Congestive Heart Failure and Chronic Obstructive Pulmonary Disease Effect of Cardiomyopathy on the Risk of Acute Stress Disorder in Taiwan, 2000-2015

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Abstract

Background: It is now known that determining the comorbidity of COPD and HF leads to a poor prognosis. Our hypothesis that psychological problems predict mortality and that adults with cardiomyopathy will exhibit more psychological problems has predictive that has value in clinical management strategies. At present, research on physical and mental diseases of cardiomyopathy complicated with cardiopulmonary problems is limited.

Objective: To investigate whether Congestive Heart Failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD) affect cardiomyopathy and increase Acute Stress Disorder (ASD) risk.

Methods: Gender, age, and comorbidities were analyzed with 1:4 matching using the National Health Insurance Research Database (NHIRD) of Taiwan in the study. 9,709 patients with cardiomyopathy, 9,623 with ASD, were selected; 38,836 patients without cardiomyopathy, 38,482 with ASD, were also selected. The study using SPSS 22 statistical software to perform Cox regression analysis.

Results: ASD risk with cardiomyopathy is 1.635 times higher than non-cardiomyopathy. Females are 1.890 times more likely to commit ASD than males. Age 20-49 is 1.819 times more likely to develop ASD than age ?65. People with CHF have a 1.290 times higher risk of developing ASD than people without CHF. People with COPD had a 1.314 times higher risk of developing ASD than people without COPD.

Conclusions: Cardiomyopathy increases the risk of ASD, and patients with cardiomyopathy with CHF and COPD have a greater risk of ASD than those without CHF and COPD. Clinicians should be aware of the possibility that CHF and COPD in patients with cardiomyopathy may affect ASD risk.

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develop ASD than age ≥65. People with CHF have a 1.290 times higher risk of developing ASD than people without CHF. People with COPD had a 1.314 times higher risk of developing ASD than people without COPD.

Conclusions Cardiomyopathy increases the risk of ASD, and patients with cardiomyopathy with CHF and COPD have a greater risk of ASD than those without CHF and COPD. Clinicians should be aware of the possibility that CHF and COPD in patients with cardiomyopathy may affect ASD risk.

Keywords: *Acute stress disorder (ASD); Cardiomyopathy; Congestive Heart Failure (CHF); Chronic Obstructive Pulmonary Disease (COPD)*

1.Introduction

Cardiomyopathy is an umbrella term for diseases of the heart muscle, which are anatomical and pathological diagnoses associated with cardiac muscle or electrical dysfunction that dilate, hypertrophy, and stiffen ventricle and reduce the ability of the cardiac to pump blood throughout the body [1]. Dilated cardiomyopathy is the most common form, with prevalence estimates ranging from 1 in 250 [2] and is most commonly characterized by left ventricular or biventricular dilatation and systolic function Barriers [3].

Acute stress disorder (ASD) is an acute trauma response [4], defined in the DSM-IV as a disorder following experiencing, witnessing, or facing an event involving actual or threatened death, bodily harm, or a threat to one's bodily integrity [5]. ASD is a predictor of later development of post-traumatic stress disorder (PTSD) [6], causes negative emotions, occurs in people who have experienced stressful or traumatic events [7], develops cardiac Post-illness patients may face acute stress disorder as a sequelae of heart disease[8], and while the impact of acute stress disorder on mental health has long been recognized in the past, more people with stress disorders are at increased risk of impaired physical health, especially with regard to heart disease.

Many studies have also analyzed the possible pathogenesis of multiple diseases, cardiovascular disease and chronic obstructive pulmonary disease (COPD), with many of the same risk factors and pathogenic relationships that aggravate the disease course [9]. COPD is often associated with systemic comorbidities, Cardiovascular comorbidities are significantly associated with mortality, and in COPD patients, even taking into account the risk of smoking, the risk of cardiovascular

disease(CVD) is on average higher than for their peers in the general population 2-3 times, approximately 40% of patients with mild to moderate COPD die from cardiovascular disease [10], rather than simply attributable to common risk factors such as smoking [11]. Cardiopulmonary disease is often interactive [12], and a two to three-fold increase in cardiovascular morbidity and mortality in COPD patients is associated with disease severity [13]. Five points One in three COPD patients is diagnosed with left heart failure for the first time, and one third of patients with heart failure suffer from obstructive ventilatory disorders, and these are associated not only with difficulty in diagnosis but also with poorer prognosis [14].

