The Arrhythmogenic Impact of Heart Failure With Preserved Ejection Fraction on Diabetics

Type II diabetes milletus (DM) is associated with an increased risk of heart failure with preserved ejection fraction (HFpEF).[1] This is postulated to be due to an increased fatty acid utilization that can increase the production of toxic intermediates predisposing to myocyte and endocardial dysfunction.[2] Nearly half of HFpEF patients have DM,[3] and it is known that DM increases cardiovascular morbidity and mortality, primarily through increasing the risk of coronary artery disease.[4] Nonetheless, coronary artery disease alone does not fully explain the high prevalence of sudden cardiac deaths of nearly 20% that was reported in HFpEF primarily in diabetics.[5] DM arrhythmogenic effects have recently emerged as a concern. This was depicted in the 38-year follow-up of the Framingham heart study, where DM was found to be an independent risk factor for atrial fibrillation.[6] Moreover, both DM and HFpEF were linked to an increased risk of ventricular arrhythmias (VA) owing to their effect on the potassium channels, leading to a prolonged action potential duration manifesting as a prolonged QT interval repolarization and risks of multiple re-entry circuits.[7,8] Notwithstanding this, the exact burden of VA in diabetics with HFpEF remain largely unexamined. Hence, we attempted to evaluate the probable synergistic effects of DM and HFpEF on VA risk and to understand outcome predictors in this patients' cohort.

We queried the national inpatient sample from 2012 to 2014 for patients age >=18 years. We excluded heart failure patients with reduced ejection fraction and hypertrophic cardiomyopathy. Subsequently, we used ICD-9-CM codes to identify discharges associated with DM, HFpEF, VT, ventricular fibrillation (VF), and QTc prolongation. Diabetic patients were divided into HFpEF and non-HFpEF groups. Outcomes of interest were the prevalence of VT, VF, QTc prolongation, and in-hospital mortality; also, the length of stay. We use propensity score matching to limit the effect of confounders. Standardized mean difference <0.1 indicated covariate homogeneity. We used multivariate logistic regression to devise the propensity scores. The results were considered significant at p <0.05. We identified 326,545 hospitalizations in the HFpEF group and 362,513,0 in the non-HFpEF group. Compared with the non-HFpEF group, the HFpEF group tended to have older and had more co-morbidities (Table 1). Charlson score as a measurement of

Table 1
Patient characteristics of both the unmatched and propensity-score−matched cohort of patients

Variable	Unmatched		p Value	SMD	OR	95% CI	Propensity score matched		p Value	SMD	OR	95% CI
	Without HFpEF	With HFpEF					Without HFpEF	With HFpEF				
Number	36,25,130	326,545					326,544	326,544				
Year (%)			<0.001	0.088					<0.001	0.013		
2012	12,33,623 (34.0)	99,137 (30.4)					100,463 (30.8)	99,137 (30.4)				
2013	11,98,795 (33.1)	108,403 (33.2)					109,025 (33.4)	108,403 (33.2)				
2014	11,92,712 (32.9)	119,005 (36.4)					117,056 (35.8)	119,004 (36.4)				
Age (mean (SD))	64.15 (15.26)	71.87 (12.16)	<0.001	0.56			72.23 (11.49)	71.87 (12.16)	<0.001	0.031		
LOS (mean (SD))	5.10 (6.26)	6.41 (6.64)	<0.001	0.203			5.92 (6.50)	6.41 (6.64)	<0.001	0.074		
Race (%)			<0.001	0.127					0.251	0.006		
White	23,35,071 (64.4)	220,834 (67.6)					221,754 (67.9)	220,834 (67.6)				
Black	641,323 (17.7)	61,814 (18.9)					61,350 (18.8)	61,813 (18.9)				
Hispanic	423,096 (11.7)	27,207 (8.3)					26,922 (8.2)	27,207 (8.3)				
Asian	88,976 (2.5)	6,826 (2.1)					6,733 (2.1)	6,826 (2.1)				
Native American	30,168 (0.8)	1,898 (0.6)					1,922 (0.6)	1,898 (0.6)				
Others	106,496 (2.9)	7,966 (2.4)					7,863 (2.4)	7,966 (2.4)				
Female (%)	18,73,932 (51.7)	196,977 (60.3)	<0.001	0.174			194,137 (59.5)	196,976 (60.3)	<0.001	0.018		
Tobacco (%)	10,27,254 (28.3)	87,583 (26.8)	<0.001	0.034			89,109 (27.3)	87,583 (26.8)	<0.001	0.011		
Alcohol (%)	56,018 (1.5)	2,577 (0.8)	<0.001	0.07			2,515 (0.8)	2,577 (0.8)	0.391	0.002		
Obesity (%)	813,603 (22.4)	109,699 (33.6)	<0.001	0.25			104,894 (32.1)	109,698 (33.6)	<0.001	0.031		
Hypertension (%)	20,12,838 (55.5)	113,187 (34.7)	<0.001	0.429			114,555 (35.1)	113,187 (34.7)	<0.001	0.009		
Dyslipidemia (%)	17,52,331 (48.3)	173,911 (53.3)	<0.001	0.099			174,102 (53.3)	173,910 (53.3)	0.636	0.001		
CAD (%)	10,92,560 (30.1)	155,100 (47.5)	<0.001	0.362			157,619 (48.3)	155,099 (47.5)	<0.001	0.015		
ACS (%)	236,578 (6.5)	32,073 (9.8)	<0.001	0.121			31,718 (9.7)	32,073 (9.8)	0.14	0.004		
Stroke (%)	275,119 (7.6)	21,435 (6.6)	<0.001	0.04			21,795 (6.7)	21,435 (6.6)	0.074	0.004		
CKD (%)	868,793 (24.0)	169,362 (51.9)	<0.001	0.6			167,922 (51.4)	169,361 (51.9)	<0.001	0.009		
OSA (%)	328,986 (9.1)	69,191 (21.2)	<0.001	0.343			64,284 (19.7)	69,190 (21.2)	<0.001	0.037		
PVD (%)	284,115 (7.8)	37,938 (11.6)	<0.001	0.128			38,786 (11.9)	37,937 (11.6)	0.001	0.008		
Charlson (mean (SD))	2.27 (1.16)	3.72 (1.07)	<0.001	1.301			3.73 (1.22)	3.72 (1.07)	0.002	0.008		
VT (%)	40,098 (1.1)	6,714 (2.1)	<0.001	0.076	1.88	1.83-1.93	6,315 (1.9)	6,714 (2.1)	<0.001	0.009	1.06	1.03-1.10
V.fib (%)	7,332 (0.2)	601 (0.2)	0.027	0.004	0.91	0.84-0.99	1,026 (0.3)	601 (0.2)	<0.001	0.026	0.59	0.53-0.65
LOS (mean (SD))	5.10 (6.26)	6.41 (6.64)	<0.001	0.203			5.92 (6.50)	6.41 (6.64)	<0.001	0.074		
DIED (%)	83,33 (2.3)	10,873 (3.3)	<0.001	0.062	1.46	1.43-1.49	15,344 (4.7)	10,873 (3.3)	<0.001	0.07	0.7	0.68-0.72
Qtc (%)	970 (0.0)	113 (0.0)	0.011	0.004	1.29	1.06-1.57	119 (0.0)	113 (0.0)	0.743	0.001	1.03	0.79-1.34

