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Risk of Myocardial Infarction After Carbon Monoxide Poisoning: A Nationwide Population-Based Cohort Study

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Abstract

Carbon monoxide poisoning (COP) may lead to ischemic changes in organs, and heart is one of the most susceptible targets to ischemic condition. The objective of this study is to evaluate the risk of myocardial infarction following COP. Using a nationwide database of insurance claims in Taiwan, we conducted a population-based cohort study to identify COP patients diagnosed between 1999 and 2012. At a ratio of 3:1, we identified non-COP patients who were matched by the index date and age and compared the risk of myocardial infarction between the two cohorts by time after the index dates of the COP patients, until 2013. We identified 22,258 COP patients and 66,774 non-COP patients. COP patients had an increased risk of myocardial infarction, with an incidence rate ratio of 1.45 (95% confidence interval 1.06–1.98) in comparison with the non-COP patients after adjusting for other independent predictors, including older age, male sex, and underlying comorbidity of hypertension, diabetes, and renal disease. Stratified analyses showed that the increased risk was more prominent in patients with a young age (< 34 years), female sex, and liver disease, and occurred only in the first month of follow-up. We concluded that COP increased the risk of myocardial infarction, but the increased risk was only observed in the first month after COP, which indicated that the impact of COP on the heart was mainly acute. Patients who were younger than 34 years, female, and with liver diseases were more prone to myocardial infarction after COP.

Keywords Carbon monoxide · Heart · Myocardial infarction · Myocardial injury · Poisoning

Abbreviations

COP	Carbon monoxide poisoning
CO	Carbon monoxide
NPD	Nationwide Poisoning Database
LHID2000	Longitudinal Health Insurance Database 2000
CAD	Coronary artery disease
ICD-9	International Classification of Diseases-9
HIV	Human immunodeficiency virus
NTD	New Taiwan Dollars
IRR	Incidence rate ratios
CI	Confidence interval
AHR	Adjusted hazard ratio
HBOT	Hyperbaric oxygen therapy

Introduction

Carbon monoxide (CO) comes from an incomplete combustion of organic matter and is known as a "silent killer" due to its 200- to 240-fold affinity for hemoglobin compared with oxygen [1, 2]. In the United States, carbon monoxide poisoning (COP) contributes to 50,000 emergency department visits and 2700 deaths annually [2, 3]. In Taiwan, COP occurs not only from unintentional causes such as malfunctioning heating appliances, but also frequently from suicide attempts [4]. Because CO is odorless and fatal, COP by charcoal burning became a popular method for suicide in Chinese society since the first case was reported in Hong Kong [5]. A study in Taiwan reported that charcoal burning became the second most-favored method for suicide and accounted for 33.5% of total suicide deaths in Taiwan in 2006 [4]. The incidence of charcoal-burning suicide was 0.22 per 100,000 in 1999 but increased to 6.48 per 100,000 in 2006 [4].

Hypoxia due to CO's competitive binding with hemoglobin is the major mechanism for the toxicity of COP [1, 2, 6]. The heart and brain have the highest oxygen demands and

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therefore are the organs most commonly damaged by COP [1, 2, 6–8]. Myocardial infarction has been found to occur in patients with acute COP [9, 10]. In addition, COP induces inflammatory and immunological reactions in the heart [1, 2, 11–21], which may also increase the risk of subsequent myocardial infarction. However, the long-term effects of COP on myocardial infarction are rarely evaluated, and subgroup analyses by age, sex, and co-morbidities have seldom been carried out. To fill the data gaps, we conducted a retrospective nationwide population-based cohort study.

Methods

Data Sources

We conducted this study using two sub-databases from the National Health Insurance Database: the Nationwide Poisoning Database (NPD) and the Longitudinal Health Insurance Database 2000 (LHID2000). The NPD contains data on all patients of poisoning (including COP) in Taiwan between 1999 and 2013. The LHID2000 contains the registration and claim data of 1,000,000 individuals randomly selected from the original National Health Insurance Research Database [22]. Large, computerized databases derived from this system by the National Health Insurance Administration (the former Bureau of National Health Insurance), Ministry of Health and Welfare (the former Department of Health), Taiwan, and maintained by the National Health Research Institutes, Taiwan, are provided to scientists in Taiwan for research purposes [22].

