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Association between hemorrhoid and risk of coronary heart disease

A nationwide population-based cohort study

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Abstract

The purpose of the study was to address the association between hemorrhoid and the subsequent risk of coronary heart disease (CHD) development.

This retrospective cohort study used reimbursement claims data from the Longitudinal Health Insurance Database 2000 in Taiwan. Thirty-three thousand thirty-four patients with hemorrhoids and 132,136 age-, gender-, and index year matched controls between 2000 and 2010 were identified. Cox model was performed to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) of CHD development for the hemorrhoid cohort compared with the nonhemorrhoid cohort.

During a follow-up period of 12 years, the overall incidence rate of CHD was 9.91 per 1000 person-years in the hemorrhoid patients and was 1.36-fold higher than in the nonhemorrhoid cohort (7.28 per 1000 person-years) with an adjusted hazard ratio (aHR) of 1.27 (95% CI = 1.21–1.34). Moreover, compared with the nonhemorrhoid patients without these comorbidities, among patients with hemorrhoids, those with any 2 comorbidities were at a significantly increased risk of CHD (HR = 7.12, 95% CI = 6.61–7.67; $P < .001$), followed by those with any 1 comorbidity (HR = 3.23, 95% CI = 2.94–3.54; $P < .001$).

We found that hemorrhoid patients had a 1.27-fold higher risk of CHD compared with those without hemorrhoids after adjusting for the potential confounding factors.

Abbreviations: CHD = coronary heart disease, CI = confidence interval, COPD = chronic obstructive pulmonary disease, HR = hazard ratio, ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification, LHID 2000 = Longitudinal Health Insurance Database 2000, NHI = National Health Insurance, NHIRD = National Health Insurance Research Database.

Keywords: cohort study, coronary heart disease, hemorrhoid

1. Introduction

Hemorrhoid is an increasing prevalent gastrointestinal disorder contributing to reduced quality of life.[1,2] Clinical manifestations were in great diversity, ranging from asymptomatic to rectal bleeding.[1–3] Increased intraabdominal pressure and fragile supporting structure were the principal causes of the increased incidence of hemorrhoid.[1–3]

The presentations of coronary heart disease (CHD) were varied, including stable angina, unstable angina, and acute myocardial infarction.[4–6] CHD imposed a great medical burden worldwide because of high mortality rate.[4–6] Several CHD-associated risk factors have been well defined according to previous investigations.[4–7]

Although hemorrhoid and CHD shared several risk factors[1–7]; however, to our best knowledge, there is limited investigation on the correlation between hemorrhoid and the risk of CHD development in the literature. Using a nationwide, population-based dataset, the study was aimed to assess the association between hemorrhoid and the subsequent risk of CHD development.

2. Methods

2.1. Data source

This retrospective cohort study used reimbursement claims data from the Longitudinal Health Insurance Database 2000 (LHID2000) in Taiwan, which was part of the Taiwan National Health Insurance Research Database (NHIRD). The NHIRD has been described in detail in previous studies.[8,9] In brief, it consisted of detailed healthcare data from 23.74 million enrollees, representing 99% of Taiwan's entire population.[10] We used the LHID2000 containing complete data of 1,000,000 randomly sampled beneficiaries between 1996 and 2011 from the original NHIRD. All diagnoses were recorded according to

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International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The Ethics Review Board of China Medical University and Hospital in Taiwan approved this study (CMUH-104-REC2-115).

2.2. Sampled participants

The hemorrhoid cohort was identified between January 1, 2000 and December 31, 2010, with newly diagnosed hemorrhoid (ICD-9-CM code 455) and the index date was set as the first diagnosed day. Patients with a history of CHD (ICD-9-CM codes 410–414) before the index date and those aged < 20 years were excluded. The nonhemorrhoid cohort was randomly retrieved from the LHID2000 during the same period of 2000 to 2010, and the exclusion criteria were the same as the hemorrhoid cohort. For each corresponding hemorrhoid patient, 4 nonhemorrhoid subjects were frequency matched by sex, age, and index year. Finally, a total of 33,034 patients with hemorrhoids and 132,136 subjects without hemorrhoids were included in this study.

