Selection of Regional Factors Related to Cerebral Function after Out-of-Hospital Cardiac Arrest in Japan

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Abstract

The rate of good cerebral function after out-of-hospital cardiac arrest (OHCA) remains poor and the difference in the rate exists in the regional level in Japan. Large-scale administrative data are available for research of social and demographic variables (SDV). The purpose of the present study was to find SDVs associated with cerebral function after OHCA using the Utstein database of Japan using correlation coefficient (CC) and coefficient of determination (R2). The rates of good cerebral function after OHCA at 1 month and SDVs from administrative data were surveyed in each prefecture. Five variables were found using CC and R2 by multiple regression. We concluded that the combination of CC and R2 would contribute to the selection of regional factors from the many variables in the large-scale database.

Keywords: Cerebral Function; Out-of-Hospital Cardiac Arrest; Utstein Database; Regional Factors; Social and Demographic Variable; Correlation Coefficient; Adjusted R2

Abbreviations

OHCA: Out-of-Hospital Cardiac Arrest; EMS: Emergency Medical Services; GCFR: Rate of Good Cerebral Function; SDV: Social and Demographic Variables

Introduction

Emergency cases of out-of-hospital cardiac arrest (OHCA) from all over the world are recorded in the Utstein database [1-3]. Each year, 120,000 people suffer from OHCA, which are all recorded by nationwide emergency medical services (EMS), and 7% of all deaths occur in Japan [4-8]. The Utstein database showed that the rate of good cerebral function (GCFR) after OHCA in Japan is still poor and that the difference in the rate exists in the prefectural level [9]. However, it was difficult to explain the regional differences [10]. The extent of regional variation in OHCA outcomes suggests underlying differences in rural and urban features, characteristics of patients, and patient care. Explanatory variables are classified into individual and environmental (neighborhood) levels in case of multivariate analysis. Evidence from other disciplines suggests that neighborhood-level factors influence health outcomes [11-14]. Numerous studies have evaluated socioeconomic status and race/ethnicity and their association with OHCA survival, but the results have been inconsistent [15-18] and none has considered these regional factors to account for survival and cerebral function in addition to the Utstein database variables.

Large-scale administrative data are available for research of social and demographic variables (SDV) in Japan [19]. A great number of these variables are available to use; however, the number of regions is rather small. Therefore, we need efficiently select the potentially

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related variables from the SDV provided. We tried to elucidate SDV related to the regional factors in the good cerebral function of patients after OHCA.

Purpose of the Study

The purpose of this study was to find SDV related to cerebral function after OHCA using the Utstein database of Japan using a combination of correlation coefficient (CC) and coefficient of determination ($R^2$).

Materials and Methods

Study setting

The 2014 Utstein database of Japan was analyzed in this study. EMS were managed by 1703 fire stations and 120,766 staff in 2014. EMS comprised basic life support ambulances staffed with paramedics. Ambulances were dispatched from municipal fire defense stations. Request calls for an ambulance (phone: 119) were received by a telephone operator or a dispatcher. EMS is financed by taxes, and completely free access to EMS is guaranteed. The data of patients with OHCA were electronically recorded in the Utstein database at each fire station and the prognosis of OHCA cases was surveyed in 1 month and sent to the Fire Defense and Disaster Agency. All patients with OHCA were gathered and recorded nationwide in the Utstein database, which has been run in all fire stations since 2008 in Japan. The annual reported number of the Utstein database of Japan is the greatest in the world.

Japan consists of 47 prefectures. The median population of each prefecture is 1,668,000, with a minimum of 574,000 and a maximum of 13,390,000. The median area of each prefecture is 4819 km², with a minimum of 574 km² and a maximum of 78,420 km². Japan is covered by a universal public health insurance system for Japanese people and foreigners are entitled to register. The health insurance system is mainly managed by the Health Insurancce, the National Healthcare Insurance and the Long Life Medical Care System that have high-cost medical care expense system.

The Japanese Government provides administrative statistical data of Japan at the portal site e-Stat, where SDV are provided by the Japanese Government Statistics [19]. The SDV have 13 statistical tables (Table 1). These data are summarized by prefectures and fiscal years. A fiscal year means the interval from April of the current year to March of the following year.

