Mortality and Causes of Death in a National Sample of Diabetic Patients in Taiwan

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OBJECTIVE — To determine the mortality rate, causes of death, and standardized mortality ratio (SMR) in Taiwanese diabetic patients.

RESEARCH DESIGN AND METHODS — A cohort of 256,036 diabetic patients (118,855 men and 137,181 women, aged 61.2 ± 15.2 years) using the National Health Insurance were assembled during the years 1995–1998 and followed up to the end of 2001. Deaths were verified by indexing to the National Register of Deaths. Underlying causes of death were determined from death certificates coded according to the ninth revision of the International Classification of Diseases. The general population of Taiwan was used as reference for SMR calculation.

RESULTS — With a total of 1,124,348.4 person-years of follow-up, 43,888 patients died and the crude mortality rate was 39.0/1,000 person-years. Mortality rates increased with age, and diabetic men had a significantly higher risk of death than women. However, mortality rate ratio for men versus women attenuated with increasing age. The overall SMR was 1.63 (1.62–1.65), and SMRs also attenuated in the elderly. Causes of death ascribed to diabetes; cancer; cardiovascular diseases; accidents; and suicide were 28.8, 18.5, 9.0, 10.5, 0.3, 4.8, 6.4, 7.9, 3.2, and 0.8%, respectively.

CONCLUSIONS — Approximately 71.2% of the diabetes-related deaths would not be ascribed to diabetes on death certificates in Taiwan. The diabetic men have higher risk of dying than women, and diabetic patients have excess mortality when compared with the general population. For underlying causes of death not listed as diabetes, total cardiovascular death, including cardiopulmonary disease, stroke, and disease of arteries, arterioles, and capillaries, is the most common cause of death, followed by cancer.

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Although diabetic patients have an excess risk of mortality in other races and ethnic groups (1–7), data on diabetes-related mortality are limited in Taiwan. A study using data of vital statistics demonstrated that mortality ascribed to diabetes has increased 6.3-fold from 1960 to 1988 in Taiwan. Because diabetes is rarely mentioned as a cause of death on the death certificates of diabetic patients (1,4,9,10), vital statistics unavoidably underestimate the impact of diabetes-related death. Longitudinal follow-up of a cohort of diabetic patients will surely provide more information than using the data. Therefore, the purpose of this study was 1) to determine the mortality rate and causes of death in a national sample of known diabetic patients covered by the National Health Insurance (NHI) in Taiwan and 2) to assess standardized mortality ratios (SMRs) compared with the general population.

RESEARCH DESIGN AND METHODS — The study was approved and supported by the Department of Health, Executive Yuan, Republic of China. Because >96% of the total population of Taiwan is covered by the compulsory and universal NHI since March 1995, almost all diabetic patients have been using the NHI (12). Most diabetic patients receive their care in hospitals, and a diabetic patient will visit the outpatient clinic on average 35.8 times per year for any cause (13). Therefore, the hospitals’ databases for NHI claims are appropriate for deriving a national sample of diabetic patients. To assemble such a cohort, 66 hospitals distributed evenly across Taiwan were selected to participate in the recruitment. All of these hospitals provided the basal demographic data of all patients with a diagnosis of diabetes who submitted claims to the NHI for every month for 1 year. The diagnosis of diabetes was defined by the ninth revision of the International Classification of Diseases (ICD)-9 code 250 or the A-code...
Mortality in diabetic patients in Taiwan

Table 1—Age- and sex-specific mortality rates (per 1,000 person-years) and SMRs and mortality rate ratios for the diabetic men versus diabetic women

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Deaths</td>
</tr>
<tr>
<td>&lt;45</td>
<td>16,506</td>
<td>1,009</td>
</tr>
<tr>
<td>45–49</td>
<td>9,717</td>
<td>894</td>
</tr>
<tr>
<td>50–54</td>
<td>12,053</td>
<td>1,244</td>
</tr>
<tr>
<td>55–59</td>
<td>11,933</td>
<td>1,833</td>
</tr>
<tr>
<td>60–64</td>
<td>14,595</td>
<td>2,698</td>
</tr>
<tr>
<td>65–69</td>
<td>15,659</td>
<td>3,635</td>
</tr>
<tr>
<td>70–74</td>
<td>16,829</td>
<td>4,119</td>
</tr>
<tr>
<td>≥75</td>
<td>21,563</td>
<td>7,421</td>
</tr>
</tbody>
</table>

Data are SMR (95% CI) or MR ratio (95% CI), unless noted otherwise. MR, mortality rate.