2.3. Outcome and comorbidities

Each study subject was followed until a diagnosis of CHD, or until the subject was censored due to withdrawal from the database, death, or the end of follow-up on December 31, 2011. The baseline comorbidity included hypertension (ICD-9-CM codes 401–405), diabetes mellitus (ICD-9-CM code 250), hyperlipidemia (ICD-9-CM code 272), asthma (ICD-9-CM code 493), chronic obstructive pulmonary disease (COPD) (COPD; ICD-9-CM codes 491, 492, and 496), chronic liver disease (ICD-9-CM code 571), atrial fibrillation (ICD-9-CM code 427.31), heart failure (ICD-9-CM code 428), cancer (ICD-9-CM codes 140–208), and obesity (ICD-9-CM code 278).

2.4. Statistical analysis

The distributions of demographic data and comorbidities were compared between the hemorrhoid cohort and the nonhemorrhoid cohort using the Chi-square test (for category variables) and the Student *t* test (for continuous variables). We estimated the cumulative incidence curves of CHD for both hemorrhoid and non-hemorrhoid cohorts by Kaplan–Meier method and tested the curve difference between the 2 cohorts by log-rank test. The incidence densities of CHD (per 1000 person-years) were estimated for each cohort and stratified by sex, age, and comorbidity. Univariable and multivariable Cox proportional hazard regression analyses were performed to estimate the hazard ratios (HRs) and 95% CIs of CHD development for the hemorrhoid cohort compared with the nonhemorrhoid cohort. The multivariable Cox models were adjusted for comorbidities of hypertension, diabetes mellitus, hyperlipidemia, asthma, COPD, chronic liver disease, atrial fibrillation, heart failure, cancer, and obesity. Additional data were analyzed to evaluate the joint effect of hemorrhoid and CHD-associated risk factors on the risk of CHD development. All analyses were performed using SAS statistical software (Version 9.4, SAS Institute, Cary, NC). The 2-sided significance level was set at $P < .05$.

3. Results

Baseline demographic characteristics and comorbidities of the hemorrhoid patients and the nonhemorrhoid patients are shown in Table 1 (1:4 matching for age and sex). Most people were men (54.0% vs 54.0%) and aged ≤49 years (67.4% vs 67.4%). The mean ages of the hemorrhoid and the nonhemorrhoid cohorts were 44.7 (±14.7) and 44.3 years (±15.0), respectively. The prevalence of comorbidities, including hypertension, hyperlipidemia, asthma, COPD, chronic liver disease, atrial fibrillation, heart failure, cancer, and obesity were significantly higher in the hemorrhoid cohort than in the nonhemorrhoid cohort. The median follow-up period was 6.87 years for the hemorrhoid cohort and 6.78 years for the nonhemorrhoid cohort. The results of the Kaplan–Meier analysis for the cumulative incidence of CHD in the hemorrhoid cohort were significantly higher than in

Table 1

Demographic characteristics and comorbidities in patients with and without hemorrhoids.

Variable	Hemorrhoid		*P*
	No, N = 132,136	Yes, N = 33,034	
Sex	n (%)	n (%)	.99
Female	60,820 (46.0)	15,205 (46.0)	
Male	71,316 (54.0)	17,829 (54.0)	
Age, mean (SD)*	44.3 (15.0)	44.7 (14.7)	<.001*
Stratify age			.99
≤49	89,124 (67.4)	22,281 (67.4)	
50–64	28,716 (21.7)	7179 (21.7)	
≥65	14,296 (10.8)	3574 (10.8)	
Comorbidity			
Hypertension	19,687 (14.9)	6107 (18.5)	<.001
Diabetes mellitus	5839 (4.42)	1437 (4.35)	<.001
Hyperlipidemia	12,708 (9.62)	4844 (14.7)	<.001
Asthma	4533 (3.43)	1622 (4.91)	<.001
COPD	6111 (4.62)	2406 (7.28)	<.001
Chronic liver disease	16,183 (12.3)	6780 (20.5)	<.001
Atrial fibrillation	3410 (2.58)	1374 (4.16)	<.001
Heart failure	664 (0.50)	220 (0.67)	<.001
Cancer	1858 (1.41)	891 (2.70)	<.001
Obesity	1046 (0.79)	432 (1.31)	<.001