Definitions, Variables, and Outcomes

We identified COP patients using the International Classification of Diseases-9 (ICD-9) codes 986, E868, E952, and E982 either during admission or ambulance care, listed in the NPD between 1999 and 2012 (Fig. 1). Non-COP patients were identified from the LHID2000 by matching the index date and age with COP patients at a ratio of 3:1. The index date was defined as the date of admission or ambulatory care for COP patients. We excluded patients who had coronary artery disease (CAD) (ICD-9: 410–414) before the index date and stratified the age as < 20, 20–34, 35–49, 50–64, and ≥ 65 years. The underlying co-morbidities included in this study were hypertension (ICD-9: 401–405), diabetes (ICD-9: 250), hyperlipidemia (ICD-9: 272), malignancy (ICD-9: 140–208), stroke (ICD-9: 436–438), dementia (ICD-9: 290), congestive heart failure (ICD-9: 428), chronic obstructive pulmonary disease (ICD-9: 496), liver disease (ICD-9: 570–576), renal disease (ICD-9: 580–593), connective tissue disease (ICD-9: 710), HIV infection (ICD-9: 042, 07953, V08), drug abuse (ICD-9: 303–305), and mental disorder

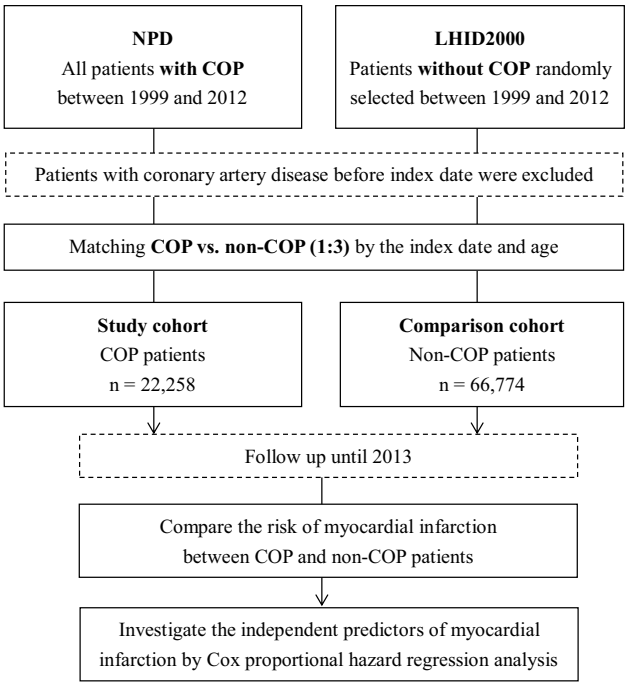

Fig. 1 Flowchart of this study. *NPD* Nationwide Poisoning Database, *LHID* Longitudinal Health Insurance Database, *COP* carbon monoxide poisoning

(ICD-9: 290–302, 306–319). Monthly income was classified as < 19,999, 20,000–39,999, and ≥ 40,000 New Taiwan Dollars (NTD). Myocardial infarction was defined as ICD-9 410.

Comparison of the Risk of Myocardial Infarction Between COP and Non-COP Patients

Following up the two cohorts until 2013, we compared the risk of myocardial infarction between them. We performed both overall analyses and stratified analyses according to age, sex, underlying co-morbidities, and follow-up period (Fig. 1). In addition, we tried to identify the independent predictors for myocardial infarction and evaluate their effects.

Statistical Analyses

We used the two-sample *t* test and the Chi square test to evaluate the differences in continuous variables and categorical variables, respectively. Estimated incidence rate ratios (IRRs) were obtained using Poisson regression with adjustment for sex, underlying co-morbidities (hypertension, diabetes, hyperlipidemia, malignancy, stroke, dementia, chronic obstructive pulmonary disease, liver disease, renal disease, connective tissue disease, and mental disorder), and monthly income. Kaplan–Meier analysis and the log-rank test were used to compare the risks of myocardial infarction

between the two cohorts during the follow-up period. Stratified analyses by age, sex, underlying co-morbidities, and follow-up periods were performed to investigate potential effect modifications. In addition, we used Cox proportional hazard regressions to identify independent predictors of myocardial infarction and estimate their effects. Specifically, we constructed a "full model" which included all the variables with p values < 0.05 in the univariate analyses, and then a "reduced model" in which all the variables were statistically significant. All the analyses were performed using SAS 9.4 for Windows (SAS Institute, Cary, NC, USA) at a two-tailed significance level of 0.05.

