Risk of dementia after charcoal-burning suicide attempts: a nationwide cohort study in Taiwan

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ABSTRACT
This study aimed to investigate the association between charcoal-burning suicide attempts and the risk of developing dementia. A nationwide, matched cohort, population-based study enrolled a total of 4103 patients with newly diagnosed charcoal-burning suicide attempts, between 2000 and 2010, which were selected from the National Health Insurance Research Database of Taiwan, along with 12,309 controls matched for sex and age. After adjusting for confounding factors, Fine and Gray's competing risk analysis was used to compare the risk of developing dementia during the 10-year follow-up period. Of the enrolled patients (n=16,412), dementia developed in 303 (1.85%), including 2.56% in the study group (105 in 4103) and 1.61% (198 in 12,309) in the control group. The Fine and Gray's survival analysis revealed that the patients with charcoal-burning suicide attempts were likely to develop dementia, with a crude HR of 5.170 (95% CI 4.022 to 6.644, p<0.001). After adjusting for age, sex, comorbidity, geographic area and urbanization level of residence, and monthly insured premium, the adjusted HR was 4.220 (95% CI 3.188 to 5.586, p<0.001). Suicide attempts were associated with an increased risk of degenerative dementia in this study. Patients with charcoal-burning suicide attempts had a fourfold risk of dementia than the control group.

INTRODUCTION
Charcoal-burning suicides became an epidemic in Hong Kong,[1] Taiwan,[1–4] China,[5–7] Korea,[8] Japan,[9] Singapore,[10] and some Western countries such as the UK[11] and the USA[12] over the last two decades, which were precipitated by wide media reports[13] or by internet browsing.[14] Charcoal-burning survivors would suffer from delayed neurologic sequelae, with diffuse demyelination in the brain accompanied by lethargy, behavioral changes, forgetfulness, memory loss, and parkinsonian features, and additionally sometimes toxic or ischemic peripheral neuropathies,[15] which could impair attempters' cognitive and motor functions.

Between 2011 and 2012, 130,000 people, or 4.97%, of those aged 65 years and over in Taiwan had dementia,[16] which is a heavy burden for the patients and their caregivers,

Significance of this study

What is already known about this subject?
► Previous studies have found that charcoal-burning survivors would suffer from delayed neurologic sequelae, involving diffuse demyelination in the brain accompanied by lethargy, behavioral changes, forgetfulness, memory loss, and parkinsonian features.
► The association between charcoal-burning suicide attempts and the risk of dementia has not yet been studied.

What are the new findings?
► Comparing with previous research on the association between carbon monoxide intoxication and the risk of dementia, this population-based study focused on the association between charcoal-burning suicidal attempts and the risk of dementia.
► The charcoal-burning suicide attempters were more likely to develop dementia (HR 4.22, 95% CI 3.19 to 5.59, p<0.001), when adjusting for sex, age, monthly income, urbanization level, geographic region, and comorbidities.
► Charcoal-burning suicide attempts were associated with an increased risk of degenerative dementia in this study.

How might these results change the focus of research or clinical practice?
► If the association between charcoal-burning suicide attempts and the risk of dementia is causal, then the results would remind clinicians who care for charcoal-burning suicide survivors to provide careful monitoring of these patients' cognitive function in clinical practice.

community, or society.[17–20] Injuries on the brain such as traumatic brain injury (TBI),[21] stroke,[22] or even attention deficit hyperactivity disorder and related brain injury[23 24] would also contribute to the development of dementia. Studies on delayed neurologic or neuropsychiatric syndrome revealed that carbon monoxide (CO) intoxication from charcoal-burning

resulted in the diffuse demyelination in the brain.[15] Another study found that the fronto-insular-caudate areas represented the target degenerative network in the CO intoxication.[25] Therefore, we hypothesize that CO intoxication in patients with suicide attempts would also be associated with dementia, and we conducted this study to clarify whether coal-burning suicide attempts would be associated with subsequent dementia.

METHODS
Data sources
The National Health Insurance (NHI) program was launched in Taiwan in 1995, and as of June 2009 it has included contracts with 97% of medical providers with approximately 23 million beneficiaries, or more than 99% of the entire population.[26] The National Health Insurance Research Database (NHIRD), which contains all claims data of the beneficiaries, uses the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes to record diagnoses.[27] All the diagnoses of dementia in Taiwan are made by board-certified psychiatrists or neurologists. All patients with suicide attempts by charcoal-burning would be attended and treated by emergency physicians, chest medicine specialists, intensive care physicians, or other medical experts, and the diagnosis would then be confirmed from their medical history and arterial blood gas tests. The NHI Administration randomly reviews the records of ambulatory care visits and inpatient claims to verify the accuracy of the diagnoses.[28] Several studies have demonstrated the accuracy and validity of several diagnoses in the NHIRD, including diabetes mellitus (DM),[29 30] cancer,[31–33] myocardial infarction,[29 34 35] central nervous system diseases such as Tourette syndrome,[36] stroke,[29 37–40] outcomes,[33] mortality,[29 41] or comorbidity.[33 41] In a wide spectrum of conditions, some studies also demonstrated concordance between Taiwan's National Health Survey and the NHIRD on a variety of diagnoses,[42] medication use,[42] and health system utilizations.[42 43] In this study, we used data from the Longitudinal Health Insurance Database (2000–2010), a subset of the NHIRD, to investigate the association between charcoal-burning suicide attempts and dementia over a 10-year period.

