Impact of Diabetes Mellitus (DM) on the Health-Care Utilization and Clinical Outcomes of Patients with Stroke in Singapore

Yan Sun, PhD, Matthias Paul Han Sim Toh, MBBS, MMED(Public Health), FAMS (Singapore)
Department of Health Services & Outcomes Research, National Healthcare Group, Singapore

ABSTRACT

Objective: This study aims to assess the impact of diabetes mellitus (DM) on the health-care utilization and clinical outcomes of patients with acute stroke.

Methods: This is a retrospective cohort study. All patients who were admitted for the first time to one of the three public hospitals in the National Healthcare Group in Singapore from January 2005 to June 2007 with a primary diagnosis of acute stroke were included and were followed up for 1 year after the index hospitalization. The study population was divided into two groups: with DM and without DM. Both univariate and multivariate analyses were applied to compare the hospital length of stay (LOS), hospitalization costs, mortality, as well as the 1-year hospital readmissions between the DM and non-DM groups.

Results: There were 9766 study patients, and 38.5% of them had DM. DM patients with ischemic stroke (IS) and transient ischemic attack (TIA) stayed 1-day and 0.6-day longer, and incurred 10% and 26% higher hospital cost during index admission, respectively, compared with their counterparts in the non-DM group. They also had more hospital readmission within 1 year. The mortality rate in IS patients with diabetes was 24% higher. After risk adjustment, subarachnoid hemorrhage patients with diabetes had more hospitalizations. Intracerebral hemorrhage (ICH) and IS patients in the DM group had all worse outcomes but the 1-year stroke recurrence; TIA patients with DM incurred longer LOS and hospital costs.

Conclusion: DM predicts worse clinical outcomes and higher health-care expenditures in the 1-year poststroke especially for the IS, ICH, and TIA stroke subtypes.

Keywords: clinical outcomes, diabetes mellitus, health-care utilization, stroke.

Introduction

Stroke is one of the leading causes of mortality and morbidity in developed countries. Diabetes mellitus (DM) is a well-recognized risk factor for ischemic stroke (IS) [1,2]. The significance of DM as a risk factor for hemorrhagic stroke could differ depending on ethnicity [1,2]. DM has been independently associated with some forms of large artery disease and with small artery infarctions detected by neuroimaging studies [1–4]. DM significantly increases the risk of stroke, but it is not clear how DM affects the clinical and functional outcomes. In some studies, stroke patients with DM were reported to be associated with reduced survival after stroke [5–9], worse clinical and functional outcomes, and more health-care utilization [6–9], but in some other studies, the impact was not significant [10,11].

Stroke is the fourth leading cause of death and hospitalization, as well as the biggest cause of long-term disability in Singapore [12,13]. According to the Singapore National Health Survey in 2004, the prevalence rate of DM in the whole population was about 8.2%, and the rate was 17.9% in the population aged 40 years [14]. There are about 10,000 stroke incidences annually, and more than 30% stroke patients also have DM [13]. It is not known how DM affects the health-care utilization and clinical outcomes of stroke patients in Singapore.

The objective of this study is to assess the impact of DM as a comorbid condition on the health-care utilization (hospital length of stay [LOS] and cost of the index hospital admission, and total cost of hospital admissions within 1 year of the index admission due to any reason other than DM and its related complications) and the clinical outcomes (mortality of index admission, 1-year hospital readmission rate due to stroke recurrence, and 1-year hospital readmission due to any reason other than DM or DM-related complications) among patients hospitalized with different subtypes of acute strokes in Singapore.

Methodology

Study Design

This is a retrospective cohort study. In Singapore, the National Healthcare Group (NHG) is one of the two public health-care delivery clusters that manage three acute hospitals, several specialty centers, and nine primary care clinics serving a population of 2.2 million. Patients admitted to one of the three public hospitals in the NHG in Singapore from January 2005 to June 2007 with a primary diagnosis of acute stroke were included and followed up for 1 year. Patients who had any previous admission during year 2000 to 2004 with a primary or secondary diagnosis of acute stroke were excluded from the study. Study patients were categorized into four stroke subtypes based on the primary diagnosis coded by ICD9CM: subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), IS, and transient ischemic attack (TIA).

