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Hassan AlHarbi

Mohammed AlAhmari

Abdulrahman M. Alanazi

Bander Al-Ghamdi

See next page for additional authors

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Authors

Hassan AlHarbi, Mohammed AlAhmari, Abdulrahman M. Alanazi, Bander Al-Ghamdi, Abdullah AlSuayri, Ahmed AlHaydhal, Amr A. Arafat, Khaled D. Algarni, Wiam Abdelsalam, Sameera AlRajwi, Abdulrahman AlMoghairi, Hussin AlAmri, Saeed AlAhmari, and Mohammed AlOtaiby

ORIGINAL ARTICLE

Outcomes After Transcatheter Aortic Valve Replacement in Patients with Severe Aortic Stenosis and Diastolic Dysfunction☆

Hassan AlHarbi [a], Mohammed AlAhmari [a], Abdulrahman M. Alanazi [a], Bander Al-Ghamdi [a], Abdullah AlSuayri [a], Ahmed AlHaydhal [a], Amr A. Arafat [b,^,*], Khaled D. Algarni [b,#], Wiam Abdelsalam [a], Sameera AlRajwi [c], Abdulrahman AlMoghairi [a], Hussin AlAmri [a], Saeed AlAhmari [a], Mohammed AlOtaiby [a]

[a] Adult Cardiology Department, Prince Sultan Cardiac Center, Riyadh, Saudi Arabia
[b] Adult Cardiac Surgery Department, Prince Sultan Cardiac Center, Riyadh, Saudi Arabia
[c] Adult Cardiology Department, King Abdulaziz Cardiac Centre, Ministry of National Guard Riyadh, Saudi Arabia

Abstract

Objectives: **Left ventricular diastolic dysfunction (LVDD) in patients undergoing transcatheter aortic valve replacement (TAVR) is associated with poor outcomes; however, the effect of its severity is controversial. We sought to assess the impact of diastolic dysfunction on hospital outcomes and survival after TAVR and identify prognostic factors.**

Methods: **We included patients who underwent TAVR for severe aortic stenosis with preexisting LVDD from 2009 to 2018 (n = 325). Patients with prior mitral valve surgery (n = 4), atrial fibrillation (n = 39), missing or poor baseline diastolic dysfunction assessment (n = 36) were excluded. The primary endpoint was all-cause mortality. 246 patients were included in the study.**

Results: **The median age was 80 years (25th and 75th percentiles:75−86.7), 154 (62.6%) were males and the median EuroSCORE II was 4.3 (2.2−8). Patients with severe LVDD had significantly higher EuroSCORE, and lower ejection fraction (p < 0.001). There was no difference in post-TAVR new atrial fibrillation (p = 0.912), pacemaker insertion (p = 0.528), stroke (p = 0.76), or hospital mortality (p = 0.95). Patients with severe LVDD had longer hospital stay (p = 0.036). The grade of LVDD did not affect survival (log-rank = 0.145) nor major adverse cardiovascular events (log-rank = 0.97). Predictors of mortality were; low BMI (HR: 0.95 (0.91−0.99); p = 0.019), low sodium (0.93 (0.82−2.5); p = 0.021), previous PCI (HR: 1.6 (1.022−2.66); p = 0.04), E-peak (HR: 1.01 (1.002−1.019); p = 0.014) and implantation of more than one device (HR: 3.55 (1.22−10.31); p = 0.02).**

Conclusion: **Transcatheter aortic valve replacement is feasible in patients with diastolic dysfunction, and the degree of diastolic dysfunction did not negatively affect the outcome. Long-term outcomes in those patients were affected by the preoperative clinical state and procedure-related factors.**

Keywords: Transcatheter aortic valve replacement, Diastolic dysfunction, Survival

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* *Corresponding author*.
E-mail address: amr.arafat@med.tanta.edu.eg (A.A. Arafat).
^ affiliated with Cardiothoracic Surgery Department, Tanta University, Tanta, Egypt.
# affiliated with Cardiac Science Department, King Saud University, Riyadh, Saudi Arabia.

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1. Introduction

The indications of transcatheter aortic valve replacement (TAVR) have been expanded to treat high, intermediate, or low-risk surgical risk patients [1]. Thus, high-risk patients with associated comorbidities previously deemed unfit for surgery are currently managed with TAVR. These patients are prone to complications, even after minimally invasive interventions.

Aortic stenosis (AS) is associated with left ventricular hypertrophy and impairment of the diastolic function. Several studies have demonstrated an association between diastolic dysfunction in patients with AS and morbidity and mortality after surgical and transcatheter aortic valve replacement [2,3].

Patients with diastolic dysfunction are frequently readmitted after TAVR because of left ventricular failure [4]. The impact of the degree of LVDD on the outcomes after TAVR is not fully established, and the results from the literature are controversial. This study's objectives were to assess the effect of the degree of diastolic dysfunction in patients with severe AS on hospital outcomes and survival after TAVR and to identify the prognostic factors.