COPD and heart failure (HF) Killed more than 21 million people each year, and an estimated 52% of HF patients have COPD [15]. COPD patients have a 450% higher risk of developing HF [16]. COPD and HF are progressive and irreversible [15,16]. Cardiomyopathy can progress to HF a poor prognosis. A common comorbidity in heart failure patients is COPD, and the two diseases often coexist. It is related to clinical prognosis and is also accompanied by a significant impact on mental health [17]. With the advancement of medical technology, the prevention of poor prognosis of cardiopulmonary problems caused by cardiomyopathy has gradually attracted attention, but the underlying mechanism has not yet been Totally sure.

It is now known that determining the comorbidity of COPD and HF leads to a poor prognosis. Our hypothesis that psychological problems predict mortality and that adults with cardiomyopathy will exhibit more psychological problems has predictive that has value in clinical management strategies. At present, research on physical and mental diseases of cardiomyopathy complicated with cardiopulmonary problems is limited. Therefore, we assume that Congestive Heart Failure (CHF) and COPD effect of Cardiomyopathy on the risk of ASD. We used National Health Insurance Research Database (NHIRD) to track whether CHF and COPD effect of Cardiomyopathy on the risk of ASD from 2000-2015 through long-term follow-up in Taiwan.

2.Method

2.1 Data sources

At present, the National Health Insurance (NHI) coverage rate in Taiwan has reached more than 99%, making NHIRD representative empirical data from medical and health-related research. The research results can be used as a reference for medical and health policies and an important research resource. NHIRD contains multiple health registries for most Taiwanese populations, included outpatient, emergency, and inpatient clinic data. The clinical codes were diagnosed according to the International Classification of Diseases, Ninth Clinical Revision (ICD-9-CM). Therefore, NHIRD provides data that is broadly representative of medically relevant research. Additionally, NHIRD converts national ID numbers into encryption to protect the privacy of each national in the process. The study was approved by the Triservices General Hospital Institutional Review Board (TSGHIRB: No. E202216032)

2.2 Study Design and Participants

This study recruited 1,978,082 outpatient and inpatient patients between January 1, 2000 and December 31, 2015 from the Taiwan Longitudinal National Health Insurance Database (LHID). A total of 798,450 patients over 20 years of age, diagnosed with cardiomyopathy (ICD-9-CM) were included in this study. Code: 425.4, ,Diagnosed with at least 3 outpatient visits or 1 hospitalization. Patients diagnosed with cardiomyopathy before January 1, 2000 and patients with ASD were excluded from this study. In total, 9,709 participants (9,623 ASD patients) who meet our inclusion criteria. Among control patients, patients with a history of cardiomyopathy and medical history during the study were excluded according to our exclusion criteria. A control group of 38,836 patients with undiagnosed cardiomyopathy (38,482 with ASD) was randomly selected and matched 1:4 to the cardiomyopathy of the study was grouped by age, sex, index date, and comorbidities. Figure 1 shown the flowchart of the study design.