Data Collection

Records of study patients’ hospitalization were extracted from the hospital administrative databases. These included the index admission (first admission due to stroke) and all the subsequent admissions within 1 year of the index admission because of stroke recurrence or any cause other than DM and DM-related complications that were identified by ICD9CM codes of 250.*
The main outcomes of this study were the LOS, cost of the index hospital admission, total cost of all hospital admissions (including index admission), the mortality of index admission, readmission due to stroke recurrence, and readmission due to any reason other than DM and its complications. The LOS was extracted from the hospital billing database, and the cost was from the NHG’s financial database, which had been standardized across different hospitals using the same unit price on each service and consumable item. Costs in this study were from health care provider’s perspective. Important variables included patient demographic characteristics of race, sex, age, and residential status; stroke subtype; all causes of hospital admission within 3 months before index admission (yes or no); presence of comorbid conditions, in particular, hypertension, dyslipidemia, atrial fibrillation or flutter (AFF), and ischemic heart disease (IHD); and DM. All these factors except DM were controlled as confounders in the multiple regression models.

Statistical Analysis
The study population was divided into two groups for comparison: patients with DM (history of DM or fasting plasma glucose level of >7.0 mmol/L) and patients without DM. For univariate analysis, nonparametric Mann–Whitney U and chi-square tests were applied to compare the differences in outcomes between the two groups.

Health-care utilization that consisted of LOS and costs of the hospitalizations (from hospital’s perspective) were compared using generalized linear models (GLMs) with gamma distribution and log link because the data were highly skewed to the right. GLM is an extension of the linear modeling process that allows models to be fitted to data that follow probability distributions other than the normal distribution. The exp(B) estimated from the model represents the odds ratio (OR) of the outcomes in the DM group, with the non-DM group as reference. Ninety-five percent confidence interval (CI) of the OR was also reported.

Cox proportional hazards models were used to estimate the relative risk (RR) of mortality in hospital (with discharged alive from hospital as the censoring event and death during hospital stay as the event of interest), the RR of the 1-year readmission due to stroke recurrence, as well as the RR of the 1-year readmission due to other reasons (only including patients discharged alive in the model, with no readmission as the censoring event and readmission as the event of interest) by adjusting the risk factors mentioned above. The maximum likelihood approach was used to estimate weights of the regression parameters. The exp(B) estimated from the model represents the RR of the outcomes in the DM group, with the non-DM group as reference. Ninety-five percent CI of the RR was also reported.

All statistical analyses were carried out using SPSS version 15 (SPSS, Chicago, IL). P-values <0.05 were considered as significant.

Results
There were 9766 patients admitted to the three hospitals with acute stroke during January 2005 to June 2007. Among them were 414 (4.2%) patients with SAH, 1567 (16.0%) with ICH, 6464 (66.2%) with IS, and 1321 (13.5%) with TIA (Table 1 shows the descriptive characteristics of the stroke patients with and without DM). The overall prevalence of DM among the patients with stroke was 38.5%. It was significantly higher for IS (44.4%) and TIA patients (33.8%) compared with ICH (25.0%) and SAH (12.6%) patients ($P < 0.001$ by chi-square test). With the exception of IS, the mean ages of patients with DM were higher than non-DM patients for SAH, ICH, and TIA. Overall,
there were more males than females, except in SAH where the females largely outnumbered the males. The ethnic distribution of stroke patients was similar to the profile of the general population in Singapore: Chinese (75.2%), Malays (13.6%), Indians (8.8%), and others (2.4%). There was, however, disproportionately more Malays and Indians among the patients with DM compared with the non-DM group. For all stroke subtypes, the prevalence of hypertension, dyslipidemia, and IHD was higher in the DM group. They were also more likely to be admitted to a hospital during the 3 months preceding the acute stroke event. Table 2 compares the outcomes by type of stroke.

