Article

Association between accessibility to emergency cardiovascular centers and cardiovascular mortality in Japan

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Abstract

Objective: The aim of this study was to examine the association between accessibility to cardiovascular emergency centers and cardiovascular mortality in Japan.

Design: A semi-ecological study.

Setting: Three databases were generated: accessibility to emergency cardiovascular centers, population records and death records.

Main Outcome Measures: The standardized mortality ratio (SMR) for cardiovascular disease was adjusted by age and sex. Accessibility was represented by transfer time, number of cardiovascular emergency hospitals, and the proportion of habitable areas. Combinations of the three were divided into Categories 1–8 from the worst to the best, and the association with SMR was analyzed.

Results: There were 1998 cardiovascular emergency hospitals. The median of crude mortality was 0.16%. The median SMR of the reference Category 8 (transfer time <30 min and habitable area ≥50% with cardiovascular emergency hospitals) was 0.96, but that of the low accessibility Category 1 (transfer time ≥30 min and habitable area <50% without cardiovascular emergency hospitals) was 1.10. The SMR of accessibility Category 1 : Category 8 was 1.18 (95% confidence interval: 1.14–1.21).

Conclusions: Decreased accessibility to cardiovascular emergency hospitals was associated with increased SMR. Areas with less accessibility and higher cardiovascular mortality were characterized by geographical variability in Japan.

Key words: emergency medical system, cardiovascular mortality, accessibility
Introduction

Long transfer time to cardiovascular emergency (CE) centers may cause pre-hospital delay for patients with time-sensitive conditions, such as acute myocardial infarction (AMI). Emergency treatment of acute coronary syndrome has advanced in recent years, especially in cardiac care units (CCUs), and the in-hospital mortality rate of AMI has decreased to <10% in Japan [1]. However, delays between the onset of AMI and admission to hospital remain a problem. Immediate treatment of patients is important to improve prognosis, especially in patients with AMI [2–4]. Emergency medical systems (EMSs) play an essential role in minimizing time from onset of the disease to the administration of reperfusion therapy in a CE center. In Japan, EMS and CE centers are present in all areas and provide universal health coverage; however, patient accessibility to CE centers differs by region. There is little information regarding the association between accessibility to CE centers and patient outcomes. Therefore, our goal was to examine the association between accessibility to CE centers by EMS and cardiovascular mortality in Japan.

Methods

Study design and setting

The present study had a semi-ecological study design, in which individual-level data were collected on the basis of outcome and co-founders with exposure arising from another source [5]. It was challenging to capture all individual data on death and survival, and hospital accessibility in Japan. Data regarding mortality and the associated characteristics were collected individually, and data on accessibility were obtained using a database created as described below. Individual data were collected for each death and the mortality rate was subsequently calculated as the aggregated mortality in each area using population data. Three databases were used: death records, population records and the created database of accessibility to CE centers. Records of deaths from cardiovascular diseases from 2005 were obtained from the vital statistics of the Ministry of Health and Welfare, Japan. The cause of death was determined according to the International Classification of Diseases (ICD-10). The cases identified by ICD codes 100–109, 116–119 and 180–199 as circulatory system: acute rheumatic fever; chronic rheumatic heart diseases; pulmonary heart disease and diseases of pulmonary circulation; other forms of heart disease; diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified; and other unspecified disorders of the circulatory system were considered cardiovascular disease-related mortalities. The population data were taken from the national population census of 2005 conducted by the Ministry of Internal Affairs and Communications [6]. To generate the accessibility database, first, we identified hospitals with EMSs. Using the database of hospital information for Japan (Japan Medical Press, Inc., http://www.ijimippo.co.jp/k/index.php), we searched the words ‘cardiovascular’, ‘CCU’, ‘catheter’ and ‘emergency’. CE facilities were identified by the presence of the following words: (i) ‘CCU’ and (ii) ‘cardiovascular’, ‘catheter’ and ‘emergency’. We identified hospitals that were included on the list of cardiovascular training centers and related hospitals associated with cardiovascular training and certified by the Japanese Circulation Society (http://www.j-circ.or.jp/). Other combinations of these four search words were used to identify EMS. CE hospitals known to treat AMI with reperfusion therapy were identified in all areas of Japan. According to the training hospitals of the Japanese Circulation Society, board members of the Japanese Circulation Society carefully investigated identified hospitals in order to determine whether they had sufficient EMS capacity. We postulated that the strongest measurement of accessibility was transfer time to the hospital. We defined the average transfer time to the hospital for each area as: the time lapsed during transfer from a city center with a local public office to the nearest hospital in each area based on the shortest traffic route measured using an electronic map of MapPaint 2006 (Mapquest.co.jp). If a CE hospital was not present in the area, we searched the nearest hospital within neighboring areas. Annexation of the municipality area was adjusted in 2007. The islands were excluded.

