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ORIGINAL ARTICLE / KLİNİK ÇALIŞMA

Impact of the recovery of left ventricular ejection fraction after TAVI on mortality in patients with aortic stenosis

Aort darlığı olan hastalarda TAVI sonrası sol ventriküler ejeksiyon fraksiyonunun düzelmesinin mortaliteye etkisi

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ABSTRACT

Objective: To assess the effects of transvalvular aortic valve implantation (TAVI) on the outcomes of the patients with symptomatic severe aortic stenosis (AS), and predict the effect of left ventricular ejection fraction (LVEF) and cardiac structural recovery on mortality after the TAVI in patients with different stage of LV function.

Methods: Out of 191 patients, 151 consecutive patients in 3 centers were evaluated for outcome analysis. Patients were classified into 3 subgroups as AS with reduced ejection fraction (ASrEF) (LVEF <40%), AS with mildly reduced EF (ASmrEF) (LVEF 40-49%) and AS with preserved EF (ASpEF) (LVEF ≥50%).

Results: The mean follow-up period was 19.4±12.4 (up to 54) months. All-cause mortality was not different among all 3 groups. (p=0.901). In multivariate analysis, stroke volume index (SVI) (Exp(B): 0.039, 95% confidence interval [CI]: 0.011-0.013, p<0.001), baseline blood urea nitrogen (Exp(B): 1.022, 95% CI: 1.006-1.038, p=0.006), and percent LVEF change after TAVI (d-LVEF) (Exp(B): 0.046, 95% CI: 0.004-0.610, p=0.046) were the independent predictors for mortality after TAVI. The receiver operating characteristic curve analysis showed that the cutoff value of "≤10%" for d-LVEF had sensitivity of 50%, specificity of 75%, and an area under the curve of 0.72 in predicting mortality in patients with SVI <35 mL/m^2.

Conclusion: Improvement of LVEF after TAVI, which reflected the marked LV reverse remodeling, has an impact on the prediction of the survival in patients with AS, and this is more prominent in patients with low SVI.

ÖZET

Amaç: Transvalvüler aort kapak implantasyonunun (TAVI) semptomatik şiddetli aort darlığı (AD) olan hastaların sonuçları üzerindeki etkilerini değerlendirmek ve işlem sonrası sol ventrikül ejeksiyon fraksiyonu (LVEF) değişiminin ve kardiyak yapısal değişimin mortalite üzerindeki etkisini tahmin etmek.

Yöntemler: Taranan 191 hasta arasından 151 hasta 3 merkezde analiz edildi. Hastalar, düşük ejeksiyon fraksiyonlu AD (LVEF <%40), hafif düşük EF'li AD (LVEF %40-49) ve korunmuş EF'li AD (LVEF ≥%50) olarak üç alt gruba ayrıldı.

Bulgular: Ortalama takip süresi 19.4±12.4 (54'e kadar) ay idi. Tüm nedenlere bağlı mortalite her üç grup arasında benzer saptandı (p=0.901). Çok değişkenli analizlerde, strok volüm indeksi (SVİ) (Exp (B): 0.039, %95 CI: 0.011-0.013, p<0.001), başlangıç kan üre azotu (Exp (B): 1.022, %95 CI: 1.006-1.038, p=0.006) ve TAVI sonrası LVEF değişim yüzdesi (d-LVEF) (Exp (B): 0.046, %95 CI: 0.004-0.610, p=0.046) mortalite için bağımsız faktörlerdi. ROC eğrisi analizine göre, SVİ <35 mL/m^2 olan hastalarda d-LVEF ≤ %10 olması mortaliteyi öngörmede %50 duyarlılık ve %75 özgüllük (0.72 AUC) değerine sahiptir.

Sonuç: Belirgin LV tersine yeniden şekillenmesini yansıtan, TAVI'den hemen sonra LVEF'nin iyileşmesinin, AD hastalarında sağ kalımı öngörmede etkisi vardır ve SVİ düşük olan hastalarda daha önemlidir.

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Aortic stenosis (AS) is one of the most common valvular heart diseases in elderly patients.[1] Surgical aortic valve replacement (SAVR) has been shown to improve the symptoms and survival, and has been the preferred treatment method for symptomatic severe AS for many years.[2] In some high-risk patients, SAVR has high mortality and morbidity rates, and has no advantage over medical treatment.[1] Recently, transvalvular aortic valve implantation (TAVI) has emerged as an alternative treatment for those patients who have high risk co-morbidities for SAVR or considered inoperable for AS.[3] Left ventricular dysfunction (LVD) is one of the most important high-risk factors and associated with poor survival in patients with AS. SAVR has shown to reverse LVD and reduce all-cause mortality by improving the clinical outcomes. Additionally, immediate recovery of left ventricular ejection fraction (LVEF) after SAVR was shown to be associated with improved prognosis.[2] Besides, TAVI was also shown to improve LVEF, and LVEF improvement was associated with improved survival.[4,5] Several studies suggested that TAVI improved the mortality and morbidity rates in patients with severe AS and moderate LVD; however, there is a little data on advanced heart failure (HF) patients because such patients have been generally excluded from studies.[2] In this study, we aimed to assess the effects of TAVI on the outcomes of the patients with AS, and compare the effect of pre-procedural and post-procedural variables on mortality outcomes in patients with AS. The main goal of this study is to predict the effect of LVEF recovery and cardiac structural recovery on mortality after the TAVI procedure in patients with different LVEF values.