Study design

Outcome

Among 125,951 patients with OHCA in the 2014 Utstein database, our outcome was good cerebral function, which was defined as category 1 or 2 in the cerebral performance categories at 1 month after OHCA. The GCFR was calculated in each prefecture (Figure 1).

![Figure 1: Flowchart of the study.](image-url)
Combination of correlation coefficient and $R^2$

**Correlation coefficient**

We downloaded 2800 variables from 13 statistical tables from the SDV in the e-Stat. The original variables were divided by population or area. We obtained a total of 4839 variables for explanatory variables (Table 1). We calculated CC between GCFR and 4839 variables in each prefecture. We chose 17 variables with CC that were ≥ 0.4. We performed multiple regression between GCFR and 17 variables and calculated variance inflation factors (VIF) in each variable to prevent multicollinearity. When the VIFs were over 10, we deleted the variable of the smaller CC.

<table>
<thead>
<tr>
<th>Statistical table</th>
<th>Example variables</th>
<th>Number of original variables</th>
<th>Number of modified variables</th>
<th>Number of total variables</th>
<th>Number of variables chosen by correlation coefficients</th>
<th>Number of variables to prevent multicolinearity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population and households</td>
<td>Population, death, marriage, divorce</td>
<td>136</td>
<td>124</td>
<td>260</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Natural environment</td>
<td>Area, habitable area, temperature, rain</td>
<td>23</td>
<td>16</td>
<td>39</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Economic base</td>
<td>Income, product, shipment, deposit</td>
<td>307</td>
<td>268</td>
<td>575</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Administrative base</td>
<td>Finance, expenditure of health/welfare/education</td>
<td>180</td>
<td>179</td>
<td>359</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Education</td>
<td>School, college and university, teacher, student, graduation</td>
<td>203</td>
<td>117</td>
<td>320</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Labor</td>
<td>Labor force, unemployment rate, part-time work</td>
<td>202</td>
<td>265</td>
<td>467</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Culture and sports</td>
<td>Library, sports facility, swimming pool, travel</td>
<td>90</td>
<td>67</td>
<td>157</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dwelling</td>
<td>Owned/rented house, floor area, flush toilet, rate of recycling</td>
<td>268</td>
<td>268</td>
<td>536</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Health and medical care</td>
<td>Life expectancy, cause of death, hospital/clinic, medical expense</td>
<td>236</td>
<td>144</td>
<td>380</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Welfare and social security</td>
<td>Livelihood protection, welfare center, visiting care giver, rehabilitation</td>
<td>180</td>
<td>152</td>
<td>332</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Safety</td>
<td>Fire, traffic accident, criminal offence, insurance</td>
<td>154</td>
<td>439</td>
<td>593</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Family budget</td>
<td>Income, wage, expenditure, consumer price index</td>
<td>607</td>
<td>0</td>
<td>607</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Daily time</td>
<td>Type of activity, hobby, TV/radio/newspaper/magazine</td>
<td>214</td>
<td>0</td>
<td>214</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>—</td>
<td>2800</td>
<td>2039</td>
<td>4839</td>
<td>17</td>
<td>16</td>
</tr>
</tbody>
</table>

*Table 1: System of social and demographic statistics and selected variables.*

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R² and R²_adj

R² was defined as 1-SS_res/SStot and R²_adj was defined as 1-{SS_res/df_r}/(SStot/df_t), where SStot was the total sum of squares, SS_res was the residual sum of squares, df_r is n-1, df_t is n-p-1, p was the total number of explanatory variables, and n was the sample size.

GCFR was a response variable, and we adopted the top variables from the list (Table 2) as explanatory variables in each model. We repeated the regression analysis 16 times from 1 to 16 explanatory variables of table 2 and gained R² and R²_adj in each model. We plotted R² and R²_adj and the number of explanatory variables (Figure 2). We also performed stepwise regression with backward elimination to search predictable variables by Akaike information criterion (AIC).

