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Etiology and clinical characteristics of patients with severely impaired consciousness in prehospital settings: A retrospective study

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Abstract

Aim: To examine the causes of patients with severely impaired consciousness and the clinical characteristics in prehospital settings that are useful for differential diagnosis, especially stroke.

Methods: We retrospectively examined patients aged ≥16 years with Japan Coma Scale III-digit codes during paramedic contact and transported to our hospital between January 2018 and December 2018. Furthermore, we examined background and physical findings of patients at final diagnosis, and also examined factors associated with stroke.

Results: Overall, 227 patients were included in this study. One hundred and twelve patients (49.3%) were male, and the median age was 71 years (interquartile range, 50–83 years). Stroke was the most common cause (30%). Intoxication and psychiatric disorders were significantly more common in younger patients ($p < 0.01$). Systolic blood pressure was the highest in patients with stroke. Mortality was the highest in stroke (55.9%). Systolic blood pressure, airway compromise, and ocular abnormalities were factors associated with stroke, with odds ratios of 1.03 (95% confidence interval [CI], 1.02–1.04), 6.88 (95% CI, 3.02–15.64), and 3.86 (95% CI, 1.61–9.27), respectively.

Conclusion: Stroke was the most common cause of severely impaired consciousness. Age could be a useful indicator to consider intoxication and psychiatric disorders. Systolic blood pressure, airway compromise, and ocular abnormalities were factors associated with stroke in the prehospital setting.

KEYWORDS
airway, coma, differential diagnosis, ocular abnormality, prehospital emergency services

INTRODUCTION

Impaired consciousness is a clinical problem in approximately 25% of patients transported to the emergency department (ED) and constitutes 5%–10% of all patients presenting to the ED.[1,2] Nontraumatic impaired consciousness has many differential diagnoses; however, it is difficult to obtain a detailed history and accurate physical examination

The corresponding author was transferred to the current institution (Osaka Red Cross Hospital) after completing the data collection for this study at the original institution (Kobe City Medical Center General Hospital).

Results of Kruskal–Wallis test for male gender, age, systolic blood pressure (sBP), heart rate (HR), atrial fibrillation (Af), airway compromise, ocular abnormalities, and mortality.

of patients with severely impaired consciousness.[3] Stroke is one of the emergency conditions that cause severely impaired consciousness, and delays in treatment affect the patient's prognosis. Therefore, accurate judgment and early transport by paramedics are necessary. However, accurate diagnosis of patients with severely impaired consciousness in the prehospital setting is difficult,[3,4] and conditions such as seizures, syncope, migraine, dizziness, and traumatic intracranial hemorrhage are often difficult to differentiate from stroke in the prehospital setting. It has been reported that 30% of patients transported for suspected stroke have diseases other than stroke.[5,6] It is challenging for paramedics to accurately determine stroke as the cause of the impaired consciousness, especially if the stroke is severe, resulting in severely impaired consciousness.[7] Therefore, the aim of this study was to examine the causes of severely impaired consciousness and to examine clinical characteristics of patients to identify useful indicators for differential diagnosis, particularly to differentiate between stroke and nonstroke, in prehospital settings.

TABLE 1 Japan Coma Scale.

Level	Grade
Alert	0
The patient is awake without any stimuli	I-digit code
Almost fully conscious but not normal	1
Unable to recognize time, place, and person	2
Unable to recall name or date of birth	3
The patient can be aroused, then reverts to previous state after cessation of stimuli	II-digit code
Easily with a normal call	10
With loud voice	20
Only with repeated painful stimuli	30
The patient cannot be aroused with any painful stimuli	III-digit code
Responds with movements to avoid the stimuli	100
Responds with slight movements including decerebrate and decorticate posture	200
Fails to respond	300

METHODS

Study design and population

We undertook a single-center retrospective cohort study using data from the Kobe City Fire Department database. Our institution is a tertiary care hospital located at the center of a city with a population of approximately 1.5 million people, and approximately 30,000 patients visit the hospital ED annually.

At our facility, emergency physicians initially assess all patients who visit the ED, and those who are determined to require hospitalization are referred to specialists for inpatient care.