Abbreviations:

AF	*Atrial fibrillation*
AoMNGR	*Aortic mean gradient*
AoPGR	*Aortic peak gradient*
AS	*Aortic stenosis*
ASmrEF	*AS with mildly reduced EF*
ASpEF	*AS with preserved EF*
ASrEF	*AS with reduced EF*
AUC	*Area under curve*
AV	*Atrioventricular*
AVA	*Aortic valve area*
AVG	*Aortic valve gradients*
BUN	*Blood urea nitrogen*
CAD	*Coronary artery disease*
d-LVDD	*Delta left ventricular end-diastolic diameter*
d-LVEF	*Delta LVEF*
d-LVSD	*Delta left ventricular end-systolic diameter*
DM	*Diabetes mellitus*
FG	*Fasting glucose*
GFR	*Glomerular filtration rate*
Hbg	*Hemoglobin*
HF	*Heart failure*
HT	*Hypertension*
Htc	*Hematocrit*
Log	*Logistic*
LVD	*Left ventricular dysfunction*
LVDD	*Left ventricular diastolic diameter*
LVEF	*Left ventricular ejection fraction*
LVOT	*LV outflow tract*
LVSD	*Left ventricular systolic diameter*
NYHA	*New York Heart Association*
ROC	*Receiver operating characteristic*
SAVR	*Surgical aortic valve replacement*
SPAP	*Systolic pulmonary artery pressure*
STS	*The Society of Thoracic Surgery*
SV	*Stroke volume*
SVI	*Stroke volume index*
TAVI	*Transvalvular aortic valve implantation*

METHODS

Patient population

This study is a retrospective, multicenter observational cohort analysis of consecutive patients with severe AS (aortic valve area [AVA] <1 cm^2 or aortic valve index <0.5 cm^2/m^2) who referred for TAVI treatment. 191 consecutive patients with severe AS who underwent TAVI procedure in 3 centers namely, Health Science University Tepecik Research Hospital, İzmir; Dokuz Eylül University Hospital, İzmir; and Dicle University Hospital, Diyarbakır were screened between 2016 and 2018, and 151 patients were evaluated for outcome analysis. Patients were excluded from the study if the data were missing on baseline clinical and echocardiographic measurements. Only the first admission data for each patient were included in this analysis. All patients underwent clinical and echocardiographic evaluation at baseline in his/her own center. In order to comply with international guidelines and the main objective of the study, patients were classified into 3 subgroups as AS with reduced EF (ASrEF) (LVEF <40%), AS with mildly reduced EF (ASmrEF) (LVEF 40–49%) and AS with preserved EF (ASpEF) (LVEF ≥50%). All data (clinical, echocardiographic, and procedural variables) for the study cohort were collected from the hospitals' administrative databases. All-cause mortality during follow-up were obtained from either hospital's database or national health insurance database. Study protocol and activities have been approved by the Health Science University İzmir Tepecik Training and Research Hospital, Local Ethics Department (Approval Date: January 23, 2020; Approval Number: 2020/1-22). The investigation confirms with the principles outlined in the Declaration of Helsinki. The author order in this paper was defined according to the number of patients enrolled from each center.

TAVI procedure

All TAVI procedures were performed at the catheterization laboratory under general anesthesia with flu-

oroscopy guidance. Three different types of valves were implanted in TAVI procedures (61 patients [40.4%] with balloon-expandable Edwards SAPIEN valve [Edwards Lifesciences, Irvine, CA, USA], 32 patients [21.2%] with self-expandable CoreValve Evolut R [Medtronic, Minneapolis, Minnesota, USA], and 58 patients [38.4%] with self-expandable Portico valve [St. Jude Medical, St. Paul, Minnesota, USA]). All procedures were performed via the transfemoral approach as previously described.[6] Procedural success was defined as the implantation of a functioning aortic prosthetic valve without intraprocedural mortality.

Data collection

The mean follow-up period was 19.4±12.4 (up to 54) months. All-cause mortality was defined as death occurred in any time including during in-hospital period and follow-up period. In-hospital mortality was defined as death that occurred during TAVI procedure and before hospital discharge. Intraprocedural complications were defined events such as coronary occlusion, valve migration, atrioventricular (AV) conduction block, cardiac tamponade, and others that occurred during procedure.

