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ORIGINAL RESEARCH

The Impact of COPD on in-Hospital Outcomes in Patients with Takotsubo Cardiomyopathy

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Purpose: Chronic obstructive pulmonary disease (COPD) is a known comorbidity of takotsubo cardiomyopathy (TCM), and COPD exacerbation is a potential triggering factor of TCM. The association between COPD and in-hospital outcomes and complications among TCM patients is not well established. We sought to assess the effect of COPD on hospitalized patients with a primary diagnosis of TCM.

Methods: We conducted a retrospective cohort study in patients with a primary diagnosis of TCM with or without COPD using the latest National Inpatient Sample from 2016–2017. We identified 3139 patients admitted with a primary diagnosis of TCM by the ICD-10-CM coding system; 684 of those patients also had a diagnosis of COPD. We performed propensity score matching in a 1:2 ratio (n=678 patients, matched COPD group; n=1070, matched non-COPD group) and compared in-hospital outcomes and complications between TCM patients with and without a COPD diagnosis.

Results: Before matching, the COPD group had worse outcomes compared with the non-COPD group in inpatient death (2.9% vs 1.3%, p=0.006), length of stay (LOS) (4.02±2.99 days vs 3.27±3.39 days, p<0.001), hospitalization charges ($55,242.68±47,637.40 vs $48,316.97±47,939.84, p=0.001), and acute respiratory failure (ARF) (22.5% vs 7.7%, p<0.001), respectively. After propensity score matching, the matched COPD group, compared with the matched non-COPD group, had a higher inpatient mortality rate (2.9% vs1.0%, p=0.005), longer LOS (4.02±3.00 days vs 3.40±3.54 days, p<0.001), higher hospitalization charges ($55,409.23±47,809.13 vs $46,469.60±42,209.10, p<0.001), and a higher incidence of ARF (22.6% vs 8.2%, p<0.001) and cardiogenic shock (5.6% vs 3.3%, p=0.024), respectively.

Conclusion: Patients with COPD who are hospitalized for TCM have higher rates of inpatient mortality, ARF, cardiogenic shock, as well as a longer LOS, and higher charges of stay than those without COPD. Prospective studies are warranted to examine the effect of early intervention or treatment of COPD on short- and long-term outcomes of TCM.

Keywords: takotsubo cardiomyopathy, chronic obstructive pulmonary disease, in-hospital outcomes

Introduction

Takotsubo cardiomyopathy (TCM), first described in Japan in 1990, is characterized by regional wall motion abnormalities that extend beyond a single coronary artery distribution, and a lack of evidence of coronary artery occlusion.[1] The term "takotsubo" in Japanese refers to an octopus trap, which resembles the typical finding of the left ventricle in systole on echocardiograms.[2] TCM's clinical presentation, electrocardiographic findings, and biomarker profiles resemble acute myocardial infarction (AMI).[1,3,4] Once thought to be a temporary, reversible

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condition, TCM has been found to have a mortality rate similar to acute coronary syndrome.[3] Approximately 1–2% of individuals who initially present with AMI patients are in fact sufferers of TCM.[5] In addition, the TCM hospitalization rate has increased from 5.7 per 100,000 person-years in 2007 to 17.4 in 2012.[6] Many pre-existing factors have been identified that affect the outcomes of TCM include age,[7] sex,[8] race,[9] conventional cardiovascular risk factors (such as obesity,[10] and diabetes mellitus (DM)[11]), psychiatric disorders (such as anxiety, depression[12]), and chronic kidney disease (CKD).[13,14]

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of death worldwide.[15,16] It is often seen in patients with TCM, with an even higher prevalence in patients with acute coronary syndrome.[17–20] Many studies have found that TCM could be triggered by acute exacerbation of COPD, though the evidence of COPD affecting the outcomes of admitted TCM patients is lacking.[21–23] In this study, we used the latest data available in the National Inpatient Sample (NIS) 2016 and 2017 – the largest inpatient discharge database in the United States – to identify the association between COPD and the inpatient outcomes of TCM.