Results

The mean age of the COP cohort was 34.6 years, with a standard deviation of 14.0 years (Table 1). The majority of COP patients were in the age group 20–34 years (41.81%), followed by 35–49 years (32.48%). In the COP patients, 51.0% were females. In comparison with the non-COP patients, the COP patients had higher prevalence rates of hypertension, diabetes, malignancy, stroke, dementia, congestive heart failure, chronic obstructive pulmonary disease, liver disease, renal disease, HIV infection, drug abuse, and mental disorder, and had lower monthly incomes (all $p < 0.05$).

We observed a higher risk of myocardial infarction in COP patients during the follow-up, with an IRR of 1.45 after adjustment for sex; the underlying co-morbidities of hypertension, diabetes, hyperlipidemia, malignancy, stroke, dementia, chronic obstructive pulmonary disease, liver disease, renal disease, connective tissue disease, and mental disorder; and monthly income (95% confidence interval [CI] 1.06–1.99) (Table 2). We did not adjust for HIV infection and drug abuse because there were zero cases of myocardial infarction in the COP patients who had HIV infection or drug abuse. Both the Kaplan–Meier analysis and the log-rank test showed a significant difference between the two cohorts ($p = 0.0175$) (Fig. 2). In stratified analyses, we found the increased risk was more prominent in young (< 34 years old) patients (IRR 3.62; 95% CI 1.31–10.00), female patients (IRR 1.76; 95% CI 1.02–3.04), patients with liver disease (IRR 2.06; 95% CI 1.04–4.08), and the first month of follow-up (IRR 7.73; 95% CI 1.50–39.85), which indicated that these variables were effect modifiers. No significant differences in the risk of myocardial infarction were observed after 1 month of follow-up between COP and non-COP cohorts.

Cox proportional hazard regression analyses showed that independent predictors of myocardial infarction included COP (adjusted hazard ratio [AHR] 1.45; 95% CI 1.06–1.98), older age, male sex (AHR 2.31; 95% CI 1.68–3.17), hypertension (AHR 2.17; 95% CI 1.47–3.19), diabetes (AHR 1.98; 95% CI 1.30–3.02), and renal disease (AHR 1.80; 95% CI 1.23–2.62) (Table 3). There were no remarkable differences in the AHR estimates between the full and the reduced models.

Table 1 Comparison of age, sex, underlying co-morbidities, and monthly income between COP and non-COP patients

Variable	COP patients $n = 22,258$	Non-COP patients $n = 66,774$	p Value
Age (years)	34.6 ± 14.0	34.6 ± 14.0	0.996
Age (years)			
< 20	2666 (12.0)	8000 (12.0)	> 0.999
20–34	9305 (41.8)	27,913 (41.8)	
35–49	7229 (32.5)	21,687 (32.5)	
50–64	2390 (10.7)	7170 (10.7)	
≥ 65	668 (3.0)	2004 (3.0)	
Sex			
Female	11,340 (50.9)	34,873 (52.2)	0.001
Male	10,918 (49.1)	31,901 (47.8)	
Underlying comorbidity			
Hypertension	1599 (7.2)	4476 (6.7)	0.014
Diabetes	947 (4.3)	2266 (3.4)	< 0.001
Hyperlipidemia	1215 (5.5)	3446 (5.2)	0.084
Malignancy	456 (2.0)	1089 (1.6)	< 0.001
Stroke	291 (1.3)	546 (0.8)	< 0.001
Dementia	61 (0.3)	108 (0.2)	< 0.001
Congestive heart failure	117 (0.5)	183 (0.3)	< 0.001
Chronic obstructive pulmonary disease	151 (0.7)	302 (0.5)	< 0.001
Liver disease	2644 (11.9)	6857 (10.3)	< 0.001
Renal disease	1869 (8.4)	4033 (6.0)	< 0.001
Connective tissue disease	155 (0.7)	436 (0.7)	0.490
HIV infection	64 (0.3)	49 (0.1)	< 0.001
Drug abuse	997 (4.5)	585 (0.9)	< 0.001
Mental disorder	6501 (29.2)	8493 (12.7)	< 0.001
Monthly income (NTD)			
< 19,999	15,919 (71.5)	40,863 (61.2)	< 0.001
20,000–39,999	5069 (22.8)	19,196 (28.7)	
≥ 40,000	1270 (5.7)	6715 (10.1)	