Echocardiography

All patients underwent echocardiographic evaluation at baseline and after the TAVI procedure before hospital discharge in the designated TAVI clinic according to American Society of Echocardiography recommendations[7] with a Vivid 7 instrument (General Electric, Horten, Norway) and a 2.5 MHz transducer in all centers. Standard echocardiography analysis included two-dimensional, M-mode, and Doppler flow measurements. LVEF was measured from the apical four- and two-chamber views using biplane Simpson's rule, and aortic valve gradients (AVG) were measured using continuous wave Doppler method, and AVA was calculated with continuity equation method. Other echocardiography measurements were assessed according to American Society of Echocardiography guidelines.[7] Stroke volume (SV) was calculated by pulsed-wave Doppler using the following formula.[8]

SV=LV outflow tract (LVOT) area × LVOT time integral velocity (VTI)

$SV = [\pi \times (\text{LVOT diameter}/2)^2] \times (\text{LVOT VTI})$

SV was indexed to the body surface area. Patients were evaluated in 2 groups as SVI <35 mL/m^2 and SVI >35 mL/m^2. We calculated delta left ventricular end-diastolic diameter (d-LVDD), delta left ventricular end-systolic diameter (d-LVSD), delta left atrial diameter (d-LAD) and delta LVEF (d-LVEF) as following formulas:

d-LVDD (%)=[(LVDD early after TAVI) - (Baseline LVDD) /(Baseline LVDD)]*100

d-LVSD (%)= [(LVSD early after TAVI) - (Baseline LVSD) /(Baseline LVSD)]*100

d-LVEF (%)=[(LVEF early after TAVI) - (Baseline LVEF) /(Baseline LVEF)]*100

d-LAD (%)=[(LAD early after TAVI) - (Baseline LAD) /(Baseline LAD)]*100

Statistical analysis

The baseline characteristics were summarized as mean ± SD or as median (interquartile range) for continuous variables and frequencies (percentages) for categorical variables. Months of follow-up were presented as median. Clinical and echocardiographic characteristics of patients were compared based on LV systolic function in 3 subgroups (LVEF <40% versus LVEF 40-49% versus LVEF ≥50%) at baseline. Repeated-measure analysis of variance (ANOVA) was used to analyze and compare the repeated paired continuous variables. Post-hoc analysis for significant results was performed using Bonferroni's correction. Categorical variables were compared using chi-square or Fisher's exact tests as indicated. We used a Cox proportional hazards model to identify predictors of survival after TAVI. Variables with p<0.2 in the Cox univariate analysis were used in the multivariate model. Multivariable analyses were done using stepwise backward selection. Receiver operating characteristics (ROC) analyses were used by analyzing the area under the curve (AUC), specificity, sensitivity of the delta LVEF as the gold standard of survival in whole cohorts and in the patients with SVI <35 mL/m^2. Kaplan-Meier curves were used for presenting survival curves and log-rank test was used for comparisons of survival over time between groups. P value of less than 0.05 was considered statistically significant. All analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA), R version 3.4.3, and Python 3.6.5.

Table 1. Baseline clinical characteristics of patients with a baseline LVEF <40%, LVEF between 40 and 49% and those with ≥50%

Clinical characteristics	All patients (n=151)	LVEF <40% (n=53)	LVEF 40-49% (n=40)	LVEF ≥50% (n=58)	*p*
Age (year)	76.6±7	74.5±7.8	77.9±7.2	77.7±5.5	0.02
Gender (female)	88 (58.3%)	28 (52.8%)	21 (52.5%)	39 (67.2%)	0.21
HT (n)	63 (42%)	23 (44.2%)	15 (37.5%)	25 (43.1%)	0.792
Type 2 DM (n)	95 (62.9%)	28 (52.8%)	28 (70 %)	39 (67.2%)	0.16
AF (%)	9 (15.5%)	9 (22.5%)	16 (30.2%)	34 (22.5%)	0.18
CAD (%)	78 (51.7%)	28 (52.8%)	21 (52.5 %)	29 (50%)	0.94
FG (mg/dL)	126.9±50.1	124.1±43.2	125.7±46.7	130.1±58.3	0.81
Hbg (g/dL)	11.6±1.7	12.3±1.7	11.8±1.9	10.9±1.3	<0.001
Htc (%)	35.5±5.5	36.7±6.3	36±5.2	34.6±5.5	<0.001
BUN (mg/dL)	46.7±33.5	41.5±30	40.9±32.5	55.4±35.8	0.04
Creatinine (mg/dL)	1.3±1.2	1.4±0.9	1.3±1	1.3±1.4	0.411
GFR (mL/min/1.73m^2)	64.8±22.1	70.6±24	63.6±19.9	60.5±21.1	0.061
Log. Euroscore	31.9±11.8	35.2±11.7	34.3±7.6	17.7±8.9	<0.001
STS Risk Score	20.8±12.2	20.6±13.4	22.8±10.3	15.9±11.6	0.333
SVI (<35 mL/m^2)	33 (21.9%)	23 (43.4%)	7 (17.5%)	3 (5.2%)	<0.001

AF: atrial fibrillation; BUN: blood urea nitrogen; CAD: coronary artery disease; DM: diabetes mellitus; FG: fasting glucose; GFR: glomerular filtration rate; Hbg: hemoglobin; HT: hypertension; Htc: hematocrit; Log: logistic; NYHA: New York Heart Association; STS: The Society of Thoracic Surgery; SVI: stroke volume index.