Chi-square test.

COPD = chronic obstructive pulmonary disease, SD = standard deviation.

* Student *t* test.

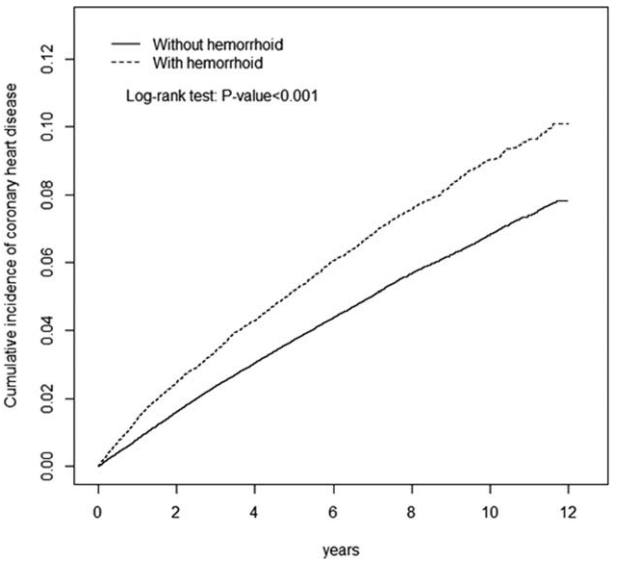

Figure 1. Cumulative incidence curves of coronary heart disease (CHD) for patients with and without hemorrhoids.

Table 2

Comparison of incidence and hazard ratio of coronary heart disease stratified by sex, age and comorbidity between patients with and without hemorrhoids.

	Hemorrhoid							
	No			Yes				
Variable	Event	PY	Rate†	Event	PY	Rate†	Crude HR (95% CI)	Adjusted HR‡ (95% CI)
All	6321	868,591	7.28	2177	219,606	9.91	1.36 (1.30, 1.43)**	1.27 (1.21, 1.34)**
Sex								
Female	2391	410,496	5.82	815	103,386	7.88	1.36 (1.25, 1.47)**	1.21 (1.11, 1.31)**
Male	3930	458,095	8.58	1362	116,220	11.7	1.37 (1.29, 1.46)**	1.23 (1.15, 1.30)**
P for interaction								0.85
Stratify age								
≤49	2062	619,233	3.33	762	157,419	4.84	1.45 (1.34, 1.58)**	1.28 (1.18, 1.40)**
50–64	2477	173,606	14.3	810	43,139	18.8	1.32 (1.22, 1.43)**	1.24 (1.14, 1.34)**
≥65	1782	75,752	23.5	605	19,048	31.8	1.35 (1.24, 1.49)**	1.29 (1.18, 1.42)**
P for interaction								0.09
Comorbidity§								
No	2223	622,617	3.57	597	130,335	4.58	1.28 (1.17, 1.40)**	1.28 (1.17, 1.40)**
Yes	4098	245,974	16.7	1580	89,271	17.7	1.07 (1.01, 1.13)*	1.07 (1.07, 1.13)*
P for interaction								<.001

CI = confidence interval, crude HR = crude hazard ratio, PY = person-year.

† Rate, incidence rate, per 1000 person-years.