COP carbon monoxide poisoning, *NTD* New Taiwan Dollars. Data are expressed as means ± SD or *n* (%)

Discussion

This retrospective nationwide population-based cohort study showed that the risk of myocardial infarction increased after COP. Stratified analysis showed that the increased risk was more prominent in patients with a young (< 34 years)

Table 2 Comparison of the risk of myocardial infarction Between COP and non-COP patients by estimating the IRR with Poisson regression

Variable	COP patients			Non-COP patients			IRR (95% CI)[a]	*p* Value
	Case (%)	PY	Rate	Case (%)	PY	Rate		
Overall analysis	57 (0.26)	110,487	0.52	128 (0.19)	360,648	0.35	1.45 (1.06–1.99)	0.019
Stratified analysis								
Age (years)								
< 34	8 (0.07)	63,678	0.13	7 (0.02)	201,968	0.03	3.62 (1.31–10.00)	0.013
35–49	21 (0.29)	34,764	0.60	49 (0.23)	115,938	0.42	1.43 (0.86–2.38)	0.171
50–64	12 (0.50)	9434	1.27	31 (0.43)	32,854	0.94	1.35 (0.69–2.62)	0.380
≥ 65	16 (2.40)	2612	6.13	41 (2.05)	9888	4.15	1.48 (0.83–2.63)	0.186
Sex								
Female	20 (0.18)	58,058	0.34	37 (0.11)	189,491	0.20	1.76 (1.02–3.04)	0.041
Male	37 (0.34)	52,429	0.71	91 (0.29)	171,158	0.53	1.33 (0.91–1.95)	0.146
Underlying comorbidity								
Hypertension	21 (1.31)	5964	3.52	50 (1.12)	19,729	2.53	1.39 (0.83–2.31)	0.206
Diabetes	9 (0.95)	3383	2.66	30 (1.32)	9555	3.14	0.85 (0.40–1.78)	0.663
Hyperlipidemia	11 (0.91)	4378	2.51	24 (0.70)	14,018	1.71	1.47 (0.72–3.00)	0.292
Malignancy	4 (0.88)	1394	2.87	4 (0.37)	4518	0.89	3.24 (0.81–12.96)	0.096
Stroke	6 (2.06)	1015	5.91	12 (2.20)	2388	5.03	1.18 (0.44–3.13)	0.745
Dementia	1 (1.64)	179	5.58	4 (3.70)	434	9.23	0.60 (0.07–5.41)	0.653
Chronic obstructive pulmonary disease	2 (1.32)	503	3.98	4 (1.32)	1389	2.88	1.38 (0.25–7.54)	0.709
Liver disease	14 (0.53)	10,663	1.31	20 (0.29)	31,374	0.64	2.06 (1.04–4.08)	0.038
Renal disease	10 (0.54)	7717	1.30	27 (0.67)	18,188	1.48	0.87 (0.42–1.80)	0.713
Connective tissue disease	1 (0.65)	581	1.72	1 (0.23)	1801	0.56	3.10 (0.19–49.56)	0.424
Mental disorder	16 (0.25)	25,814	0.62	27 (0.32)	37,531	0.72	0.86 (0.46–1.60)	0.637
Follow-up period								
< 1 month	5 (0.02)	1791	2.79	2 (< 0.01)	5539	0.36	7.73 (1.50–39.85)	0.015
1–6 months	3 (0.01)	8629	0.35	10 (0.02)	27,120	0.37	0.94 (0.26–3.43)	0.929
7–12 months	4 (0.02)	9790	0.41	6 (0.01)	31,105	0.19	2.12 (0.60–7.51)	0.245
1–2 years	6 (0.03)	17,866	0.34	15 (0.03)	57,444	0.26	1.29 (0.50–3.31)	0.602
2–4 years	11 (0.07)	28,853	0.38	30 (0.06)	94,403	0.32	1.20 (0.60–2.39)	0.606
≥ 4 years	28 (0.23)	43,559	0.64	65 (0.16)	145,038	0.45	1.43 (0.92–2.23)	0.111

COP carbon monoxide poisoning, *IRR* incidence rate ratio, *PY* person-year, *CI* confidence interval.