RESULTS

Patient population and baseline characteristics

A total of 151 patients who underwent TAVI procedure between January 2016 and May 2018 were included in the study. Patients were classified in 3 groups; 53 patients as ASrEF (LVEF <40%), 40 patients as ASmrEF (LVEF 40–49%), and 58 patients as ASpEF (LVEF ≥50%). The baseline clinical characteristics of the patients are listed in Table 1. ASrEF group was younger than the ASmrEF and ASpEF groups (ASrEF vs ASmrEF vs ASpEF; 74.5±7.8 vs. 77.9±7.2 vs 77.7±5.5 years, p=0.021). As expected, higher logistic Euro risk score were observed for the ASrEF (35.2±11.7 vs 34.3±7.6 vs. 17.7±8.9, p<0.001). There were no statistically significant differences in other baseline characteristics.

Echocardiographic findings

Echocardiographic measurements are listed in Table 2. At the baseline, LVDD (ASrEF vs ASmrEF vs ASpEF; 55.1±6.7 vs. 50.1±5.5 vs 47.4±5 mm, p<0.001), LVSD (44.8±7.5 vs. 35.2±5 vs. 29.9±5.7 mm, p<0.001), and LAD (47±6 vs. 45.5±5.3 vs. 42.3±5.7 mm, p<0.001) measurements were higher in ASrEF and found significantly different among all groups. Aortic valve peak gradient (AvPGR) (66.5±19.4 vs. 76.9±15.5 vs. 85±19 mmHg, p<0.001), aortic valve mean gradient (AvMnGR) (39.4±12.3 vs. 46.4±9.6 vs. 50.9±11.5 mmHg, p<0.001), and AVA (0.66±0.16 vs. 0.71±0.15 vs. 0.76±0.12 cm^2, p<0.001) were lower in ASrEF patients.

Immediately post-TAVI, significant reductions in AoPGR from 76.4±19.8 to 16.2±5.7 mmHg (p<0.001) and AoMnGR from 45.7±12.3 to 8.4±3.4 mmHg (p<0.001) were observed and found similar between groups. In addition, LVSD (from 36.5±8.9 to 35.2±8.3 mm, p<0.001) and LVDD (from 50.8±6.6 to 49.9±6.4 mm, p<0.001) were decreased and LVEF (from 44±12.5 to 48.5±11.2%, p<0.001) was increased in all groups. Change in the cardiac chamber dimensions immediately after TAVI were different between groups. d-LVDD (ASrEF vs ASmrEF vs ASpEF; -5.3±11.4 vs 0.6±9.4 vs 0.8±10.3%, p<0.001) and d-LVSD (ASrEF vs ASmrEF vs ASpEF; -9.1±15.7 vs 0.1±12.9 vs -0.7±17.8%, p<0.001) were found to be decreased in ASrEF patients and additionally d-LVEF (ASrEF vs ASmrEF vs ASpEF; 31.1±38.3 vs 12.3±15.4 vs 2.1±7%, p<0.001) was higher in ASrEF patients than those of other groups (Figure 1).

Table 2. Echocardiographic characteristics of patients with a baseline LVEF <40%, LVEF between 40 to 49% and those with ≥50%