(abridged code) of A181. Since the claim data included both inpatients and outpatients, it was believed that this recruitment procedure would not tend to select sicker patients. Although it is not easy to answer the question of sensitivity/specificity of this approach, both sensitivity and specificity were believed to be good for the following reasons: hospitals would tend to report all cases of diabetes in the claim data if the patients had diabetes in order to get better reimbursement and false report of diagnosis would face severe penalty from the Bureau of NHI.

Because the claim data were compiled every 1 month, there might be overlapping cases in the same hospitals in different months or the same case might appear in different hospitals. These cases were identified by using a unique identification number. The earliest date he or she appeared in the claim data was used as the date of entry into the study. This recruitment process began on 1 November 1995 and ended on 31 December 1998. All of the patients were then followed until the end of the year 2001.

The date and cause of death for a person was obtained by matching the computerized data file of the National Register of Deaths with an identification number. Because the contributing causes of death were not available in either the annual report or computer file, only the underlying cause of death was used for analyses in this study. The causes of death in the government computer files have been coded according to ICD-9 since 1981 (14).

Mortality rates were computed using a person-years denominator. The person-years of follow-up for each patient were calculated as the duration from the date of recruitment until the end of 2001 for those who were alive or to the date of death for those who died. Age- and sex-specific mortality rates were calculated, and the mortality rate ratios and their 95% CIs for men versus women in each stratum of age were estimated by Cox proportional hazard models.

Standardization was applied to compute the SMR using data for the Taiwan area (average of 1995–2001 midyear population) as the standard population. Byar’s approximation was used to calculate the 95% CIs for SMRs (15). Specific causes of death were classified into the following categories according to ICD-9 codes: diabetes (250), cancer (140–208), cardiopulmonary disease (401–429), stroke (430–438), disease of arteries, arterioles, and capillaries (440–448), nephropathy (580–589), infection (001–139, 320, 321, 326, 421, 460–466, 480–487, 510, 513, 531, 567, 590, 599, 680–686, 711, 730), digestive diseases (520–579, excluding 551), accidents (800–949), suicide (950–959), other causes (codes other than the above), and all causes.

RESULTS—At the end of recruitment, there were 256,036 diabetic individuals (118,855 men and 137,181 women). The mean age (±SD) of the patients was 61.2 ± 15.2 years.

With a total of 1,124,348.4 person-years of follow-up, 43,888 patients died and the crude mortality rate was 39.0/1,000 person-years. The age- and sex-specific mortality rates and SMRs and the mortality rate ratios for men versus women in each stratum of age are shown in Table 1. The mortality rates in the diabetic patients were age dependent, which increased from 14.1 to 86.3 per 1,000 person-years in patients aged <45 to ≥75 years, respectively, in the diabetic men and from 4.5 to 77.8 per 1,000 person-years in the diabetic women. Furthermore, the mortality rate ratios suggested a higher risk of mortality in the diabetic men. However, this sexual difference in mortality risk attenuated with increasing age. Excess mortality in the diabetic patients relative to the general population can be demonstrated by SMRs. A greater SMR in the diabetic men than in the diabetic women was observed in patients aged <45 years; and on the contrary, SMRs were greater in the diabetic women than the diabetic men in the older age-groups.