Abbreviations

AS	aortic stenosis
CT	computed tomography
LVDD	left ventricular diastolic dysfunction
MACE	Major adverse cardiovascular events
TAVR	transcatheter aortic valve replacement
TTE	transthoracic echocardiography

2. Patients and methods

2.1. Study design and patients

This research is a retrospective cohort study that included patients who had transcatheter aortic valve replacement (TAVR) for severe aortic stenosis and had a concomitant left ventricular diastolic dysfunction (LVDD) during the period from April 2009 till February 2018. TAVR was performed in 325 consecutive patients, and patients with prior mitral valve surgery (n = 4), atrial fibrillation (n = 39), missing echocardiographic data, or poor baseline diastolic dysfunction assessment (n = 36) were excluded. Patients were grouped into three groups based on pre-procedural LVDD (mild (n = 156), moderate (n = 66), and severe (n = 24)) (Fig. 1).

The institutional review board approved the study, and the need for patients' consent was waived. (Reference number: R19009).

2.2. Procedure details

A comprehensive preoperative evaluation was performed on all patients in the outpatient clinic. Patients had pre-procedural transthoracic and transesophageal echocardiography, cardiac catheterization, and computed tomography (CT) angiography of the chest, abdomen, and pelvis. Procedure risk was assessed using EuroSCORE ll [5]. Our interdisciplinary adult cardiac team consists of adult interventional cardiologists, cardiac surgeons, and echocardiographers. The team reviewed the patients before the intervention in a multidisciplinary meeting. A consensus on appropriate treatment was reached based on individual risk assessment, anatomical, and technical considerations as well as patients' preferences. We decided about the access site (transfemoral vs. transapical) according to the anatomical characteristics. We used two valves during the study period, either the Medtronic CoreValve System (Medtronic Inc., Minneapolis, Minnesota, USA) or the Edwards SAPIEN valve (Edwards Life science, Irvine, CA, USA). We chose the device according to vascular access dimensions and aortic annular diameter.

2.3. Assessment of LVDD

Pre-procedure diastolic dysfunction was assessed using transthoracic echocardiography (TTE) and collected from our echocardiography database. LV diastolic function was evaluated using two tissue Doppler parameters, one CW-Doppler, and one 2D parameter [6]. Left ventricular diastolic dysfunction was diagnosed using annular e′ velocity, average E/e′ ratio, left atrium maximum volume index, and deceleration time. Patients who met the diagnostic criteria of LVDD were further graded into mild, moderate, and severe. Mild LVDD was defined as a lateral E/e′ ratio of greater than 10, a peak velocities of early (E) and late (A) (E/A) ratio of less than 0.8, and deceleration time (DT) a greater than 200 ms; moderate LVDD was defined by a lateral E/e′ ratio of greater than 10, an E/A ratio between 0.8 and 1.5, and DT of between 160 and 200 ms; and severe LVDD was defined as a lateral E/e' ratio of greater than 10, an E/A ratio of greater than 2 and DT of less than 160 ms. In patients with mitral annular calcification and mitral valve disease, pulmonary artery systolic pressure (PASP) estimated from the tricuspid regurgitation (TR) jet was our index of left

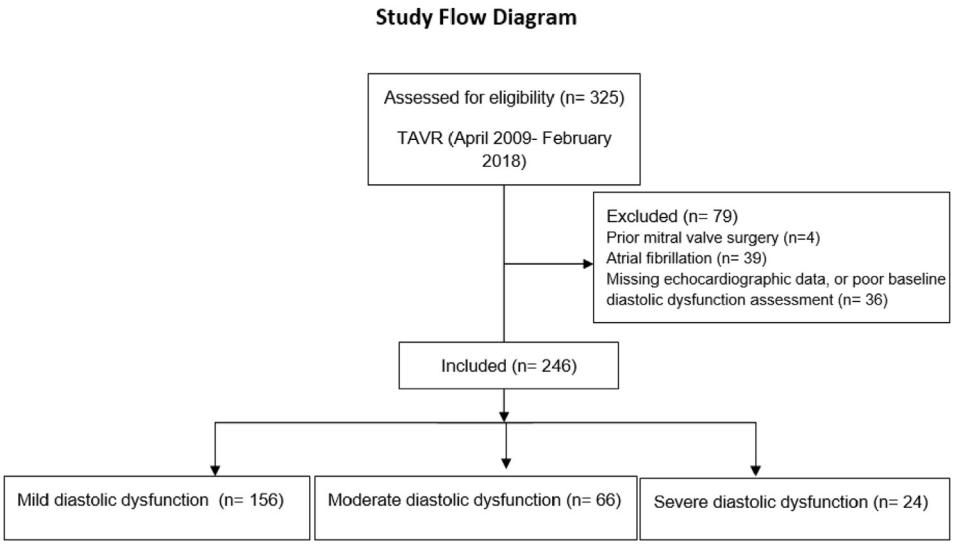

Fig. 1. The study flowchart.

atrial pressure (LAP), provided there is no evidence of pulmonary vascular or parenchymal disease.

2.4. Clinical follow-up

Clinical follow-up was performed after one month, six months, then yearly. The patients' vital status was confirmed during the last clinical follow-up or phone calls conducted in August 2018. Eighty-two percent of the patients completed a year follow-up, 57% two-year follow-up, and 43% achieved a three-year follow-up. Procedure-related mortality was defined as any death occurring during the admission for the procedure or within 30-days after the procedure. Re-hospitalization was recorded, and the causes of readmission were re-evaluated.

2.5. Study endpoints

The primary endpoint was all-cause mortality during the follow-up. Secondary endpoints included hospital outcomes (procedure mortality, new-onset atrial fibrillation, permanent pacemaker insertion, vascular complications, stroke, length of coronary care unit (CCU), and hospital stay). Additionally, long-term major cardiovascular events (MACE) (stroke, re-hospitalization for heart failure, and reintervention) were compared among groups. Study data were retrospectively retrieved from our prospectively maintained database.

