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COVID-19, POCUS, and Takotsubo

As of November 26, 2020, 62 articles could be accessed in PubMed in response to the MeSH term "COVID-19 and takotsubo,"[1–3] and describe or review cases of afflicted patients with the SARS-CoV-2, who were also diagnosed with the co-morbidity of Takotsubo syndrome (TTS). These 62 articles discuss patients with the COVID-19/TTS co-morbidity, and constitute a small part of the 74,342 articles accessed in PubMed, in response to the MeSH term "COVID-19," which discuss patients who were diagnosed solely with COVID-19. Review of these 62 reports reveals that many of the patients with TTS in the setting of a hospitalization with COVID-19, appeared to have been diagnosed with TTS, almost fortuitously, in the sense that while the main pathology of concern of their physicians was COVID-19, these patients complained of chest pain, or had excessive dyspnea in the absence of severe pneumonic involvement, or had cardiac complications, or showed increased biomarkers, or had prior history of heart disease, or had risk factors for coronary artery disease, or had an imaging test without any particular diagnostic intention. This implies that TTS, of varying severity must be underdiagnosed in patients with COVID-19. All health workers must keep in mind that patients with COVID-19 are at risk for development of acute coronary syndromes, heart failure, arrhythmias, and TTS,[1–3] in addition to specific infectious myocarditis with detection of SARS-CoV-2 in myocardial biopsies.[4] Indeed, the catecholamine surge, the intense inflammatory activation of the cytokine storm, and other physical and emotional triggers, associated with COVID-19, are perfect breeding grounds for the emergence of TTS co-morbidity.

Considering the intense activity to manage patients with COVID-19 and its dramatic complications, and the understandable efforts to limit physical exposure of members of the caring team, who ordinarily when TTS is suspected, will perform certain imaging studies (e.g., conventional transthoracic echocardiography, cardiac catheterization, CT-scan/angiography, and cardiac magnetic resonance imaging), and record one or several electrocardiograms during hospitalization, one is left with very little to diagnose a possible underlying TTS co-morbidity. In this setting, implementing frequently point of care hand-held ultrasound (POCUS) devices,[5] by many members of the caring team for the detection of TTS and other cardiac afflictions in patients with COVID-19, may prove revealing (i.e., show the true incidence of TTS) and life-saving (i.e., alter the management plan to include interventions for the underlying cardiac pathology, in addition to the ones directed at the pulmonary, and systemic complications of COVID-19).

Conflicts of Interest

The authors have no conflicts of interest to disclose.

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Impact of Malnutrition on Outcomes Among Patients Undergoing Transcatheter Aortic Valve Implantation

In geriatric patient population, poor nutritional status has been shown to be an independent risk factor for long-term mortality and morbidity among patients with severe aortic stenosis undergoing transcatheter aortic valve implantation (TAVI).[1-4] In our study, we utilized a nationwide cohort to assess the impact of malnutrition on in-hospital outcomes amongst the patients undergoing TAVI.

We identified all hospitalizations in patients who underwent TAVI (*International Classification of Diseases*, *Ninth Revision, Clinical Modification* [ICD-9-CM] procedure code 35.05 or 35.06 and *International Classification of Diseases*, *Tenth Revision, Clinical Modification* [ICD-10-CM] procedure codes 02RF37H, 02RF37Z, 02RF38H, 02RF38Z, 02RF3JH, 02RF3JZ, 02RF3KH, and 02RF3KZ) from 2014 to 2017 using the national inpatient sample (NIS) database. Malnutrition was defined as ICD-9-CM diagnosis codes 262, 2630, 2631, 2632, 2638, 2639, and ICD-10-CM diagnosis codes E43, E440, E441, E45, and E46. Overweight and obesity were defined as ICD-9-CM code 278 and ICD-10-CM code E66. A propensity score matching model was developed using logistic regression to derive 2 matched groups, malnutrition versus no malnutrition for comparative outcome analysis. The study population was entered into a