In Japan, paramedics extensively use the Japan Coma Scale (JCS) to assess a patient's consciousness level in prehospital settings. In this study, evaluation and recording using the JCS was done in all patients, but evaluation and recording of consciousness level using the Glasgow Coma Scale was very rare, so we used JCS to evaluate impaired consciousness. Previous studies have reported that the JCS correlates with patient outcomes.[8,9] The JCS comprises four categories as follows: 0, I-, II-, and III-digit codes. Each code has three subcategories as follows: 1, 2, and 3 in the I-digit code; 10, 20, and 30 in the II-digit code; and 100, 200, and 300 in the III-digit code, respectively (Table 1). The I-, II-, and III-digit codes correspond to E4, E3 or E2, and E1 on the Glasgow Coma Scale, respectively.

We evaluated patients aged ≥16 years for whom emergency services were called for acute illness, who were in JCS III-digit codes at the time of paramedic contact, and who were transported to our ED between January and December 2018. In reference to previous reports on the differentiation of impaired consciousness or stroke mimics for evaluation items,[10–14] we retrospectively verified age, sex, systolic blood pressure (sBP), heart rate (HR) at ED arrival, presence of atrial fibrillation (Af), airway compromise, ocular abnormalities, including conjugate eye deviation or pupillary irregularities, final diagnosis, and mortality from paramedic transport and electronic medical records. In addition, we excluded patients with cardiopulmonary arrest, trauma, original conscious state of JCS III-digit codes, improved consciousness from JCS III-digit codes on arrival at the ED, and missing data. The final diagnosis was based on the diagnosis at discharge evaluated by specialists certified by each specialty board and classified as follows with reference to previous reports of differential diagnosis for impaired consciousness[5,6,14,15]: stroke, intoxication, seizure, infections, psychiatric disorders, metabolic disorders (hypoglycemia and hepatic encephalopathy, among others), environmental disorders (hypothermia and heat stroke), cardiovascular diseases, and others. Airway compromise was defined as cases in which the emergency physician or paramedics determined that airway management (manual mandibular elevation, use of naso-/oropharyngeal airway, or endotracheal intubation) is necessary. In Japan, endotracheal intubation by paramedics is not permitted except for cases of cardiopulmonary arrest, and paramedics use other methods to maintain the airway.

Statistical analysis

Continuous variables are represented as medians and interquartile ranges, and binary variables are presented as absolute values and percentages (%). The distribution of age, sBP, HR, and rates of male gender, Af, airway compromise, ocular abnormalities, and mortality were verified and compared in each disease group excluding "others". The Kruskal–Wallis test was used for testing, followed by the Steel–Dwass multiple

comparison test. The Steel-Dwass test used a table of significance levels determined by the number of comparison groups and degrees of freedom to determine significant differences. In addition, we compared and validated these characteristics between stroke and nonstroke. Statistically significant was set at $p < 0.05$. For comparisons between stroke and nonstroke, we applied the Mann–Whitney *U*-test, χ^2-test, and multiple logistic regression analysis to identify factors associated with stroke. We included sex, age, sBP, HR, airway compromise, Af, and ocular abnormalities as factors that could influence stroke in the logistic regression analysis. Statistical analysis was carried out using the Bell Curve for Excel (Social Survey Research Information Co., Ltd.).

The ethics board of the Kobe City Medical Center General Hospital approved this study (registration number: zn22148).

RESULTS

Background

During the study period, 587 patients aged ≥16 years had JCS III-digit codes at the time of paramedic contact. Of these, we excluded 61 patients for whom emergency services were requested for transfer and 99 patients for whom emergency services were requested for trauma. Of 407 patients who requested emergency services for acute illness, 227 patients were eligible for validation after excluding 179 patients who met the exclusion criteria (Figure 1). Table 2 shows the patient characteristics. One hundred twelve patients (49.3%) were male, and the median age was 72 years. The numbers of patients with JCS III-100, III-200, and III-300 were 71 (31.3%), 71 (31.3%), and 85 (37.4%), respectively. Stroke was the most common final diagnosis (68 patients [30%]) in patients. Patients classified as "others" comprised six with unknown causes, four with carbon dioxide narcosis, one with gastrointestinal bleeding, one with serotonin syndrome, and one with senility.