[a]Adjusted for sex, underlying comorbidities (hypertension, diabetes, hyperlipidemia, malignancy, stroke, dementia, chronic obstructive pulmonary disease, liver disease, renal disease, connective tissue disease, and mental disorder), and monthly income

age, female sex, and liver disease, and occurred in the first month of follow-up only. After the acute poisoning period (< 1 month), changes in the risk of myocardial infarction in COP patients did not reach statistical significance. The independent predictors of myocardial infarction identified in our study were COP, older age, male sex, hypertension, diabetes, and renal disease.

This study showed that the effect of COP on myocardial infarction was acute and occurred mainly in the first month after the exposure to CO. In other words, COP did not increase the long-term risk of myocardial infarction, and this finding is compatible with a previous study [9]. Some studies that used cardiac biomarkers or electrocardiography for defining myocardial infarction reported that 37% of the patients with moderate to severe COP had a concomitant myocardial infarction [10, 23]. In these patients, the in-hospital mortality was 5%, and the long-term all-cause mortality was 38% after a median follow-up of 7.6 years; both were higher than those in the COP patients without myocardial infarction [10, 23]. Another study reported that all COP patients with myocardial infarction were found to have normal coronary arteries without evidence of vasospasm shown by coronary angiogram [9]. The systolic function of the left ventricle may be normal or mildly to severely impaired, but most of the myocardial dysfunction disappeared within 1 day [9], suggesting that the mechanism of COP-related myocardial infarction is not via the coronary artery, but via other processes such as tissue hypoxia and myocardial stunning

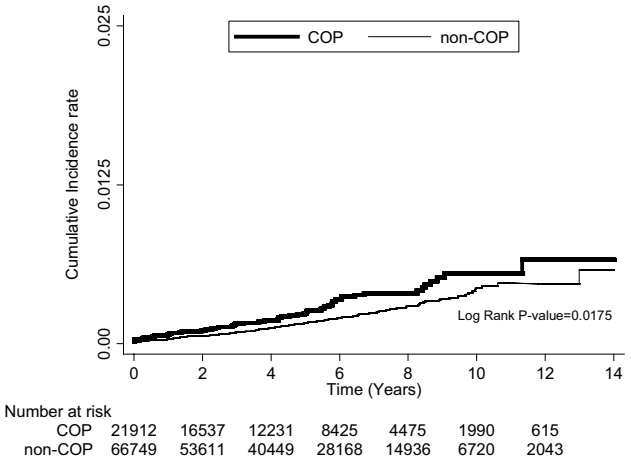

Fig. 2 Comparison of the risk of myocardial injury between COP and non-COP patients by Kaplan–Meier analysis and log-rank test. *COP* carbon monoxide poisoning

[9, 10, 24]. In some case reports, coronary artery occlusion was found in COP patients, but these reports could not determine a causal relationship between COP and coronary artery occlusion [25–27]. In addition to acute intoxication as we studied, CO is an important air pollutant, and a meta-analysis showed that CO increased the risk for myocardial infarction (relative risk 1.048; 95% CI 1.026–1.070) [28], which support the conclusion of an association between COP and myocardial infarction in our study. In addition to hypoxia, COP may induce immunological and inflammatory damages to the heart via reactive oxygen species production by the following mechanisms: (1) binding to intracellular proteins, (2) nitric oxide generation and peroxynitrite production, (3) lipid peroxidation by neutrophils, (4) mitochondrial oxidative stress, (5) apoptosis (programmed cell death), (6) immune-mediated injury, and (7) delayed inflammation [1, 2, 11–21].

In this study, age was matched between COP and non-COP patients, and therefore we could not identify the high risk age of COP. However, through stratified analyses, we found that age was an effect modifier of COP, with young (< 34 years) being more vulnerable to COP-associated myocardial infarction. We also found that sex is an effect modifier of COP, with the female sex being more vulnerable. These results are compatible with those in a previous nationwide cohort study which reported that COP increased mortality especially in the younger (< 30 years) and female patients [29]. Previous studies on risk factors for myocardial infarction also revealed that females were more sensitive than males to the harmful effects of smoking, diabetes, elevated triglycerides, and left ventricular hypertrophy [30, 31]. Interactions between the risk factors (including smoking) and hormonal factors (including oral contraceptive use and hormone replacement therapy) may be involved in the development of myocardial infarction [30, 31]. This may also be true in the case of COP. While we found that liver disease was also an effect modifier like age and sex, we could not find any previous reports by using "liver disease," "myocardial injury," "myocardial infarction," and "carbon monoxide" to search literature indexed by the PubMed. Therefore, this is very likely to be a novel finding. In addition, our study also showed that older age, male sex, hypertension, diabetes, and renal disease were independent predictors for myocardial infarction, which are known as conventional risk factors for myocardial ischemia reported in the literature [29, 32, 33].