2.6. Statistical analysis

Continuous variables were presented as median (25th − 75th percentiles) and were compared by the Kruskal-Wallis test, and Dunn's test was used for posthoc analysis. Categorical variables were presented as number and percent and compared with Pearson's Chi-square test or Fisher's exact test if the expected frequency is less than 5. Time-related variables were assessed nonparametrically using Kaplan-Meier methods. The log-rank test was used to test the equality of survival distributions. Multivariable Cox regression was used to study the predictors of time-related events, the Efron method to handle ties was used, and the proportional hazard assumption was tested with Schoenfeld residual tests. Univariable Cox regression was used, and variables with p-value <0.1 were included in the multivariable model. We included all variables listed in Tables 1 and 2 and the operative variables in Table 3 in the univariable analysis. Components of the EuroSCORE were not added to the multivariable analysis to avoid collinearity. The interaction between LVDD and low EF and low pressure AS were tested. A P-value of less than 0.05 was considered significant. Stata 16 (Stata Corp, College Station, Texas, USA) was used to perform all analyses.

3. Results

3.1. Baseline patients' characteristics

The median age was 80 years (25th- 75th percentiles: 75−86.7), and EuroSCORE was significantly higher in patients with severe LVDD ($p < 0.001$). (Table 1).

To adjust for the effect of time, the study period was divided into the early time era (2009−2013) and

Table 1. Comparison of patients' baseline characteristics. (Continuous variables are presented as median (25th and 75th percentiles and categorical data as number and percent).

	All (n = 246)	Diastolic Dysfunction Grade			P
		Mild (n = 156)	Moderate (n = 66)	Severe (n = 24)	
Age	80 (75, 86.7)	78 (73.3, 82.8)	78 (70, 81)	77.5 (70,85.8)	0.453
Male	154 (62.6)	88 (56.4)	48 (72.7)	18 (75)	0.030
BMI (kg/m^2)	28.7 (25.1, 33.2)	29.6 (26, 34.4)	29.3 (25.9,33.4)	29.6 (24.9, 34.7)	0.792
Risk Stratification:					
Euro Score II	4.3 (2.2, 8)	2.9 (1.9, 4.8)	3.3 (2.2, 7.2)	5.2 (3.6, 9.4)	<0.001
Comorbidities:					
Hypertension	198 (80.5)	125 (80.1)	53 (80.3)	20 (83.3)	0.933
Diabetes Mellitus	159 (64.6)	103 (66)	41 (62.1)	15 (62.5)	0.834
Chronic lung disease	52 (21.1)	32 (20.5)	16 (24.2)	4 (16.7)	0.703
Previous MI	28 (11.4)	17 (10.9)	8 (12.1)	3 (12.5)	0.950
Previous Cardiac Surgery	33 (13.4)	14 (9)	14 (21.2)	5 (20.8)	0.027
Previous PCI	86 (35)	56 (35.9)	20 (30.3)	10 (41.7)	0.559
Extracardiac vasculopathy	44 (17.89)	24 (15.38)	13 (19.70)	7 (29.17)	0.236
Recent HF	53 (21.54)	24 (15.38)	18 (27.27)	11 (45.83)	0.001
Poor mobility	46 (18.70)	34 (21.79)	7 (10.61)	5 (20.83)	0.130
Clinical status:					
NYHA III-IV	220 (89.4)	136 (87.2)	60 (90.9)	24 (100)	0.148
Clinical preop state	7 (2.8)	2 (1.3)	3 (4.5)	2 (8.3)	0.096
Laboratory tests:					
Hemoglobin (mg/dl)	12.2 (11, 13.4)	12.4 (11.25, 13.35)	11.75 (10.7, 13.2)	12.45 (11.3, 13.65)	0.316
Creatinine (μmol/l)	61 (44.8, 80)	83.5 (69, 103)	80 (69.105.2)	89.5 (72.3, 107)	0.625
Sodium (mEq/l) (n = 238)	138 (136, 140)	138 (135.5, 140)	138.5 (135, 141)	138 (137, 141)	0.748
Era:					
Time era (2014–2018)	137 (55.69)	88 (56.41)	35 (53.03)	14 (58.33)	0.865

BMI: body mass index, HF: heart failure, MI: myocardial infarction, NYHA: New York Heart Association, PCI: percutaneous coronary intervention.

the recent time era (2014–2018). Patients were equally distributed among the groups in both the time era (p = 0.865).

Patients with severe diastolic dysfunction had significantly lower ejection fraction (p < 0.001). Preoperative echocardiographic data were presented in Table 2.

3.2. Procedure and hospital outcomes

Four patients had valve-in-valve (1.6%), and 15 patients (6.1%) had concomitant percutaneous coronary intervention (PCI). Self-expandable valves were used in 142 patients (57.7%). Grade II paravalvular leak occurred in 23 patients (9.35%) and grade III in one patient (0.4%), and no

Table 2. Pre-procedural echocardiographic characteristics. (Continuous variables are presented as median (25th and 75th percentiles and categorical data as number and percent).

