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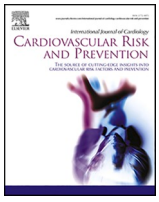

Seasonal variation in in-hospital outcomes of Takotsubo-syndrome-related admissions: A National Inpatient Analysis, 2019

We used data from the Nationwide Inpatient Sample (NIS) database, a nationally representative survey of hospitalizations conducted by the Healthcare Cost and Utilization Project in collaboration with participating states [1], to identify seasonal fluctuation based on meteorological classification of the northern hemisphere's Spring, Summer, Fall, and Winter. NIS is the largest all-payer inpatient dataset in the United States and includes a 20% sample of US community hospitals that approximates 20% of all US community hospitals. In the past, the NIS database has been used to conduct health quality and outcome-focused studies on TTS hospitalization [2]. Each hospitalization is identified and maintained as a distinct entry in the NIS with one primary discharge diagnosis and $\leq$14 secondary diagnoses. All TTS-related admissions among adults in the United States in 2019 were identified using the prior validated International Classification of Diseases (10th Edition) Clinical Modification (ICD-10-CM) diagnosis code I51.81 (Takotsubo syndrome) as the admission diagnosis. Categorical and continuous data were compared using Pearson's Chi-square test and Mann Whitney *U* test, respectively. Multivariable regression models were subsequently applied to assess the odds of outcomes of TTS-related admissions among adults in the US adjusting for baseline patient and hospital level characteristics and relevant preexisting comorbidities using complex survey sample models. Results were reported in adjusted odds ratio and 95% confidence interval for odds of outcomes. A two-tailed p-value below 0.05 was considered a threshold for statistical significance. IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA) was used to perform all analyses.

The TTS cohort (n = 41,830) in 2019 was primarily caucasian (80.6%), female (82.1%), and had a median age of $\geq$65 years (61.9%), similar to the findings in Ahuja et al. [3]. Fall admissions were the greatest (25.9%), followed by summer (25%), spring (24.6%), and winter (24.5%), which was similar to what was reported by Aryal et al. [4] and Deshmukh et al. [2]. Despite a similar median length of stay (4 days; $p < 0.001$), winter hospitalization expenditures (USD 56763) were the highest and fall the lowest (USD 51649). Winter admissions showed higher all-cause mortality (7.3% vs.6.7%) and dysrhythmias (29.8% vs.28.5%), including Atrial fibrillation (AF) (20.7% vs. 19.7%) [5]. Spring hospitalizations had a greater rate of cardiac arrest (4.8% vs.4.1%) and Acute Venous Thromboembolism (VTE) (4.7% vs.3.5%) than total TTS-related admissions [Table 1]. With confounders controlled, there was a higher risk of dysrhythmias in winter (OR:1.20; 95%CI:1.03–1.39), spring (OR:1.15; 95% CI:1.00–1.33), and fall (OR:1.18; 95% CI:1.03–1.36) compared to summer ($p = 0.063$). When compared to summer, there was a greater incidence of AF in winter (OR:1.22; 95% CI:1.02–1.45) [4], spring (OR:1.20; 95% CI:1.02–1.42), and fall (OR:1.28; 95% CI:1.08–1.51). Spring admissions had a greater risk of VTE than summer admissions [(OR:1.54; 95% CI:1.09–2.16) vs. summer; $p = 0.067$] which is what was reported by Zhao H et al. [6]. Other outcomes, such as all-cause mortality and cardiogenic shock, were not associated after controlling for confounding variables.

In conclusion, this nationwide retrospective cohort study found that hospitalizations throughout the winter increased the risk of dysrhythmia and atrial fibrillation (AF). At the same time, admissions during the spring showed a higher risk of venous thromboembolism (VTE). Seasonal variations in hospitalization and mortality have clinical and economic consequences. During vulnerable times, emergency care and other hospital resources should be available. Susceptible patients should be aware of the increased risk throughout the winter, and the increased risk may assist health practitioners to boost causative prevention measures, treatment, and educational methods [7]. Enhanced vigilance and improved access to emergency services and other hospital resources during the vulnerable period can improve in-hospital outcomes and ultimately reduce hospitalization costs.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Table 1
TTS hospitalizations and outcomes by seasons, 2019.