Comparative verification for each final diagnosis

Figure 2 showed the validation results for age, sBP, and HR for each final diagnosis. Young patients were more likely when intoxication or psychiatric disorders were the cause ($p < 0.01$). When stroke was the cause, sBP was significantly higher compared to diagnoses excluding seizures and metabolic disorders ($p < 0.01$). There were few significant differences in HR between causes. In addition, 87 patients (38.3%) had airway compromise on arrival at the ED, of whom 50 (73.5%) had a stroke. Stroke was more often associated with airway compromise than other differential diagnoses except for environmental disorders and cardiovascular diseases ($p < 0.01$) Ocular abnormalities were significantly more likely to be found in patients with seizures than in patients with other final diagnoses ($p < 0.01$). Sex and Af showed no significant differences by final diagnosis. Among the 227 eligible patients, 56 (25.6%) died. Stroke was the most common cause of death, with a significant difference compared to other causes except for environmental and cardiovascular diseases (intoxication, seizures, and psychiatric disorders, $p < 0.01$, infection, $p = 0.04$; metabolic disorders, $p = 0.03$) (Table 3). The results of the Kruskal–Wallis test for sex, age, sBP, HR, Af, airway compromise, ocular abnormalities, and mortality are presented in the additional file.

Comparative verification of stroke and nonstroke and factors associated with stroke

Univariate analysis showed a significant difference between stroke and nonstroke in age (77.5 vs 69 years; $p < 0.01$), sBP (172 vs 123 mmHg; $p < 0.01$), airway compromise (73.5% vs 25.2%; $p < 0.01$), Af (23.5% vs 16.1%; $p = 0.01$), and ocular abnormalities (55.9% vs 12.6%; $p < 0.01$) (Table 4). In multiple logistic regression analysis, sBP (odds ratio [OR] 1.03; 95% CI, 1.02–1.04), airway

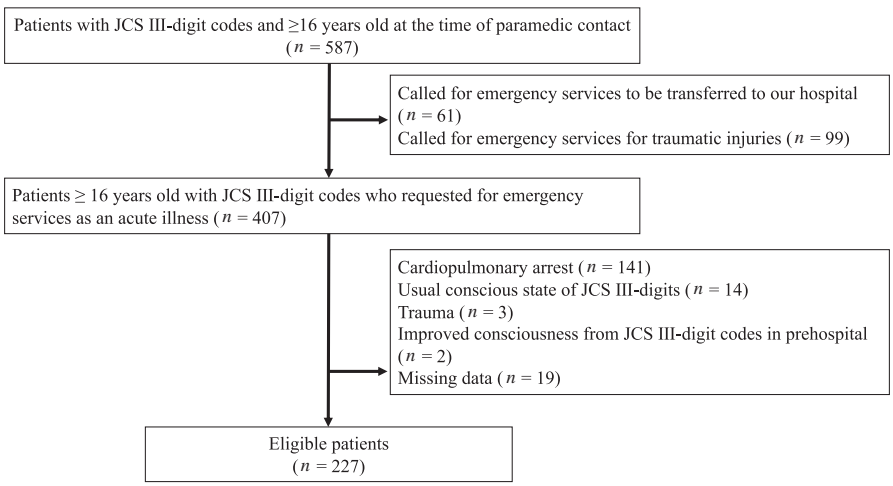

FIGURE 1 Flowchart of patient inclusion in this study of etiology and clinical characteristics of patients with severely impaired consciousness in prehospital settings. JCS, Japan Coma Scale.

TABLE 2 Characteristics of patients with severely impaired consciousness in prehospital settings.

N	227
Sex, male (%)	112 (49.3)
Age (years), median (IQR)	72 (50–83)
JCS, *n* (%)	
III-100	71 (31.3)
III-200	71 (31.3)
III-300	85 (37.4)
Final diagnosis, *n* (%)	
Stroke	68 (30.0)
Intoxication	34 (15.0)
Seizure	29 (12.8)
Infection	27 (11.9)
Psychiatric disorders	22 (9.7)
Metabolic disorders	16 (7.0)
Environmental disorders	9 (4.0)
Cardiovascular diseases	9 (4.0)
Others	13 (5.7)
Mortality	58 (25.6)

Abbreviations: IQR, interquartile range; JCS, Japan Coma Scale.

compromise (OR 6.88; 95% CI, 3.02–15.64), and ocular abnormalities (OR 3.86; 95% CI, 1.61–9.27) were associated with stroke as the cause of severely impaired consciousness (Table 5).