‡ Adjusted HR: Multivariable analysis including comorbidities of hypertension, diabetes mellitus, hyperlipidemia, asthma, chronic obstructive pulmonary disease, chronic liver disease, atrial fibrillation, heart failure, cancer, and obesity.

§ Comorbidity: Patients with any one of the comorbidities: hypertension, diabetes mellitus, hyperlipidemia, asthma, chronic obstructive pulmonary disease, chronic liver disease, atrial fibrillation, heart failure, cancer, and obesity were classified as the comorbidity group.

* $P < .05$.

** $P < .001$.

the nonhemorrhoid cohort by the end of the 12-year follow up (Fig. 1, log rank test, $P < .001$).

Table 2 illustrates the incidence density rate and HR of CHD stratified by sex, age, and comorbidity between patients with and without hemorrhoids. The overall incidence rate of CHD was 9.91 per 1000 person-years in the hemorrhoid patients and was 1.36-fold higher than in the nonhemorrhoid cohort (7.28 per 1000 person-years) with an adjusted hazard ratio (aHR) of 1.27 (95% CI = 1.21–1.34). Both cohorts were male dominant regarding the incidence densities of CHD. The gender-specific aHR of CHD for the hemorrhoid cohort relative to the nonhemorrhoid cohort was significantly higher for both men (aHR = 1.23, 95% CI = 1.15–1.30) and women (aHR = 1.21, 95% CI = 1.11–1.31). The incidence of CHD increased with age in both cohorts. The risk of CHD for the hemorrhoid cohort relative to the nonhemorrhoid cohort was significant higher for all age groups (aHR = 1.28, 95% CI = 1.18–1.40 for aged ≤49 years; aHR = 1.24, 95% CI = 1.14–1.34 for aged 50–64 years; aHR = 1.29, 95% CI = 1.18–1.42 for aged ≥65 years). Moreover, patients with comorbidities had an increased CHD incidence in both cohorts. Regardless of comorbidities, the hemorrhoid cohort showed a higher aHR of CHD than the nonhemorrhoid cohort. In the interaction analysis, comorbidity significantly modified the association between hemorrhoid and CHD (*P*-value for interaction < .001).

Table 3

Joint effects for coronary heart disease between hemorrhoid and coronary heart disease-associated risk factors.

Variable	N	No. of events	Rate†	Crude HR	95% CI
None	89,024	2223	3.57	1	(Reference)
Only hemorrhoid	18,075	597	4.58	1.28	(1.17, 1.40)**
Only hypertension	6488	953	21.8	6.13	(5.68, 6.61)**
Only diabetes mellitus	686	68	15.6	4.41	(3.46, 5.61)**
Only hyperlipidemia	2214	191	13.0	3.65	(3.15, 4.23)**
Only asthma	1576	53	5.53	1.56	(1.19, 2.05)*
Only COPD	1518	102	10.6	3.00	(2.46, 3.66)**
Only chronic liver disease	6837	269	5.39	1.51	(1.33, 1.72)**
Only atrial fibrillation	971	79	12.3	3.46	(2.76, 4.33)**
Only heart failure	36	3	13.5	3.84	(1.24, 11.9)**
Only cancer	694	28	7.44	2.11	(1.45, 3.06)**
Only obesity	364	12	5.53	1.57	(0.89, 2.76)
Hemorrhoid with any 1 comorbidity	7354	571	11.5	3.23	(2.94, 3.54)**
Hemorrhoid with any 2 comorbidities	7605	1009	25.4	7.12	(6.61, 7.67)**

CI = confidence interval, COPD = chronic obstructive pulmonary disease, HR = hazard ratio.

† Rate, per 1000 person-year.

* $P < .01$.

