Long-term Mortality Risk After Hyperglycemic Crisis Episodes in Geriatric Patients With Diabetes: A National Population-Based Cohort Study

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OBJECTIVE

Hyperglycemic crisis is one of the most serious diabetes-related complications. The increase in the prevalence of diabetes in the geriatric population leads to a large disease burden, but previous studies of geriatric hyperglycemic crisis were focused on acute hyperglycemic crisis episode (HCE). This study aimed to delineate the long-term mortality risk after HCE.

RESEARCH DESIGN AND METHODS

This retrospective national population-based cohort study reviewed, in Taiwan's National Health Insurance Research Database, data from 13,551 geriatric patients with new-onset diabetes between 2000 and 2002, including 4,517 with HCE (case subjects) (ICD-9 code 250.1 or 250.2) and 9,034 without HCE (control subjects). The groups were compared and followed until 2011.

RESULTS

One thousand six hundred thirty-four (36.17%) case and 1,692 (18.73%) control subjects died ($P < 0.0001$) during follow-up. Incidence rate ratios (IRRs) of death were 2.82 times higher in case subjects ($P < 0.0001$). The mortality risk was highest in the first month (IRR 26.56; 95% CI 17.97–39.27) and remained higher until 4–6 years after the HCE (IRR 1.49; 95% CI 1.23–1.81). After adjustment for age, sex, selected comorbidities, and monthly income, the mortality hazard ratio was still 2.848 and 4.525 times higher in case subjects with one episode and two or more episodes of hyperglycemic crisis, respectively. Older age, male sex, renal disease, stroke, cancer, chronic obstructive pulmonary disease, and congestive heart failure were independent mortality predictors.

CONCLUSIONS

Patients with diabetes had a higher mortality risk after HCE during the first 6 years of follow-up. Referral for proper education, better access to medical care, effective communication with a health care provider, and control of comorbidities should be done immediately after HCE.

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Hyperglycemic crises, a disease continuum of acute diabetes-related complications, include three subtypes: diabetic ketoacidosis (DKA), hyperosmolar hyperglycemic state (HHS), and mixed syndrome (both DKA and HHS as a mixed state of acidosis and hyperosmolality) (1). The basic underlying mechanism is the combination of insulin deficiency and an increase in counterregulatory hormones, viz., catecholamines, cortisol, glucagon, and growth hormone (2). Preventive care for adults with diabetes has improved substantially in the past two decades (3). The death rate for patients with hyperglycemic crisis declined 64.4% between 1990 and 2010 in the U.S.; however, a large burden of disease persists because of the continued increase in the prevalence of diabetes (3). Furthermore, despite the decreased death rate in the U.S., hyperglycemic crises remain a serious health problem in developing countries (1).

The prevalence of diabetes in the elderly is extremely high and growing. It is estimated that seven million people in the U.S. are elderly (≥65 years old) and that ~20.1% have physician-diagnosed diabetes (4). This is nearly four times the prevalence of diagnosed diabetes in all adults 20 years old and older (5.1%) (4). In addition, undiagnosed diabetes and prediabetes rates have been estimated to be 6.2% and 14%, respectively, in the group aged 60–74 years, which is more than twice the prevalence for all other adults (4). Overall, nearly half of the elderly are exposed to the risk of hyperglycemic crises. As people age, insulin secretory reserve, insulin sensitivity, and thirst mechanisms decrease, and the elderly are at a particularly greater risk for developing hyperglycemic crises (5).