	All (n = 246)	Diastolic Dysfunction Grade			p
		Mild (n = 156)	Moderate (n = 66)	Severe (n = 24)	
LV EF	55 (45,55)	55 (50,60)	55 (48.8, 56.3)	45 (25, 53.8)	<0.001
AV mean gradient (mmHg)	45.8 (38.7, 54.4)	46.1 (40, 56)	49.5 (40.6, 56.6)	44 (35.4, 58.4)	0.509
Aortic regurgitation grade					
No AR	69 (28)	49 (31.4)	11 (16.7)	9 (37.5)	0.084
Mild AR	119 (48.4)	74 (47.4)	39 (59.1)	6 (25)	
Moderate AR	53 (21.5)	30 (19.2)	15 (22.7)	8 (33.3)	
Moderately severe AR	3 (1.2)	2 (1.3)	0	1 (4.2)	
Severe AR	2 (0.8)	1 (0.6)	1 (1.5)	0	
E peek (m/s)	90 (70.9, 109)	76.8 (63.2, 92)	107.6 (98, 118.5)	122 (102, 138)	<0.001
A peek (m/s)	97 (78, 113)	105 (92, 119)	83 (63.1, 99)	45.9 (39, 65.2)	<0.001
E/A ratio	0.82 (0.7, 1.2)	0.75 (0.7, 0.8)	1.3 (1.1, 1.7)	2.6 (1.9, 3.3)	<0.001
Septal E (m/s)	4.4 (3.6, 5.4)	4.6 (3.8, 5.5)	4.8 (4, 6)	4 (3.3, 6.8)	0.236
E/E ratio	19 (15, 27)	16.4 (13, 22)	22 (17, 29)	29.65 (21.5, 35.2)	<0.001
Deceleration time (ms)	0.23 (0.19, 0.30)	0.26 (0.22, 0.30)	0.21 (0.17, 0.25)	0.16 (0.15, 0.20)	<0.001

AV: aortic valve, AR: aortic regurgitation, LVEF: left ventricle ejection fraction.

Table 3. Procedural characteristics and hospital outcomes. (Continuous variables are presented as median (25th and 75th percentiles and categorical data as number and percent).

	All	Diastolic Dysfunction Grade			P
		Mild (n = 156)	Moderate (n = 66)	Severe (n = 24)	
AV valve-in-valve	4 (1.6)	3 (1.9)	1 (1.5)	0	0.784
Revascularization:					
Concomitant PCI	15 (6.1)	9 (5.8)	4 (6.1)	2 (8.3)	0.887
Valve type:					
Balloon expandable valve	104 (42.3)	67 (42.9)	27 (40.9)	10 (41.7)	0.959
Self-expandable valve	142 (57.7)	89 (57.1)	39 (59.1)	14 (58.3)	
Number of valves implanted (>1)	7 (2.85)	5 (3.21)	0	2 (8.33)	0.077
Outcomes:					
Procedure mortality	9 (3.66)	6 (3.85)	2 (3.03)	1 (4.17)	>0.99
New AF	14 (5.69)	10 (6.41)	3 (4.55)	1 (4.17)	0.912
Permanent PM	59 (23.98)	36 (23.08)	15 (22.73)	8 (33.33)	0.528
Vascular complications	44 (17.89)	33 (21.15)	8 (12.12)	3 (12.50)	0.245
Stroke	6 (2.4)	4 (2.6)	1 (1.5)	1 (4.2)	0.760
Paravalvular leak (Grade II or higher)	24 (9.76)	15 (9.62)	6 (9.09)	3 (12.5)	0.892
CCU stay (days)	3 (1, 5)	3 (1, 5)	3 (1, 5)	3 (1.5, 6)	0.52
Hospital stay (days)	5 (4, 8)	5 (4, 8)	5 (4, 7)	6 (5, 12)	0.036

AF: atrial fibrillation, AV: aortic valve, CCU: coronary care unit; PCI: percutaneous coronary intervention, PM: pacemaker.

difference was observed among groups (p = 0.892). There was no difference in operative complications among groups (Table 3); however, patients with severe LVDD had longer hospital stays (p = 0.036).

3.3. Long-term outcomes

The median follow-up period was 30 (25th- 75th percentiles: 15–56) months. Kaplan-Meier survival distribution was presented in Fig. 2. Mortality was reported in 81 patients (32.9%) during follow-up; 47 (30.1%) with mild LVDD, 26 (39.4%) with moderate LVDD and 8 (33.3%) in patients with severe LVDD. The grade of LVDD did not affect survival (log-rank p = 0.145) nor major adverse cardiovascular events (log-rank p = 0.97). Predictors of mortality were; low body mass index (BMI) (HR: 0.95 (95% CI: 0.91–0.99); p = 0.019), low sodium (0.93 (95% CI: 0.82–2.5); p = 0.021); previous PCI (HR: 1.6 (95% CI: 1.022–2.66); p = 0.04); E-peak (HR: 1.01 (95% CI: 1.002–1.019); p = 0.014) and implantation of more than one device (HR: 3.55 (95%CI: 1.22–10.31); p = 0.02). (Table 4). MACE was reported in 44 patients (17.9%); 28 (18%) in patients with mild LVDD, 11 (16.7%) in moderate LVDD and 5 (20.8%) in severe LVDD. There was no difference among groups in MACE (log-rank p = 0.97). (Fig. 3, Table 5).

There was no interaction between LVDD and low EF and low pressure AS.