** $P < .001$.

The joint effects for CHD development between hemorrhoid and CHD-associated risk factors are shown in Table 3. The risk of CHD in the patients with only hemorrhoid relative to those with neither hemorrhoid nor comorbidity was statistically significant, with a HR of 1.28 (95% CI = 1.17–1.40). Compared with the nonhemorrhoid patients without these comorbidities, those with only hypertension had the highest risk of CHD (HR = 6.13, 95% CI = 5.68–6.61), followed by those with only diabetes mellitus (HR = 4.41, 95% CI = 3.46–5.61), those with only heart failure (HR = 3.84, 95% CI = 1.24–11.9), those with only hyperlipidemia (HR = 3.65, 95% CI = 3.15–4.23), those with only atrial fibrillation (HR = 3.46, 95% CI = 2.76–4.33), those with only COPD (HR = 3.00, 95% CI = 2.46–3.66), those with only cancer (HR = 2.11, 95% CI = 1.45–3.06), those with only asthma (HR = 1.56, 95% CI = 1.19–2.05), and those with only chronic liver disease (HR = 1.51, 95% CI = 1.33–1.72). Moreover, compared with the nonhemorrhoid patients without these comorbidities, among patients with hemorrhoids, those with any 2 comorbidities were at a significantly increased risk of CHD (HR = 7.12, 95% CI = 6.61–7.67), followed by those with any 1 comorbidity (HR = 3.23, 95% CI = 2.94–3.54).

4. Discussion

This is the first study to address the association between hemorrhoid and the subsequent risk of CHD development. After adjustment for the potential confounding factors, subjects with hemorrhoids had a 1.27-fold higher risk of CHD compared with those without hemorrhoids. The advantage of this study is that it is a nationwide cohort study which includes a very big case numbers of study and control cohorts with long follow-up period.[10] Therefore, the association between hemorrhoid and risk of incident CHD demonstrated in the present study is highly convincing.

In this study, most patients in the hemorrhoid cohort were men (54.0%), and their mean age was 44.7 years. Our finding is consistent with previous investigations[1–3]; indicative of the accuracy and verity of NHIRD hemorrhoid patient population. This study showed that patients with hemorrhoids displayed a 27% increased risk of CHD after adjustment for the confounding factors. Risk factors for the development of CHD are more common among subjects with hemorrhoids than those without hemorrhoids except for diabetes mellitus. However, after minimizing the confounding factors, hemorrhoid still imposes the risk of the development of CHD with steadily increased within 12 years of follow up. A subgroup analysis was conducted to address the joint effects for CHD development between hemorrhoid and CHD-associated risk factors. Although the impact of hemorrhoid on CHD development was not as high as that for conventional CHD-associated risk factors, a greater CHD risk was found in the hemorrhoid patients with any concomitant comorbidity than in patients with only hemorrhoid. Additional studies are required to confirm our finding.

Several possible theories could explain the increased CHD risk among patients with hemorrhoids.[1–3,11–16] First, subjects taking high fat diet are at an increased risk of hemorrhoid development because of increased intraabdominal pressure secondary to strenuous bowel movement.[1–3,11–16] Second, hemorrhoid is prevalent among obese population because of increased stress on the rectal muscle.[1–3,11–16] Finally, physical inactivity may contribute to the development of hemorrhoid due to blood stasis in the pelvis.[1–3,11–16] All these factors were strongly associated with atherosclerotic process, hence contributing to the development of CHD.[17–20]

5. Limitations

First, the encoded data of hemorrhoid, CHD, and other comorbidities were completely by ICD codes; therefore, one may argue the accuracy. However, Taiwan's NHI has set up a thorough method to evaluate the diagnosis accuracy. Second, family history of CHD, cigarette smoking, body mass index, physical activity, and psychologic stress were unavailable from Taiwan's NHI database. Finally, the severity of hemorrhoid was uncertain due to the limitation of Taiwan's NHI Database. Therefore, further large studies are necessary to verify the clinical significance of our finding.

6. Conclusions

In summary, our finding suggested that patients with hemorrhoids had a 1.27-fold higher risk of CHD compared with those without hemorrhoids after adjusting for the potential confounding factors.

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