The effectiveness of using magnetic resonance imaging in syncope patients visiting an emergency department: A case-control study

Go Eun Choi, Byung Hyun Moon, Sung Do Lee, Eu Jen Jeung, Dong Hun Lee, Yong Soo Cho, Yang Jun Kang, Byeong Kook Lee, Seong Min Choi, Seung Han Lee, Hyun Ho Ryu, Jeong Mi Moon, Byeong Jo Chun, Tag Heo, Yong Il Min

Abstract
Objective: To evaluate the effectiveness of brain magnetic resonance imaging in excluding neurological causes in patients with syncope.
Methods: This retrospective, observational, cohort study was conducted at the Chonnam National University Hospital, Gwangju, South Korea, and comprised medical record of patients with syncope from January 2011 to February 2016. The ratio of abnormal findings, the characteristics of the patients who showed abnormal findings and the relationships between the presence of neurological problem and other clinical factors were analysed. SPSS 18 was used for statistical analysis.
Results: Of the 1,045 patients, 142(13.5%) underwent additional magnetic resonance imaging. The results showed that 15(10.6%) patients had abnormal findings indicating neurological problems; of them, 9(60%) showed vascular stenosis, 4(27%) showed cerebral infarction, and 2(13%) showed brain tumors. The neurological problems shown were significantly higher for older patients (p=0.006) and those with the underlying diseases of hypertension (p=0.014) and coronary artery disease (p=0.008). Of these patients in particular, age (p=0.036) and history of coronary artery disease (p=0.029) were significantly associated with abnormal findings in their magnetic resonance imaging.
Conclusion: Although there are no specific neurological examinations or computed tomography findings currently used in patients with syncope in the emergency department, magnetic resonance imaging may be performed to exclude neurological causes in older patients as well as those with a history of coronary artery disease.
Keywords: Syncope, Emergency department, Brain magnetic resonance imaging, Age, Coronary artery disease.

Introduction
Syncope is defined as a transient loss of consciousness that the patient rapidly recovers from. Patients with syncope commonly visit emergency departments due to the sudden onset. Patients experiencing syncope account for about 6% of emergency patients, about 0.7% of those expire within 10 days, and about 6% expire within a year after an episode of syncope. Causes of syncope may be associated with cardiac, neurological, vasovagal, and orthostatic systems and patient prognosis also varies depending on the cause. In the case of vasovagal syncope, a benign prognosis is shown and the mortality rate is not increased compared to patients without syncope. In the case of syncope with a cardiac cause, however, the mortality rate more than doubles, syncope with a neurological cause increases mortality by 1.5 times, and the danger of cerebral infarction due to syncope with a neurological cause is three times higher compared to patients without syncope episodes. Because syncope in patients can lead to a serious prognosis, in instances where patients present at an emergency department, doctors will carry out various examinations to come to a diagnosis.
Syncope patients not showing neurological symptoms cannot be rest assured due to the danger of asymptomatic lesions, the high mortality rate for neurological syncope, and the danger of cerebral infarction. Emergency doctors should mention to syncope patients the danger of syncope in their prognosis and the possibility of neurological asymptomatic lesions. Moreover, more active neurological examinations are needed to consider potential syncope caused by neurological problems and related diseases and the possibility of further cerebral infarction. Possible neurological examinations performed after an episode of syncope are electroencephalography (EEG) and brain imaging. Due to the difficulty in the application of EEG in the emergency department, brain imaging may be considered. The diagnostic efficacy of brain computed tomography (CT) in patients with syncope has been widely researched previously, and between 5%
and 6% of patients with syncope showed abnormal findings.7,8 The researchers paid attention to magnetic resonance imaging (MRI) which can be provided a more detailed analysis compared to a CT. This study presents the beginning stage of research to find out potential neurological problems using MRI with patients who have no abnormal findings in their neurological examination and CT. The current study was planned to investigate the clinical factors associated with the cerebral comorbidity on brain MRI of syncope patients.