4. Discussion

Diastolic dysfunction is common in patients with aortic stenosis, which results from mechanical obstruction of the left ventricle with LV hypertrophy and abnormalities in the collagen fibers [7,8]. It was found that mortality was correlated to the degree of LVDD rather than the degree of AS [9]. Moderate and severe left ventricular diastolic dysfunction was associated with increased late mortality and adverse events after aortic valve replacement [2,10]. The effect of diastolic dysfunction on survival after transcatheter aortic valve replacement is still controversial. In our study on 246 patients, the degree of LVDD was not associated with long-term mortality. Sato and colleagues in their study on 237 patients had 57% mortality in a median follow-up of 3.6 years, and mortality was not associated with the degree of LVDD; however, severe pre-procedural LVDD combined with post-procedural aortic regurgitation were predictors of mortality [11]. A similar finding was confirmed in another study [12]. In our study, neither the degree of LVDD nor the post-procedure paravalvular leak was associated with mortality either by univariable or multivariable analysis, which could be attributed to the small number of events in our study.

In a study by Kampaktsis and coworkers on 359 TAVR patients, LVDD was associated with increased mortality in a mean follow-up of 13 months. However, after propensity-score adjustment, the STS score was the only predictor of mortality [13]. On the other hand, in a study on 222 TAVR patients, severe LVDD and NT-pro BNP were associated with increased mortality in a one-year median follow-up [14]. Blair and colleagues found that LVDD was an independent predictor of mortality after TAVR [15].

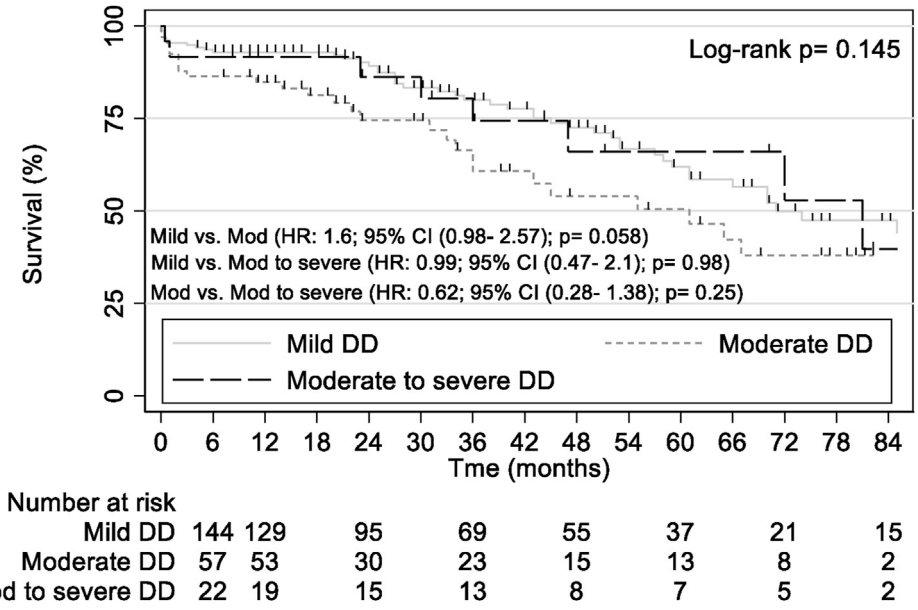

Fig. 2. Plot of survival function in patients with diastolic dysfunction stratified by the degree of dysfunction with a comparison of survival function among the three grades.

Table 4. Legend: Univariable and multivariable Cox regression analysis for predictors of mortality.

	Univariable Cox		Multivariable Cox	
	Crude HR (95% CI)	P	Adjusted HR (95%CI)	p
Time era (2014–2018)	0.61 (0.34–1.07)	0.085	0.54 (0.29–1.007)	0.053
Euro Score II	1.03 (1.013–1.051)	0.001	1.019 (0.99–1.05)	0.164
BMI (kg/m2)	0.96 (0.92–0.996)	0.032	0.95 (0.91–0.99)	0.019
Na (mg/dl)	0.93 (0.88–0.98)	0.012	0.93 (0.82–2.5)	0.021
Recent HF	1.96 (1.24–3.11)	0.004	1.78 (1.089–2.91)	0.206
Previous PCI	1.66 (1.07–2.58)	0.024	1.6 (1.022–2.66)	0.040
E-peak (m/s)	1.01 (1.005–1.02)	0.001	1.01 (1.002–1.019)	0.014
Number of devices used	2.83 (1.03–7.84)	0.044	3.55 (1.22–10.31)	0.02
Type of the valve	0.66 (0.43–1.038)	0.073	0.81 (0.49–1.34)	0.415

BMI: body mass index; HF: heart failure; PCI: percutaneous coronary intervention.

Several risk factors predicted the outcomes after TAVR in patients with diastolic dysfunction. In a study by Conte and colleagues on 166 TAVR patients with LVDD, paravalvular leak independently predicted mortality [16]. The volume overload that occurs because of the paravalvular leakage or aortic regurgitation may exacerbate the LVDD. This finding was not confirmed in our study, which could be related to the number of patients and events in our study were low. Asami and coworkers did not find an association between the degree of post-procedure aortic regurgitation and mortality [3].