comorbidities was significantly higher in the HFpEF group. On propensity score matching + multivariate logistic regression, HFpEF group had higher VT odds (2.1% vs 1.9%; OR, 1.06; 95% CI, 1.03 to .10; p <0.001) and higher length of stay (6.41% vs 5.92%; p <0.001). Nonetheless, VF and in-hospital mortality were surprisingly higher in the non-HFpEF group. No difference in QTc prolongation between both groups was noted. A subgroup analysis of the VT prevalence revealed that the female gender and age of 65 or higher carried the highest risk in the HFpEF cohort.

Our finding is consistent with the findings of McHugh et al who studied the HFpEF with DM in THE GWTG-HF REGISTRY,[2] and supported by an earlier report by Jae Hyung Cho et al showing that HFpEF predisposed to VA in rats.[7] To our knowledge, this is the first retrospective analysis that evaluated this association, utilizing such a large patient sample. Our study failed to depict the association between DM and QTc prolongation, likely owing to the paucity of data describing QTc prolongation in the retrieved sample for both groups. Our analysis is subject to the inherent limitations associated with retrospective studies as well as the nature of the national inpatient sample database itself. Although our findings are consistent with other database-based work, further prospective studies in settings of more controlled confounding factors are needed to explore this relation further and examine interventions that are likely to mitigate morbidity associated with this synergism.

Disclosures

All authors declare that they have no conflicts of interest to disclose.

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Myocardial Contractile Reserve and Mortality in Patients With Severe Aortic Stenosis With Impaired Left Ventricular Function Who Underwent Transcatheter Aortic Valve Implantation

Low-flow, low-gradient aortic stenosis (LFLG AS) with reduced left ventricular ejection fraction (LVEF) remains a challenging subgroup of severe AS. In these patients, dobutamine stress echocardiography (DSE) is routinely used to establish the diagnosis of true severe AS. The 2014 ACC/AHA Valve Guidelines endorse a class IIa recommendation for low−dose DSE in AS patients with LVEF <50% to confirm AS severity and to assess myocardial contractile reserve (CR), which is defined as stroke volume increase of ≥20%. Earlier studies have shown that patients with LFLG AS and no CR have increased mortality with conservative management as well as with surgical aortic valve replacement (SAVR).[1] However, it is not known if CR portends similar prognostic significance in patients who underwent transcatheter aortic valve implantation (TAVI). Hence, we performed a meta-analysis to systematically review the impact of the presence or absence of CR on all-cause mortality in patients with LFLG AS who underwent TAVI.

We conducted a systematic literature search of PubMed, Scopus, Embase, and Cochrane Library, from 2002 to October 31, 2020. We used the following key words and Medical Subject Headings: "contractile reserve," "flow reserve," "dobutamine stress echocardiography," "DSE," "transcatheter aortic valve replacement," "transcatheter aortic valve implantation," "TAVR," "TAVI," "aortic