DISCUSSION

This retrospective, observational study showed that age, sBP, airway compromise, and ocular abnormalities could be indicators for the differential diagnosis of severe impaired consciousness. Furthermore, stroke was the most common cause of severely impaired consciousness, similar to that in a previous study,[15] and sBP, airway abnormalities, and ocular abnormalities were particularly useful in differentiating stroke from nonstroke. Although there are many differential diagnoses of the cause of impaired consciousness, it is difficult to obtain a detailed history and physical examination of patients with severely impaired consciousness. The concordance rate between prehospital and final diagnoses is approximately 60%.[4] Stroke and cardiovascular disease often require early treatment and have high mortality rates[16]; thus it is crucial to diagnose these diseases early and accurately.

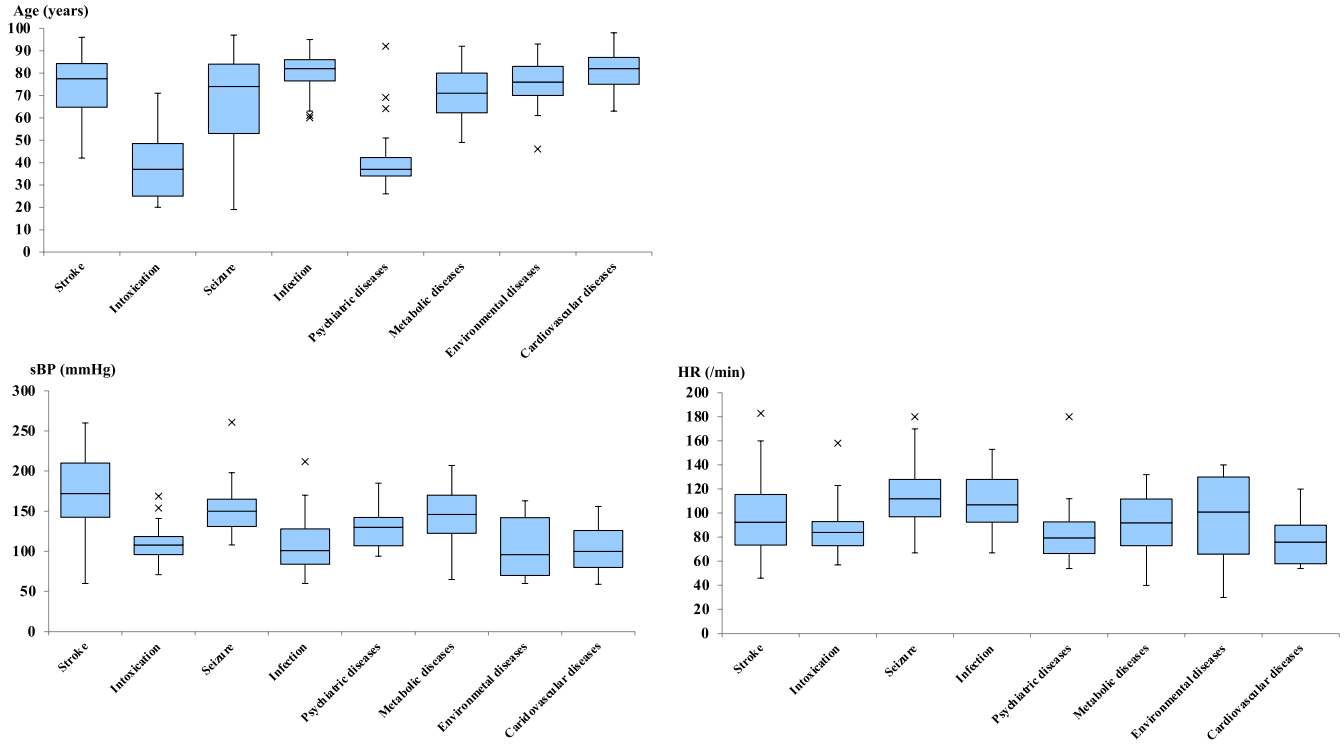

FIGURE 2 Distribution of age, systolic blood pressure, and heart rate depending on each final diagnosis in patients with severely impaired consciousness in prehospital settings. The bottom to top edge each box indicates the first quartile to third quartile, respectively. The upper and lower whiskers indicate the upper and lower limits of 1.5 times the quartile range (interquartile ranges), with × indicating outliers. The centerline indicates the median value. Patients with intoxication and psychiatric diseases were significantly younger than those with other diseases ($p < 0.01$). Significant differences were found between patients with stroke and those with intoxication, infection, psychiatric disorders, environmental disorders, or cardiovascular diseases ($p < 0.01$). No significant differences were found in patients with seizures or metabolic disorders ($p = 0.15$ and 0.28, respectively). HR, heart rate; sBP, systolic blood pressure.

TABLE 3 Rate of male gender, atrial fibrillation (Af), airway compromise, ocular abnormalities, and mortality for each final diagnosis in patients with severely impaired consciousness.

	Number of patients	Male gender	Af	Airway compromise	Ocular abnormalities	Mortality
Stroke	68	37 (54.4)	16 (23.5)	50 (73.5)[a]	31 (45.6)	38 (55.9)[c]
Intoxication	34	21 (61.8)	2 (5.9)	7 (20.6)	1 (2.9)	0 (0.0)