Scoring systems inconsistently predicted mortality after TAVR. EuroSCORE II predicted mortality in our series in the univariable analysis; however, it became insignificant predictors by multivariable analysis. Similar to our finding, log EuroSCORE was not a predictor of mortality by Asami and colleagues [3] and Conte and coworkers [16]. However, STS independently predicted mortality in another study [13]. The inconsistency in these results could be attributed to different patients' populations; on the other hand, several other factors unique to TAVR may affect the outcomes and were not included in the scoring systems.

Lower BMI was an independent predictor of mortality after TAVR in patients with diastolic dysfunction. In a study by Mancio and colleagues, lower BMI and visceral abdominal fat index were associated with higher mortality after TAVR [17]. This finding could be attributed to the better metabolic reserve in obese patients, which supported them to survive the catabolic state of heart failure and the procedure. Additionally, lower BMI and

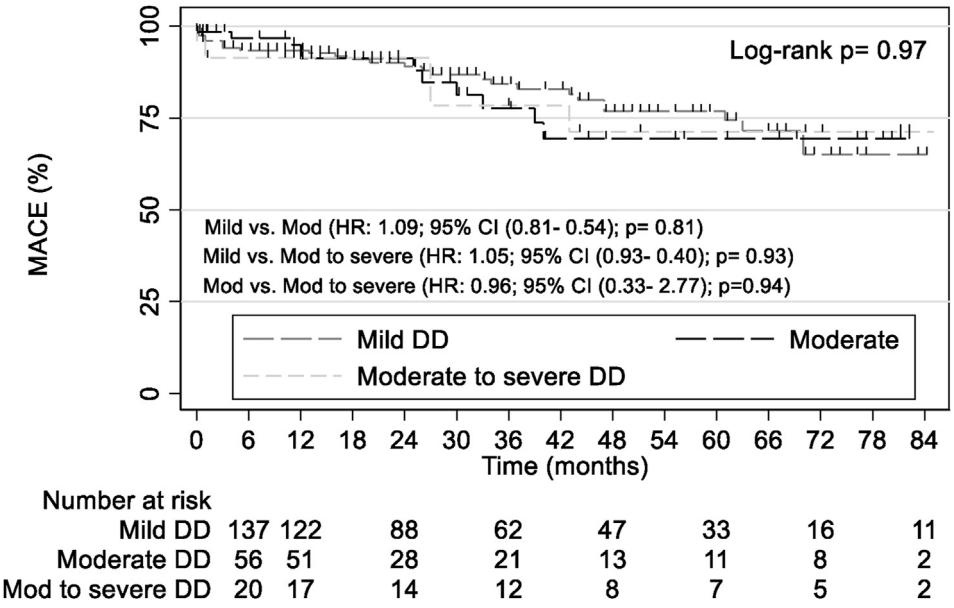

Fig. 3. Plot of time to event distribution of major adverse cardiovascular events in patients with diastolic dysfunction stratified by the degree of dysfunction with a comparison of survival function among the three grades.

Table 5. Legend: Univariable and multivariable Cox regression analysis for predictors of major adverse cardiovascular events.

	Univariable Cox		Multivariable Cox	
	Crude HR (95% CI)	P	Adjusted HR (95%CI)	p
DM	2.01 (0.97–4.19)	0.062	1.73 (0.82–3.67)	0.149
Recent HF	1.85 (0.98–3.5)	0.057	1.55 (0.81–2.97)	0.186
Self-expandable valve	0.57 (0.31–1.04)	0.066	0.65 (0.34–1.2)	0.171

MACE: major adverse cardiovascular events; DM: diabetes mellitus; HF: heart failure.

unintentional weight loss may indicate disease progression in those patients [18].

Hyponatremia was associated with increased perioperative morbidity and mortality in patients undergoing surgery [19] and heart failure patients [20]. The effect of hyponatremia on the outcome after TAVR was evaluated in a study by Kagase and associates [21]. Pre-procedure hyponatremia was associated with increased all-cause mortality in patients who had TAVR. In our study, low serum sodium was an independent predictor of mortality after TAVR in patients with diastolic dysfunction.

In a meta-analysis of 4 observational studies including 209 who had TAVR, concomitant PCI did not affect the outcomes of the procedure [22]; a finding similar to our results. Witberg and associates [23] found that complete revascularization before TAVR improved the outcomes of the procedure. In our study, prior PCI predicted the mortality after TAVR; however, prior CABG was not associated with increased mortality. This finding could be related to the completeness of revascularization in CABG versus PCI, as Witberg and colleagues suggested [23]. Our study showed the feasibility of TAVR in patients with diastolic dysfunction with no increase in the procedure risk in paitents with severe degree of LVDD [24].

4.1. Study limitations

The study is a single-center experience, and generalization of the results may not be applicable. Assessment of diastolic function was not done routinely because of the study's retrospective nature, and patients with incomplete evaluation of diastolic function were excluded. There could be intra or inter-observational variability in the assessment of the diastolic function in the included patients since a single echocardiographer assessed the function prior to the procedure.

5. Conclusion

Transcatheter aortic valve replacement can be safely performed in patients with diastolic dysfunction, and the degree of diastolic dysfunction

did not negatively affect the outcome. Long-term outcomes in those patients were affected by the preoperative clinical state and procedure-related factors.