Methods

Data Source

The NIS database, compiled by the Agency for Healthcare Research and Quality (AHRQ), includes more than 7 million patients per year in the United States, and approximates a 20% stratified sample of all discharges from US community hospitals (excluding rehabilitation and long-term acute care hospitals).[24] It contains information on patient demographics, administrative codes for primary diagnosis and secondary diagnoses, procedures, discharge status, disposition, hospital charges, and length of stay (LOS). It has been widely used in examining the utilization of hospital health services, practice variation, cost, and the impact of health policy interventions in the inpatient setting.[25] As a de-identified publicly available database, Institutional Review Board (IRB) approval is not required in using NIS. Beginning with the data year 2016, the NIS includes a full calendar year of data with diagnosis codes reported using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) coding system. NIS 2016 and 2017 are the latest available NIS using the ICD-10-CM coding system.

Study Population

All patients admitted to a hospital from January 1, 2016 to December 31, 2017 with the primary diagnosis of TCM were selected in this study, using ICD-10-CM codes (Supplementary Table 1). Patients without discharge status were excluded. Eligible patients in this study were designated into two groups based on whether or not the patient carried a diagnosis of COPD. The process of patient selection in this study is shown in Figure 1.

Study Variables

Patients' demographic data were collected from NIS 2016 and 2017, including age, sex, race, geographic location, household income, primary payer, hospital type, region

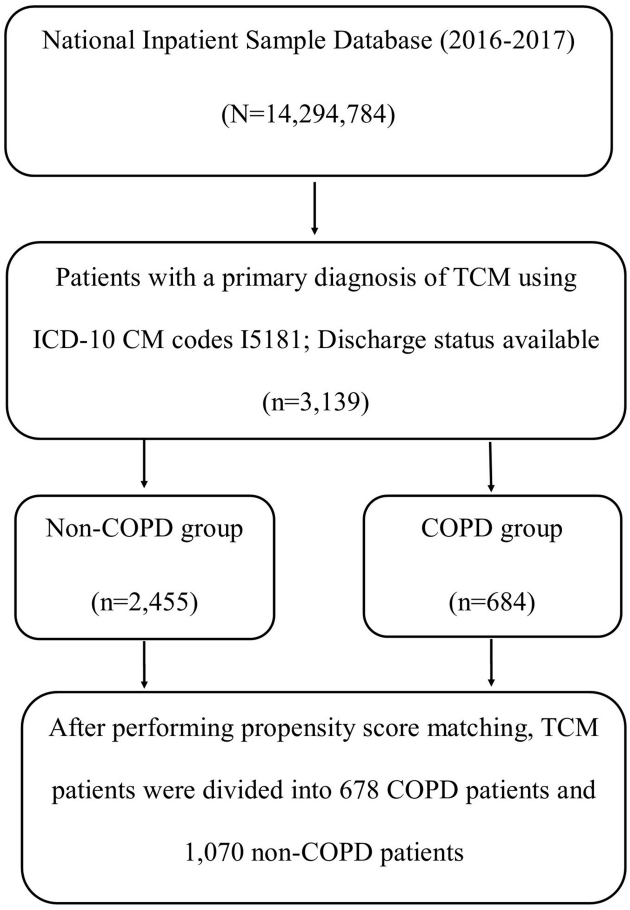

Figure 1 Flow chart of the selection process for the final patient sample used in this study.

Notes: We selected 3139 patients with a primary diagnosis of TCM from the 2016 and 2017 NIS database using the ICD-10-CM of I5181. All eligible patients were divided into two groups based on whether they had the diagnosis of COPD; 684 patients were in the COPD group and 2455 in the non-COPD group. After the propensity score matching in a target ratio of 1:2, 678 COPD patients and 1070 non-COPD patients remained. We then compared inpatient outcomes between two groups.

Abbreviations: TCM, takotsubo cardiomyopathy; COPD, chronic obstructive pulmonary disease; ICD-10-CM code, Tenth Revision, Clinical Modification Code.

and bed size. Comorbidities collected include hypertension, DM, hyperlipidemia, obesity, smoking, obstructive sleep apnea (OSA), depression, anxiety disorders and CKD, by the ICD-10-CM codes from the discharge diagnosis. (Supplement Table 1)

Outcomes

The primary outcome of this study is inpatient mortality. The secondary outcomes were LOS, total charges of stay, and certain severe inpatient complications: cardiac arrest, cardiogenic shock, ventricular arrhythmia, acute kidney injury (AKI), and acute respiratory failure (ARF).