Studies about geriatric hyperglycemic crises are scarce, and almost all are focused on acute episodes (4–7). The elderly have a higher mortality risk for hyperglycemic crises. Mortality rates for HHS range from 10% for those under 75 years of age to 19% for those 75–84 years old and 35% for those over 84 years old (8). Similar outcomes have been reported (9) for DKA: mortality rates of 8% for patients 60–69 years old, 27% for patients 70–79 years old, and 33% for patients older than 79 years. In a recent study, the overall mortality of hyperglycemic crises in the elderly was 14.7% (6). In 2013, Huang et al. (6) proposed that infection, absent tachycardia, cancer history, and severe coma are independent mortality predictors in geriatric patients with hyperglycemic crises. The mortality risk apparently rises with the number of independent mortality predictors: in the patients with all four predictors, 100% died, but in patients with none of the predictors, mortality was 0% (6). Poor compliance leading to uncontrolled diabetes is the most common precipitating factor of geriatric HCE, which suggests that close follow-up and secondary prevention after an HCE are crucial (6). The long-term effect of uncontrolled diabetes contributes to various complications, including death (2). However, the long-term mortality risk after HCE in geriatric patients with diabetes has never been clarified. We wanted to analyze a population-based cohort taken from Taiwan's National Health Insurance Research Database (NHIRD) to determine the long-term mortality risk of geriatric patients with diabetes after HCE.

RESEARCH DESIGN AND METHODS

Data Sources

The Taiwan National Health Insurance (NHI) program, launched in 1995, is a universal health care system that covers 99% of the country's population of 23.3 million (10). It has one of the largest and most complete population-based health care claim data sets in the world. The NHIRD contains encrypted patient identification numbers, ICD-9-CM codes for applied clinical diagnoses and procedures, details of prescribed drugs, dates of admission and discharge, and basic sociodemographic information, including sex and date of birth. All the expenses of HCE therapy are covered by NHI (but not hospital room and board). Data used in this study came from the Longitudinal Cohort of Diabetes Patients (LHDB) of the NHIRD, which contains randomized selected data (120,000 patients/year) from patients with newly diagnosed diabetes. The definitions of diabetes in the LHDB are as follows: *1*) inpatient, at least one hospitalization with a diagnosis of diabetes or a prescription for antidiabetes medication and *2*) ambulatory care, at least two visits with a diagnosis of diabetes or one visit with both a diagnosis of diabetes and a prescription for antidiabetes medication within a year. The criteria for the diagnosis of diabetes were *1*) symptoms of diabetes plus casual plasma glucose concentration ≥200 mg/dL (11.1 mmol/L), *2*) fasting plasma glucose ≥126 mg/dL (7.0 mmol/L), or *3*) 2-h oral glucose tolerance test ≥200 mg/dL (11.1 mmol/L) (11). There were no significant differences in age, sex, or health care costs between the sample group and all NHI enrollees.

Design

In this longitudinal cohort study, we selected all geriatric patients (≥65 years) in the LHDB who had been diagnosed with HCE (ICD-9 code: DKA, 250.1, or HHS, 250.2) between 1 January 2000 and 31 December 2002. The control subjects (two geriatric patients with a diagnosis of diabetes and without HCE for every geriatric patient with diabetes with HCE) were also randomly selected from the LHDB. The index date in the HCE group was the date that HCE was first diagnosed in the database and the index date in the control group corresponded with the index date of the HCE group so that mortality follow-up in both case and the control subjects began on the same date. Candidates for the control group who died before the HCE index date were deleted from the control candidate pool. The control subjects were matched with the HCE patients by the age at which diabetes was diagnosed (±30 days), duration between diabetes diagnosis date to HCE index date, sex, selected comorbidities, and monthly income by propensity score. Propensity-score matching was used to reduce selection bias because it can bundle many confounding covariates that may be present in an observational study with this number of variables. In our study, propensity scores were computed by modeling a logistic regression model with the dependent variable as the odds of diagnosis of HCE and the independent variables as the age at which diabetes was diagnosed (±30 days), duration between diabetes diagnosis date and HCE index date, sex, selected comorbidities, and monthly income. Afterward, an SAS matching macro "%OneToManyMTCH" proposed in the proceedings of the 29th SAS Users Group International was used in this study (12). It allows

propensity score matching from 1-to-1 to 1-to-*N* based on specification from the user. The macro makes "best" matches first and "next-best" matches next in a hierarchical sequence until no more matches can be made. Each control subject is selected at most once. The final matched-pair samples contain both closely matched individual pairs and balanced case and control groups. Figure 1 shows the selection and propensity score matching of the HCE and control subjects.