Variable		WINTER	SPRING	SUMMER	FALL	Total TTS	P-value
		n = 10,255	n = 10,275	n = 10,450	n = 10,850	n = 41,830	
Age (years) at admission	*Median [IQR]*	69 [59–77]	69 [59–77]	68 [59–77]	69 [59–78]	68 [59–77]	0.724
	18–44	6.4%	6.6%	7.4%	6.8%	6.8%	0.020
	45–64	32.4%	30.9%	31.0%	31.2%	31.4%	
	> = 65	61.2%	62.5%	61.7%	62.0%	61.9%	
Sex	*Male*	17.6%	18.6%	17.2%	17.9%	17.9%	0.059
	Female	82.4%	81.4%	82.8%	82.1%	82.1%	
Race	*White*	80.9%	81.2%	81.2%	79.2%	80.6%	<0.001
	Black	7.9%	8.9%	7.8%	7.5%	8.0%	
	Hispanic	5.8%	5.0%	6.7%	7.8%	6.4%	
	Asian or Pacific Islander	1.8%	2.6%	1.7%	1.9%	2.0%	
	Native American	0.6%	0.5%	0.6%	0.7%	0.6%	
	Others	2.9%	1.7%	2.0%	2.8%	2.4%	
Median household income national quartile for patient ZIP Code	*0*-25th	25.6%	25.0%	24.5%	25.9%	25.3%	0.001
	76-100th	22.8%	23.5%	21.8%	21.4%	22.4%	
Primary expected payer	*Medicare*	63.6%	63.6%	63.8%	63.4%	63.6%	<0.001
	Medicaid	9.6%	10.7%	10.0%	10.4%	10.2%	
	Others	2.3%	2.1%	2.1%	1.8%	2.1%	
Non-elective admission		93.2%	92.7%	93.5%	93.0%	93.1%	0.159
Location/teaching status of hospital	*Rural*	6.4%	6.2%	6.6%	5.9%	6.3%	0.004
	Urban non-teaching	15.2%	15.4%	15.2%	16.9%	15.7%	
	Urban teaching	78.4%	78.4%	78.2%	77.2%	78.1%	
COMORBIDITIES							
Hypertension, complicated		31.8%	32.7%	32.2%	28.3%	31.2%	<0.001
Hypertension, uncomplicated		31.5%	30.0%	31.0%	35.2%	32.0%	<0.001
Diabetes, chronic complications		13.9%	13.3%	12.8%	13.8%	13.5%	0.070
Diabetes without chronic complications		9.2%	9.2%	9.2%	9.5%	9.3%	0.770
Hyperlipidemia		45.9%	47.1%	46.5%	47.0%	46.6%	0.291
Obesity		11.7%	11.5%	11.9%	11.6%	11.7%	0.824
Smoking		17.6%	18.6%	17.4%	18.4%	18.0%	0.071
Peripheral vascular disease		9.0%	11.2%	9.7%	10.0%	10.0%	<0.001
Prior MI		11.1%	11.2%	10.6%	12.3%	11.3%	0.002
Prior PCI		0.4%	0.3%	0.5%	0.3%	0.4%	0.030
Prior CABG		4.7%	4.9%	3.7%	5.3%	4.6%	<0.001
Prior TIA/Stroke		6.8%	7.1%	6.0%	7.7%	6.9%	<0.001
Prior VTE		6.1%	5.7%	5.7%	5.9%	5.9%	0.498
Drug abuse		5.0%	5.9%	5.1%	5.9%	5.5%	0.001
Depression		19.1%	19.3%	19.2%	18.8%	19.1%	0.734
COPD		32.7%	32.8%	30.7%	28.8%	31.2%	<0.001
Cancer		8.2%	7.5%	8.3%	9.3%	8.4%	<0.001
Prior Radiation		2.5%	2.1%	1.9%	2.5%	2.2%	0.002
Chemotherapy		0.3%	0.3%	0.6%	0.5%	0.4%	0.019
OUTCOMES							
All-cause Mortality		7.3%	7.1%	6.3%	6.1%	6.7%	0.001
Dysrhythmia		29.8%	29.1%	26.1%	29.0%	28.5%	<0.001
AF		20.7%	20.3%	17.3%	20.6%	19.7%	<0.001
Cardiogenic Shock		7.1%	7.1%	7.4%	7.2%	7.2%	0.808
Cardiac arrest		3.9%	4.8%	3.9%	4.1%	4.1%	0.003
Acute VTE		4.1%	4.7%	3.2%	3.5%	3.9%	<0.001
Multivariate odds [aOR (95% CI)] of outcomes in TTS-related Hospitalizations by Season 2019							
All-cause Mortality		1.16 (0.90–1.50)	1.14 (0.87–1.48)	Referent	0.97 (0.74–1.27)		0.426
Dysrhythmia		1.20 (1.03–1.39)	1.15 (1.00–1.33)	Referent	1.18 (1.03–1.36)		0.063
AF		1.22 (1.02–1.45)	1.20 (1.02–1.42)	Referent	1.28 (1.08–1.51)		**0.028**
Cardiogenic Shock		0.93 (0.73–1.19)	0.92 (0.71–1.19)	Referent	0.97 (0.77–1.24)		0.906
Acute VTE		1.15 (0.81–1.65)	1.54 (1.09–2.16)	Referent	1.11 (0.79–1.58)		0.067

A $p < 0.05$ indicates statistical significance. Multivariable regression analyses were adjusted for baseline characteristics, hospital-level characteristics, and relevant cardiac-extra cardiac comorbidities.
MI = myocardial infarction, PCI = percutaneous coronary intervention, CABG = coronary artery bypass grafting, TIA = transient ischemic attack, VTE = venous thromboembolic events, COPD = chronic obstructive pulmonary disease, AF = atrial fibrillation, aOR = adjusted odds ratio, CI = confidence interval.

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