Statistical Analyses

Descriptive data are shown in percentages or mean ± standard deviation (SD), and tested with the chi-square and *t*-test for categorical and continuous variables, respectively.

To reduce the bias in the unmatched data, we use propensity score matching analysis to match patients from the COPD group and the non-COPD group. Compared to a multivariable regression model, the propensity score matching model has the following advantages: 1) the number of confounders used in propensity score matching is not limited by the number of outcome events, 2) propensity score matching eliminates the linearity assumption between the propensity score and outcome, and 3) estimates the treatment effect by modelling covariates and treatment assignment. It mirrors a randomized experiment by separating the study design from the outcome analysis, which protects against actual or suspected bias from the researchers.[26]

To measure propensity scores, we built a multivariate logistic regression model and adjusted it for individual characteristics (age, sex, race, and mean household income), hospital-level characteristics (hospital type, region, and size) and the comorbidities mentioned above, using the nearest neighbor matching of both groups with a caliper match tolerance of 0.05. A match ratio of 1:2 (COPD: non-COPD patients) was used based on initial findings, as there were 684 TCM patients with COPD and 2455 without. In other words, for each TCM patient with COPD, an effort was made to match the patient with two patients without COPD with similar demographic characteristics. After matching, 678 patients with COPD were identified, along with 1070 patients without COPD. Finally, we compared the in-hospital outcomes and complications between the COPD and non-COPD groups in both the unmatched and the propensity score–matched cohorts.

All statistical analysis was performed by the R statistics software (version 3.6.1, R Development Core Team). The matching process was conducted using the MatchIt package in R software. All tests were two-sided. The results were considered significant at $p < 0.05$.

Standardized mean difference is used to examine the balance of the covariate distribution between matched COPD group and non-COPD group. Standardized mean differences less than 0.1 were considered balanced.[27]

Results

Baseline Characteristics

3139 patients with a primary diagnosis of TCM from the 2016 and 2017 NIS database were identified. Among them, 684 carried the comorbidity of COPD while 2455 did not. Once matched in a 1:2 target ratio, there are 678 patients in COPD subgroup and 1070 in non-COPD subgroup.

In the unmatched cohorts, the majority of patients in both groups were female (89.2% in COPD group, 90.8% in non-COPD group, $p = 0.306$). Compared with the non-COPD group, TCM patients with COPD tended to be older (68.07 ± 10.47 vs. 66.28 ± 13.21, $p = 0.001$), whiter (82.3% vs. 78.7%, $p = 0.037$), and had more comorbidities, including smoking (74.1% vs. 35.2%, $p < 0.001$), anxiety (30.4% vs. 23.8%, $p = 0.001$), depression (23.0% vs. 16.2%, $p < 0.001$), and OSA (7.5% vs. 4.9%, $p = 0.012$). There was no significant difference between the two groups when comparing conventional cardiovascular risk factors, including hypertension (48.4% vs. 49.1%, $p = 0.768$), DM (20.9% vs. 19.6%, $p = 0.479$), hyperlipidemia (48.4% vs. 48.8%, $p = 0.87$), obesity (10.8% vs. 13.2%, $p = 0.112$), CKD (9.2% vs. 8.6%, $p = 0.669$).

After propensity score matching, all baseline characteristics, including patient and hospital-level, were comparable in COPD and non-COPD groups ($p > 0.05$ in all categories). All standardized mean differences between two matched groups were less than 0.1 after propensity score matching (Figure 2). For simplicity, we only showed the standardized mean difference of continuous covariate age and binary covariates in Figure 2. The dotted vertical line at 0.1 indicates the threshold below which the balance is considered to be achieved. The baseline characteristics before and after propensity score matching are shown in Table 1.