We linked to the diagnostic codes through the inpatient and ambulatory care claim databases of the NHI. Our data collection included not only the patients' survival status but also their date of death, demographics, baseline comorbidities, and monthly income. Baseline comorbidities affecting mortality that may have presented before the index date were defined as follows: hypertension (HTN) (ICD-9 codes 401–405), renal disease (ICD-9 codes 582, 583, 585, 586, and 588), coronary artery disease (CAD) (ICD-9 codes 410–414), stroke (ICD-9 codes 430–438), cancer (ICD-9 codes 140–208), chronic obstructive pulmonary disease (COPD) (ICD-9 codes 490–496, 500–505, and 5064), congestive heart failure (CHF) (ICD-9 code 428), and liver disease (ICD-9 codes 5712, 5714, 5715, 5716, 4560–4562, and 5722–5728). We counted these comorbid conditions if they occurred either in the inpatient setting or in three or more ambulatory care claims coded 12 months before the index medical care date. Patients were followed from the index date to the date of death or 31 December 2011, the end of the database period. According to the law, enrollment in the NHI is mandatory for all citizens and other legal residents of Taiwan, and it must be withdrawn within 30 days after death. Therefore, those patients recorded as deceased in the inpatient claim or as withdrawing their NHI enrollment within 30 days after being discharged from their last hospitalization were presumed dead, and the discharge date was designated as the date of death.

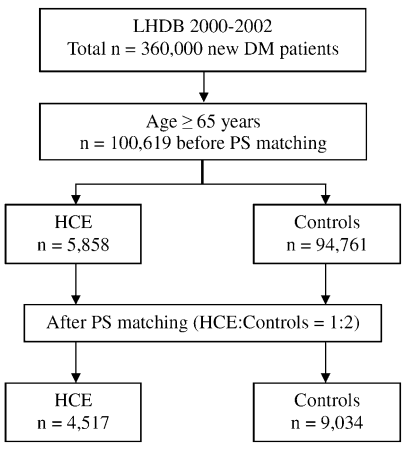

Figure 1—The selection and propensity score matching of the HCE and control subjects. DM, diabetes; PS, propensity score.

This study was conducted according to the Declaration of Helsinki and was approved by the institutional review board at Chi Mei Medical Center. The institutional review board waived the need for informed consent (written and oral) from the patients because the data set used in this study consists of nationwide, unidentifiable, secondary data released to the public for research purposes. This waiver does not adversely affect the rights and welfare of the patients.

Statistical Analysis

The normality of the variables was verified by Kolmogorov-Smirnov test. We used standardized difference, which was proposed by Ho et al. (13), to assess the balance of measured variables between HCE and control subjects in the matched sample, since assessment of balance in baseline variables between treated and untreated subjects should use methods that are not influenced by sample size and that are sample specific and do not refer to a hypothetical population (14). A standardized difference of 0.1 or more was considered indicative of imbalance (14). All of the following analyses were performed in the matched sample, using methods appropriate for the analysis of matched data in estimating the outcome effect.

The risk of death between geriatric patients with diabetes in the HCE and control groups was compared by estimating the incidence rate ratio (IRR) with conditional Poisson regression. Besides, a separate Cox proportional hazards regression was done to compute the risk of death between the HCE and control groups after adjustment for HCE, age, sex, HTN, renal disease, CAD, stroke, cancer, COPD, CHF, liver disease, and monthly income. The SAS procedures GENMOD (for conditional Poisson regression) and PHREG (for Cox proportional hazards regression on the matched pairs) can be used to analyze matched-pair cohort data. Afterward, Kaplan-Meier analysis was used to calculate the cumulative survival rate among three groups (two or more episodes of hyperglycemic crisis, one episode of hyperglycemic crisis, and control subjects), and the log-rank test was used to analyze the differences between the survival curves. SAS 9.3.1 for Windows (SAS Institute, Cary, NC) was used for all analyses. Significance was set at $P < 0.05$.