Patients and Methods

This retrospective, observational, cohort study was conducted at the Chonnam National University Hospital, a university-affiliated hospital in Gwangju, South Korea, and comprised medical record of patients admitted to the emergency department with syncope from January 2011 to February 2016. The patients were selected and analysed if their chief complaints were relevant to syncope, i.e. ‘a transient loss of consciousness that is rapidly recovered from’. ‘Syncope’ patients were identified according to International Classification of Disease (ICD) 10.9 The inclusion criteria were ICD code R 55 and age >15 years. Patients aged under 15 years, with abnormal neurologic exam at presentation, or with abnormal brain CT finding were excluded. When patients with episodes of syncope visited the emergency department, residents and physicians in emergency medicine performed medical examinations using interviews in taking a medical history, a physical health assessment, and a neurological examination. If a local neurological defect was shown which raised suspicions of cerebral infarction, such as altered consciousness, sensory or motor paralysis, visual field defects, or loss of coordination, they regarded as an abnormal findings.

After taking a patient history and performing a neurological examination, an electrocardiogram (ECG) and blood tests were done. A brain CT was performed to exclude any structural brain problems. Patients who did not show any local neurological defects or abnormal findings, in their brain CT, received a full explanation about the need for a brain MRI and allowed us to perform a brain MRI with informed consent for a more detailed evaluation. Patients were asked about age, sex, recent head injuries, any underlying diseases like hypertension and diabetes mellitus, cerebral infarction, brain tumours and cerebral haemorrhage, prodromal symptoms and any accompanying symptoms in their past. After having an ECG in the emergency department, emergency medicine and internal medicine residents and emergency physicians looked at the results and classified bradycardia, supraventricular tachycardia (SVT), atrial fibrillation (AF), atrial flutter (AF), ventricular tachycardia (VT) and ventricular fibrillation (VF) as abnormal findings.

Brain CTs and MRIs were performed and interpreted by radiologists and they classified the results of the examinations. Cerebral haemorrhage, cerebral infarction and brain tumours on brain CTs were classified as abnormal conditions (=positives). Acute cerebral infarction, brain tumours, and vascular stenosis on brain MRIs were also added as positives. In the results of brain MRIs, old and previous cerebral embolisms and lesions were excluded from classification. Two emergency residents, three emergency physicians, and one neurologist reviewed the records of the brain CTs and brain MRIs, and one radiologist looked at and interpreted the imaging records of the brain CTs and brain MRIs.

SPSS 18 was used for statistical analysis. Categorical variables were expressed as a percentage and chi-square tests and a Fisher’s exact test were used for comparing the two groups in accordance with the conditions. As all the continuous variables are non-normally distributed in a normal distribution test, a median value was indicated. The Mann-Whitney U test was used to compare the two groups. A binary multivariate logistic regression analysis was used to find an independent variable related to abnormal findings in brain MRIs. The backward selection method was used for choosing the final model. Through the use of the multivariate logistic regression analysis, the result for the multivariate analysis was p<0.20 and only variables were included.

Results

Of the 1,146 patients, general characteristics were examined for 1,045(91.2%) as 31(2.7%) were excluded as they were aged below 15 years and 70(6.1%) had abnormal findings in their neurological examinations and brain CTs. There were two groups: those who had a brain MRI (group A), and those who did not (group B). They comprised 142(13.6%) and 903(86.4%) patients, respectively. Both groups showed a high frequency of visiting the emergency department in autumn and winter and more patients came during the day rather than at night. Regarding the ECGs, most patients had a normal sinus rhythm (NSR); however, about 160(15.7%) of all the participants showed sinus bradycardia. The median value with interquartile ranges (IQR) of door-to-CT time was 12(6-24) minutes and the time difference between CT and MRI was 180(90-320) minutes. Group A patients presented with more underlying diseases such as hypertension (HTN), but there were no significant differences for any
Table 1: Clinical Opinions on the Research Groups (*p<0.05).

<table>
<thead>
<tr>
<th>Previous Illness</th>
<th>Abnormal (N = 15)</th>
<th>Normal (N = 127)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD</td>
<td>0.452 (0.036 - 5.628)</td>
<td>0.537</td>
<td></td>
</tr>
<tr>
<td>SHD</td>
<td>6.400 (1.000 - 39.821)</td>
<td>0.008*</td>
<td></td>
</tr>
<tr>
<td>HTN</td>
<td>2.612 (0.694 - 9.822)</td>
<td>0.155</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: MRI comparisons between the normal group and the abnormal group (*p<0.05).