These three databases were combined using an identifying number for each area. Mortality was calculated using the number of mortalities from the death record database and the number of populations from the population databases, for each area. For variables pertaining to accessibility, the number of CE hospitals and transfer times were derived from the accessibility database, while the habitable area was derived from the population database.

Outcome measures and data analysis

Accessibility was measured by transfer time, number of CE hospitals, and the percentage of habitable areas, which was obtained after subtracting the forest and lake areas from the total area [7]. Transfer time was divided by 30 min, because the mean transfer time to the hospital by emergency medical assistance was 33.4 min, in 2007 in Japan [8]. Considering the mean of the demographic statistics [7], a 50% cut-off was used to divide the habitable area. All measurements were obtained for each municipality. We categorized accessibility by the combination of CE hospitals (yes or no), transfer time (<30 or ≥30 min) and the percentage of habitable areas (<50 or ≥50%). In total, there were eight categories.

The aggregated, not individual, mortality in each area was calculated as the standardized mortality ratio (SMR) for cardiovascular mortality adjusted for age (≤14, 15–64 and ≥65 years) and sex [9]. The median SMR of each category was used. The association between accessibility and the log scale of SMR was calculated using a linear regression model weighted by the number of deaths in each area. To compare effects between the categories, we set the reference categories as existence of CE hospitals, lower transfer times, and larger habitable areas, because they showed the smallest value of median SMR. We then ordered Categories 1–8 from the worst (1) to the best (8) combinations. The SMR of Categories 1–7 to Category 8 (CE hospital = yes, transfer time <30 min and habitable area ≥50%) was estimated.

We further determined the effect of accessibility using different cut-off values for these three variables. The cut-off values were 0, 1 and 5 for hospital numbers; 30, 50 and 70 for percentage of habitable areas and 10, 30 and 60 min for transfer times. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Inc., Cary, NC, USA).

Results

We identified 1998 CE hospitals with widespread distribution in Japan. The map in Fig. 1 shows that there are more hospitals in the plains than in mountain areas. The analysis included 1864 regions. The median (interquartile range) transfer time was 13 min (range 4–32 min) and the median (interquartile range) percentage of the habitable area was 45% (range 24–82%). The median (interquartile range) of crude mortality was 0.16% (0.13–0.21%) for all regions (Table 1).

We further displayed accessibility on the map according to categories (Fig. 2). The distribution of accessibility was variable, similar to the geographical characteristics. There were 468 regions (25.1%) with CE hospitals, with transfer times <30 min, and with ≥50% habitable
There were 450 regions (24.1%) without CE hospitals, with transfer times \( \geq 30 \) min and with <50% habitable areas. The regions with CE hospitals (Categories 5–8) had better median SMR than the regions without CE hospitals (Categories 1–4). Low accessibility and median SMR increased concomitantly in each categorized subgroup. The reference category was 8 (transfer time <30 min and percentage of habitable area \( \geq 50\% \) with a CE hospital), and included 25% of regions. The median SMR of the reference category was 0.96. Conversely, the least accessible region (transfer time \( \geq 30 \) min and <50% of habitable area without a CE hospital) that included 24% of regions, had a median SMR of 1.18 (95% confidence interval [CI]: 1.14–1.21). The low accessibility categories showed a higher SMR than the reference category (transfer time \( \geq 30 \) min and percentage of habitable area \( \geq 50\% \) without a CE hospital, SMR of Category 2: Category 8 = 1.18, 95% CI: 1.09–1.27; transfer time <30 min and percentage of habitable area <50% without a CE hospital, SMR of Category 3: Category 8 = 1.16, 95% CI: 1.12–1.20; Table 2). There were only two regions in Category 5 (transfer time \( \geq 30 \) min and percentage of habitable area <50% with a CE

Figure 1 Distribution of cardiovascular emergency hospitals. Dots represent cardiovascular emergency hospitals.