Echocardiographic characteristics	All patients (n=151)	LVEF <40% (n=53)	LVEF 40-49% (n=40)	LVEF ≥50% (n=58)	*p*
LVEF (%)	44±12.5	29.9±5.2	43.3±2.8	57.3±4.4	<0.001
LVDD (mm)	50.8±6.6	55.1±6.7	50.1±5.5	47.4±5.0	<0.001
LVSD (mm)	36.5±8.9	44.8±7.5	35.2±5	29.9±5.7	<0.001
LAD (mm)	44.8±6	47±6	45.5±5.3	42.3±5.7	<0.001
AoPGR (mmHg)	76.4±19.8	66.5±19.4	76.9±15.5	85±19	<0.001
AoMnGR (mmHg)	45.7±12.3	39.4±12.3	46.4±9.6	50.9±11.5	<0.001
SPAP (mmHg)	48.1±14.9	47.8±12.3	48.1±16.1	48.4±16.7	0.981
AVA (cm^2)	0.71±0.15	0.66±0.16	0.71±0.15	0.76±0.12	<0.001
LVDD (mm) (Post-TAVI)	49.9±6.4	51.7±7.3	50.3±5.7	47.6±5.1	<0.001
LVSD (mm) (Post-TAVI)	35.2±8.3	40.2±7.9	35.6±6.8	29.6±6.1	<0.001
LAD (mm) (Post-TAVI)	43.8±6.3	45.2±5.9	45.4±7.3	41.1±5	-
LVEF (%) (Post-TAVI)	48.5±11.2	38.5±9.7	48.8±6.9	58.2±4.6	<0.001
AoPGR (mmHg) (Post TAVI)	16.2±5.7	16.9±7.4	15.3±4.9	16.1±4.4	0.442
AoMnGR (mmHg) (Post-TAVI)	8.4±3.4	8.7±4.3	7.9±3	8.4±2.6	0.592
AVA (cm^2) (Post-TAVI)	1.7±0.2	1.6±0.2	1.8±0.3	1.7±0.2	0.241
SPAP (mmHg) (Post-TAVI)	38.7±12.9	39±9.6	38.5±13.2	38.5±15.7	0.921
Delta LVDD (%)	-1.5±10.8	-5.3±11.4	0.6±9.4	0.8±10.3	<0.001
Delta LVSD (%)	-3.6±16.3	-9.1±15.7	0.1±12.9	-0.7±17.8	<0.001
Delta LVEF (%)	15.5±27.8	31.1±38.3	12.3±15.4	2.1±7	<0.001
Delta LAD (%)	-1.6±11.2	-2.8±11.2	-1±8.2	-0.8±13	0.611

AoMNGR: aortic mean gradient; AoPGR: aortic peak gradient; AVA: aortic valve area; LAD: left atrial diameter; LVDD: left ventricular diastolic diameter; LVEF: left ventricular ejection fraction; LVSD: left ventricular systolic diameter; SPAP: systolic pulmonary artery pressure; TAVI: transvalvular aortic valve implantation.

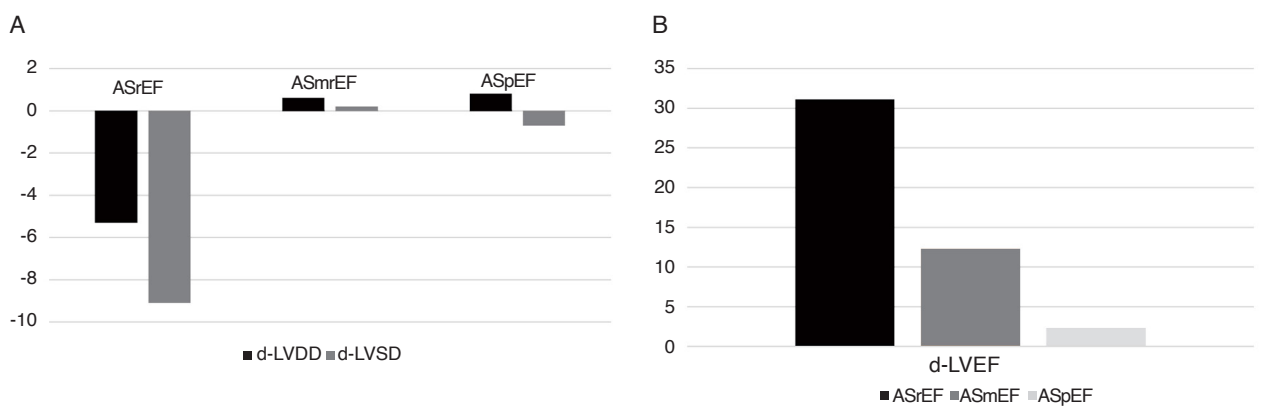

Figure 1. (A) Delta changes in LVDD and LVSD after TAVI procedure, **(B)** Delta change in LVEF after TAVI procedure. ASmrEF: AS with mildly reduced EF; ASpEF: AS with preserved EF; ASrEF: AS with reduced EF; d-LVDD delta left ventricular end-diastolic diameter; d-LVEF: delta LVEF; d-LVSD: delta left ventricular end-systolic diameter; LVDD: left ventricular diastolic diameter; LVEF: left ventricular ejection fraction; LVSD: left ventricular systolic diameter; TAVI: transvalvular aortic valve implantation.

Procedural and clinical outcomes

Procedural success rate was 91% (n=138) among study population and similar among the 3 study groups (p=0.791). Valve types were different among groups (p<0.001). However, we did not find any correlation between mortality and valve types (p=0.881). Procedural complication rate was similar in all groups (p=0.682). Procedural characteristics are demonstrated in Table 2. In-hospital mortality was observed in 12 patients (8.3%) and was not different among groups (p=0.791). The mean follow-up period was 19.4±12.4 (up to 53) months and not different among the groups (p=0.582). 37 patients (24.5%) died during follow-up period and all-cause mortality rate was similar among the groups (p=0.901) (Table 2).