Study design
This study has a population-based, matched-cohort design. Patients with newly diagnosed charcoal-burning suicide attempts were selected from the hospitalization data set from January 1, 2000 to December 31, 2010, according to the diagnosis of the charcoal-burning suicide attempts (ICD-9-CM code: E952). Patients before 2000 were excluded. In addition, patients diagnosed with dementia before 2000 or before the first visit for charcoal-burning suicide attempts were also excluded. All patients aged <20 years were also excluded. All patients with other suicide attempts (ICD-9-CM codes: E950-E951, E953-E959) were also excluded. A total of 16,412 patients were enrolled, including 4103 subjects with charcoal-burning suicide attempts and 12,309 randomly selected sex-matched, age-matched, and index year-matched controls without charcoal-burning suicide attempts in a ratio of 1:3, with a statistical power of up to 0.875, similar

to the design of our previous studies (online supplementary figure 1).[23 44] Age was grouped into 20–29, 30–39, 40–49, 50–59, 60–69, and ≥70 years.

Covariates
The covariates included geographic area of residence (north, center, south, west, and east of Taiwan), urbanization level of residence (levels 1–4) and monthly income (in New Taiwan Dollars (NT$): <18,000, 18,000–34,999, ≥35,000).[8] Other covariates such as complications from acute respiratory failure, rhabdomyolysis, acidosis, encephalopathy, procedures of hyperbaric oxygenation (HBO) therapy, and mechanical ventilations were also recorded.

Comorbidity
In this study, the comorbidity was used with reference to previous cohort studies on the risk factor of dementia.[44 45] In these two previous studies, the comorbidity was according to the RxDx-Dementia Risk Index, a useful tool to identify the risk of dementia, which has a c-statistics value of 0.806 (95% CI 0.799 to 0.812).[45] Therefore, the baseline comorbidities (in ICD-9-CM codes) included DM (250), hypertension (401.1, 401.9, 402.10, 402.90, 404.10, 404.90, 405.1, 405.9), hyperlipidemia (272.x), coronary artery disease (411, 413, 414), myocardial infarction (410, 412), peripheral vascular disease (444-449), heart failure (428), obesity (278), chronic kidney disease (580, 581–589, 753, 403, 404, 250.4, 274.1, 440.1, 442.1, 447.3, 572.4, 642.1, 646.2), cerebrovascular disease (433, 434, 436), TBI (800–804, 850–854, 905.0, 950.1, 950.3, 907.0, 959.01, 959.9, 310.2, V15.52), primary cancer (140–239, with the exceptions of 190–199 and 210–229), metastatic tumor (190-199), chronic pulmonary diseases (490-496), rheumatologic disease (725-729), peptic ulcer disease (533), hemiplegia or paraplegia (342, 344), liver disease (571), AIDS (042), epilepsy (345), tuberculosis (010–018), Parkinson's disease (332), cardiac atherosclerotic cardiovascular disease (440, 441, 442, 443), glaucoma (365), cystic fibrosis (277.0x), transplantation (V42), thyroid disorder (240-246), gout (274), Crohn's disease and ulcerative colitis (555, 556), pain (338), pain and inflammations (710-719), depression (296.2, 296.3, 296.82, 300.4, 311), bipolar disorders (296.4x, 296.5x, 296.6x, 296.89), anxiety disorders (300.00, 300.01, 300.02), and psychotic illness (295.xx, 298.x).

Main outcome measures
All of the study subjects were followed from the index date until the onset of dementia (ICD-9-CM codes: 290.0, 290.10, 290.11, 290.12, 290.13, 290.20, 290.21, 290.3, 290.41, 290.42, 290.43, 290.8, 290.9, and 331.0), withdrawal from the NHI program, or at the end of year 2010. Dementia was divided into three subgroups: Alzheimer-type dementia (331.0), vascular dementia (ICD-9-CM codes: 290.4x), and other degenerative dementia (ICD-9-CM codes: 290.x, with the exception of 290.4x). As mentioned above, all the diagnoses of dementia in Taiwan are made by board-certified psychiatrists or neurologists, and for the types of dementia the NHI Administration also randomly reviews the records of ambulatory care visits and inpatient claims to verify the accuracy of the diagnoses.[28]

Statistical analysis

All statistical analyses were performed using SPSS for Windows, V.22.0. χ^2 and t-tests were used to evaluate the distribution of categorical and continuous variables, respectively, with the Fisher's exact examination. Fine and Gray's competing risk analysis was used to determine the risk of dementia, since death can act as a competing risk factor,[44 46 47] and the results were presented as HR with 95% CI. Differences in the risk of dementia between the study and control groups were estimated using the Kaplan-Meier method with the log-rank test. A two-tailed p value <0.05 was considered to indicate statistical significance.

RESULTS

Sample characteristics

Table 1 shows the proportion of outcomes (with or without suicide) among exposure groups of sex, age, comorbidities, urbanization, and area of residence, and the income of the charcoal-burning cohort and controls. For most of the exposure groups with comorbidities, the proportions of outcome with charcoal-burning suicides were lower than the proportions of outcome without suicide, except DM. For the exposure groups with HBO therapy, the proportions of outcome with charcoal-burning suicide were higher than the proportions of outcome without suicide. With regard to the exposure groups in different urbanization levels and location of residence, the patients in urbanization level 2, middle, southern and eastern Taiwan showed higher proportions of outcome with charcoal-burning suicide. The exposure group with monthly insured premium lower than NT$18,000 revealed higher proportion of outcome with suicide.