In order to evaluate the effect of CAD, which was excluded in the initial analysis, we performed a comparison between COP patients with history of CAD and non-COP patients with history of CAD and found that COP patients with history of CAD were more vulnerable to myocardial injury than non-COP patients with history of CAD (IRR 2.00; 95% CI 1.52–2.63 and Fig. 3). The current result is compatible with previous human and environmental studies. Some prospective studies on males with CAD revealed that low levels of carboxyhemoglobin exacerbate myocardial ischemia during graded exercise [34, 35]. A multicenter cohort study in European also showed that ambient CO increased risk of hospital cardiac readmissions in patients with CAD [36]. Another multicenter study in the United States reported a positive association between short-term exposure to ambient CO and the risk of hospitalizations for cardiovascular disease [37]. A recent meta-analysis revealed that myocardial infarction can be triggered by air pollution, physical exertion, alcohol, and coffee; however, these estimates did not account for the contribution of CO [38]. The current study found that COP is a triggering factor for myocardial infarction and suggested that in addition to particular matters, CO may be another air pollutant that may contribute to the occurrence of myocardial infarction.

Various methods have been suggested for diagnosing myocardial infarction caused by COP, including electrocardiogram, echocardiography, scintiscanning, coronarography, single photon emission computed tomography, and levels of troponin I, B-type natriuretic peptide, creatine kinase, and creatine kinase-MB [9, 39–41]. Further studies are warranted to identify the ones that are best for screening and monitoring after COP, the standard treatment for COP is administration of oxygen via non-rebreathing mask or endotracheal intubation in order to provide nearly 100% of oxygen, which shortens the half-life of CO from 320 min on normal air to 80 min [1]. Hyperbaric oxygen therapy (HBOT) is also suggested for patients with COP, especially for those with severe poisoning, to reduce neurological sequelae, which are the most common and concerning complication [1]. However, the benefit of HBOT in limiting

Table 3 Predictors of myocardial infarction in all patients by Cox proportional hazard regression analysis

Variable	Crude HR (95% CI)	Full model[a] AHR (95% CI)	Reduced model[b] AHR (95% CI)
Cohort			
COP patients	1.46 (1.07–1.99)	1.45 (1.06–1.99)	1.45(1.06–1.98)
Non-COP patients	1 (reference)	1 (reference)	1 (reference)
Age (years)			
< 34	1 (reference)	1 (reference)	1 (reference)
35–49	8.34 (4.78–14.57)	7.33 (4.17–12.88)	7.33 (4.17–12.88)
50–64	18.84 (10.46–33.94)	12.16 (6.59–22.45)	12.18 (6.60–22.47)
≥ 65	82.84 (46.90–146.34)	36.38 (19.28–68.64)	36.36 (19.27–68.60)
Sex			
Female	1 (reference)	1 (reference)	1 (reference)
Male	2.49 (1.82–3.40)	2.33 (1.69–3.13)	2.31 (1.68–3.17)
Underlying comorbidity			
Hypertension	11.42 (8.47–15.39)	2.17 (1.47–3.19)	2.17 (1.47–3.19)
Diabetes	9.99 (7.00–14.25)	1.98 (1.30–3.01)	1.98 (1.30–3.02)
Hyperlipidemia	6.13 (4.23–8.89)	1.16 (0.75–1.79)	–
Malignancy	3.66 (1.80–7.44)	1.08 (0.52–2.22)	–
Stroke	15.43 (9.48–25.12)	1.72 (1.00–2.98)	–
Dementia	22.21 (9.12–54.05)	1.74 (0.66–4.64)	–
Chronic obstructive pulmonary disease	8.60 (3.81–19.41)	0.96 (0.42–2.22)	–
Liver disease	2.38 (1.64–3.46)	0.82 (0.55–1.23)	–
Renal disease	4.45 (3.10–6.39)	1.79 (1.23–2.62)	1.80 (1.23–2.62)
Connective tissue disease	2.26 (0.56–9.09)	1.32 (0.32–5.36)	–
Mental disorder	2.04 (1.45–2.88)	1.01 (0.70–1.48)	–
Monthly income (NTD)			
< 19,999	1.14 (0.68–1.92)	1.04 (0.61–1.79)	–
20,000–39,999	0.68 (0.37–1.24)	1.03 (0.56–1.90)	–
≥ 40,000	1 (reference)	1 (reference)	–