Table 1 Regional characteristics

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>Interquartile range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>31 080</td>
<td>10 884–80 255</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>14 928.5</td>
<td>5225–39 300</td>
</tr>
<tr>
<td>Women</td>
<td>16 105.5</td>
<td>5657–40 669</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \leq 14 )</td>
<td>4180.5</td>
<td>1391–11 264</td>
</tr>
<tr>
<td>15–64</td>
<td>19 300.5</td>
<td>7335–52 749</td>
</tr>
<tr>
<td>( \geq 65 )</td>
<td>6927</td>
<td>2879–16 348</td>
</tr>
<tr>
<td>Area (ha)</td>
<td>10 888</td>
<td>3962–25 377</td>
</tr>
<tr>
<td>Habitable area (ha)</td>
<td>3952</td>
<td>1972–8163</td>
</tr>
<tr>
<td>Percentage of habitable area</td>
<td>0.45</td>
<td>0.24–0.82</td>
</tr>
<tr>
<td>Length of roads (km)</td>
<td>402</td>
<td>233–732</td>
</tr>
<tr>
<td>Area/length (ha/km)</td>
<td>24</td>
<td>10.8–50.0</td>
</tr>
<tr>
<td>No. of hospitals</td>
<td>0</td>
<td>0–1</td>
</tr>
<tr>
<td>Transfer time (min)</td>
<td>13</td>
<td>4–32</td>
</tr>
<tr>
<td>Distance (km)</td>
<td>5.9</td>
<td>1.8–15.6</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>0.16</td>
<td>0.13–0.21</td>
</tr>
</tbody>
</table>
hospital), and no region in Category 6 (transfer time ≥30 min and percentage of habitable area ≥50% with a CE hospital); thus, these categories were not compared with Category 8 for estimating the ratio.

Areas with an SMR >1.2 were highlighted on the map (Fig. 3). These regions are mainly distributed in low accessibility areas, such as mountains or peninsulas.

We further determined various patterns of accessibility with changing cut-off values for the number of CE hospitals (0, 1 and 5), percentage of habitable areas (30, 50 and 70%) and transfer times (10, 30 and 60 min) as presented in Supplementary Fig. S1. When using different cut-off values, a higher number of CE hospitals, a higher percentage of habitable areas and lower transfer times were all associated with lower mortality. The three patterns on the left in the figure show a higher SMR value, although these values were >1.15 only in the case of Table 2.

The relationship between accessibility and SMR was also analyzed according to sex, which showed no differences between the SMR per accessibility category by sex, and CIs overlapped (Supplementary Table S1). In the present study, the population was determined after excluding patients aged <18 years, because they are unlikely to benefit

<table>
<thead>
<tr>
<th>Category</th>
<th>Cardiovascular emergency hospital</th>
<th>Transfer time (min)</th>
<th>Habitable area (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>≥30</td>
<td>&lt;50</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
<td>≥30</td>
<td>≥50</td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>&lt;30</td>
<td>&lt;50</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>&lt;30</td>
<td>≥50</td>
</tr>
<tr>
<td>7</td>
<td>Yes</td>
<td>&lt;30</td>
<td>&lt;50</td>
</tr>
<tr>
<td>8</td>
<td>Yes</td>
<td>&lt;30</td>
<td>≥50</td>
</tr>
</tbody>
</table>

Figure 2 Distribution according to transfer time, the presence of cardiovascular emergency hospitals, and percentage of habitable areas. The gray scale from black to white represents the accessibility categories; 1, no cardiovascular emergency hospital, transfer time ≥30 min, habitable area <50%; 2, no cardiovascular emergency hospital, transfer time ≥30 min, habitable area ≥50%; 3, no cardiovascular emergency hospital, transfer time <30 min, habitable area <50%; 4, no cardiovascular emergency hospital, transfer time <30 min, habitable area ≥50%; 7, with cardiovascular emergency hospital, transfer time <30 min, habitable area <50%; 8, with cardiovascular emergency hospital, transfer time <30 min, habitable area ≥50%.
from reperfusion or, indeed, to experience a myocardial infarction. Results were similar for the analysis of the total population.

**Discussion**

Categories in regions with CE hospitals showed better median SMR than the categories without CE hospitals. In addition, low accessibility to CE hospitals was associated with an increased SMR.

Delays in the initiation of reperfusion therapy for AMI can be divided into two distinct periods: pre-hospital and in-hospital [10]. In the present study, we focused on pre-hospital delay. Pre-hospital delay can further be divided into decision delay and transportation delay. Khraim and Carey [10] previously categorized factors associated with pre-hospital delay, such as socio-demographic, contextual, cognitive, affective/psychological, behavioral and clinical factors. These factors are patient-dependent; therefore, these factors have a greater effect on decision delay times [10]. For transportation delays, the distribution of EMS hospitals and access to EMS systems were shown to be important. Regarding access to EMS, transport distance was not associated with survival, despite adjustment for potential patient-related confounders [11].