For IS and TIA, the average LOS, cost of index admission, and total 1-year hospitalization costs of patients with DM were significantly higher \( (P < 0.001) \) than non-DM patients. For average LOS, DM patients with IS and TIA stayed 1-day and 0.6-day longer, respectively, than non-DM patients. DM patients with IS and TIA were 10% and 26% higher in cost of index admission than the non-DM patients, respectively. There was, however, no significant difference in health-care utilization in both SAH and ICH.

SAH patients with DM had a lower mortality rate by 10% compared with non-DM patients, whereas the rate in IS patients with DM was about 24% higher than patients without DM. The mortality rate among TIA patients was very low; 0.1% among non-DM patients and 0.4% among DM patients. For IS and TIA, patients with DM were significantly more likely to have stroke recurrence within 1 year. This was not evident for patients with hemorrhagic stroke. The 1-year rehospitalization rates due to any reason other than DM and its related complications ranged from 30.7% to 78.4%. They were significantly higher in patients with DM than non-DM patients for all stroke subtypes except in ICH, which was marginally higher. Table 3 compares the outcomes of the DM group with the non-DM group (reference) by multivariate analyses.

After adjusting for the confounding factors of age, sex, race, residential status (resident or not), previous admission (yes or no), and comorbid conditions of hypertension (yes or no), dyslipidemia (yes or no), AFF (yes or no), and IHD (yes or no), the DM group had significantly poorer outcomes than the non-DM group for all types of stroke. DM patients with IS and TIA had 20% and 17% longer LOS, respectively. ICH, IS, and TIA patients with DM incurred higher cost during the index admission. The total 1-year hospital expenditures incurred by ICH, IS, and TIA patients with DM were 32%, 31%, and 48% higher than the non-DM patients, respectively.

The mortality rates during index admission for ICH and IS patients with DM were significantly higher than non-DM patients. The adjusted RR for ICH was 1.37 (95% CI 1.07–1.76), and IS was 1.44 (95% CI 1.16–1.79). Because the mortality of TIA patients was very low, TIA patients were excluded from the multiple analysis of mortality. The RRs of stroke recurrence in all stroke subtypes were not significantly different between both groups. With the exception of TIA, the RRs for readmission within 1 year were significantly higher in patients with DM than in patients with non-DM, with the highest for SAH \( (P < 0.001) \) and TIA patients with DM were 32%, 31%, and 48% higher

### Discussion

Stroke is one of the common macrovascular complications among patients with DM. In several studies around the world, the prevalence of DM among stroke patients was reported to be 6% to 23% \[5–11\]. In our study, the overall prevalence of DM was as high as 38.5%, contributed mainly by patients with stroke of ischemic origin. The stroke patients with DM had significantly

<table>
<thead>
<tr>
<th>Type of stroke</th>
<th>Without DM</th>
<th>With DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS (days)</td>
<td>Mean</td>
<td>15.7</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>9.6</td>
</tr>
<tr>
<td></td>
<td>1-year cost ($5)</td>
<td>27,477</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>9.95</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>6.25</td>
</tr>
<tr>
<td></td>
<td>Total 1-year cost ($5)</td>
<td>1,497</td>
</tr>
<tr>
<td>Mortality rate (%)</td>
<td>Without DM</td>
<td>29.3</td>
</tr>
<tr>
<td></td>
<td>Without DM</td>
<td>25.3</td>
</tr>
<tr>
<td></td>
<td>With DM</td>
<td>26.9</td>
</tr>
<tr>
<td>1-year recurrence rate (%)</td>
<td>Without DM</td>
<td>7.0</td>
</tr>
<tr>
<td></td>
<td>With DM</td>
<td>8.5</td>
</tr>
<tr>
<td>1-year readmission rate (%)</td>
<td>Without DM</td>
<td>41.6</td>
</tr>
<tr>
<td></td>
<td>With DM</td>
<td>38.4</td>
</tr>
</tbody>
</table>