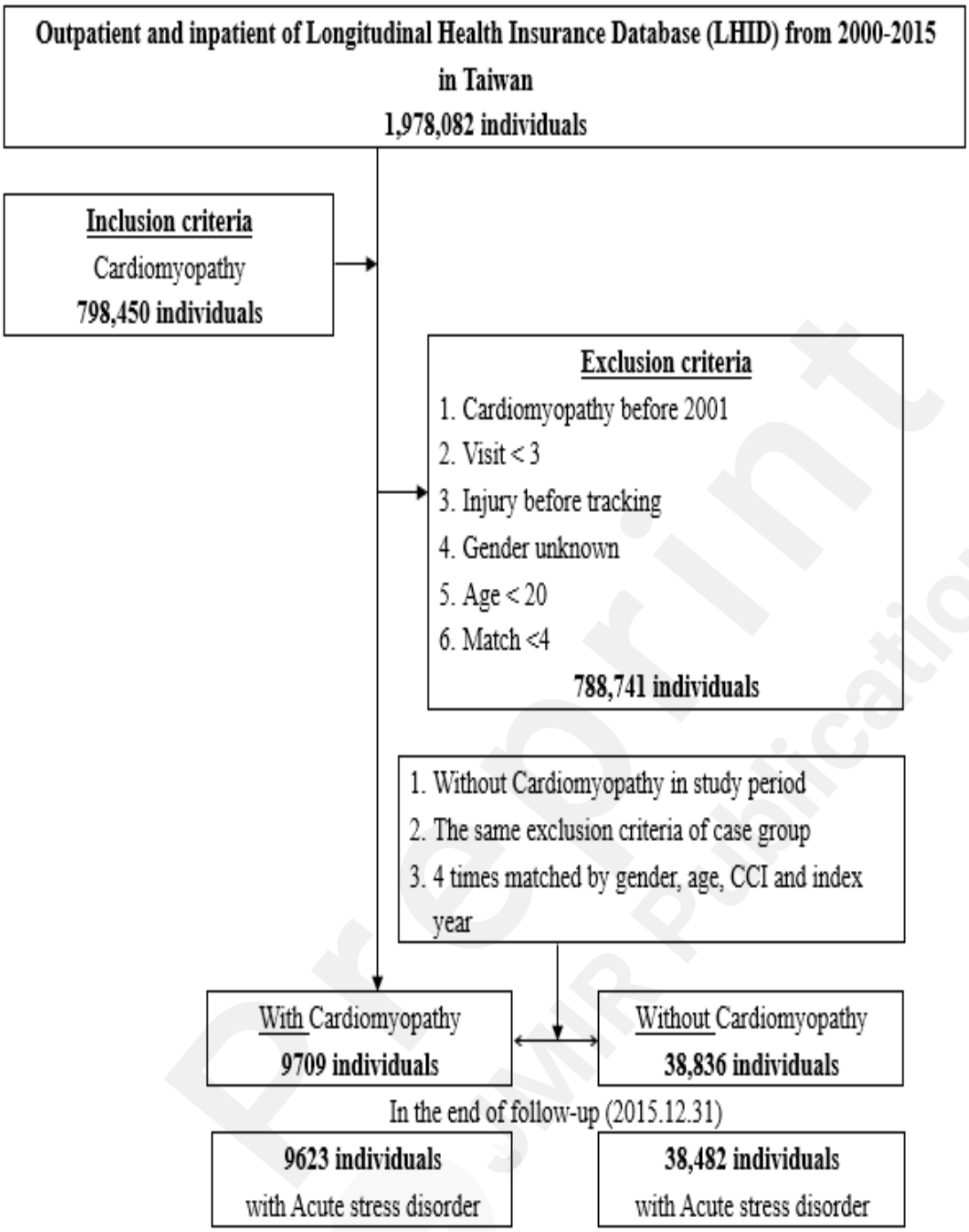

Figure1. Research Database Research Sample Selection Flowchart

2.3 Statistical analysis

Chi-square tests compared the demographic characteristics and common comorbidities of individuals with and without cardiomyopathy. And use the t-test to calculate the mean patient age in the two pairs of columns. This study adjusted for age, sex, and concomitant comorbidities for inclusion in the multivariate model analysis. This study calculated hazard ratios (HR) and 95% confidence intervals (CI) using a multivariate Cox proportional hazards model. SPSS 22.0 software was used for statistical analysis, and $p<0.05$ was considered statistically significant.

3. Results

3.1 Baseline characteristics of the patients in the study

Table 1 showed the data on the demographic characteristics of cardiomyopathy and common comorbidities. 9,709 patients in the cardiomyopathy cohort and 38,836 patients in the control group included in the study from 2000-2015. The average age of ccardiomyopathy cohort was 61.93 ±14.77 years, and the proportion of male patients was 57.70%. In the study population, 48.15% of patients were over 65 years old, 28.46% of patients were 50-64 years old, and 23.39% of patients were 20-49 years old. Significant variables between the study and control groups were low income and level of care ($p < .001$).