Table 1
Characteristics and outcomes of study population

Variable	Unmatched cohorts			Propensity score matching (PSM)		
	Malnutrition (N = 852)	No malnutrition (N = 26023)	p-value	Malnutrition (N = 787)	No malnutrition (N = 787)	p Value
Age (years)	80.06 (9.52)	80.27 (8.43)	<0.001	80.15 (8.71)	80.78 (8.52)	0.139
Women	49.21%	45.94%	0.078	50.06%	52.36%	0.391
Elective	52.51%	80.44%	<0.001	53.36%	54.38%	0.723
Race			0.004			0.345
White	87.28%	85.89%		85.52%	84.90%	
Black	4.24%	4.48%		4.44%	6.22%	
Hispanics	4.41%	3.84%		4.04%	5.46%	
Heart failure	87.69%	74.24%	<0.001	87.92%	86.66%	0.495
Chronic lung disease	37.53%	33.59%	0.017	39.78%	37.22%	0.325
Diabetes mellitus controlled	15.45%	22.42%	<0.001	15.12%	17.16%	0.304
Diabetes mellitus uncontrolled	17.03%	14.82%	0.070	16.26%	15.38%	0.678
Hypertension controlled	23.97%	37.97%	<0.001	24.52%	24.90%	0.907
Hypertension uncontrolled	56.78%	50.56%	<0.001	56.92%	55.02%	0.477
Peripheral vascular disease	28.70%	25.76%	0.055	28.20%	27.44%	0.778
Solid tumor without metastasis	3.47%	2.42%	0.088	3.44%	2.80%	0.561
Metastatic cancer	1.57%	0.58%	<0.001	1.52%	1.40%	>0.99
Lymphoma	1.57%	0.99%	0.181	1.66%	1.66%	>0.99
Overweight or Obesity	9.14%	17.48%	<0.001	8.26%	7.36%	0.573
Atrial fibrillation	51.10%	40.80%	<0.001	51.46%	52.74%	0.649
Chronic dialysis	9.14%	3.56%	<0.001	9.52%	8.38%	0.656
Carotid artery disease	5.04%	7.00%	0.045	5.08%	5.60%	0.736
Cardiogenic shock	10.09%	5.86%	<0.001	9.78%	11.30%	0.367
Coronary artery disease	64.66%	69.48%	0.002	64.54%	65.06%	0.874
Chronic kidney disease	48.26%	36.49%	<0.001	46.64%	45.88%	0.800
Chronic liver disease	7.86%	3.18%	<0.001	7.76%	7.12%	0.700
Endovascular TAVI	97.47%	97.99%	0.28	97.46%	97.20%	0.875
Hospital region			0.175			0.144
Northeast	23.02%	24.39%		24.66%	29.60%	
Midwest	26.18%	22.84%		23.64%	20.72%	
South	32.49%	33.24%		34.44%	33.30%	
West	18.61%	19.51%		17.28%	16.40%	
Hospital bed size			0.237			0.832
Small	6.01%	5.99%		6.10%	5.46%	
Medium	19.16%	17.03%		17.02%	17.66%	
Large	74,83%	77.28%		76.88%	76.88%	
Outcomes						
In-hospital mortality	8.21%	1.74%	<0.001	7.88%	3.30%	<0.001
Mechanical ventilation	13.24%	2.29%	<0.001	13.60%	4.06%	<0.001
In hospital sepsis	9.14%	2.09%	<0.001	8.90%	3.56%	<0.001
Acute kidney injury	37.54%	11.79%	<0.001	37.10%	20.34%	<0.001
Blood transfusion	18.61%	9.28%	<0.001	19.18%	13.98%	0.006
Stroke	4.15%	1.64%	<0.001	4.04%	1.83%	0.014
Vascular complications	6.62%	3.25%	<0.001	6.74%	2.92%	0.006
New pacemaker insertion	10.72%	9.55%	0.249	10.54%	10.42%	>0.99
Length of stay, days (SD)	14.29 (14.35)	4.96 (5.33)	<0.001	14.37 (14.52)	7.34 (7.19)	<0.001
Hospitalization charges, $ (SD)	349441.59 (309065.27)	212300.82 (127219.60)	<0.001	357896.32 (316967.73)	246177.57 (156926.48)	<0.001