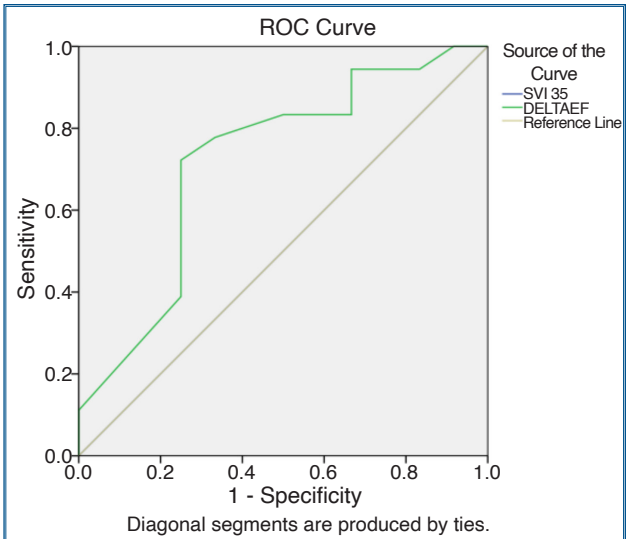

Figure 2. ROC analysis of "Delta LVEF" for mortality in the patients with SVI<35 mL/m². (Cut-off value ≥10%, AUC=0.72) (Sensitivity=50%, Specificity=75%).
AUC: area under curve; LVEF: left ventricular ejection fraction; ROC: receiver operating characteristic; SVI: stroke volume index.

In univariate analysis, baseline hematocrit, blood urea nitrogen (BUN), creatinine levels, baseline LAD, AvPGR, AvMnGR, SVI values and d-LVEF, d-LVDD, d-LVSD and d-LVEF values were all associated with mortality; thus, were entered into the multivariate analyses. In multivariate analysis, SVI (Exp(B):0.039, 95% CI: 0.011-0.013, p<0.001), baseline BUN (Exp(B):1.022, 95% CI: 1.006-1.038, p=0.006), and d-LVEF (Exp(B):0.046, 95% CI: 0.004-0.610, p=0.046) were found to be the independent predictors for mortality following TAVI in patients with AS.

Using ROC curve analysis, we determined that d-LVEF could predict mortality after TAVI in patients with SVI <35 mL/m². A cutoff value of "£10%" for d-LVEF had sensitivity of 50%, specificity of 75% and an AUC of 0.72 (95% CI: 0.66-0.76) in predicting mortality after TAVI in patients with SVI<35 mL/m² (Figure 2).

In Kaplan-Meier analysis of mortality, the percentage of patients free of mortality were similar be-

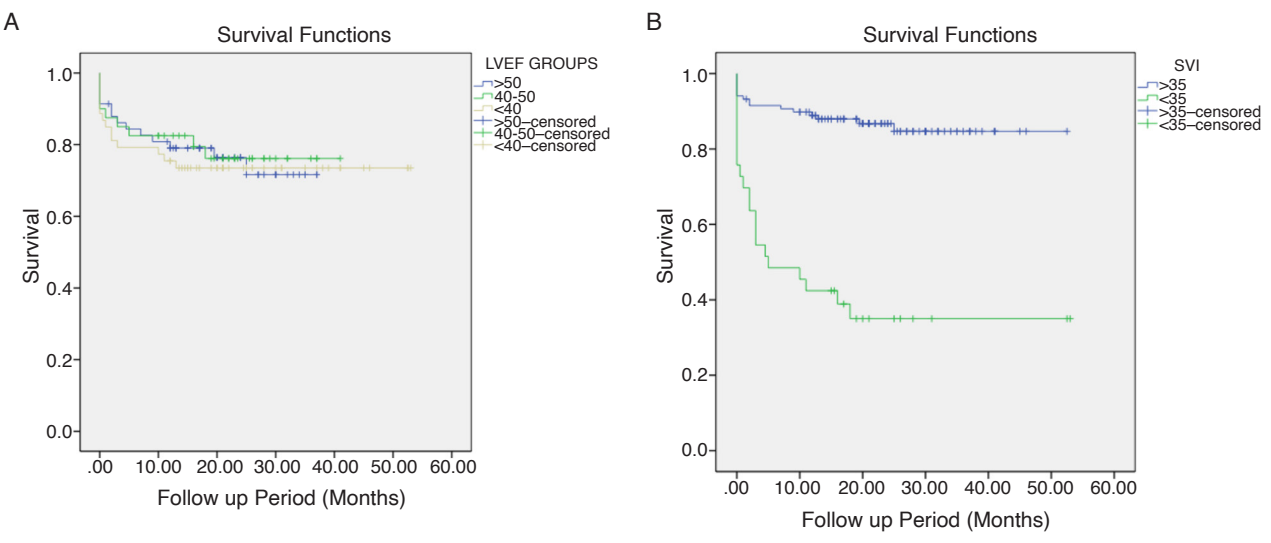

Figure 3. (A) Kaplan-Meier curves of survival for patients who underwent TAVI with a baseline LVEF <40%, 40-49% and ≥50% (p=0.903). **(B)** Kaplan-Meier curves of survival for patients who underwent TAVI with a baseline SVI <35 mL/m² and SVI ≥35 mL/m² (p<0.001).
LVEF: left ventricular ejection fraction; SVI: stroke volume index; TAVI: transvalvular aortic valve implantation.