Table 1. Characteristics of the Baseline Study

Cardiomyopathy	**Total**		**With**		**Without**		***p*-value**
Variables	***n***	**%**	***n***	**%**	***n***	**%**	
Total	48,545		9,709	20.00	38,836	80.00	
Gender							
Male	28,010	57.70	5,602	57.70	22,408	57.70	0.177
Female	20,535	42.30	4,107	42.30	16,428	42.30	
Age (mean ± SD, year)	61.70 ±15.73		61.93 ±14.77		62.31 ± 15.47		0.836
Age groups (years)							
20-49	11,355	23.39	2,271	23.39	9,084	23.39	0.278
50-64	13,815	28.46	2,763	28.46	11,052	28.46	
≥65	23,375	48.15	4,675	48.15	18,700	48.15	
Low-income							
without	48,089	99.06	9,562	98.49	38,527	99.20	<0.001
with	456	0.94	147	1.51	309	0.80	
Season							
Spring (3-5)	13,255	27.30	2,651	27.30	10,604	27.30	0.999
Summer (6-8)	11,700	24.10	2,340	24.10	9,360	24.10	
Autumn (9-11)	11,570	23.83	2,314	23.83	9,256	23.83	
Winter (12-2)	12,020	24.76	2,404	24.76	9,616	24.76	
Location							
Northern Taiwan	23,287	47.97	4,688	48.29	18,599	47.89	0.672
Middle Taiwan	9,038	18.62	2,030	20.91	7,008	18.05	
Southern Taiwan	14,515	29.90	2,431	25.04	12,084	31.12	
Eastern Taiwan	1,533	3.16	519	5.35	1,014	2.61	
Missing Data	172	0.35	41	0.42	131	0.34	
Urbanization level							
1 (The highest)	12,474	25.70	2,367	24.38	10,107	26.02	0.978
2 (Second)	13,996	28.83	2,589	26.67	11,407	29.37	
3 (Third)	15,592	32.12	3,252	33.49	12,340	31.77	
4 (The lowest)	6,261	12.90	1,453	14.97	4,808	12.38	

Missing data	222	0.46	48	0.49	174	0.45	
Level of care							<0.001
Medical center	7,376	15.19	3,135	32.29	4,241	10.92	
Regional hospital	9,008	18.56	3,707	38.18	5,301	13.65	
Local hospital	6,911	14.24	1,911	19.68	5,000	12.87	
Clinic	25,250	52.01	956	9.85	24,294	62.56	

p-value (category variable: Chi-square/Fisher exact test; continue variable: t-test)

3.2 Endpoint characteristics of the study

Table 2 shows the endpoint characteristics. ASD events occurred in 9,623 patients in the cardiomyopathy cohort and 38,482 in the control group. The cardiomyopathy cohort group differed from the control group by the following factors: low income; Charlson comorbidity index (CCI); season; level of care. The ASD variable was significant between the study and control groups (p=0.005).

Table 2 Study characteristics at the end of follow-up

Cardiomyopathy	**Total**		**With**		**Without**		***p*-value**
Variables	***n***	**%**	***n***	**%**	***n***	**%**	
Total	48,545		9,709	20.00	38,836	80.00	
Outcomes							
Without	32,736	67.43	6,410	66.02	26,326	67.79	0.444
With	15,809	32.57	3,299	33.98	12,510	32.21	
Anxiety							
Without	42,364	87.27	8,370	86.21	33,994	87.53	0.211
With	6,181	12.73	1,339	13.79	4,842	12.47	
Depression							
Without	45,506	93.74	8,973	92.42	36,533	94.07	0.657
With	3,039	6.26	736	7.58	2,303	5.93	
Manic disorder							
Without	48,448	99.80	9,684	99.74	38,764	99.81	
With	97	0.20	25	0.26	72	0.19	0.646
Bipolar disorders							
Without	48,196	99.28	9,615	99.03	38,581	99.34	0.288
With	349	0.72	94	0.97	255	0.66	
Acute stress disorder							
Without	48,105	99.09	9,623	99.11	38,482	99.09	0.005
With	440	0.91	86	0.89	354	0.91	
Eating disorder							
Without	47,881	98.63	9,550	98.36	38,331	98.70	0.941
With	664	1.37	159	1.64	505	1.30	
Gender							0.177