The observed numbers and percentages of specific causes of death and the SMRs for each specific cause and all causes of death by sex are shown in Table 2. Diabetes was listed as the underlying cause of death in about one-fourth and one-third of diabetic men and women, respectively. If diabetes was not considered as an underlying cause of death, then cancer was the most common cause of death in both sexes. However, if we considered deaths ascribed to cardiopulmonary disease, stroke, and disease of arteries, arterioles, and capillaries together as total cardiovascular deaths, then cardiovascular deaths would be ranked as the most common cause of death (19.8%) in all patients. For both sexes, the proportions ascribed to stroke were slightly greater than those ascribed to cardiopulmonary disease, and the proportions ascribed to disease of arteries, arterioles, and capillaries were actually small. Except for disease of...
CONCLUSIONS — By using cohort data of diabetic patients from the hospitals claim database of the National Health Insurance Program (NHI) of Taiwan, the demographic, cardiovascular, and cancer death rates and risks for diabetic patients were assessed. The results of these analyses were similar to those of other studies. In the Asian-Pacific region, including Taiwan, the mortality rates of diabetic patients were generally higher than those of non-diabetic persons. Diabetes is a more common cause of death than stroke in most Western countries, but in Asia-Pacific regions, including Taiwan, diabetes is a more common cause of death than heart disease. In the U.S. (1), and in 49.1% of the death certificates, diabetes was listed as the underlying cause of death. In Table 1 were shown the excess mortality with age in the diabetic patients (Table 1) was also higher risk of mortality than the general population from any of the specific causes of death listed in Table 2, as demonstrated by SMRs, and the rates for the diabetic women were higher risk of mortality than the general population from any of the specific causes of death listed in Table 2, as demonstrated by SMRs. Although the proportions ascribed to nephropathy were relatively small in both sexes, the excess mortality shown by the SMRs was greatest among all causes, except diabetes.
stroke as a more common cause of death than coronary heart disease in Asian ethnicities of the western world, but the contribution of other risk factors, such as socioeconomic status, obesity, glycemic control, hypertension, and hyperlipidemia, etc., cannot be excluded. In the present study, if deaths ascribed to cardiopulmonary disease, stroke, and disease of arteries, arterioles, and capillaries were taken together to represent total cardiovascular death, then the proportion was 19.8% (a figure close to the proportion of 18.5% for cancer) among all causes of deaths (Table 2). Diabetes was ascribed to 28.8% of the causes of death in the present study (Table 2). It was neither easy to discern how these patients died nor could we judge what proportion among these patients could be ascribed to a cardiovascular death. However, the patients in this category were less likely to die from cancer than a cardiovascular disease because cancer would be much easier to recognize and code as an underlying cause of death in death certificates if a patient with cancer died. If we considered all of these patients as dying from cardiovascular death, this would sum up to 48.6% of all deaths, a figure that would be close to the reported underlying cause of death in 49.4% in the U.S. (1) and in 49.1% in the U.K. (4). Thus, cardiovascular disease could be the most common cause of death in diabetic patients. However, whether a lesser proportion of our diabetic patients would die from cardiovascular disease when compared with that of the diabetic patients in the U.S. or U.K. is an issue requiring further investigation. The finding that only a small proportion (0.3%) of the causes of death ascribed to disease of arteries, arterioles, and capillaries in diabetic patients was consistent with the findings that the prevalence of peripheral vascular disease (20) and diabetic foot problems (21) were not as commonly seen as in Caucasians.

It was interesting to observe that diabetes was listed as an underlying cause of death in a higher proportion of women than men (Table 2). This could possibly suggest that more diabetic men might have suffered from other causes of death that were easily recognized clinically and would be entered on the death certificates, such as cancer. However, other possibilities could not be excluded.

Underreporting of diabetes as an underlying cause of death on death certificates is very common. In the present study, ~71.2% of diabetic patients in Taiwan will not have diabetes recorded as an underlying cause of death (Table 2). An early study (9) showed that only 12.5% of all death certificates in diabetic patients listed diabetes as an underlying cause and that diabetes was not mentioned on 51% of death certificates in diabetic patients. A recently published study (1) reported that diabetes was listed as the underlying cause of death for only 7.7% of diabetic men and 13.4% of diabetic women. Diabetes might not be recognized at the patient’s death, and thus it was not listed on death certificates. Another reason was that a diabetic patient could die of a cause unrelated to diabetes, such as cancer. Moreover, diabetic patients could die from other chronic diseases frequently associated with diabetes, such as ischemic heart disease, stroke, and renal disease.

The excess mortality ascribed to nephropathy was highest (if diabetes was not considered as an underlying cause of death) in our diabetic patients in both sexes (Table 2), suggesting that our diabetic patients are more prone to develop severe kidney diseases that lead to death. Excess mortality ascribed to other causes, such as cancer, infection, digestive diseases, accidents, and suicide, were all observed in our diabetic patients (Table 2). Further detailed analyses are required to explore the association between these causes and diabetes.

The strengths of this study include a large and national sample of diabetic patients and the use of national register data to allow for complete ascertainment of death cases. However, several limitations should be pointed out. First, it is not possible to make a distinction between type 1 and type 2 diabetes in this study. However, because more than one-half of the diabetes cases occurring in school-age children were of type 2 diabetes (22) and only a small proportion (<3%, data not published) of the diabetic patients had type 1 diabetes in Taiwan, it is believed that the results largely reflect the mortality of type 2 diabetic patients. Second, this study did not examine mortality in undiagnosed diabetic patients. Third, the potential misclassification of some causes of death on death certificates cannot be ruled out.

Summary
In conclusion, our data support that diabetic patients have an excess mortality compared with the general population and that diabetic men suffer from a higher mortality rate than women. These observations are especially marked in younger patients. Cardiovascular disease could be the most common cause of death in diabetic patients, followed by cancer. Whether our diabetic patients suffer from a lesser proportion of death than that ascribed to cardiovascular disease, as seen in the U.S. or the U.K., requires further investigation.

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References