Kaplan-Meier model for the cumulative risk of dementia

At the end of follow-up, 303 patients out of a total of 16,412 enrolled subjects (1.85%) had developed dementia, including 2.6% in the study group (105 in 4103) and 1.6% (198 in 12,309) in the control group, and the Kaplan-Meier analysis for the cumulative incidence of dementia in the study and control groups is shown in figure 1 (log-rank test <0.001). In addition, the percentage of use of HBO therapy in the charcoal-burning cohort was 19.0% (779 in 4103). Table 2 shows the results of Fine and Gray's competing risk analysis of the factors associated with the risk of developing dementia. The crude HR was 5.17 (95% CI 4.00 to 6.64, p<0.001). After adjusting for age, sex, comorbidities, geographic area of residence, urbanization level of residence, and monthly income, the adjusted HR was 4.22 (95% CI 3.19 to 5.87, p<0.001). In addition, male subjects were at a 1.57-fold risk than female subjects (p<0.001). With regard to age, those who were aged 60–69 and ≥70 years old had 1.66-fold and 2.88-fold risk in comparison with the reference group, that is, those aged 20–29. In addition, a 1-year increase in age increases the additional risk of dementia by 1.03%. Similarly, the charcoal-burning cohort with complications such as acute respiratory failure and encephalopathy was associated with higher risk of developing dementia than those without these complications. The adjusted HR was 2.51 (95% CI 1.20 to 3.68, p<0.001) and 2.99 (95% CI 1.30 to 7.76, p<0.001) in the charcoal-burning cohort who had received HBO therapy for 1–3 times and >3 times, respectively, in contrast to the control group.

Sensitivity analysis for the risk of dementia

We have conducted two types of sensitivity analysis to evaluate the risk of dementia. First, we excluded patients diagnosed with dementia within the first 2 years after the charcoal-burning suicide attempts, and the adjusted HR was 3.22 (95% CI 1.96 to 5.29, p<0.001) for patients with charcoal-burning suicide attempts (table 3). Second, we analyzed the risk of patients who attempted suicide by other methods, and the results showed that suicide attempts by solid or liquid ingestions, gases in domestic use, hanging, drowning, cutting or piercing implements, and jumping from building were not associated with the risk of dementia. However, the subgroup of other methods of suicides (ICD-9-CM code E958) has elevated risk of dementia (adjusted HR=3.30, 95% CI 2.44 to 6.04, p<0.001) (table 4).

Types of dementia in patients after charcoal-burning suicide attempts

With regard to the types of dementia, the study group was associated with a 4.28-fold (p<0.001) risk in developing degenerative dementia than the control group of non-attempters, and most were of the degenerative types, but not significantly associated with Alzheimer dementia (AD) or vascular dementia (VaD) (table 5).

DISCUSSION

Association between charcoal-burning suicide attempts and the risk of dementia

In this study, we found that in the 10-year follow-up of the subject group and the control group, the charcoal suicide attempts were associated with a higher risk of developing dementia. The log-rank of the Fine and Gray's competing risks regression model was significant (p<0.001). The crude HR of the subject group was 5.17 (95% CI 4.02 to 6.64, p<0.001), and the adjusted HR was 4.22 (95% CI 3.19 to 5.87, p<0.001). We have also conducted two sensitivity analyses to evaluate the influences from protopathic bias. First, even though the patients with the diagnosis of dementia within the first 2 years were excluded, the charcoal-burning suicide attempts were still associated with increased risk of dementia. Second, suicide attempts by solid or liquid ingestions, gases in domestic use, hanging, drowning, cutting or piercing implements, and jumping from building were not associated with the risk of dementia. However, the subgroup of other methods of suicides (ICD-9-CM code E958) was associated with a 3.3-fold risk of dementia (p < 0.001), and we speculate that some patients with charcoal-burning suicide attempts might have been classified into this category. Comparing with previous research about the association between CO intoxication and the risk of dementia,[48 49] this study focused on charcoal-burning suicide attempts and the risk of dementia. To our best knowledge, this is the first nationwide, population-based cohort study that focused on the association between charcoal-burning suicide attempts and the risk of dementia.

Table 1 Characteristics of the study population at baseline

Charcoal-burning suicide	Total	With suicide		Without suicide		
Variables	N	n	%	n	%	P values
Total	16,412	4103	25.0	12,309	75.0	
Sex						
Male	9120	2280	25.0	6840	75.0	0.999
Female	7292	1823	25.0	5469	75.0	0.999
Age (years)	38.43±12.75	38.00±11.92		38.58±13.02		0.077
Age groups (years)						
20–29	4812	1203	25.0	3609	75.0	0.999
30–39	5288	1322	25.0	3966	75.0	0.999
40–49	3812	953	25.0	2859	75.0	0.999
50–59	1764	441	25.0	1323	75.0	0.999
60–69	456	114	25.0	342	75.0	0.999
≥70	280	70	25.0	210	75.0	0.999
Comorbidity						
Diabetes mellitus						
Without	15,576	3914	25.1	11,662	74.9	0.064
With	836	189	22.6	647	77.4	0.053
Hypertension						
Without	15,571	3923	25.2	11,648	74.8	0.008
With	841	180	21.4	661	78.6	0.006
Hyperlipidemia						
Without	16,175	4075	25.2	12,100	74.8	<0.001
With	237	28	11.8	209	88.2	<0.001
Ischemic heart disease						
Without	15,972	4044	25.3	11,928	74.7	<0.001
With	440	59	13.4	381	86.6	<0.001
Myocardial infarction						
Without	16,320	4089	25.1	12,231	74.9	0.026
With	92	14	15.2	78	84.8	0.014
Peripheral vascular disease						
Without	16,395	4102	25.0	12,293	75.0	0.050
With	17	1	5.9	16	94.1	<0.001
Heart failure						
Without	16,328	4092	25.1	12,236	74.9	0.013
With	84	11	13.1	73	86.9	0.006
Obesity						
Without	16,407	4101	25.0	12,306	75.0	0.132
With	5	2	40.0	3	60.0	0.486
Chronic kidney disease						
Without	16,033	3960	24.7	12,073	75.3	<0.001
With	379	143	37.7	236	62.3	<0.001
Stroke						
Without	16,277	4083	25.1	12,194	74.9	0.008
With	135	20	14.8	115	85.2	0.004
Traumatic brain injury						
Without	15,099	3853	25.5	11,246	74.5	<0.001
With	1313	250	19.0	1063	81.0	<0.001
Primary cancer						
Without	15,832	4042	25.5	11,790	74.5	<0.001
With	580	61	10.5	519	89.5	<0.001
Metastatic tumor						
Without	16,250	4089	25.2	12,161	74.9	<0.001
With	162	14	8.6	148	91.4	<0.001
Chronic obstructive pulmonary disease						
Without	16,096	4053	25.2	12,043	74.8	<0.001
With	316	50	15.8	266	84.2	<0.001
Rheumatoid arthritis						
Without	15,894	3729	23.5	12,165	76.5	<0.001