Male	28,010	57.70	5,602	57.70	22,408	57.70	
Female	20,535	42.30	4,107	42.30	16,428	42.30	
Age (mean ± SD, year)	66.26 ± 15.72		66.95 ± 14.92		66.09 ± 15.90		0.688
Age groups (years)							
20-49	6,584	13.56	1,442	14.85	5,142	13.24	0.730
50-64	12,540	25.83	2,624	27.03	9,916	25.53	
≥65	29,421	60.61	5,643	58.12	23,778	61.23	
Low-income							
without	48,089	99.06	9,562	98.49	38,527	99.20	<0.001
with	456	0.94	147	1.51	309	0.80	
CCI	2.37 ± 2.68		4.04 ± 2.95		1.96 ± 2.44		<0.001
Season							
Spring (3-5)	3,054	6.29	991	10.21	2,063	5.31	<0.001
Summer (6-8)	2,925	6.03	974	10.03	1,951	5.02	
Autumn (9-11)	2,955	6.09	992	10.22	1,963	5.05	
Winter (12-2)	39,611	81.60	6,752	69.54	32,859	84.61	
Location							
Northern Taiwan	23,287	47.97	4,688	48.29	18,599	47.89	0.672
Middle Taiwan	9,038	18.62	2,030	20.91	7,008	18.05	
Southern Taiwan	14,515	29.90	2,431	25.04	12,084	31.12	
Eastern Taiwan	1,533	3.16	519	5.35	1,014	2.61	
Missing data	172	0.35	41	0.42	131	0.34	
Urbanization level							
1 (The highest)	12,474	25.70	2,367	24.38	10,107	26.02	0.978
2 (Second)	13,996	28.83	2,589	26.67	11,407	29.37	
3 (Third)	15,592	32.12	3,252	33.49	12,340	31.77	
4 (The lowest)	6,261	12.90	1,453	14.97	4,808	12.38	
Missing data	222	0.46	48	0.49	174	0.45	
Level of care							
Hospital center	7,579	15.61	2,681	27.61	4,898	12.61	<0.001
Regional hospital	9,778	20.14	3,309	34.08	6,469	16.66	
Local hospital	8,206	16.90	2,086	21.49	6,120	15.76	
Clinic	22,982	47.34	1,633	16.82	21,349	54.97	

p-value (category variable: Chi-square/Fisher exact test; continue variable: t-test)

3.3 Cox regression analysis was used to analyse the influencing factors of ASD

The results of cox regression analysis of risk factors for cardiomyopathy control and control groups are shown in Table 3. This study adjusted for age, gender, comorbidities, location, urbanization level of residence, and monthly income, ASD risk with cardiomyopathy is 1.635 times higher than non-cardiomyopathy. Females are 1.890 times to commit ASD than males. Age 20-49 is 1.819 times more to develop ASD than age ≥65. In terms of CCI, for every 1-point increase in the

score, people with cardiomyopathy had a 6.5% higher risk of developing ASD. People with CHF have 1.290 times to develop the risk of ASD compared with those without CHF. People with COPD have 1.314 times to develop the risk of ASD compared with those without COPD. The risk of ASD in winter is 0.456 times lower than in spring. The risk of ASD in medical center, regional hospitals and local hospitals was 0.338 times, 0.340 times and 0.490 times lower than in clinics, respectively.

Table 3 Using Cox regression to analyze the influencing factors of ASD

Variables	Adjusted HR	95% CI	*p*-value
Cardiomyopathy			
Without	Reference		
With	1.635	1.237-2.162	0.001
Gender			
Male	Reference		
Female	1.890	1.557-2.296	<.0001
Age groups (years)			
20-49	1.819	1.289-2.568	0.001
50-64	1.107	0.861-1.422	0.428
≥65	Reference		
Low-income			
without	Reference		
with	0.814	0.202-3.276	0.772
CCI	1.065	1.020-1.112	0.004
Diabetes mellitus	0.980	0.786-1.222	0.856
Hypertension	1.146	0.878-1.494	0.316
Chronic Kidney Disease	0.955	0.722-1.263	0.748
Congestive Heart Failure	1.290	1.011-1.646	0.040
Chronic Obstructive Pulmonary Disease	1.314	1.056-1.634	0.014
Hyperlipidemia	1.218	0.980-1.513	0.075
Season			
Spring (3-5)	Reference		
Summer (6-8)	0.958	0.540-1.700	0.884
Autumn (9-11)	1.106	0.640-1.913	0.717
Winter (12-2)	0.456	0.290-0.718	0.001
Urbanization level			
1 (The highest)	1.203	0.862-1.678	0.278
2 (Second)	1.303	0.942-1.801	0.109
3 (Third)	1.165	0.845-1.606	0.352
4 (The lowest)	Reference		
Level of care			
Medical center	0.338	0.234-0.486	<.0001
Regional hospital	0.340	0.242-0.477	<.0001
Local hospital	0.490	0.355-0.676	<.0001