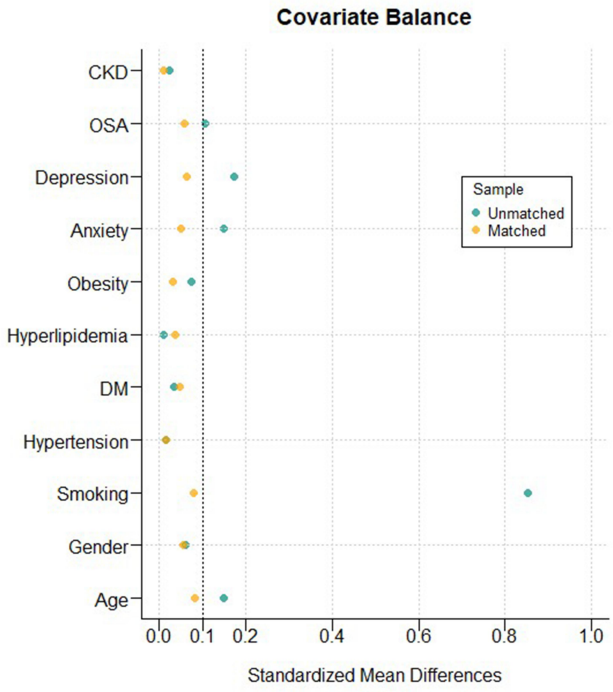

Figure 2 Standardized mean differences of covariates before and after propensity score matching between TCM patients with COPD and TCM patients without COPD.
Notes: Standardized mean difference is used to examine the balance of the covariate distribution between the matched COPD group and the non-COPD group. All standardized mean differences of covariate distributions in this study were less than 0.1, which was considered balanced.
Abbreviations: TCM, takotsubo cardiomyopathy; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; OSA, obstructive sleep apnea; CKD, chronic kidney disease.

In-Hospital Mortality

In both the unmatched and matched cohorts, the COPD group had higher inpatient mortality compared to the non-COPD group (unmatched 2.9% vs. 1.3%, p = 0.006; matched 2.9% vs. 1.0%, Odds Ratio [OR] 2.93, 95% CI 2.93, 1.39–6.15, p = 0.005) (Table 2).

In-Hospital Complications, LOS and Total Charges

In both the unmatched and matched cohorts, the COPD group had an increased risk of ARF compared to the non-COPD group (unmatched, 22.5% vs. 7.7%, p < 0.001; matched, 22.6% vs. 8.2%, OR 3.25, 95% CI 2.45–4.32, p < 0.001). After propensity score matching, the COPD group had a higher incidence of cardiogenic shock (5.6% vs. 3.3%, OR 1.76, 95% CI 1.1–2.81, p = 0.024). There was no significant difference in the two groups for incidence of cardiac arrest (unmatched, 1.6% vs. 1.8%, p = 0.818; matched, 1.6% vs. 1.4%, OR 1.16, 95% CI 0.53–2.54, p = 0.866), ventricular arrhythmia (unmatched, 3.5% vs. 4.0%, p = 0.608; matched 3.5% vs. 4.0%, OR 0.88, 95% CI 0.53–1.46, p = 0.704), and AKI (unmatched, 11.1% vs. 8.6%, p = 0.052; matched, 11.2% vs. 9.3%, OR 1.24, 95% CI 0.9–1.7, p = 0.213), before or after matching. In addition, the COPD group had a longer LOS (unmatched 4.02 ± 2.99 vs. 3.27 ± 3.39 days, p < 0.001; matched 4.02 ± 3.00 vs. 3.40 ± 3.54 days, p < 0.001) and higher total charges (unmatched 55,242.68 ± 47,637.40 vs. 48,316.97 ± 47,939.84, p = 0.001; matched 55,409.23 ± 47,809.13 vs. 46,469.60 ± 42,209.10, p < 0.001, respectively). The results can be seen in Table 2.

Discussion

To our knowledge, this is the first study to investigate the association of COPD and in-hospital outcomes among TCM patients. COPD patients who are admitted for TCM have a higher inpatient mortality rate, higher incidence of ARF, longer LOS and higher charges, compared to those without COPD. After the propensity score matching method, COPD patients still demonstrated worse prognosis in the matched cohorts.

The prevalence of COPD was 21.8% among patients with TCM, which is slightly higher than reported in previous studies (10.1% to 18.7%).[17–19] One of the most well-accepted explanations in the etiology of TCM is excessive catecholamine release related myocardial stunning.[28] Previous studies found that COPD patients had a higher catecholamine level, possibly due to the over activation of the sympathetic nervous system (SNS) and the use of β-agonists in the treatment of COPD can also mimic the actions of sympathetic adrenergic stimulation.[21,22,29,30] Also, many clinical studies reported the acute exacerbation of COPD as the potential triggering factor for TCM.[21–23] TCM and COPD may share some similar underlying pathophysiology.