COP carbon monoxide poisoning, *HR* hazard ratio, *AHR* adjusted hazard ratio, *CI* confidence interval, *NTD* New Taiwan Dollars

[a]Adjusted for age, sex, underlying comorbidities (hypertension, diabetes, hyperlipidemia, malignancy, stroke, dementia, chronic obstructive pulmonary disease, liver disease, renal disease, connective tissue disease, and mental disorder), and monthly income

[b]Adjusted for age, sex, and the underlying comorbidities of hypertension, diabetes, and renal disease

or reversing myocardial infarction is still unknown [41, 42], and further studies are needed to address this issue.

Although our study has a large sample size and thus is able to perform stratified analyses and evaluate the effects of multiple risk factors for myocardial infarction at the same time, it has some limitations. First, using ICD-9 codes to identify patients with myocardial infarction may underestimate the incidence. Despite there is a good sensitivity of 88% using ICD-9 code 410 to identify myocardial infarction or injury [43], some patients might be missed. However, this is not expected to cause remarkable bias because both COP and non-COP cohorts had the same issue of misclassification. Second, the impact of HBOT was not evaluated. But, as we discussed earlier, the effect of HBOT in such cases is still unknown [42], and thus further studies are warranted to address this issue. Third, we did not have information on smoking, which is an important risk factor for myocardial infarction. Because the prevalence of smoking in Taiwanese females is very low (4.4% in 2011 [44]), the effects of smoking on the results have been minimized when the analyses were adjusted for sex.

Conclusion

This study showed that COP increased the acute risk of myocardial infarction within 1 month, especially in patients who are < 34 years, females, or with liver disease. The independent predictors of myocardial infarction after COP include older age, male sex, and underlying comorbidity of

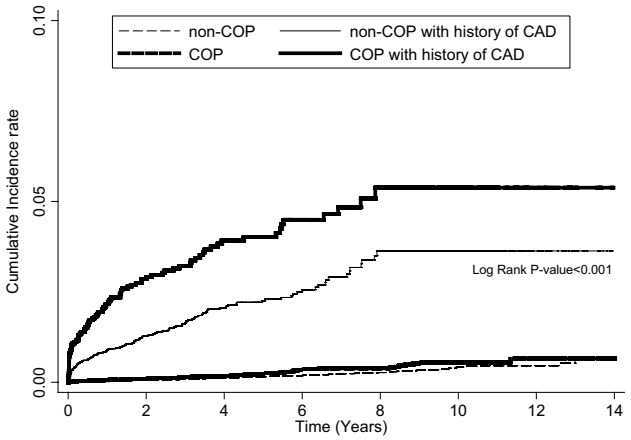

Fig. 3 Comparison of the risk of myocardial injury between COP patients with history of CAD and non-COP patients with history of CAD and between COP and non-COP patients (i.e., without history of CAD in the Fig. 2) by Kaplan–Meier analysis and log-rank test. *COP* carbon monoxide poisoning, *CAD* coronary artery disease

hypertension, diabetes, or renal disease. While the results have casted some light on the risk of myocardial infarction after COP, further studies are needed to identify the best methods for screening and monitoring myocardial infarction after COP, as well as the effect of HBOT.

Author contributions C-C Huang and H-RG designed and conceived this study and wrote the manuscript. H-CH and Y-CC performed the statistical analysis and wrote the manuscript. H-JL, C-C Hsu, J-JW, and S-BS provided professional suggestions and wrote the manuscript. All the authors have read and approved the final manuscript.

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Compliance with Ethical Standards

Conflict of interest The authors declare no potential conflicts of interest.

Ethical Approval This study involved human data and was conducted in strict accordance with the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board (IRB) at the Chi-Mei Medical Center.

Informed Consent The two databases consisted of depersonalized information, and so the requirement of informed consent was waived by the IRB as the study did not affect the welfare of the participants.

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