In the present study, we focused our analysis on accessibility, and the data revealed prolonged transfer times to a CE hospital. Areas with low accessibility were mainly distributed in mountainous areas or peninsulas. These characteristics were observed despite the fact that Japan has a healthcare system that includes free ambulance access and universal medical insurance coverage.

According to the geographical characteristics, the percentage of habitable areas is low in Japan (33%) compared with that in the USA (75%) and England (88%) [7, 12]. This should be taken into account in order to balance the efficiency and distribution of CE hospitals and access to EMS. Geography is important for establishing EMS efficiency [13, 14].

As indicated in Table 2 of the categorized regional characteristics on the SMR, the regions in categories with CE hospitals were associated with an increased SMR when the percentage of habitable area of the region is high. The region would have moderate transportation access, and it would be useful to accommodate a transfer system from neighborhoods to hospitals or to better distribute CE hospitals. When the percentage of habitable area of the region is low, mobile telemedicine would be a more efficient method to provide accessibility to CE hospitals than would the construction of a better transportation system within the region. To improve accessibility, the method should be implemented with regard to the characteristics of the region. Recently, challenges associated with the use of mobile tools [15] or transfer by helicopter have been reported [16] and the relationship between geographical characteristics and EMS has been investigated. The French administrative area of Aquitaine established a wide-area teleradiology network system in 1995, and it was evaluated by cost-minimization analysis [17]. In Australia, the cardiac Accessibility and Remoteness Index for Australia (ARIA) index was developed to address substantial inequity in access to cardiac services [18]. Using geographic information systems, an index was developed that combined the acute category—which measures the time from the emergency call to arrival at an appropriate medical facility via road ambulance—and the aftercare category, which measures access to four basic services when patients return to their community. The effect of the pre-hospital electrocardiogram on reducing hospital time delays was investigated by the Cincinnati Heart Project [19]. It would be necessary to enhance these mobile tools, transfer by hospital, and such an index of accessibility in inaccessible areas.

Another approach was the public reporting of hospital performance, which was used in a program of the Lazio region in Italy, and showed improvement for AMI outcomes [20].

**Limitations**

The present study has a semi-ecological design; therefore, the data may be subject to ecological bias. The inference is based on aggregated mortality and accessibility, and could differ from individual data. Furthermore, we did not consider individual disease severity, hypertension, diabetes, heart failure, medical history, income [21] and access to healthcare.

Processes of care [22], such as the availability of a 24-h catheterization laboratory and the number of percutaneous coronary interventions performed at a given facility, were not considered in this analysis. However, because hospitals were carefully selected for designation as CE hospitals, these factors should be minimally influential.

The average transfer time was estimated using an electronic map; therefore, this estimate did not reflect the actual individual transfer time. Average transfer time was calculated as time from a city center with a local public office to the nearest hospital in each area, regardless of the shape of the geographical area or the location of the hospital. Accurate measurement of transfer time would require collecting all transfer data in Japan. In addition, the transfer time was calculated according to hospital addresses in 2007, which may not match those in the year 2005.

In the present study, we investigated transfer times as patient-related factors. However, in-hospital factors such as waiting time [23] and walk-in access [24] were not considered.
We evaluated full population-based mortality, neither in-hospital mortality nor out-of-hospital mortality. Analysis of only out-of-hospital mortality would not allow consideration of those cases that were severe upon admittance that were caused by poor access. Analysis only of in-hospital mortality would not consider the out-of-hospital death caused by poor access. The best strategy is to evaluate mortality using the individual data of in/out-of-hospital, transfer time and the volume of CV procedures in patients transferred from hospital with a good representation of the Japanese population. However, it is very difficult to obtain the individual data. So we used three databases with selected CE hospitals, aggregated mortality, without considering in/out-of-hospital. We thought it valuable to evaluate the effects of accessibility on nationwide mortality despite these limitations. Further research is needed to determine the effect of accessibility to CE centers on cardiovascular mortality in more representative areas and populations in Japan.

Conclusions
Low accessibility was associated with increased SMR. The areas with low accessibility and high mortality were characterized by geographical...
variation, despite the universal coverage of the medical insurance system in Japan. These variations should be taken into account in order to make EMS more effective, including the special transfer systems using helicopter emergency medical service and mobile telemedicine.

Supplementary material
Supplementary material is available at International Journal for Quality in Health Care online.

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