In our study, TCM patients with COPD had a higher rate of in-hospital mortality and ARF than those without COPD. Several factors may have contributed to these results. First, it has been suggested that the activation of SNS and elevation of catecholamine, which are also seen in COPD patients, are associated with worse outcomes of TCM.[31] Second, inflammation may play a vital role in worse outcomes for TCM patients with COPD. Studies have shown that pro-inflammatory cytokine interleukin 6 (IL-6) was significantly elevated in TCM patients which may reflect endothelial and vascular smooth muscle dysfunction. In a prospective cohort study, researchers found that the increased serum levels IL-6 of were associated

Table 1 Baseline Characteristics

Variables	Unmatched Cohort		*P* value	Propensity-Matched Cohort		*P* value
	TCM without COPD	TCM with COPD		TCM without COPD	TCM with COPD	
n	2455	684		1070	678	
Age, (mean (sd))	66.28 (13.21)	68.07 (10.47)	0.001	67.09 (12.74)	68.04 (10.50)	0.107
Sex, n (%)			0.306			0.451
Male	225 (9.2)	73 (10.7)		114 (10.7)	71 (10.5)	
Female	2229 (90.8)	610 (89.2)		956 (89.3)	606 (89.4)	
Unknown	1 (0.0)	1 (0.1)		0 (0.0)	1 (0.1)	
Race, n (%)			0.037			0.985
White	1931 (78.7)	563 (82.3)		882 (82.4)	558 (82.3)	
Black	156 (6.4)	50 (7.3)		78 (7.3)	50 (7.4)	
Hispanic	146 (5.9)	30 (4.4)		54 (5.0)	30 (4.4)	
Asian/ Pacific Islander	40 (1.6)	5 (0.7)		5 (0.5)	5 (0.7)	
Native American	16 (0.7)	2 (0.3)		3 (0.3)	2 (0.3)	
Other	60 (2.4)	7 (1.0)		10 (0.9)	7 (1.0)	
Unknown	106 (4.3)	27 (3.9)		38 (3.6)	26 (3.8)	
Patient location, n (%)			0.463			0.894
"Central" counties of metro areas of ≥1 million population	572 (23.3)	149 (21.8)		236 (22.1)	149 (22.0)	
"Finge" counties of metro areas of ≥1 million population	604 (24.6)	160 (23.4)		263 (24.6)	160 (23.6)	
Counties in metro areas of 250,000–999,999 population	608 (24.8)	160 (23.4)		259 (24.2)	157 (23.2)	
Counties in metro areas of 50,000–249,999 population	250 (10.2)	76 (11.1)		111 (10.4)	75 (11.1)	
Micropolitan counties	237 (9.7)	84 (12.3)		110 (10.3)	82 (12.1)	
Non metropolitan or micropolitan counties	176 (7.2)	52 (7.6)		88 (8.2)	52 (7.7)	
NA	8 (0.3)	3 (0.4)		3 (0.3)	3 (0.4)	
Mean household income, n (%)			<0.001			0.28
$1-$42,999	543 (22.1)	206 (30.1)		283 (26.4)	201 (29.6)	
$43,000-$53,999	618 (25.2)	195 (28.5)		290 (27.1)	194 (28.6)	
$54,000-$70,999	666 (27.1)	172 (25.1)		291 (27.2)	172 (25.4)	
$71,000 or more	594 (24.2)	107 (15.6)		202 (18.9)	107 (15.8)	
Unknown	34 (1.4)	4 (0.6)		4 (0.4)	4 (0.6)	
Primary payer, n (%)			<0.001			0.493
Medicare	1404 (57.2)	463 (67.7)		677 (63.3)	458 (67.6)	
Medicaid	206 (8.4)	68 (9.9)		114 (10.7)	67 (9.9)	
Private including HMO	710 (28.9)	118 (17.3)		210 (19.6)	118 (17.4)	
Self-pay	78 (3.2)	23 (3.4)		43 (4.0)	23 (3.4)	
No charge	4 (0.2)	2 (0.3)		2 (0.2)	2 (0.3)	
Other	52 (2.1)	10 (1.5)		24 (2.2)	10 (1.5)	
Unknown	1 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
Hospital type, n (%)			0.092			0.168
Rural	125 (5.1)	49 (7.2)		54 (5.0)	49 (7.2)	
Urban non-teaching	575 (23.4)	149 (21.8)		238 (22.2)	149 (22.0)	
Urban teaching	1755 (71.5)	486 (71.1)		778 (72.7)	480 (70.8)	

(*Continued*)

Table 1 (Continued).