Seizure	29	16 (55.2)	4 (13.8)	9 (31)	21 (72.4)[b]	1 (3.4)
Infection	27	12 (44.4)	1 (3.7)	7 (25.9)	0 (0.0)	6 (22.2)
Psychiatric disorder	22	5 (22.7)	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)
Metabolic disorders	16	4 (25)	1 (6.2)	3 (18.8)	3 (18.8)	2 (12.5)
Environmental disorders	9	6 (66.7)	3 (33.3)	5 (55.5)	0 (0.0)	2 (22.2)
Cardiovascular diseases	9	4 (44.4)	2 (22.2)	6 (66.6)	1 (11.1)	5 (55.6)

Note: Data are shown as *n* (%).

[a]Stroke was significantly associated with airway compromise compared to other differential diagnoses except for environmental and cardiovascular disease. ($p < 0.01$).

[b]Seizure was significantly more associated with ocular abnormalities than with other final diagnoses except for stroke ($p < 0.01$).

[c]Stroke was the most common cause of death, with a significant difference compared to other causes except for environmental and cardiovascular diseases (intoxication, seizures, and psychiatric disorders, $p < 0.01$; infection, $p = 0.04$; metabolic disorders, $p = 0.03$).

TABLE 4 Univariate analysis of factors associated with stroke in patients with severely impaired consciousness.

	Stroke	Nonstroke			
N	**68**	**159**	***p* value**	**OR**	**95% CI**
Male	37 (54.4)	75 (47.2)	0.38	1.34	0.76–2.36
Age (years)	77.5 (64.75–84.25)	69 (41–82)	<0.01*	–	–
sBP (mmHg)	172 (142.75–210.25)	123 (98–150)	<0.01*	–	–
HR (/min)	92.5 (73.5–115.5)	92 (73–117)	0.97	–	–
Atrial fibrillation	16 (23.5)	16 (10.1)	0.01*	2.75	1.30–5.83
Airway compromise	50 (73.5)	40 (25.2)	<0.01*	8.26	4.35–15.7
Ocular abnormalities	31 (45.6)	27 (17)	<0.01*	4.10	2.19–7.68
Mortality	38 (55.9)	20 (12.6)	<0.01*	8.80	4.52–17.14

Note: Data are shown as *n* (%) or median (interquartile range).

Abbreviations: CI, confidence interval; HR, heart rate; OR, odds ratio; sBP, systolic blood pressure.

*$p < 0.05$ is statistically significant.

TABLE 5 Factors useful in differentiating stroke from nonstroke by multiple logistic regression analysis.

Factors	OR	95% CI
Male	1.98	0.88–4.51
Age	1.02	0.99–1.05
sBP	1.03	1.02–1.04
HR	0.99	0.98–1.01
Airway compromise	6.88	3.02–15.64
Atrial fibrillation	1.79	0.62–5.20
Ocular abnormalities	3.86	1.61–9.27

Abbreviations: CI, confidence interval; HR, heart rate; OR, odds ratio; sBP: systolic blood pressure.