Continued

Original research

Table 1 Continued

Charcoal-burning suicide	Total	With suicide		Without suicide		
Variables	N	n	%	n	%	P values
With	518	374	72.2	144	27.8	<0.001
Peptic ulcer disease						
Without	16,326	4095	25.1	12,231	74.9	0.001
With	86	8	9.3	78	90.7	<0.001
Hemiplegia or paraplegia						
Without	16,334	4090	25.0	12,244	75.0	0.014
With	78	13	16.7	65	83.3	<0.001
Liver disease						
Without	15,740	4028	25.6	11,712	74.4	<0.001
With	672	75	11.2	597	88.8	<0.001
AIDS						
Without	16,396	4090	25.0	12,306	75.1	<0.001
With	16	13	81.3	3	18.8	<0.001
Epilepsy						
Without	16,376	4091	25.0	12,285	75.0	0.144
With	36	12	33.3	24	66.7	0.265
Tuberculosis						
Without	16,331	4096	25.1	12,235	74.9	<0.001
With	81	7	8.61	74	91.4	0.001
Parkinson's disease						
Without	16,376	4081	24.91	12,295	75.1	<0.001
With	36	22	61.11	14	38.9	<0.001
Atherosclerotic cardiovascular disease						
Without	16,397	4103	25.0	12,294	75.0	0.013
With	15	0	0.00	15	100.0	<0.001
Glaucoma						
Without	16,394	4102	25.0	12,292	75.0	<0.001
With	18	1	5.6	17	94.4	<0.001
Cystic fibrosis						
Without	16,412	4103	25.0	12,309	75.0	0.999
With	0	0	–	0	–	
Transplantation						
Without	16,402	4103	25.0	12,299	75.0	0.058
With	10	0	0	10	100	<0.001
Thyroid disorder						
Without	16,303	4090	25.1	12,213	74.9	0.002
With	109	13	11.9	96	88.1	0.001
Gout						
Without	16,251	4080	25.1	12,171	74.9	0.003
With	161	23	14.3	138	85.71	<0.001
Crohn's disease and ulcerative colitis						
Without	16,402	4103	25.0	12,299	75.0	0.056
With	10	0	0	10	100	<0.001
Pain						
Without	16,412	4103	25.0	12,309	75.0	0.999
With	0	0	–	0	–	–
Pain and inflammations						
Without	16,159	4086	25.3	12,073	74.7	<0.001
With	253	17	6.7	236	93.3	<0.001
Depression						
Without	14,934	2676	17.9	12,258	82.1	<0.001
With	1478	1427	96.6	51	3.5	<0.001
Bipolar disorders						
Without	16,355	4074	24.9	12,281	75.1	<0.001
With	57	29	50.9	28	49.1	<0.001
Anxiety disorders						
Without	16,349	4068	24.9	12,281	75.1	<0.001

Continued

Table 1 Continued

Charcoal-burning suicide	Total	With suicide		Without suicide		
Variables	N	n	%	n	%	P values
With	63	35	55.6	28	44.4	<0.001
Psychotic illness						
Without	15,997	4016	25.1	11,981	74.9	0.037
With	415	87	21.0	328	79.0	0.028
Hyperbaric oxygenation therapy						
Without	15,631	3324	21.3	12,307	78.7	<0.001
With	781	779	99.7	2	0.3	<0.001
Urbanization level						
1 (highest)	5247	1038	19.8	4209	80.2	<0.001
2	7577	2408	31.8	5169	68.2	0.042
3	1391	269	19.3	1122	80.7	<0.001
4 (lowest)	2197	388	17.7	1809	82.3	<0.001
Location						
Northern Taiwan	6219	1308	21.07	4911	79.0	<0.001
Middle Taiwan	5112	1496	29.3	3616	70.7	<0.001
Southern Taiwan	4183	1076	25.7	3107	74.3	<0.001
Eastern Taiwan	846	221	26.1	625	73.9	<0.001
Outlets islands	52	2	3.9	50	96.2	<0.001
Insured premium (New Taiwan dollars)						
<18,000	16,033	4042	25.2	11,991	74.8	0.007
18,000–34,999	271	54	19.9	217	80.1	0.001
≥35,000	108	7	6.5	101	93.5	<0.001

P values (categorical variable: proportion test; continuous variable: t-test).