Variables	Unmatched Cohort		*P* value	Propensity-Matched Cohort		*P* value
	TCM without COPD	TCM with COPD		TCM without COPD	TCM with COPD	
Hospital Region, n (%)			0.025			0.703
Northeast	491 (20.0)	135 (19.7)		209 (19.5)	132 (19.5)	
Midwest	633 (25.8)	185 (27.0)		286 (26.7)	184 (27.1)	
South	754 (30.7)	238 (34.8)		353 (33.0)	236 (34.8)	
West	577 (23.5)	126 (18.4)		222 (20.7)	126 (18.6)	
Hospital Bed Size, n (%)			0.841			0.277
Small	345 (14.1)	99 (14.5)		157 (14.7)	96 (14.2)	
Medium	658 (26.8)	189 (27.6)		260 (24.3)	188 (27.7)	
Large	1452 (59.1)	396 (57.9)		653 (61.0)	394 (58.1)	
Comorbidities, n (%)						
Smoking	863 (35.2)	507 (74.1)	<0.001	753 (70.4)	501 (73.9)	0.124
Hypertension	1206 (49.1)	331 (48.4)	0.768	527 (49.3)	329 (48.5)	0.805
DM	481 (19.6)	143 (20.9)	0.479	206 (19.3)	143 (21.1)	0.381
Hyperlipidemia	1199 (48.8)	331 (48.4)	0.87	540 (50.5)	330 (48.7)	0.495
Obesity	324 (13.2)	74 (10.8)	0.112	126 (11.8)	73 (10.8)	0.569
Anxiety	585 (23.8)	208 (30.4)	0.001	297 (27.8)	204 (30.1)	0.319
Depression	397 (16.2)	157 (23.0)	<0.001	212 (19.8)	152 (22.4)	0.212
OSA	120 (4.9)	51 (7.5)	0.012	62 (5.8)	49 (7.2)	0.273
CKD	211 (8.6)	63 (9.2)	0.669	96 (9.0)	63 (9.3)	0.888

Notes: Descriptive data are shown in percentages or mean ± standard deviation (SD), and tested with the chi-square and *t*-test for categorical and continuous variables, respectively.

Abbreviations: TCM, takotsubo cardiomyopathy; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; OSA, obstructive sleep apnea; CKD, chronic kidney disease.

with higher adverse event rates at a mean follow-up of 178 days.[32] This association remained significant even after correction for age, LVEF, and NT-proBNP levels in multivariable Cox analysis.[33] COPD, as a chronic systemic inflammatory disease, can lead to a higher level of IL-6 than healthy individuals,[34] which may contribute to the exacerbated inflammatory process and worsen outcomes. TCM and COPD combined might lead to a higher level of inflammation than patients with TCM alone.

Moreover, a study showed that TCM patients with COPD tend to present with atypical symptoms such as progressive or relapsing dyspnea, rather than typical chest pain, known as the "bronchogenic stress cardiomyopathy".[35] The atypical symptoms may cause difficulty in diagnosing TCM and delay the treatment for TCM. Besides, dyspnea itself at presentation has been reported as an independent predictor of in-hospital complications, such as cardiogenic shock, ventricular arrhythmias and all-cause inpatient death, in TCM patients.[13]

Excessive catecholamine simulation has been thought to be one of the mechanisms of TCM and has been associated with worse outcomes in TCM patients. Though previous clinical studies yielded inconsistent results regarding the use of β-blockers in TCM patients, Kyuma M reported that intravenous propranolol can relieve the discordant ventricle by antagonizing the activation of sympathetic nerves in patients with significant intraventricular pressure gradient.[36] One meta-analysis has illustrated that early using β-blockers in general TCM patients had no significant reduction in inpatient mortality.[37] This discordance may be due to the heterogeneity within TCM patients. TCM patients with COPD, as a special subgroup, have a higher level of SNS activation and catecholamine stimulation, thus may benefit from β-blocker treatment. TCM patients with COPD, especially in the acute exacerbation state, are less likely to receive β adrenergic-blockers due to the concern for bronchospasm as a side effect. This may contribute to the poor outcomes of this group of patients, though this hypothesis needs to be validated in future controlled clinical trials in subgroup patients.