Based on previous reports[10–14] and experience, we highlighted age, sBP, HR, Af, airway compromise, and ocular abnormalities as characteristics for the differential diagnosis of severely impaired consciousness. In this study, patients with intoxication or psychiatric disorders were significantly younger, and those with stroke had the highest sBP, which showed a significant difference compared with most differential diagnoses other than seizures and metabolic disorders. Regarding the association between patients with impaired consciousness and age and sBP, it has been reported that intoxication was a more common cause in younger patients,[17] and stroke was more common when the sBP was higher than 180mmHg.[11] The results were consistent with this study and suggested that age and sBP are important factors in the differential diagnosis of severely impaired consciousness.

Airway compromise should be considered in patients with severely impaired consciousness. Although many patients with stroke-induced severely impaired consciousness require intubation, those with intoxication-induced severely impaired consciousness can be monitored without intubation[13,18]; therefore, it is crucial to confirm the necessity of airway management for patient management and to estimate the causes of impaired consciousness. Here, airway compromise was most frequently observed in patients with severely impaired consciousness due to stroke, accounting for 73.5% of cases. Among the conditions

presenting with impaired consciousness, stroke was significantly more likely to present with airway compromise, and stroke should be the first differential diagnosis in patients with impaired consciousness presenting with airway obstruction. In contrast, airway compromise was significantly less common in patients with intoxication or psychiatric disorders. In addition to previous reports,[18] the absence of the need for airway management despite severely impaired consciousness could be a useful finding when considering intoxication or psychiatric disorders as possible causes.

Clinical symptoms are significant in diagnosing stroke; however, it is challenging to confirm facial nerve palsy, paralysis, or dysarthria in the presence of severe impairment of consciousness. Here, among the patients diagnosed with a stroke, 45.6% had ocular abnormalities, including conjugate eye deviation or pupillary irregularities. Notably, conjugate eye deviation is found in 45%–50% of strokes and is associated with stroke severity and large vessel occlusion,[12,19,20] making it important to check the ocular status in patients with severely impaired consciousness for early diagnosis and treatment of stroke.

This study has several limitations. First, this was a single-center observational study. Our institution is a tertiary care hospital and is commonly selected as an institution for patients with severely impaired consciousness with JCS III-digit codes. However, it is yet to be confirmed how many patients with severely impaired consciousness are transported to other institutions. Second, the prevalence of symptoms before impaired consciousness (e.g., headache and chest pain) and comorbidities, such as atrial fibrillation, is often crucial for differential diagnosis, and we have not examined these factors. In addition, for patients with stroke, the evaluation of abnormal limb positions and ocular abnormalities might not be accurate for some paramedics. Although early transport is vital for patients with severely impaired consciousness, obtaining as much medical history and physical examination as possible and making a comprehensive assessment of the patient's condition is important. Third, diseases classified as others as the final diagnosis were not statistically validated. However, if these cases are increased and verified, the rates of airway obstruction and mortality could be higher. Finally, due to the small sample size, it is difficult to generalize the results of this verification and further verification is needed.

In conclusion, with a high mortality rate, stroke was the most common cause of severe impaired consciousness with JCS III-digit codes. Age, sBP, airway compromise, and ocular abnormalities could be useful findings in the differential diagnosis of severely impaired consciousness. In particular, sBP, airway compromise, and ocular abnormalities are important factors in differentiating stroke from other diseases in prehospital settings. However, further validation is needed.

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CONFLICT OF INTEREST STATEMENT

Authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the Kobe City Fire Department, but restrictions apply to the availability of these data, which were used under the license for the current study, and so are not publicly available. However, data are available from the corresponding author upon reasonable request and with permission from Kobe City Fire Department.

ETHICS STATEMENT

Approval of the research protocol: This study was performed according to the Helsinki Declarations and approved by the ethics committee of the Kobe City Medical Center General Hospital (registration number: zn22148).
Informed consent: N/A.
Registry and registration no. of the study/trial: N/A.
Animal studies: N/A.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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