Author's contribution

Conception and design of Study: Hassan AlHarbi, Mohammed AlAhmari. Literature review: Hassan AlHarbi, Mohammed AlAhmari, Abdulrahman M. Alanazi, Bander Al-Ghamdi, Abdullah AlSuayri, Ahmed AlHaydhal. Acquisition of data: Hassan AlHarbi, Abdulrahman AlMoghairi, Hussin AlAmri, Saeed AlAhmari, Mohammed AlOtaiby. Analysis and interpretation of data: Amr A. Arafat, Khaled D. Algarni. Research investigation and analysis: Amr A. Arafat, Khaled D. Algarni, Wiam Abdelsalam, Sameera AlRajwi. Data collection: Hassan AlHarbi, Mohammed AlAhmari, Abdulrahman M. Alanazi, Bander Al-Ghamdi, Abdullah AlSuayri, Ahmed AlHaydhal, Wiam Abdelsalam, Sameera AlRajwi. Drafting of manuscript: Amr A. Arafat, Khaled D. Algarni, Mohammed AlOtaiby. Revising and editing the manuscript critically for important intellectual contents: Hassan AlHarbi, Mohammed AlAhmari, Abdulrahman M. Alanazi, Bander Al-Ghamdi, Abdullah AlSuayri, Ahmed AlHaydhal, Amr A. Arafat, Khaled D. Algarni, Wiam Abdelsalam, Sameera AlRajwi, Abdulrahman AlMoghairi, Hussin AlAmri, Saeed AlAhmari, Mohammed AlOtaiby. Data preparation and presentation: Amr A. Arafat, Khaled D. Algarni, Mohammed AlOtaiby. Supervision of the research: Abdulrahman AlMoghairi, Hussin AlAmri, Saeed AlAhmari, Mohammed AlOtaiby. Research coordination and management: Hassan AlHarbi, Mohammed AlAhmari, Abdulrahman M. Alanazi.

Ethical approval

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None.

References

[1] Otto CM, Kumbhani DJ, Alexander KP, Calhoon JH, Desai MY, Kaul S, et al. 2017 ACC expert consensus decision pathway for transcatheter aortic valve replacement in the management of adults with aortic stenosis: a report of the American College of cardiology task force on clinical expert consensus documents. J Am Coll Cardiol 2017 Mar;69(10):1313–46. https://doi.org/10.1016/j.jacc.2016.12.006.

[2] Gjertsson P, Caidahl K, Farasati M, Oden A, Bech-Hanssen O. Preoperative moderate to severe diastolic dysfunction: a novel Doppler echocardiographic long-term prognostic factor in patients with severe aortic stenosis. J Thorac Cardiovasc Surg 2005 Apr;129(4):890–6. https://doi.org/10.1016/j.jtcvs.2004.09.004.

[3] Asami M, Lanz J, Stortecky S, Raber L, Franzone A, Heg D, et al. The impact of left ventricular diastolic dysfunction on clinical outcomes after transcatheter aortic valve replacement. JACC Cardiovasc Interv 2018 Mar;11(6):593–601. https://doi.org/10.1016/j.jcin.2018.01.240.

[4] Franzone A, Pilgrim T, Arnold N, Heg D, Langhammer B, Piccolo R, et al. Rates and predictors of hospital readmission after transcatheter aortic valve implantation. Eur Heart J 2017 Jul;38(28):2211–7. https://doi.org/10.1093/eurheartj/ehx182.

[5] Nashef SAM, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, et al. EuroSCORE II†. Eur J Cardio Thorac Surg 2012 Apr 1;41(4):734–45. https://doi.org/10.1093/ejcts/ezs043 [Internet].

[6] Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, Waggoner AD, Flachskampf FA, Pellikka PA, Evangelista A. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr 2009 Feb;22(2):107–33. https://doi.org/10.1016/j.echo.2008.11.023.PMID:19187853.

[7] Zaid RR, Barker CM, Little SH, Nagueh SF. Pre- and post-operative diastolic dysfunction in patients with valvular heart disease: diagnosis and therapeutic implications. J Am Coll Cardiol 2013 Nov 19;62(21):1922–30. https://doi.org/10.1016/j.jacc.2013.08.1619 [Internet]. 2013/09/18 Available from: https://www.ncbi.nlm.nih.gov/pubmed/24055747.

[8] Villari B, Campbell SE, Hess OM, Mall G, Vassalli G, Weber KT, et al. Influence of collagen network on left ventricular systolic and diastolic function in aortic valve disease. J Am Coll Cardiol 1993 Nov 1;22(5):1477–84. https://doi.org/10.1016/0735-1097(93)90560-n [Internet]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/8227808.

[9] Chin CWL, Everett RJ, Kwiecinski J, Vesey AT, Yeung E, Esson G, et al. Myocardial fibrosis and cardiac decompensation in aortic stenosis. JACC Cardiovasc Imaging 2017 Nov;10(11):1320–33. https://doi.org/10.1016/j.jcmg.2016.10.007 [Internet]. 2016/12/21, Available from: https://www.ncbi.nlm.nih.gov/pubmed/28017384.

[10] Metkus TS, Suarez-Pierre A, Crawford TC, Lawton JS, Goeddel L, Dodd-O J, et al. Diastolic dysfunction is common and predicts outcome after cardiac surgery. J Cardiothorac Surg 2018 Jun 15;13(1):67. https://doi.org/10.1186/s13019-018-0744-3 [Internet] Available from: https://www.ncbi.nlm.nih.gov/pubmed/29903030.