Our study had several major strengths. First, we used the latest national representative database and illustrated

Table 2 In-Hospital Outcomes and Complications

Variables	Unmatched Cohort			Propensity-Matched Cohort		*P* value
	TCM without COPD	TCM with COPD	*P* value	TCM without COPD	TCM with COPD	
n	2455	684		1070	678	
Outcomes						
Death, n (%)	32 (1.3)	20 (2.9)	0.006	11 (1.0)	20 (2.9)	0.005
LOS, (mean (sd))	3.27 (3.39)	4.02 (2.99)	<0.001	3.40 (3.54)	4.02 (3.00)	<0.001
Total charge (mean (sd))	48,316.97 (47,939.84)	55,242.68 (47,637.40)	0.001	46,469.60 (42,209.10)	55,409.23 (47,809.13)	<0.001
Complications						
Cardiac arrest, n (%)	45 (1.8)	11 (1.6)	0.818	15 (1.4)	11 (1.6)	0.866
Cardiogenic shock, n (%)	106 (4.3)	39 (5.7)	0.155	35 (3.3)	38 (5.6)	0.024
Ventricular arrhythmia	99 (4.0)	24 (3.5)	0.608	43 (4.0)	24 (3.5)	0.704
AKI, n (%)	211 (8.6)	76 (11.1)	0.052	99 (9.3)	76 (11.2)	0.213
ARF, n (%)	188 (7.7)	154 (22.5)	<0.001	88 (8.2)	153 (22.6)	<0.001

Notes: Descriptive data are shown in percentages or mean ± standard deviation (SD), and tested with the chi-square and *t*-test for categorical and continuous variables, respectively.

Abbreviations: TCM, takotsubo cardiomyopathy; COPD, chronic obstructive pulmonary disease; AKI, acute kidney injury; ARF, acute respiratory failure; LOS, length of stay.

the association between COPD and worse inpatient mortality of TCM using propensity score matching method in an effort to reduce bias from patient and hospital-level factors, which in turn could affect the outcomes of TCM. Second, as an uncommon disease, TCM in the setting of COPD has not been well studied. The common treatment options of TCM are supportive therapy and conventional cardiovascular drugs. Our findings may offer a new view on the treatment of TCM. Lastly, the poorer outcomes in TCM patients with COPD indicate that it may be beneficial to early intervene and treat COPD, and control the activity of SNS and inflammation.

Our study had several limitations. First, as a retrospective observational design, our study can help establish associations, but not causality. Further study is warranted to verify these findings. Second, due to the nature of the NIS database, data on treatment, laboratory variables, and clinical examination results are lacking, such as the use of β-adrenergic drugs, serum catecholamine concentration, the degree of cardiac injury, and total comorbidity burden, which prevents us from analyzing those factors. Third, after the propensity score-matched analysis, we got a reduced sample size, which may affect the study's final conclusions. Fourth, we are unable to validate the ICD-10 codes used for the variables and the inpatient complications in NIS database, which may affect the accuracy of our results. Finally, the severity of COPD in this study is not specified, and therefore differences between the stable COPD and acute exacerbation period were not able to be differentiated and studied.

Conclusion

Compared with patients without COPD who are admitted to hospital for TCM, those with COPD have a higher inpatient mortality rate, a higher incidence of ARF, cardiogenic shock, longer length of stay, and higher charges. Given the available evidence in our study, prospective studies are warranted to further evaluate the impact of early intervention or treatment for COPD in short- and long-term outcomes of TCM.

Abbreviations

TCM, takotsubo cardiomyopathy; COPD, chronic obstructive pulmonary disease; AMI, acute myocardial infarction; DM, diabetes mellitus; CKD, chronic kidney disease; NIS, National Inpatient Sample; AHRQ, the Agency for Healthcare Research and Quality; LOS, length of stay; IRB, Institutional Review Board; ICD-10-CM code, the International Classification of Diseases, Tenth Revision, Clinical Modification code; OSA, obstructive sleep apnea; AKI, acute kidney injury; ARF, acute respiratory failure; SD, standard deviation; SNS, the sympathetic nervous system; IL-6, interleukin 6.

Disclosure

The authors report no conflicts of interest in this work.

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