<table>
<thead>
<tr>
<th>Abnormal (N = 15)</th>
<th>Normal (N = 127)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.046 (1.003 - 1.092)</td>
<td>0.036*</td>
</tr>
<tr>
<td>Sex</td>
<td>5.404 (1.192 - 24.506)</td>
<td>0.029*</td>
</tr>
<tr>
<td>Season</td>
<td>2.595 (0.639 - 10.535)</td>
<td>0.182</td>
</tr>
</tbody>
</table>

Table 3: Logistic regression analysis of patients with abnormal findings in their brain MRIs (*p<0.05).

<table>
<thead>
<tr>
<th>Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.008*</td>
</tr>
<tr>
<td>SHD</td>
<td>0.029*</td>
</tr>
<tr>
<td>HTN</td>
<td>0.182</td>
</tr>
</tbody>
</table>

Other diseases between the two groups (Table 1).

Additional MRIs in group A showed that among the 15(10.6%) patients with abnormal findings, 9(60%) had cerebrovascular stenosis, 4(27%) had cerebral infarction, and 2(13%) had brain tumours. Of the patients with cerebrovascular stenosis, 3(33.3%) were found with previous cardiovascular problems. Of the patients with acute cerebral infarction, 12(25%) was found with previous cardiovascular disease. Moreover, 7(77.8%) patients with cerebrovascular stenosis and 2(100%) patients with brain tumours had underlying disease such as HTN.

A comparison of the groups with abnormal and normal findings in their brain MRIs showed that the difference between sex, ECG and blood pressure was insignificant. The group with abnormal findings in their brain MRIs.
were significantly associated with old age \( (p=0.005) \), HTN \( (p=0.014) \) and coronary artery disease \( (p=0.008) \). There were no meaningful differences due to underlying disease except for those three (Table-2).

Logistic regression analysis was used for two factors, age \( (p=0.036) \) and coronary artery disease \( (p=0.029) \), which indicated significant differences between the abnormal group and the normal group in the brain MRIs (Table-3).

**Discussion**

The current study found that the ratio of hypertensive patients from the group who performed the brain MRIs with informed consent was higher than those who did not have brain MRIs. Patients who showed abnormal findings in their brain MRIs had a high ratio of underlying disease like hypertension. Age and hypertension are well-known to increase the prevalence rate of cardiovascular and cerebrovascular diseases. Cardiovascular diseases also increase the prevalence rates of cerebrovascular diseases.\(^{10-12}\) On the basis of the Framingham study, some countries have executed national health polices to decrease the risk of heart and cerebrovascular disease.\(^{13,14}\) The general public, therefore, know well that old age and hypertension are the main risk factors. Doctors involved in research have asked syncope patients to have brain MRIs with informed consent as these MRIs can lead to detailed examinations of cerebral infarction, cerebrovascular diseases and brain lesions. We assume that patients with the underlying disease of hypertension may agree to an MRI as they are aware of hypertension being a main risk factor.

The need of performing a brain imaging examination in patients without a complicated syncope is controversial. According to guidelines for the diagnosis and management of syncope, initial ECG, ECG monitoring and echocardiography are recommended to distinguish syncope with a cardiac cause and patients with neurological problems are recommended to have a brain imaging examination,\(^{1,3}\) but not having neurological lesions due to having no neurological symptoms is debatable. In cases where there are no specific neurological symptoms, asymptomatic encephalopathy was found in brain imaging examinations and those having no specific neurological symptoms also showed increased stroke incidence rates or an increased prevalence of cerebral apoplexy, early death, neurological defects and cognitive impairment later.\(^{15}\) According to a study conducted by Kobayashi et al.,\(^{16}\) if there is an asymptomatic cerebral infarction lesion, the prevalence of stroke runs to 10% yearly and if there is no asymptomatic cerebral infarction lesion, the prevalence of stroke is about five times higher. Neurological diseases, however, could be a reason for syncope and doctors in the emergency department should actively deal with patients with neurological lesions considering the patient's serious prognosis. According to the results of this study, patients with no neurological symptoms and no abnormal findings in their brain CTs were found with abnormal findings in their brain MRIs. If neurological syncope is finally distinguished by whether neurological symptoms exist or not, a number of patients with syncope of neurological origin are missed by emergency doctors and emergency doctors seem not to warn patients about the potential of cerebral infarction and neurological diseases in time. According to one study, about 13.7% of patients with cerebrovascular stenosis experience cerebral infarction within two years, and 24.5% of those cause ischaemic attack.\(^{14}\) Syncope can also cause potential neurological diseases\(^{17}\) and there are research studies that show cerebrovascular stenosis and brain tumours cause syncope.\(^{18-22}\) Other results of studies which used brain MRIs targeting healthy people showed similar results with about 11% abnormal findings.\(^{23}\) A potential cerebral ischaemia caused by further cerebrovascular stenosis is not excluded but additional research is needed because of the results of the brain MRIs and the clinical importance.