nearest neighbor 1:1 variable ratio, parallel, balanced propensity score-matching model using a calliper of 0.01 to ensure matching. After propensity score matching, the standardized difference for all variables was <10%, indicating successful covariate balance between the 2 comparison groups. Baseline characteristics were compared between the groups using a Pearson $\chi 2$ test for categorical variables and an independent-samples *t* test for continuous variables. Multivariate logistic regression analysis was performed to determine the predictors/risk-factors of malnutrition in patients undergoing TAVI. Statistical analysis was performed using R 3.6.4 and p <0.05 was considered significant.

Between 2014 and 2017, a total of 26,875 unweighted hospitalizations were identified of which 852 (3.17%) had malnutrition. Patients with malnutrition were more likely to undergo a nonelective procedure, have congestive heart failure, chronic lung disease, uncontrolled hypertension, chronic kidney disease, chronic dialysis, atrial fibrillation, metastatic cancer, coagulopathy and have cardiogenic shock during the hospitalization. After propensity score matching, patients with malnutrition had significantly worse outcomes: in-hospital

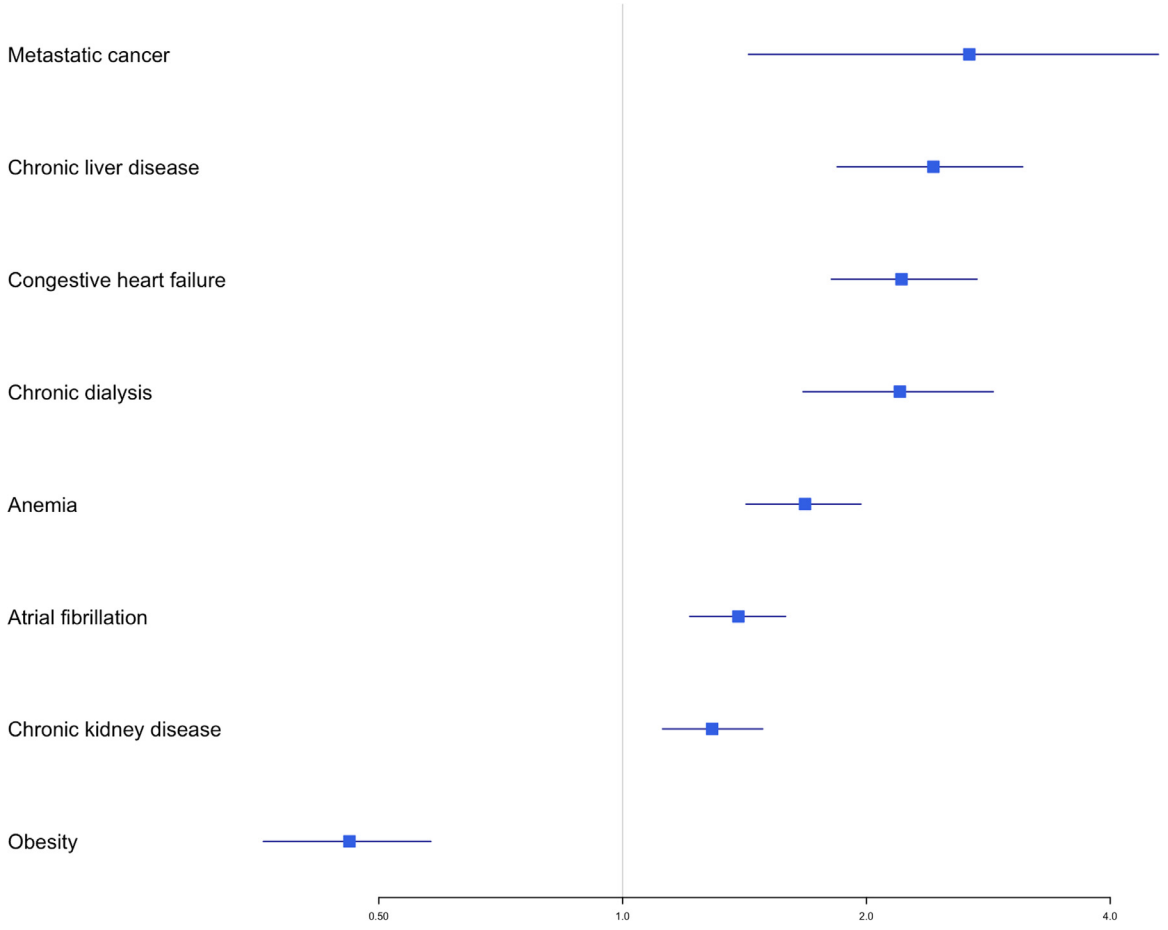

Figure 1. Multivariate predictors of malnutrition in patients undergoing TAVI., TAVI = transcatheter aortic valve implantation.

mortality (7.88% vs 3.30%, p <0.001), need for mechanical ventilation (13.60% vs 4.06%, p <0.001), in-hospital sepsis (8.90% vs 3.56%, p <0.001), acute kidney injury (37.10% vs 20.34%, p <0.001), stroke (4.04% vs 1.83%, p = 0.014), blood transfusion (19.18% vs 13.98%, p = 0.006), and vascular complications (6.74% vs 2.92%, p = 0.006). In addition, malnutrition had significant economic impact on the hospitalizations for TAVI with 2 fold increased length of stay in patients with malnutrition (14.37 [14.52] vs 7.34 [7.19], p <0.001) and 1.5 times rise in hospitalization charges ($ 357896.32 [316967.73] vs $ 246177.57 [156926.48], p <0.001) (Table 1). Malnutrition was more likely to occur in patients with metastatic cancer (odds ratio [OR]= 2.68: 95% confidence interval [CI 1.43 to 4.59]), chronic liver disease (OR = 2.42: 95% CI [1.83 to 3.12]), congestive heart failure (OR = 2.21: 95% CI [1.81 to 2.74]), chronic dialysis (OR = 2.20: 95% CI [1.67 to 2.87]), anemia (OR = 1.68: 95% CI [1.42 to 1.97]), atrial fibrillation (OR = 1.39: 95% CI [1.21 to 1.59]), and chronic kidney disease (OR= 0.46: 95% CI [0.36 to 0.58]) (Figure 1).

In our study, 3% of patients undergoing TAVI had malnutrition, a percent lower in comparison with reports from the existing studies.[1,2] This could be attributed to under reporting in the national database and varying prevalence of malnutrition based on the tool used for assessment.

The main limitation of NIS dataset is in the variation in data collection and use of ICD-CM codes which rely on fidelity of hospital billing data. In addition, variables like mobility, body mass index, albumin, and others are not available in the NIS database.

Malnutrition occurs in patients with congestive heart failure mainly because of immunological and hormonal disturbances, switching the body from anabolic to a catabolic state by an increase in the levels of catabolic markers such as proinflammatory cytokines (TNF-a, IL-1, IL-6) and glucocorticoids, and decreased activity of anabolic mediators such as insulin and growth hormone. These changes result in a hypermetabolic state and an increase in protein degradation causing muscle wasting and malnutrition. Malabsorption from the gut because of bowel wall edema and decreased appetite further worsen the malnutrition state.[5,6] Malnutrition is an under-recognized entity and has been associated with significantly worse in-hospital outcomes in patients undergoing TAVI.

