic bronchitis; and chronic obstructive pulmonary disease. The remaining patients formed the study group.

Study Parameters

Patient characteristics, including age, sex, and pertinent medical comorbidities (hypertension, hyperlipidemia, and diabetes mellitus), were collected. We collected the cause of SAH (aneurysmal or without aneurysm) and whether the aneurysm was repaired during the acute stage of SAH. We obtained the clinical and neurological statuses of the patients from the admission notes according to the Hunt–Hess score (class I: asymptomatic or mild headache; class II: moderate or severe headache, nuchal rigidity, and possible oculomotor palsy; class III: confusion, drowsiness, or mild focal signs; class IV: stupor or hemiparesis; and class V: coma, moribund, and/or extensor posturing).[22] We collected the modified Fisher score (0 or 1: no or thin SAH; 2: thin SAH, bilateral intraventricular hemorrhage; 3: thick SAH; and 4: thick SAH, bilateral intraventricular hemorrhage)[23] and the coexistence of intracerebral hematoma on CT scan. Twelve-lead ECG findings collected within 72 hours after SAH were retrieved from the patients' medical records. When the patients had multiple ECGs, the ECG obtained closest to the time of SAH was used for analysis. All ECGs were analyzed by 1 cardiologist who was blinded to the clinical data of the patient. The following parameters were collected for each ECG: heart rate (ventricular rate), heart rate-QTc interval prolongation using Bazett's formula, and predefined morphological abnormalities. Abnormalities were defined as the presence of 1 or more of the following 6 variables, which are commonly noted after SAH,[24-26] on at least 2 leads: (1) abnormal Q or QS wave (≥30 ms or a pathological R wave in V_1 to V_2); (2) ST depression (ST depression ≥ .1 mV, 80 ms post-J point); (3) ST elevation (ST elevation ≥ .1 mV); (4) peaked upright T wave (prominent peaked T wave); (5) T-wave inversion (pathologic T-wave inversion); and (6) nonspecific ST- or T-wave changes (NSSTTCs, ST- or T-wave abnormalities not meeting the above criteria).

Follow-up information, including the presence or absence of NPE, DCI, and in-hospital death, was obtained from hospital records. NPE was defined by both serial clinical and radiologic chest findings.[12] A radiologic diagnosis of NPE was made if bilateral, symmetric, smooth, and diffuse alveolar edema-like infiltrates were present on the chest radiograph. The clinical criteria for NPE included one of the following: the presence of crackles by chest auscultation, as assessed at the same time a chest radiograph was taken, or the presence of frothy pink tracheal fluid, as ascertained from the medical record.

DCI was diagnosed by neurosurgical physicians who assessed whether the clinical deteriorations fulfilled the criteria for probable or definite DCI. Probable DCI was defined as a focal deficit or deterioration of the level of consciousness that could not be explained by metabolic disturbances, infection, treatment complications, hydrocephalus, or rebleeding in the absence of new hypodensities on a repeated CT scan. Definite DCI was defined as the deterioration of the level of consciousness, the development of focal neurologic signs, or both, along with evidence of cerebral infarction on CT scan. Cases in which new hypodensities were observed on the CT scan in the absence of an obvious explanation, such as neurosurgical or endovascular intervention or perihematomal edema, were scored as definite DCI even if no clinical symptoms were present. Probable and definite DCIs were grouped together as 1 event.

Statistical Analysis

The statistical analysis was performed using commercially available statistical software (IBM SPSS 22.0, IBM, Armonk, New York, USA). A P value < .05 was considered significant. The baseline characteristics were analyzed using descriptive statistics. For baseline determinants and outcomes (NPE, DCI, and in-hospital death), univariable risk ratios (RRs) with corresponding 95% confidence intervals (CIs) were calculated using binary variable logistic regression. Multivariable logistic regression was used to identify ECG variables that were independently associated