Types of dementia in this study

In this sample, 303 patients out of a total of 16,412 enrolled subjects (1.9%) had developed dementia, including 2.6% in the study group (105 in 4103) and 1.6% (198 in 12,309) in the control group, and the percentage was close to the prevalence of 2%–5% for the population aged ≥65 in community studies.[50 51] In Taiwan, several community studies revealed that AD was the most common type of dementia (40%–60% of all dementias), followed by VaD (20%–30% of all dementias), and mixed or other dementias (7%–15%).[50 52 53] This finding reflects the fact that patients with dementia

Figure 1 Kaplan-Meier for cumulative risk of dementia among aged 20 and over stratified by charcoal-burning suicide with log-rank test.

tended to be younger in the study subject group: 95 of the 105 (90.47%) patients who developed degenerative dementia were <60 years old and related to the sequelae of charcoal-burning. Nevertheless, the charcoal-burning cohort aged >60 were associated with an increased risk of dementia: adjusted HR 1.66 (95% CI 1.01 to 2.68, p=0.045) in the charcoal-burning cohort aged 60–69, and 2.88 (95% CI 1.73 to 4.70, p<0.001) in comparison with the control group.

Possible mechanisms for the increased risk of dementia in charcoal-burning suicide attempters

Studies on delayed neurologic or neuropsychiatric syndrome revealed that CO intoxication from charcoal-burning resulted in the diffuse demyelination in the brain.[15] One study found that the fronto-insular-caudate areas represented the target degenerative network in CO intoxication.[25] The decrease in the gray matter volume in the bilateral basal ganglia, left postcentral gyrus, and left hippocampus is also correlated with the decreased perceptual organization and processing speed function in these patients.[54 55] Therefore, these wide varieties of brain damage could well play an important role in the development of dementia. In our study, the subjects with stroke, TBI, epilepsy, PD, depression, and bipolar disorder showed a higher risk in developing dementia, and these findings hint that the neurologic or psychiatric disorders were at a higher vulnerability to develop a CO-induced brain damage.

HBO therapy and dementia after charcoal-burning suicide attempts

In our study, the usage of HBO therapy in the charcoal-burning cohort was 19.0% (779 in 4103), which was compatible with another study in Taiwan in which
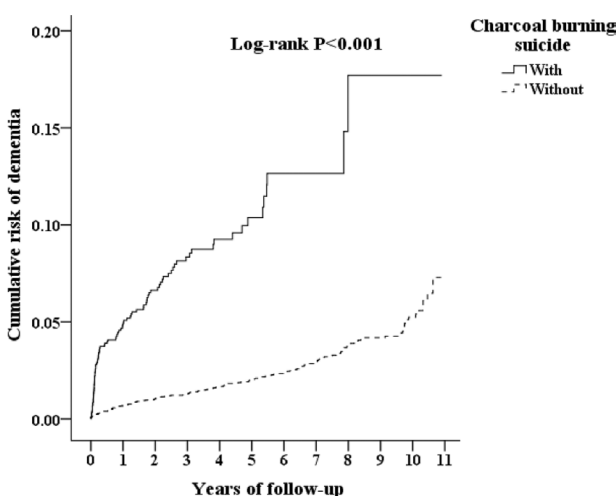
Table 2 Factors of dementia at the end of follow-up using Cox regression and Fine and Gray's competing risk model

Variables	No competing risk in the model				Competing risk in the model			
	Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values	Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values
Charcoal-burning suicide								
Without	Reference				Reference			
With	4.01	3.03	5.30	<0.001	4.22	3.19	5.59	<0.001
Sex								
Male	1.59	1.25	2.04	<0.001	1.57	1.22	2.00	<0.001
Female	Reference				Reference			
Age groups (years)								
20–29	Reference				Reference			
30–39	0.84	0.55	1.26	0.395	0.89	0.58	1.35	0.570
40–49	0.79	0.52	1.22	0.290	0.79	0.51	1.23	0.298
50–59	0.80	0.51	1.27	0.349	0.90	0.56	1.44	0.646
60–69	1.12	0.71	1.78	0.618	1.65	1.01	2.70	0.047
≥70	2.12	1.34	3.36	0.001	2.85	1.73	4.69	<0.001
Comorbidity								
Diabetes mellitus								
Without	Reference				Reference			
With	1.09	0.76	1.57	0.638	0.94	0.65	1.35	0.732
Hypertension								
Without	Reference				Reference			
With	1.19	0.84	1.70	0.328	0.96	0.68	1.37	0.834
Hyperlipidemia								
Without	Reference				Reference			
With	0.43	0.16	1.18	0.101	0.41	0.15	1.12	0.082
Ischemic heart disease								
Without	Reference				Reference			
With	0.65	0.31	1.34	0.239	0.59	0.24	1.21	0.147
Myocardial infarction								
Without	Reference				Reference			
With	0.45	0.06	3.24	0.426	0.43	0.06	3.14	0.408
Peripheral vascular disease								
Without	Reference				Reference			
With	0.91	0.13	6.59	0.923	0.83	0.11	6.06	0.856
Heart failure								
Without	Reference				Reference			
With	0.53	0.13	2.14	0.369	0.46	0.11	1.86	0.272
Obesity								
Without	Reference				Reference			
With	0.00	–	–	0.984	0.00	–	–	0.984
Chronic kidney disease								
Without	Reference				Reference			
With	1.19	0.65	2.21	0.574	1.11	0.60	2.08	0.736
Stroke								
Without	Reference				Reference			
With	3.86	2.29	6.49	<0.001	3.32	1.98	5.58	<0.001
Traumatic brain injury								
Without	Reference				Reference			
With	1.44	0.99	2.08	0.055	1.45	1.00	2.10	0.050
Primary cancer								
Without	Reference				Reference			
With	0.18	0.07	0.48	0.001	0.16	0.06	0.44	<0.001
Metastatic tumor								
Without	Reference				Reference			
With	1.52	0.51	4.53	0.449	1.51	0.51	4.46	0.457
Chronic obstructive pulmonary disease								