Patients with cerebrovascular stenosis have mostly had antithrombotic treatment. Patients with acute cerebral infarction have also taken antithrombotic medication. A patient with glioma among the patients with brain tumours underwent an operation and had radiation therapy. Six patients with abnormal findings in their brain MRIs had an EEG performed and there were no specific findings in them. In one patient with cerebrovascular stenosis and one patient with glioma it is believed the syncope was caused by convulsions and in one patient transient cerebral ischaemia is suspected. After syncope recurred in one patient it led to neurological disease and this patient is one of the four patients that experienced an acute cerebral infarction, another acute cerebral infarction occurred in this patient again within two years. Emergency doctors have to realise that patients presenting with syncope can have a serious prognosis such as neurologically mediated syncope and syncope due to a cardiac problem. The basic indicators to distinguish syncope originating in the heart in the emergency department are an ECG and a myocardial enzyme analysis. According to emergency department guidelines, if patients have no abnormal findings in two examinations, patients need to be hospitalised and have additional examinations in cardiovascular medicine such as an echocardiography and a head up tilt test depending...
on whether there are any abnormal findings.

In cases of neurological syncope, however, applicable examinations to distinguish cardiovascular syncope in the emergency department were not only restricted but also syncope with a cardiac origin, and effective treatment methods to distinguish it easily do not exist. Under complicated and special situations such as those in an emergency department, an EEG is difficult to perform at the right place with the proper staff. As these researchers distinguish syncope originating in the heart using an ECG and a myocardial enzyme analysis, and if syncope is of neurological origin it is at least distinguished through a brain MRI, emergency doctors have difficulty performing the proper diagnostic tools which can distinguish between syncope with a cardiac or neurological origin. This causes poor prognosis in the restricted emergency department. In particular, a brain MRI is effective due to the discovery of small lesions or cerebrovascular conditions which are hard to resolve in a brain CT. Even though in a brain MRI it is difficult to distinguish all the different possible neurological conditions, the brain MRIs will be helpful for patients in their diagnosis and to determine patients’ prognosis as a milestone of ECG and myocardial enzyme analysis in syncope of cardiac origin in the emergency department.

This study had a few limitations as well. First, it was carried out at a single hospital so it is hard to generalise from its findings. Second, retrospective research depending on clinical records can be swayed by an absence of records and errors due to the recorder’s subjective differences. Retrospective research can have limitations in interpreting the situation at the time. However, the calculated power of the effectiveness of brain MRI to exclude neurological causes was 1.0. Emergency residents and physicians could not consider lower level neurological symptoms such as headache and dizziness in the initial treatment. Lastly, patients with syncope who visited the emergency department could not be provided with proper cardiac examinations. In the unique emergency department set-up where this study was done, patients who were discharged came back to an outpatient department for a follow-up after the internal medicine doctors on duty initially diagnosed patients with syncope without complete medical examinations such as echocardiography and a head-up tilt test. This study did not thoroughly investigate the causes of syncope in the emergency department. In order to exclude cardiovascular syncope under minimal conditions requires an ECG, continuous monitoring and a myocardial enzyme analysis.

Conclusion
Although there were no specific neurological examinations or CT findings in patients in the current study, an MRI may be performed to exclude neurological causes in older patients as well as those with a history of coronary artery disease.

Disclaimer: None.
Conflict of Interest: None.
Source of Funding: None.

Reference