RESULTS

Demographic Data

Between 2000 and 2002, we identified 4,517 geriatric patients with diabetes and HCE and 9,034 control subjects matched for age, sex, selected comorbidities, and monthly income (with diabetes but without HCE) after ineligible patients had been excluded. The mean age in the HCE group on the diabetes date was 71.01 ± 7.38 years and in the control group was 70.95 ± 7.35 years. We subclassified these patients into three age-groups: young elderly (65–74 years old), moderately elderly (75–84 years old), and old elderly (≥85 years old). Standardized difference tests showed no significant difference in the distribution of the comorbidities of HTN, renal disease, CAD, stroke, cancer, COPD, CHF, or liver disease and monthly income in the HCE and control groups after matching (Table 1).

Incidence Rates of Death

Of the 13,551 geriatric patients with diabetes identified, 3,326 (24.54%) died during follow-up: 1,634 (36.17%) in the HCE group and 1,692 (18.73%) in the control group (Table 2). The incidence rates of death were 84.37 (HCE group) and 35.17 (control group) per 1,000 person-years (PY), which was significantly higher for the HCE group (IRR 2.82; 95% CI 2.58–3.08) (Table 2).

The mortality risk was significantly higher in the HCE group during the first 6 years of the follow-up period: first month after HCE (IRR 26.56; 95% CI 17.97–39.27), 1–6 months after (IRR 4.54; 95% CI 3.64–5.67), 6–12 months after (IRR 2.63; 95% CI 2.07–3.33), 1–2 years after (IRR 1.81; 95% CI 1.48–2.20),

Table 1—Standardized difference of baseline demographic characteristics and comorbidities for patients with HCE and matched control subjects

	HCE	Control subjects	Standardized difference
n	4,517	9,034	
Age at diabetes date (years), mean ± SD	71.01 ± 7.38	70.95 ± 7.35	0.008
Age at index date (years), mean ± SD	75.51 ± 6.78	75.39 ± 6.62	0.018
Age at index date (years)			
65–74	2,345 (51.91)	4,720 (52.25)	0.007
75–84	1,720 (38.08)	3,476 (38.48)	0.008
≥85	452 (10.01)	838 (9.28)	0.025
Duration from diabetes date to index date (years), mean ± SD/median (IQR)	4.50 ± 3.36/4.34 (5.92)	4.44 ± 3.33/4.20 (6.06)	0.018
Sex			
Male	2,223 (49.21)	4,424 (48.97)	0.005
Female	2,294 (50.79)	4,610 (51.03)	0.005
Baseline comorbidity			
HTN	2,620 (58.00)	5,193 (57.48)	0.011
Renal disease	204 (4.52)	390 (4.32)	0.010
CAD	873 (19.33)	1,672 (18.51)	0.021
Stroke	748 (16.56)	1,443 (15.97)	0.016
Cancer	343 (7.59)	650 (7.20)	0.015
COPD	713 (15.78)	1,361 (15.07)	0.020
CHF	268 (5.93)	496 (5.49)	0.019
Liver disease	344 (7.62)	661 (7.32)	0.011
Monthly income (USD)			
<501	2,959 (65.51)	5,993 (66.34)	0.018
501–791	1,483 (32.83)	2,905 (32.16)	0.014
>791	75 (1.66)	136 (1.51)	0.012

Data are mean ± SD, median (interquartile range [IQR]), or *n* (%). USD calculated as 1 USD = 31.6 New Taiwan dollars.

2–4 years after (IRR 1.89; 95% CI 1.63–2.18), and 4–6 years after (IRR 1.49; 95% CI 1.23–1.81) (Table 2). There was no significant difference after 6 years (Table 2). Kaplan-Meier survival analyses and log-rank tests showed that the HCE group patients had significantly ($P < 0.0001$) lower survival rates than control subjects during the follow-up, especially in the patients with two or more episodes of hyperglycemic crisis (Fig. 2).

All HCE group age subgroups had a higher IRR than did their control group counterparts (Table 2). HCE group patients who were ≥85 years old had the highest IRR for mortality (3.20) during the follow-up, patients 65–74 years old had the second highest (2.77), and patients 75–84 years old had the third highest (2.48) (Table 2).