Continued

Table 2 Continued

Variables	No competing risk in the model				Competing risk in the model			
	Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values	Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values
Without	Reference				Reference			
With	1.33	0.77	2.29	0.308	1.00	0.57	1.75	0.998
Rheumatoid arthritis								
Without	Reference				Reference			
With	0.70	0.29	1.70	0.425	0.71	0.29	1.71	0.440
Peptic ulcer disease								
Without	Reference				Reference			
With	2.00	0.88	4.54	0.098	1.78	0.78	4.05	0.172
Hemiplegia or paraplegia								
Without	Reference				Reference			
With	1.32	0.53	3.03	0.551	1.37	0.55	3.42	0.505
Liver disease								
Without	Reference				Reference			
With	1.08	0.64	1.81	0.774	1.13	0.67	1.90	0.641
AIDS								
Without	Reference				Reference			
With	1.01	0.14	7.23	0.996	1.30	0.18	9.38	0.794
Epilepsy								
Without	Reference				Reference			
With	4.10	2.23	7.52	<0.001	4.50	2.45	8.28	<0.001
Tuberculosis								
Without	Reference				Reference			
With	1.63	0.52	5.14	0.406	1.55	0.49	4.92	0.455
Parkinson's disease								
Without	Reference				Reference			
With	4.61	2.34	9.81	<0.001	3.33	1.66	6.67	0.001
Atherosclerotic cardiovascular disease								
Without	Reference				Reference			
With	0.00	–	–	0.978	0.00	–	–	0.978
Glaucoma								
Without	Reference				Reference			
With	3.95	0.55	28.32	0.171	3.08	0.43	22.08	0.264
Cystic fibrosis								
Without	Reference				Reference			
With	–	–	–	–	–	–	–	–
Transplantation								
Without	Reference				Reference			
With	0.00	–	–	0.974	0.00	–	–	0.974
Thyroid disorder								
Without	Reference				Reference			
With	0.74	0.18	3.01	0.673	0.76	0.19	3.10	0.702
Gout								
Without	Reference				Reference			
With	0.72	0.23	2.28	0.578	0.66	0.21	2.07	0.474
Crohn's disease and ulcerative colitis								
Without	Reference				Reference			
With	3.24	0.45	23.32	0.243	3.24	0.45	23.29	0.243
Pain								
Without	Reference				Reference			
With	–	–	–	–	–	–	–	–
Pain and inflammations								
Without	Reference				Reference			
With	0.88	0.39	2.00	0.77	0.78	0.34	1.76	0.547

Table 2 Continued

Variables	No competing risk in the model				Competing risk in the model			
	Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values	Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values
Depression								
Without	Reference				Reference			
With	2.46	1.70	3.56	<0.001	2.49	1.72	3.61	<0.001
Bipolar disorders								
Without	Reference				Reference			
With	2.81	1.37	5.73	0.005	2.76	1.35	5.64	0.005
Anxiety disorders								
Without	Reference				Reference			
With	0.00	–	–	0.953	0.00	–	–	0.953
Psychotic illness								
Without	Reference				Reference			
With	1.03	0.62	1.70	0.918	1.13	0.68	1.86	0.646
Hyperbaric oxygenation therapy								
Without	Reference				Reference			
With	2.71	1.12	6.57	0.027	2.80	1.15	6.77	0.023
Urbanization level								
1 (highest)	1.04	0.75	1.45	0.797	1.05	0.75	1.45	0.792
2	0.78	0.57	1.07	0.126	0.78	0.57	1.08	0.131
3	0.96	0.62	1.48	0.856	1.02	0.66	1.57	0.929
4 (lowest)	Reference				Reference			
Location								
Northern Taiwan	Had collinearity with urbanization level				Had collinearity with urbanization level			
Middle Taiwan	Had collinearity with urbanization level				Had collinearity with urbanization level			
Southern Taiwan	Had collinearity with urbanization level				Had collinearity with urbanization level			
Eastern Taiwan	Had collinearity with urbanization level				Had collinearity with urbanization level			
Outlets islands	Had collinearity with urbanization level				Had collinearity with urbanization level			
Insured premium (New Taiwan dollars)								
<18,000	Reference				Reference			
18,000–34,999	0.80	0.26	2.50	0.700	0.80	0.25	2.49	
≥35,000	0.00	–	–	0.939	0.00	–	–	

Adjusted HR, adjusted variables listed in the table.

hyperbaric oxygen therapy was only used in 18.8% of patients.[14] Evidence of HBO therapy for CO intoxication from charcoal-burning is yet to be established.[56–58] However, the charcoal-burning cohort who had received HBO therapy still had an increased risk of dementia in contrast to the control group, with an adjusted HR of 2.80 (95% CI 1.15 to 6.77, p=0.023), and with an adjusted HR of 2.51 (95% CI 1.20 to 3.68, p<0.001) and 2.99 (95% CI 1.60 to 7.76, p<0.001) in the charcoal-burning cohort who had received the HBO therapy for 1–3 times and >3 times, respectively, in contrast to the control group, which were lower than the overall adjusted HR of as high as 4.28. However, further studies were indicated for the association among charcoal-burning attempts, HBO therapy and the risk of dementia.

Psychiatric disorders and risk of dementia in charcoal-burning suicide attempters

In the charcoal-burning cohort, the comorbidities of depression, bipolar disorders, and anxiety disorders were higher than the control groups. This observation indicates that the prevention of charcoal-burning as a suicide method in some populations is, indeed, important. Furthermore, in the charcoal-burning cohort with stroke, TBI, epilepsy,

PD, depression and bipolar disorder, the risk of developing dementia was higher than those without these comorbidities. These findings revealed that the prevention of the charcoal-burning suicide in these patients could be important. Since one study showed in its preliminary results that a charcoal-restriction program reduced the method-specific and overall suicides,[59] a larger scale and longer follow-up study is needed to evaluate the results of charcoal restriction and their effects on the prevention of suicide.