[11] Sato K, Harb S, Kumar A, Kapadia SR, Mick S, Krishnaswamy A, et al. Impact of left ventricular diastolic function and survival in patients with severe aortic stenosis undergoing transcatheter aortic valve replacement. PloS One 2018 May 2;13(5). https://doi.org/10.1371/journal.pone.0196031. e0196031–e0196031. [Internet] Available from: https://www.ncbi.nlm.nih.gov/pubmed/29718948.

[12] Kampaktsis PN, Bang CN, Chiu Wong S, Skubas NJ, Singh H, Voudris K, et al. Prognostic importance of diastolic dysfunction in relation to post procedural aortic insufficiency in patients undergoing transcatheter aortic valve replacement. Cathet Cardiovasc Interv 2017 Feb 15;89(3):445–51. https://doi.org/10.1002/ccd.26582 [Internet]. 2016/05/24 Available from: https://www.ncbi.nlm.nih.gov/pubmed/27218599.

[13] Kampaktsis PN, Vavuranakis M, Choi DY, Sherifi I, Christofi A, Triantafyllou D, et al. Prognostic role of diastolic dysfunction in patients undergoing transcatheter aortic valve replacement. Cathet Cardiovasc Interv 2020;95(5):1024.–1031. https://doi.org/10.1002/ccd.28426 [Internet] n/a(n/a).

[14] Anantha-Narayanan M, Malik U, Mbai M, Megaly M, Florea V, Sharma A, et al. Impact of diastolic dysfunction on long-term mortality and quality of life after transcatheter aortic valve replacement. Cathet Cardiovasc Interv 2020; 95(5):1034–41. https://doi.org/10.1002/ccd.28444. n/a(n/a). [Internet].

[15] Blair JEA, Atri P, Friedman JL, Thomas JD, Brummel K, Sweis RN, et al. Diastolic function and transcatheter aortic valve replacement. J Am Soc Echocardiogr 2017 Jun;30(6): 541–51 [Internet]. 2017/03/14 Available from: https://www.ncbi.nlm.nih.gov/pubmed/28314622. DOI: 10.1016/j.echo.2017.01.003.

[16] Conte L, Fabiani I, Pugliese NR, Giannini C, La Carruba S, Angelillis M, et al. Left ventricular stiffness predicts outcome in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation. Echocardiography 2017 Jan 1;34(1):6–13. https://doi.org/10.1111/echo.13402 [Internet].

[17] Mancio J, Fonseca P, Figueiredo B, Ferreira W, Carvalho M, Ferreira N, et al. Association of body mass index and visceral fat with aortic valve calcification and mortality after transcatheter aortic valve replacement: the obesity paradox in severe aortic stenosis. Diabetol Metab Syndr 2017 Oct;9:86. https://doi.org/10.1186/s13098-017-0285-2.

[18] Zamora E, Díez-López C, Lupón J, de Antonio M, Domingo M, Santesmases J, et al. Weight loss in obese patients with heart failure. J Am Heart Assoc 2016 Mar;5(3). https://doi.org/10.1161/JAHA.115.002468. e002468–e002468.

[19] Leung AA, McAlister FA, Rogers Jr SO, Pazo V, Wright A, Bates DW. Preoperative hyponatremia and perioperative complications. Arch Intern Med 2012 Oct;172(19):1474–81. https://doi.org/10.1001/archinternmed.2012.3992.

[20] Gheorghiade M, Abraham WT, Albert NM, Gattis Stough W, Greenberg BH, O'Connor CM, et al. Relationship between admission serum sodium concentration and clinical outcomes in patients hospitalized for heart failure: an analysis from the OPTIMIZE-HF registry. Eur Heart J 2007 Apr;28(8): 980–8. https://doi.org/10.1093/eurheartj/ehl542. 2007/02/19.

[21] Kagase A, Yamamoto M, Shimura T, Kodama A, Kano S, Koyama Y, et al. Impact of pre-procedural hyponatremia on clinical outcomes after transcatheter aortic valve replacement: a propensity-matched analysis. Cathet Cardiovasc Interv 2018 Aug;92(2):E125–34. https://doi.org/10.1002/ccd.27483. 2018/01/11.

[22] Yang Y, Huang F-Y, Huang B-T, Xiong T-Y, Pu X-B, Chen S-J, et al. The safety of concomitant transcatheter aortic valve replacement and percutaneous coronary intervention: a systematic review and meta-analysis. Medicine (Baltim) 2017 Dec;96(48). https://doi.org/10.1097/MD.0000000000008919. e8919–e8919.

[23] Witberg G, Zusman O, Codner P, Assali A, Kornowski R. Impact of coronary artery revascularization completeness on outcomes of patients with coronary artery disease undergoing transcatheter aortic valve replacement: a meta-analysis of studies using the residual syntax score (synergy between PCI with taxus and cardiac surgery). Circ Cardiovasc Interv 2018 Mar;11(3). https://doi.org/10.1161/CIRCINTERVENTIONS.117.006000. e006000–e006000.

[24] Alharbi H, Alotaiby M, AlAhmari M, Alanazi A, AL Ghamdi B, Alsuayri A, et al. Outcomes after transcatheter aortic valve replacement in patients with severe aortic stenosis and diastolic dysfunction. JACC (J Am Coll Cardiol) March 2020;75(11):1257. https://doi.org/10.1016/S0735-1097(20)31884-2. Suppl (1).