Disclosure

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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The Utility of CHA(2)DS(2)-VASc Scores as a Risk Assessment Tool in Low-Risk In-Hospital Patients With Coronavirus Disease 2019 Infection

Coronavirus disease 2019 (COVID-19) infections can have serious consequences such as cardiac manifestations, severe coagulopathy, and thromboembolism.[1–4] We read with interest the study by Ruocco et al published in *the American Journal of Cardiology*.[5] This study, performed on an Italian cohort, showed that the CHA(2)DS(2)-VASc score could aid prognostication of mortality and a composite end-point of inpatient death or invasive ventilation across CHA(2)DS(2)-VASc tertiles in COVID-19 patients.

In Singapore, there has been a demographic shift in COVID-19 cases initially involving at-risk elderly population in the community, and transitioning to cluster outbreaks in densely-populated foreign worker dormitories.[6] Active case finding of dormitory residents resulted in a surge of swab-positive COVID-19 patients who were either asymptomatic or mildly symptomatic. They were admitted to hospital for risk assessment before transfer to a nonhospital isolation facility. This policy provided an opportunistic insight into the low-risk COVID-19 cohort.

Our hospital registry of 554 in-hospital COVID-19 patients, recruited between 23rd January to 30th April 2020, were admitted to a tertiary

Table 1
Clinical characteristics and outcomes of patients hospitalised for COVID-19 infection categorised according to CHA(2)DS(2)-VASc score

Variable	All patients (N = 554)	CHA(2)DS(2)-VASc scores			p Value
		≤1 (N = 532)	2-3 (N = 18)	≥4 (N = 4)	
Sex (male)	482 (87.0)	473 (88.9)	9 (50.0)	0	<0.001
Age (years)	36 (11)	36 (10)	54 (13)	67 (19)	<0.001
Smoking status					0.330
Current smoker	30 (5.6)	27 (5.3)	3 (16.7)	0	
Ex-smoker	3 (0.6)	3 (0.6)	0	0	
Hypertension	53 (12.3)	34 (8.3)	16 (88.9)	3 (75.0)	<0.001
Diabetes mellitus	21 (5.1)	8 (2.0)	10 (62.5)	3 (75.0)	<0.001
Hyperlipidemia	34 (8.1)	17 (4.3)	13 (72.2)	4 (100.0)	<0.001
Atrial fibrillation	0	0	0	0	
Ischemic heart disease	5 (1.2)	1 (0.3)	3 (16.7)	1 (25.0)	<0.001
Congestive heart disease	3 (0.7)	0	1 (6.3)	2 (50.0)	<0.001
Stroke	2 (0.5)	0	0	2 (50.0)	<0.001
Chronic kidney disease	3 (0.7)	1 (0.3)	0	2 (50.0)	<0.001
Medications					
Statin	26 (6.2)	11 (2.8)	11 (61.1)	4 (100)	<0.001
Beta-blocker	8 (1.9)	4 (1.0)	3 (16.7)	1 (25.0)	<0.001
Calcium channel blocker	29 (6.9)	17 (4.3)	10 (55.6)	2 (50.0)	<0.001
ACE-I	6 (1.5)	2 (0.5)	3 (16.7)	1 (25.0)	<0.001
ARB	12 (2.9)	8 (2.0)	3 (16.7)	1 (25.0)	<0.001
Diuretics	5 (1.2)	3 (0.8)	0	2 (50.0)	<0.001
Metformin	18 (4.3)	8 (2.0)	10 (62.5)	0	<0.001
Insulin	4 (1.0)	2 (0.5)	1 (6.3)	1 (25.0)	<0.001
Study outcomes					
Mortality	2 (0.5)	2 (0.5)	0	0	0.952
Intensive care unit admission	19 (3.4)	15 (2.8)	2 (11.1)	2 (50.0)	<0.001
Mechanical ventilation	16 (2.9)	12 (2.3)	2 (11.1)	2 (50.0)	<0.001
Composite end-point	59 (10.6)	52 (9.8)	3 (16.7)	4 (100.0)	<0.001

ACE-I = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; COVID-19 = coronavirus disease 2019.