Male HCE patients had a mortality rate of 90.94/1,000 PY, but male control subjects had a death rate of only 38.75/1,000 PY (IRR 2.51; 95% CI 2.26–2.79) (Table 2). The difference between female HCE patients and female control subjects was also significant (IRR 2.81; 95% CI 2.48–3.18).

HCE patients comorbid with HTN (83.17/1,000 PY), renal disease (123.54/1,000 PY), CAD (85.26/1,000 PY), stroke (119.12/1,000 PY), cancer (188.44/1,000 PY), COPD (117.63/1,000 PY), CHF (141.56/1,000 PY), and a liver disease (106.91/1,000 PY) had a higher IRR for death than did control patients comorbid with the same diseases (Table 2).

Risk Factors for All-Cause Mortality in Patients With Diabetes

Cox proportional hazards regressions were used to determine crude and adjusted hazard ratios (HRs) for death during the follow-up by cohort for the total sample. After adjustment for patient age, sex, selected comorbidities, and monthly income, HCE was still an independent risk factor for death in the total sample (Table 3). The adjusted HR of two or more HCEs and one HCE was 4.525 (95% CI 3.364–6.086) and 2.848 (95% CI 2.599–3.119), respectively. Other risk factors for death included older age (≥75 years old), male sex, renal disease, stroke, cancer, COPD, and CHF.

CONCLUSIONS

This is the first national population-based study to evaluate the association between HCE and long-term mortality risk in geriatric patients with diabetes. We found that HCE raised the risk of long-term mortality in geriatric patients with diabetes, that the incidence rate of mortality was significantly high during the first 6 years of follow-up after HCE but not after 6 years, and that the risk of HCE-associated mortality was still >2.848 times that of the control subjects after adjustment for potential confounding factors. Poorer prognosis was found in patients with more episodes of hyperglycemic crisis. Early referral of geriatric patients with diabetes and HCE for proper patient education, better access to medical care, effective communication with a health care provider (2), and control of comorbidities such as renal disease, stroke, cancer, COPD, and CHF may be urgently needed.

Poor compliance, which leads to uncontrolled diabetes, is the most common precipitating factor (~60%) of HCE (1). Therefore, HCE indicates uncontrolled diabetes (2). The clues for uncontrolled diabetes can be traced from a patient's medical history or from objective data such as HbA_{1c}. A recent study (15) reported that the mean HbA_{1c} of patients with HCE was 11.8%. Uncontrolled diabetes may have long-term effects that contribute to various serious complications, such as renal disease, CAD, stroke, peripheral arterial disease, neuropathy, and retinopathy (2,16), and to all-cause mortality, as in the current study. Resources need to be redirected toward prevention by funding better access to care and educational programs tailored to individual needs, including ethnicity and personal health care beliefs (2).

Mortality during the first 6 years after HCE was significantly higher in the HCE patients than in the control subjects. In particular, the IRR was extremely high during the first month after HCE owing to acute illness. A recent study (6) reports a first-month mortality rate of 14.7%. Patients who survive the acute episode will most often fully recover. The long-term effects of HCE may be due to persistent uncontrolled diabetes