tween ASrEF, ASmrEF and ASpEF (73.6%, 77.5%, and 75.9%, respectively; log-rank P=0.903). The percentage of patients free of mortality were lower in patients with SVI <35 mL/m^2 compared with patients with SVI ³35 ml/m^2 (36.4 vs 86.4%, respectively; log-rank p<0.001) (Figure 3).

DISCUSSION

LVD is one of the most important risk factors, and is associated with poor survival in patients with AS who referred to TAVI.[2] However, there is no consensus on the prediction of survival in patients with AS and LVD after TAVI. In this study, we showed that the baseline LVEF prior to TAVI did not have significant effect on predicting survival in patients with AS. In addition, improvement of LVEF early after the TAVI has predictive value on survival in patients with AS, and this LVEF improvement is more important in patients with low SVI.

Multiple mechanisms are responsible for the transition from concentric hypertrophy to dilatation and reduced LVEF in patients with severe AS.[9] HF with reduced EF (HFrEF) in patients with AS caused by afterload excess is potentially reversible; depending on the underlying pathophysiology and substantial LV recovery may occur after mechanical interventions.[10] In a previous study, it was shown that ventricular unloading by TAVI appears to benefit prognosis in HF with mid-range EF and HF with preserved EF patients, whereas its effects are less impressive once systolic LV function has significantly failed in HFrEF patients.[11] TVT Registry showed that severe LVD was associated with higher rate of mortality compared with preserved LVEF in TAVI patients at 1 year.[12] However, a recently published study showed that mortality rates at 5 years were similar for ASrEF, ASmrEF, and ASpEF patients without significant differences in procedural efficacy or safety outcomes, and they showed that TAVI improves LV function with reversibility of LV diameters and improvement in retrograde cardiac pressure measurements.[13] These results were compatible with our results. In our study, we evaluated patients in 3 groups; ASmrEF patients were evaluated in a separate group and we did not find any significant difference in mortality rate among these 3 groups (Figure 3A). Our results showed that baseline LVEF did not have significant effect on survival. However, d-LVEF was increased and d-LVSD and d-LVDD were decreased significantly early after the TAVI. These changes were more prominent in ASrEF patients. Changes were limited in ASmrEF and ASpEF patients. These changes reflected marked reverse remodeling of the LV. Depending on the underlying pathophysiology, reduced LVEF can potentially be reversible,[10] and LVEF recovery after TAVI may be important for keeping survival gain in patients with reduced LVEF and AS.[14] At this point, it will be important to determine which ventricle has recovering capacity. Previously, it was reported that various LV remodeling changes have been shown in AS and LV dilatation is frequent and associated with adverse outcomes.[15] In our study, we found that d-LVEF predicted mortality after TAVI in patients with AS.

Patients with severe AS and low EF with low transvalvular gradients are at higher risk for worse outcomes compared with patients with high transvalvular gradients.[16] Recently, flow status quantified using SVI, was introduced as a better surrogate of LV function to identify patients with true severe AS.[13] In patients with preserved LVEF, preprocedural SVI was not associated with prognosis. However, patients with reduced SVI are characterized by worse cardiac conditions such as lower LVEF, lower aortic valve gradient, and myocardial fibrosis.[17] Accordingly, increased short- and long-term mortality after TAVI has also been reported in patients with reduced SVI.[18] In our study, mortality rates were increased in patients with low SVI (<35 mL/m^2) (Figure 3B). We also showed that SVI <35 mL/m^2 was one of the significant predictors of mortality after TAVI in patients with AS. Additionally, we found that a cutoff value of "£10%" for d-LVEF in patients with SVI <35 mL/m^2 had sensitivity of 50% and specificity of 75% in predicting mortality (Figure 2). This means that LV reverse remodeling revealed with increase of LVEF immediately after the TAVI has an impact on survival in patients with AS and low SVI. To the best of our knowledge, prognostic association of LVEF improvement early after TAVI in patients with low SVI has not been reported in the literature before.

In our study, increased levels of BUN independently predicted mortality. In previous studies, it was suggested that impaired kidney functions increased mortality after TAVI.[19] Our result is compatible with previous studies.