| No | Variable (unit) | Statistical table | Estimate | Standard error | t value | Pr(|t|) |
|----|----------------|-------------------|----------|----------------|---------|--------|
| 1  | Rate of arrests to recognitions of criminal offenses (/100,000) | Safety | 0.006 | 0.002 | 2.784 | 0.009 |
| 2  | Average time of primary activities among 25- to 34-year-old females (minutes) | Daily time | -0.015 | 0.011 | -1.352 | 0.187 |
| 3  | Rate of 0- to 14-year-old children (%) | Population and households | 0.362 | 0.304 | 1.191 | 0.243 |
| 4  | Rate of owned houses renovated to be earthquake resistant (%) | Dwelling | 0.002 | 0.002 | 1.092 | 0.283 |
| 5  | Rate of reports of pregnancy (/100,000) | Health and medical care | -0.002 | 0.002 | -1.02 | 0.316 |
| 6  | Rate of outpatient rehabilitation stations (/100,000) | Health and medical care | 0.004 | 0.004 | 0.951 | 0.349 |
| 7  | Average time of schoolwork among males (hours) | Education | -0.033 | 0.036 | -0.922 | 0.364 |
| 8  | Rate of users of visiting bathing and nursing care (/100,000) | Welfare and social security | -0.007 | 0.009 | -0.78 | 0.442 |
| 9  | Lowest temperature among monthly averages of daily lowest (°C) | Natural environment | -0.035 | 0.057 | -0.616 | 0.543 |
| 10 | Rate of persons killed by fires (/100,000) | Safety | -0.171 | 0.300 | -0.572 | 0.572 |
| 11 | Changes of consumer price index (%) | Family budget | -0.239 | 0.483 | -0.493 | 0.625 |
| 12 | Average time of tertiary activities (leisure) among males ages 75 years and older (minutes) | Daily time | 0.003 | 0.007 | 0.366 | 0.717 |
| 13 | Rate of electral roll subscribers (%) | Administrative base | 3.766 | 12.444 | 0.303 | 0.764 |
| 14 | Height among males of the fifth grade at elementary school (cm) | Health and medical care | 0.069 | 0.265 | 0.26 | 0.797 |
| 15 | Rate of Births weighing under 2,500g (/100,000) | Health and medical care | 0.005 | 0.027 | 0.196 | 0.846 |
| 16 | Rate of construction-started residential buildings (/100,000) | Dwelling | 0.001 | 0.005 | 0.137 | 0.892 |

Table 2: Result of multiple regression of 16 selected variables in ascending order by p-value.

We used the open statistical software R (version 3.4.2; The R Foundation, Austria) for analysis.

**Ethics**

The Utstein database was used with permission from the Fire and Disaster Management Agency of the Ministry of Internal Affairs and Communications. This study was approved by the Ethical Committee of Kokushikan University (No. 27-010).

**Results**

**GCFR in each prefecture**

The median was 3.1%, the maximum was 5.9%, the minimum was 2.1%, and the mean was 3.1% among 47 prefectures. The distribution of GCFR shown at the prefectural levels was left-sided monophasic and right-tailed (Figure 2).

**Selected variables from the e-Stat**

Of the original and modified 4839 variables, 17 variables were selected as the correlation coefficients of GCFR and the variables were ≥ 0.4 (variables chosen by correlation coefficients in table 1). Consequently, 16 variables were selected to prevent multicollinearity (variables to prevent multicollinearity in table 1). Then, we obtained the list of 16 variables in ascending order by p-value (Table 2).

**R² and R²(adj) of multiple regression**

R² showed a plateau as the number of explanatory variables increased. R²(adj) also showed plateau-shaped and gradually decreased when the number increased (Figure 3). The maximum R² was 0.627 in 16 variables, however the maximum R²(adj) was 0.522 in four variables (Figure 3). Only the first variable of "Rate of arrests to recognitions of criminal offenses" (safety) had statistical significance (p = 0.0092) in table 2 and its R² and R²(adj) were 0.220 and 0.202 (Figure 3). The second variable was "Average time of primary activities among 25- to 34-year-old females (daily time)", the third was "Rate of 0 to-14-year-old children (population and households)", the fourth was "Rate of owned houses renovated to be earthquake resistant (dwelling)", and the fifth was "Rate of reports of pregnancy (health and medical care)" (Table 2).

**Figure 2**: Distribution of GCFR at 1 month after OHCA by prefecture.
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Stepwise regression showed four predictive variables that were the same as the four top variables in table 2.