**Table 2** Univariate comparison of outcomes of patients with and without diabetes mellitus (DM) by type of stroke.
higher prevalence of dyslipidemia and hypertension compared with non-DM patients ($P < 0.001$ by chi-square tests). DM is a well-established risk factor for IS and TIA, and a marginal risk factor for ICH [1,2]. Hence, early screening and optimal control of cardiovascular risk factors, including blood pressure, cholesterol, and blood glucose levels, are essential to prevent stroke.

The RR of mortality in patients with DM was higher than in non-DM patients, 44% higher in IS and 37% higher in ICH. This association however was not evident in SAH. These results were consistent with findings in other studies [5–8].

The average LOS of the index admission for patients with DM was 20% and 17% longer for IS and TIA, respectively, compared with those without DM, and in ICH, it was marginally longer by 13% ($P = 0.06$). These results were consistent with reports in other studies [5,6]. Lithner et al. [6] reported that 4 days after hospital admission, more stroke patients with DM than without DM were still confined to bed. DM may affect the rate of recovery of the neurological function after a stroke. With a longer LOS, the cost of index admission was also correspondingly higher, likely because of additional treatment of DM or its related complications and more clinical interventions.

In this study, we did not find an association that DM increases the risk of early stroke recurrence within 1 year in patients with the four types of stroke. In the Copenhagen Stroke Study [5], although patients with DM were noted to recover more slowly than patients without diabetes, the amount of neurological deficit at hospital discharge was equivalent between the two groups. This may explain why the stroke recurrence rate was not affected by DM even though the hospital LOS was longer than patients without DM.

Readmission rates to hospital within 1 year of acute stroke for reasons other than DM or its related complications were significantly higher in both hemorrhagic stroke and IS patients with DM compared with those without DM, after adjusting for confounding factors. The top three reasons for readmission were cardiovascular disease, pneumonia, and urinary tract infection (UTI). A possible explanation could be that the patients with DM had a higher prevalence of cardiovascular risk factors such as hypertension, dyslipidemia, and IHD, and being diabetic made them more prone to develop chest pain and UTI, requiring a hospital admission. The costs of subsequent hospitalizations in 1 year were significantly higher in DM patients with ICH, IS, and TIA.

There were several limitations with this study involving the use of administrative data. We were only able to extract and compare the comorbid conditions of patients that were recorded during the hospital stay. The clinical parameters indicative of the stroke severity at onset and the functional status of patients before or after their stroke could not be compared. Smoking status, lifestyle practices, degree of obesity, and socioeconomic factors that may affect the outcome of stroke patients could not be adjusted in this study. Some patients might be lost to follow-up when they sought treatment at other hospitals outside the NHG or in other countries. It would be ideal if the study period be extended to study health-care utilization and clinical outcomes of patients over a longer period of time.

### Conclusion
Stroke is a major cause of morbidity and mortality in Singapore. This study showed that by having diabetes as a comorbid condition, patients with IS, TIA, and ICH had higher mortality, stayed longer initially in hospital, and incurred higher hospitalization costs in the year after index admission compared with their counterparts without diabetes. All stroke patients with DM except TIA are more likely to be hospitalized in the first year poststroke.

It is important to identify and treat medical complications early in an attempt to reduce the morbidity and mortality associated with stroke. This is especially pertinent for patients with...
DM. Future studies and specific interventions could be more targeted to reduce the mortality and readmissions associated with stroke patients with DM.

Source of financial support: None. Yan Sun and Matthias Paul Han Sim Toh have no conflicts to declare.

References