Limitations

Our study has several limitations. Most importantly, we used retrospective cohort in our study, prospective-

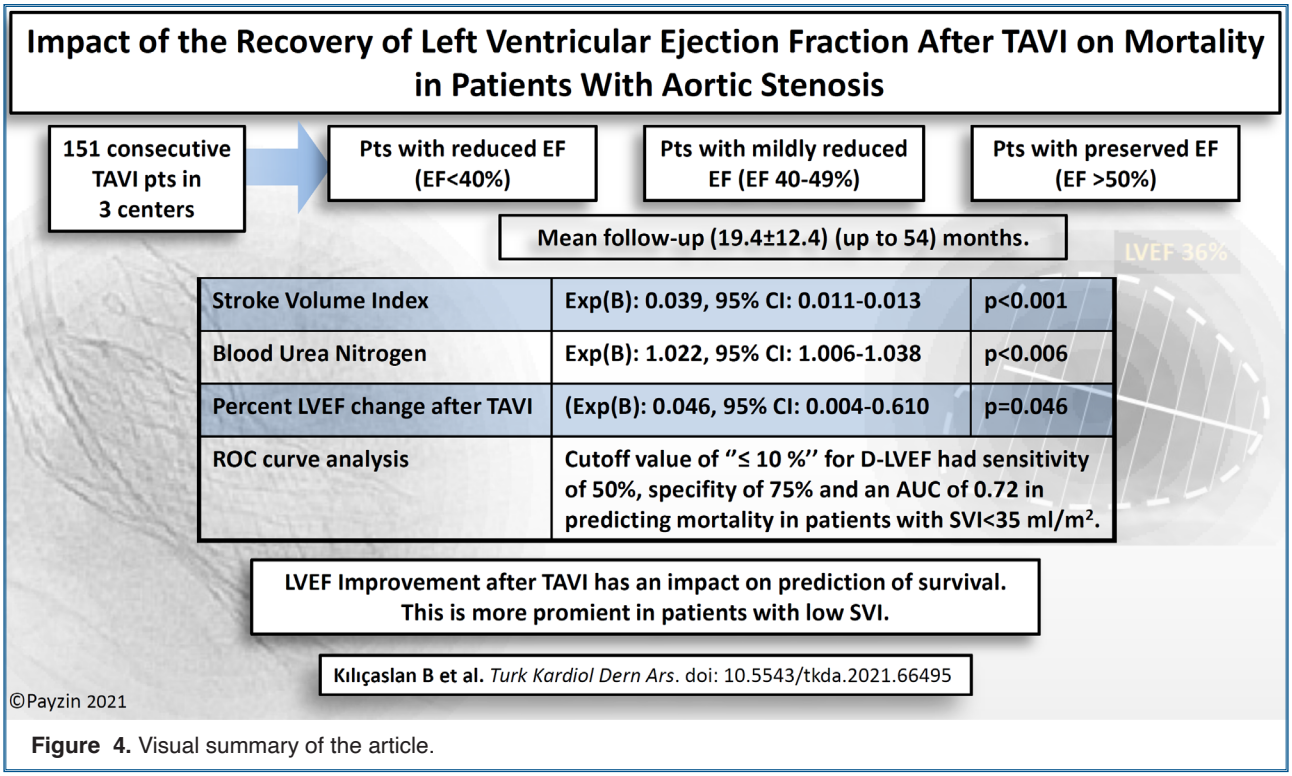

Figure 4. Visual summary of the article.

ly designed studies will be more valuable for predicting survival. Our study population was too small when compared with similar mortality studies. Myocardial function in HF patients may be evaluated with some sophisticated methods such as strain echocardiography and magnetic resonance imaging. Thus, it will be possible to detect more ideal patients for TAVI procedure in HF patients. Another limitation of this study was that echocardiographic measurements were made by different operators without a central core laboratory and also SVI was determined by Doppler echocardiography, which implies angle-dependent errors. Another limitation of the current study was that aortic paravalvular regurgitation after the TAVI was not taken into consideration. Finally, dobutamine stress echocardiography findings for low EF patients were not reported because of the missing data.

Conclusion

TAVI procedure has become one of the main treatment methods for AS patients and HF incidence is increased in this AS era. It is important to define patients' risk profile before TAVI procedure and which patient will need more care after the procedure. This study shows that recovery in LV systolic function immediately after TAVI procedure is more important than baseline LVEF to predict survival in patients with AS. Increase in LVEF more than 10% has an impact on prediction of survival in patients with AS and SVI <35 mL/m^2 who underwent TAVI. It remains to be validated among prospective and multicentric cohorts.

The visual summary of the article can be seen in Figure 4.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Health Science University İzmir Tepecik Training and Research Hospital (Approval Date: January 23, 2020; Approval Number: 2020/1-22).

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Keywords: Aortic stenosis; heart failure; transcatheter aortic valve implantation; stroke volume index; ventricular remodeling

Anahtar Kelimeler: Aort darlığı; kalp yetersizliği; transkatater aort kapak implantasyonu; atım hacim indeksi, ventriküler yeniden şekillenme