Discussion

$R^2$ increased and reached the plateau, however, $R^2_{\text{adj}}$ did not increase at four variables afterward (Figure 3) when the number of explanatory variables increased. $R^2$ was 0.0.561 (89.5% of the maximum) and the $R^2_{\text{adj}}$ was 0.520 and the maximum in four explanatory variables (Figure 3), which were quite similar to that of the five or six ones. Stepwise regression with backward elimination showed that four explanatory variables were selected and were the same variables of the four top ones in table 2. Only "Rate of arrests to recognitions of criminal offenses" was statistically significant among 16 social and demographic variables; however, it showed an $R^2_{\text{adj}}$ of 0.2025. As the $R^2$ and the $R^2_{\text{adj}}$ mean the descriptive power of the regression model that includes a diverse number of explanatory variables, the four top variables in table 2 seem to demonstrate well regional property in this study.

Correlation coefficient is a measure of association that indicates the degree to which two variables have a linear relationship. The number of regions is limited as there are only 47 prefectures in Japan. Recently, we can use many social and demographic variables that are provided in large-scale databases. However, we have to choose even the smaller number of social and demographic variables, although multilevel analysis is applied to demonstrate regional property. We showed the method of selecting the suitable variables from many ones with a combination of simple correlation and $R^2_{\text{adj}}$ by multiple regression analysis in this study.

Health outcomes were reported to be influenced by socioeconomic inequities such as health-care access, quality of health care [20], education [21], health services [22], number of practitioners/hospital beds [23] and workforce [24]. Of the 4839 SDV, we could find no relationship between GCFR and socioeconomic variables of the prefectural income per person, the rate of people having completed colleges and universities, and the rate of hospitals and clinic per population and habitual prefectural area.

We have great concern as to which factor influences the regional differences of good cerebral function after OHCA. The most significant factor was "Rate of arrests to recognitions of criminal offenses" (safety), which means security in the communities and also seems...
to imply good communication in the communities to keep the community safe. Okubo, et al. demonstrated regional variation in favorable outcomes after OHCA using the hierarchical model; however, the suitable variables were still not demonstrated among cases with OHCA [10]. Buick, et al. studied the measures of poverty, ethnicity, instability, crime rate, and the density of family physicians as neighborhood variables using hierarchical logistic regression analysis, and only census tracts with a moderate ethnic concentration had an increased likelihood of survival-to-hospital charge [25]. We could select several variables that have correlation with GCFR itself.

The four top variables belonged to diverse fields that were safety, daily time, population and households and dwelling (Table 2). The second variable, “Average time of primary activities among 25- to 34-year-old females” is supposed to be related to allowance and richness. In fact, the four explanatory variables are interesting but much complicated, therefore, further studies would require medical and sociological analyses.

We often postulate the relationship between explanatory variables and outcome variables as a linear model when we use multiple logistic regression or multilevel analysis. We used the multiple regression analysis to demonstrate the relationship between GCFR and finally selected 16 social and demographic variables in this study. However, as the relationship would not always be linear, we need to clarify the nonlinear relationship between exposures and outcomes using methods of machine learning or deep learning.

**Limitations of the Study**

This method explored the significant factors from many social and demographic variables; however, it did not imply the causality of OHCA and the factors in this study. After meaningful and proper variables were chosen from among the social and demographic variables, multivariate analysis such as multilevel analysis would be required to prove regional property.

Principal component analysis is often used for multiple variables in sociology and psychology, and the statistical method helps the reduction of variables. We used a combined conventional method of correlation coefficient and $R^2$ to exclude many variables in this study. However, as far as we have surveyed, we could find no reports that described the selection of regional factors from many social and demographic variables among patients with OHCA.

**Conclusion**

We selected five social and demographic variables related to good cerebral function after OHCA from the Utstein database. The selected variables were the age of arrests to recognitions of criminal offenses, the average time of primary activities among 25- to 34-year-old females, the rate of 0- to 14-year-old children, the rate of owned houses renovated to be earthquake resistant and the rate of reports of pregnancy.

The combination of correlation coefficient and $R^2_{adj}$ would contribute to the selection of regional factors from the many variables in the large-scale database.

**Conflicts of Interest**

There were no conflicts of interest through the development of this study.

**Authors’ Contributions**

Kuboyama helped in the study concept, drafting of the manuscript, and design. R. Sagisaka helped in the acquisition of data. S. Ito helped in the statistical analysis. E. Saito helped in the interpretation of data. S. Toyokawa helped in correcting the manuscript. All authors read and approved the final manuscript.

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Bibliography


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