Clinic	Reference		

**: $p < 0.05$ (category variable: Chi-square/Fisher exact test; continue variable: t-test), HR = Hazard Ratio

4. **Discussion**

ASD risk with cardiomyopathy is 1.635 times higher than non-cardiomyopathy. Females are 1.890 times more likely to commit ASD than males. Age 20-49 is 1.819 times more likely to develop ASD than age ≥65. People with CHF have 1.290 times to develop the risk of ASD compared with those without CHF. People with COPD have 1.314 times to develop the risk of ASD compared with those without COPD. The link between cardiomyopathy and CHF is strong [18]. CHF is a complex clinical syndrome caused by ventricular dysfunction or structural dysfunction, resulting in symptomatic left ventricular (LV) dysfunction resulting from insufficient cardiac output to keep up with the body's metabolic demands [19]. CHF is a chronic progressive disease that may be the ultimate common pathway for many structural or functional heart diseases that impair the heart's ability to fill or empty [20]. Heart failure occurs when the heart muscle becomes weak or stiff and does not relax properly [21]. Previous findings contributed to the understanding of the association between COPD and cardiomyopathy in this study [22-26]. Among the long list of comorbidities present in patients with COPD, cardiomyopathy is generally considered important [27]. One of the most common comorbidities of COPD is cardiomyopathy and increases the risk of death [28]. COPD patients are as likely to die from cardiomyopathy as from respiratory disease [29]. Previous findings add to our understanding of the association between COPD and cardiomyopathy [30-33].

A large population study in Sweden found a strong link between mental illness, which may follow extreme stressful experiences, and the risk of several types of cardiovascular disease [34]. Previous study suggests that link between CHF and ASD may be bidirectional [35]. Decades of research has shown several, sometimes surprising, links between CHF and ASD, even suggesting that the two may actually cause each other [36]. Inflammation may be a common cause of ASD and cardiomyopathy [37]. The role of inflammation in tumorigenesis and prognosis of cardiomyopathy has been extensively described in the cardiovascular literature [37]. Previous studies have shown that inflammation promotes the development and progression of atherosclerosis [38-40]. Inflammation leads to endothelial dysfunction (characterized by loss of vasodilating and increased vasoconstrictor [41,42]. People with COPD under acute event stress experience more depressive symptoms and a worse quality of life than people without COPD [43], which is consistent with our study. In summary, our study found that ASD risk with cardiomyopathy is 1.635 times higher than non-cardiomyopathy. Females are 1.890 times more likely to commit ASD than males. Age 20-49 is 1.819 times more likely to develop ASD than age ≥65. People with CHF have 1.290 times to develop the risk of ASD compared with those without CHF. People with COPD have 1.314 times to develop the risk of ASD compared with those without COPD. CHF and COPD effect of Cardiomyopathy on the risk of ASD.

This study has several limitations worth considering. First, similar to previous studies using the NHI research database, genetic, environmental, severity, or psychological assessments of patients with cardiomyopathy could not be assessed because these values were not recorded in the NHIRD [44]. Second, some unexplained heterogeneity exists, and comparability between studies may be reduced due to the lack of uniform diagnostic criteria. Third, because data from many studies were not available, we did not have all the data to summarize them. Therefore, the results of this study are a set of data that is unlikely to be replicated. Validation of our results requires a more robust approach.

5.Conclusions

The results of this study suggest that cardiomyopathy develop with a higher risk of ASD compared with patients without cardiomyopathy. People with CHF have a greater risk of ASD than

people without CHF. Compared with people without COPD, people with COPD have a greater risk of ASD than people without COPD. Cardiomyopathy patients with CHF and COPD have a greater risk of ASD than patients without cardiomyopathy. CHF and COPD in cardiomyopathy have the greatest impact on ASD risk. Therefore, in addition to striving to avoid ASD events, healthcare providers should be aware of the cardiomyopathy and ASD risks associated with CHF and COPD.

Ethics approval and consent to participate: This study was conducted according to the Code of Ethics of the World Medical Association (Declaration of Helsinki). The Institutional Review Board of the Tri-Service General Hospital approved this study (TSGHIRB No. E202216032) and waived the need for individual consent since all the identification data were encrypted in the NHIRD.
Consent to publish: Not applicable.

Availability of data and materials: The data that support the findings of this study are available from NHIRD, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the corresponding author upon reasonable request and with permission of NHIRD**.**

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Competing interests: The authors declare no conflict of interest.

Authors' contributions: P.-C.Y., R.-J.C., Y.-C.H., H.-T.H., and W.-C.C.: conception and design, analysis and interpretation of the data, critical review, and approval of the final version submitted for publication. Y.-C.H., and P.-C.Y.: statistical analysis, critical review, and approval of the final version submitted for publication. P.-C.Y., R.-J.C., Y.-C.H., H.-T.H. and W.-C.C.: drafting of the paper, critical review, and approval of the final version submitted for publication. All authors have read and agreed to the published version of the manuscript.

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