Table 2—Risk of death for patients with HCE and control subjects

	HCE				Control subjects					
	n	Death	PY	Rate*	*n*	Death	PY	Rate*	IRR (95% CI)	*P*
All	4,517	1,634	19,367.73	84.37	9,034	1,692	48,109.75	35.17	2.82 (2.58–3.08)	<0.0001
Age at index date (years)										
65–74	2,345	685	11,383.58	60.17	4,720	641	26,966.72	23.77	2.77 (2.45–3.13)	<0.0001
75–84	1,720	702	6,694.28	104.87	3,476	772	17,438.12	44.27	2.48 (2.21–2.79)	<0.0001
≥85	452	247	1,289.87	191.49	838	279	3,704.91	75.31	3.20 (2.43–4.22)	<0.0001
Sex										
Male	2,223	860	9,456.95	90.94	4,424	925	23,870.04	38.75	2.51 (2.26–2.79)	<0.0001
Female	2,294	774	9,910.78	78.1	4,610	767	24,239.71	31.64	2.81 (2.48–3.18)	<0.0001
Comorbidity										
HTN	2,620	882	10,604.66	83.17	5,193	1,010	26,591.99	37.98	2.53 (2.26–2.84)	<0.0001
Renal disease	204	93	752.79	123.54	390	138	2,023.73	68.19	1.79 (1.33–2.41)	<0.0001
CAD	873	322	3,776.89	85.26	1,672	351	8,686.88	40.41	2.14 (1.82–2.52)	<0.0001
Stroke	748	333	2,795.58	119.12	1,443	405	7,618.38	53.16	2.32 (1.96–2.74)	<0.0001
Cancer	343	192	1,018.88	188.44	650	206	2,946.28	69.92	3.05 (2.34–3.97)	<0.0001
COPD	713	335	2,848.02	117.63	1,361	427	7,096.62	60.17	2.01 (1.72–2.36)	<0.0001
CHF	268	137	967.82	141.56	496	173	2,401.6	72.04	2.03 (1.53–2.71)	<0.0001
Liver disease	344	149	1,393.75	106.91	661	143	3,591.69	39.81	2.76 (2.14–3.55)	<0.0001
Follow-up period										
0–1 month	4,517	362	353.643	1,023.63	9,034	31	748.710	41.40	26.56 (17.97–39.27)	<0.0001
1–6 months	4,124	247	1,625.52	151.95	8,938	126	3,632.19	34.69	4.54 (3.64–5.67)	<0.0001
6–12 months	3,739	147	1,795.84	81.86	8,511	131	4,141.67	31.63	2.63 (2.07–3.33)	<0.0001
1–2 years	3,442	189	3,212.44	58.83	8,037	251	7,626.38	32.91	1.81 (1.48–2.20)	<0.0001
2–4 years	2,967	324	5,074.61	63.85	7,153	426	12,567.81	33.90	1.89 (1.63–2.18)	<0.0001
4–6 years	2,113	190	3,543.17	53.62	5,411	332	9,163.97	36.23	1.49 (1.23–1.81)	<0.0001
6–8 years	1,431	107	2,282.03	46.89	3,807	231	6,143.28	37.60	1.25 (0.99–1.57)	0.0588
≥8 years	877	68	1,480.48	45.93	2,391	164	4,085.74	40.14	1.14 (0.86–1.52)	0.3469

*Per 1,000 PY.

and prior hyperglycemia-induced microvascular and macrovascular injury (16). Despite the long-term effect, the mortality rate was not significantly different between HCE patients and control subjects 6 years after HCE. This highlights the importance of initiating better diabetes care as soon as possible after HCE to minimize the mortality right after the event.

Although controlling diabetes and preventing HCE can lower long-term mortality risk, there is no evidence that tight glycemic control in the elderly is beneficial (17). For the elderly, it is harmful to use medications to achieve HbA_{1c} levels of <6.5% (18). The complications of tight glycemic control include hypoglycemia and mortality in addition to the benefits of reductions in myocardial infarctions and mortality with metformin (18). Given the long time frame needed to achieve a reduction in microvascular complications of retinopathy, neuropathy, and nephropathy, glycemic goals should reflect patient goals, health status, and life expectancy (17). The American Diabetes Association (19) recommends a less stringent target, such as 8.0%, for frail elderly, for patients with limited life expectancy or extensive comorbid conditions, and for others for whom the risks of intensive glycemic control appear to outweigh the potential benefits.