Limitations

There are several limitations to this study. First, patients with dementia could be identified using the insurance claims data; however, data on severity, stage, and impact on their caregivers were not available. The types of dementia were also identified from the ICD codes in these claims data. Second, even though only newly diagnosed dementia would be included in the follow-up period, a protopathic bias, in which the initiation of an exposure occurs in response to an undiagnosed disease (outcome) under study,[60] should also be considered since some of the subjects with charcoal-burning suicide attempts suffered cognitive decline before their suicide attempts. Third, in this study, we

Table 3 Factors of dementia (first 2 years excluded) using Cox regression and Fine and Gray's competing risk model

Variables	No competing risk in the model				Competing risk in the model			
	Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values	Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values
Charcoal-burning suicide (reference: without)	3.22	1.96	5.30	<0.001	3.22	1.96	5.29	<0.001
Sex (reference: male)	1.70	1.18	2.45	0.005	1.72	1.19	2.49	0.004
Age groups (years) (reference: 20–29)								
30–39	0.63	0.30	1.31	0.213	0.63	0.31	1.32	0.223
40–49	0.47	0.22	1.01	0.054	0.48	0.22	1.02	0.058
50–59	0.67	0.31	1.46	0.318	0.69	0.32	1.49	0.345
60–69	1.20	0.55	2.62	0.641	1.24	0.57	2.71	0.583
≥70	2.03	0.94	4.41	0.073	2.14	0.98	4.66	0.056
Comorbidity (reference: without)								
Diabetes mellitus	3.22	1.96	5.30	<0.001	1.03	0.64	1.66	0.908
Hypertension	1.70	1.18	2.45	0.005	1.02	0.64	1.63	0.931
Hyperlipidemia					0.35	0.08	1.49	0.156
Ischemic heart disease	0.63	0.30	1.31	0.213	0.32	0.10	1.04	0.059
Myocardial infarction	0.47	0.22	1.01	0.054	0.83	0.11	6.07	0.852
Peripheral vascular disease	0.68	0.31	1.46	0.318	0.00	–	–	0.975
Heart failure	1.20	0.55	2.62	0.641	0.68	0.16	2.83	0.592
Obesity	2.03	0.94	4.41	0.073	0.000	–	–	0.988
Chronic kidney disease	0.92	0.39	2.14	0.841	1.03	0.44	2.42	0.947
Stroke	4.70	2.44	9.06	<0.001	4.71	2.44	9.10	<0.001
Traumatic brain injury	1.33	0.78	2.27	0.301	1.38	0.81	2.38	0.238
Primary cancer	0.31	0.10	0.93	0.037	0.32	0.11	0.97	0.045
Metastatic tumor	1.08	0.23	5.10	0.923	1.15	0.24	5.41	0.859
Chronic obstructive pulmonary disease	1.45	0.77	2.72	0.254	1.50	0.80	2.83	0.206
Rheumatoid arthritis	0.66	0.16	2.68	0.561	0.66	0.16	2.70	0.565
Peptic ulcer disease	2.68	0.96	7.45	0.059	2.65	0.95	7.35	0.062
Hemiplegia or paraplegia	0.00	–	–	0.970	0.00	–	–	0.970
Liver disease	0.98	0.47	2.05	0.957	1.01	0.48	2.12	0.973
AIDS	0.00	–	–	0.986	0.00	–	–	0.987
Epilepsy	5.21	2.36	11.47	<0.001	5.79	2.61	12.88	<0.001
Tuberculosis	2.18	0.51	9.41	0.295	2.26	0.52	9.87	0.277
Parkinson's disease	2.27	0.67	7.65	0.186	2.27	0.67	7.67	0.187
Atherosclerotic cardiovascular disease	0.00	–	–	0.982	0.00	–	–	0.982
Glaucoma	7.97	1.07	59.077	0.04	7.86	1.06	58.33	0.044
Cystic fibrosis	–	–	–	–	–	–	–	–
Transplantation	0.00	–	–	0.981	0.00	–	–	0.981
Thyroid disorder	0.51	0.06	4.01	0.519	0.49	0.06	3.93	0.500
Gout	1.16	0.36	3.74	0.809	1.13	0.35	3.65	0.845
Crohn's disease and ulcerative colitis	4.81	0.65	35.67	0.125	4.67	0.63	34.67	0.132
Pain	–	–	–	–	–	–	–	–
Pain and inflammations	0.42	0.10	1.72	0.228	0.41	0.10	1.67	0.221
Depression	3.61	1.95	6.67	<0.001	3.51	1.90	6.50	<0.001
Bipolar disorders	2.32	0.72	7.52	0.160	2.27	0.70	7.35	0.172
Anxiety disorders	0.00	–	–	0.97	0.00	–	–	0.972
Psychotic illness	0.61	0.25	1.53	0.294	0.61	0.24	1.51	0.284
Hyperbaric oxygenation therapy (reference: without)	0.00	–	–	0.994	0.00	–	–	0.994
Urbanization level (reference: 4, the lowest)								
1 (highest)	1.07	0.64	1.79	0.790	1.01	0.66	1.84	0.726
2	0.87	0.55	1.38	0.561	0.89	0.56	1.41	0.605
3	1.07	0.59	1.94	0.823	1.09	0.60	1.98	0.777
Insured premium (New Taiwan dollars) (reference: <18,000)								
18,000–34,999	0.59	0.35	0.98	0.042	0.57	0.34	0.96	0.033
≥35,000	0.68	0.46	1.01	0.055	0.67	0.45	0.99	0.046

Adjusted HR, adjusted variables listed in the table.

Table 4 Factors of the subgroup of dementia using Cox regression and Fine and Gray's competing risk model

Comparison cohort	Charcoal-burning suicide (reference: without)	No competing risk in the model				Competing risk in the model			
		Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values	Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values
Without charcoal-burning suicide	All dementia	4.01	3.03	5.30	<0.001	4.22	3.19	5.59	<0.001
(Without ICD-9-CM E952)	AD	4.00	0.56	29.76	0.298	4.13	0.75	30.03	0.211
	VaD	7.96	0.50	38.45	0.265	8.00	0.60	48.88	0.194
	Other degenerative dementia	4.16	3.00	5.49	<0.001	4.28	3.00	5.99	<0.001
Solid or liquid suicide	All dementia	1.03	0.46	1.882	0.256	1.03	0.48	2.00	0.565
(ICD-9-CM E950)	AD	1.00	0.30	1.31	0.142	1.00	0.34	1.51	0.452
	VaD	0.99	0.22	1.25	0.667	1.00	0.23	1.49	0.701
	Other degenerative dementia	1.24	0.57	1.95	0.298	1.29	0.58	2.01	0.384
Gases in domestic use	All dementia	1.00	0.56	2.99	0.725	1.02	0.60	2.13	0.765
(ICD-9-CM E951)	AD	0.89	0.25	1.79	0.668	0.91	0.34	1.86	0.604
	VaD	1.01	0.68	3.01	0.595	1.10	0.70	3.90	0.588
	Other degenerative dementia	0.97	0.42	1.90	0.480	1.00	0.45	3.00	0.484
Hanging	All dementia	0.86	0.20	7.56	0.823	0.87	0.30	8.65	0.842
(ICD-9-CM E953)	AD	0.81	0.17	7.11	0.772	0.83	0.24	8.11	0.701
	VaD	0.76	0.12	6.81	0.682	0.80	0.20	7.46	0.655
	Other degenerative dementia	0.90	0.26	8.62	0.783	0.99	0.33	9.03	0.806
Drowning	All dementia	0.46	0.18	1.00	0.047	0.51	0.21	1.06	0.062
(ICD-9-CM E954)	AD	0.86	0.55	3.59	0.598	0.87	0.60	4.76	0.498
	VaD	0.73	0.43	3.10	0.892	0.76	0.55	3.89	0.797
	Other degenerative dementia	0.43	0.17	0.98	0.040	0.44	0.19	1.00	0.050
Cutting or piercing implements	All dementia	2.99	0.99	21.10	0.062	3.00	0.99	25.41	0.058
(ICD-9-CM E956)	AD	1.07	0.24	16.25	0.774	1.13	0.29	20.00	0.735
	VaD	2.14	0.46	18.48	0.688	2.19	0.50	20.15	0.612
	Other degenerative dementia	3.09	0.99	28.45	0.060	3.24	1.00	33.77	0.053
Jumping from building	All dementia	0.77	0.25	8.45	0.792	0.80	0.28	9.45	0.774
(ICD-9-CM E957)	AD	0.80	0.30	9.07	0.801	0.85	0.31	10.25	0.797
	VaD	0.74	0.22	8.266	0.883	0.76	0.26	9.00	0.812
	Other degenerative dementia	0.71	0.21	8.01	0.767	0.72	0.25	8.94	0.735
Other methods of suicide	All dementia	3.27	2.40	5.89	<0.001	3.30	2.44	6.04	<0.001
(ICD-9-CM E958)	AD	3.14	0.54	29.12	0.294	3.24	0.64	31.46	0.339
	VaD	7.98	0.47	38.56	0.188	8.264	0.60	43.98	0.273
	Other degenerative dementia	3.11	2.07	5.13	<0.001	3.20	2.12	5.27	<0.001

Adjusted HR, adjusted for all the variables listed in table 2.
AD, Alzheimer dementia; ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification; VaD, vascular dementia.

Table 5 Factors of the subgroup of dementia at the end of follow-up using Cox regression and Fine and Gray's competing risk model

Variables	Charcoal-burning suicide	No competing risk in the model				Competing risk in the model			
		Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values	Adjusted HR	95% CI Lower limit	95% CI Upper limit	P values
Total	105	4.01	3.03	5.30	<0.001	4.22	3.19	5.59	<0.001
Alzheimer dementia	2	4.00	0.57	29.76	0.298	4.13	0.75	30.03	0.211
Vascular dementia	1	7.99	0.50	38.45	0.265	8.00	0.598	48.88	0.194
Other degenerative dementia	102	4.16	3.00	5.50	<0.001	4.28	3.002	5.99	<0.001

Adjusted HR, adjusted for all the variables listed in table 3.

identified patients with charcoal-burning suicide attempts by ICD-9-CM code, E952. Even though there are some debates on using this code for charcoal-burning suicide,[61 62] charcoal-burning suicide deaths increased drastically from less than 2% before 1998, to 20%–30% of all suicide deaths in Hong Kong and Taiwan within the following decade,[63 64] and several authors therefore have used E952 code as charcoal-burning suicides in their studies.[1 65] Hence, we assumed that using E952 code to identify charcoal-burning suicide attempts could be a rational choice in Taiwan, even though no previous study has examined the operating characteristics of this code for charcoal-burning suicide attempts.

CONCLUSIONS

The patients with charcoal-burning suicide attempts had a nearly fourfold risk of dementia than the control group. Therefore, further studies are needed to elucidate the underlying mechanisms. If the association reflects a causal effect, this finding would remind clinicians who oversee care for charcoal-burning suicide survivors to make careful evaluations and follow-up for cognitive and behavioral manifestations.

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