This study has some limitations. First, potential disease misclassifications may exist because the diagnoses of diabetes and HCE as well as the comorbidities relied solely on the claims data. However, many studies have proven that NHIRD claim data are highly accurate and appear to be a valid resource for population research (20–22). Therefore, the misclassifications should be minimal and thus unlikely to introduce remarkable effects on the results of our study. Second, some important sociodemographic characteristics, such as education level, stress level, BMI, and smoking and alcohol drinking habits; the intensity, duration, and extent of comorbidities; results of clinical examinations; laboratory data such as degree of hyperglycemia and HbA_{1c}, blood glucose control during the follow-up period; and cause of death were not available in the NHIRD. Therefore, we could not adjust for these variables as contributing factors in this study. The impact of these missing data on the results also could not be assessed. Third, we were unable to take into account the severity of the diseases, which reduced our chances of showing the severity-related effects of comorbidities. Fourth, the precipitating factors were unavailable in the NHIRD. However, previous hospital-based studies have revealed that poor compliance, infection, new-onset

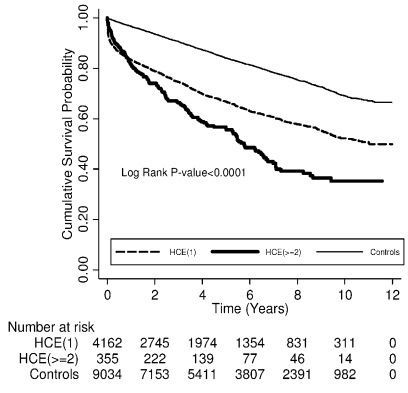

Figure 2—Long-term mortality after HCE in geriatric patients with diabetes. Survival rate for patients with an HCE and for control subjects during the follow-up period. HCE (1), one episode of HCE; HCE (≥2), two or more episodes of HCE.

Table 3—Crude and adjusted HRs of Cox proportional hazards regressions stratified on the matched pairs and 95% CIs for death during the follow-up period for the study cohort

Cohort	Crude HR (95% CI)	Adjusted HR (95% CI)
HCE (number of episodes)		
≥2 (166/355)	3.880 (2.926–5.144)*	4.525 (3.364–6.086)*
1 (1,468/4,162)	2.713 (2.489–2.957)*	2.848 (2.599–3.119)*
None (1,692/9,034)	1.000	1.000
Age (years)		
65–74	1.000	1.000
75–84	1.827 (1.595–2.093)*	1.675 (1.407–1.992)*
≥85	3.092 (2.506–3.816)*	2.675 (1.986–3.603)*
Sex		
Male	1.152 (1.026–1.294)*	1.166 (1.019–1.335)*
Female	1.000	1.000
Comorbidity		
HTN	0.853 (0.752–0.968)*	0.898 (0.757–1.065)
Renal disease	1.801 (1.447–2.241)*	1.931 (1.497–2.491)*
CAD	1.031 (0.901–1.179)	1.083 (0.922–1.273)
Stroke	1.313 (1.147–1.503)*	1.474 (1.257–1.729)*
Cancer	2.316 (1.938–2.767)*	3.079 (2.501–3.79)*
COPD	1.437 (1.258–1.642)*	1.489 (1.271–1.745)*
CHF	2.058 (1.682–2.518)*	2.155 (1.668–2.783)*
Liver disease	0.960 (0.805–1.146)	1.115 (0.898–1.384)
Monthly income (USD)		
<501	1.000	1.000
501–791	0.788 (0.693–0.895)*	0.853 (0.719–1.012)
>791	0.453 (0.291–0.705)*	0.587 (0.342–1.007)

HCE, age, sex, HTN, renal disease, CAD, stroke, cancer, COPD, CHF, liver disease, and monthly income were included in Cox proportional hazards regressions. USD calculated as 1 USD = 31.6 New Taiwan dollars. *$P < 0.05$.

diabetes, pancreatitis, and acute coronary syndrome were the common precipitating factors (1). This limitation would not decrease the value of this population-based cohort study with the aim to delineate the long-term mortality risk of HCE, which is still unclear. Fifth, despite our database being national, our findings may not be generalizable to cohorts in other nations.

In summary, HCE signified uncontrolled diabetes, which may have long-term effects that contribute to various complications, including death. Early referral of geriatric patients with diabetes and HCE for proper education, better access to medical care, effective communication with a health care provider, and control of comorbidities may be urgently needed.

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