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# Myocardial functional changes in transfemoral versus transapical aortic valve replacement



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## ABSTRACT

**Background:** Transcatheter aortic valve replacement (TAVR) has greatly expanded the treatment options available for patients with severe aortic stenosis at high surgical risk.

**Materials and methods:** We compared changes in myocardial function in TAVR with a transfemoral (TF) versus a transapical (TA) approach at a major tertiary hospital from 2012–2016. Traditional echocardiographic measures of cardiac structure and function were tracked, alongside the use of two-dimensional speckle tracking echocardiography to measure myocardial strain and strain rates.

**Results:** For the entire cohort with complete data at all time points ( $n = 42$ ), between the pre-TAVR baseline (mean: 20.1 d) and the post-TAVR 1-mo follow-up (mean: 32.7 d), global longitudinal strain significantly increased (from  $-15.6\%$  to  $-18.2\%$ ,  $P < 0.001$ ). When comparing the TF ( $n = 31$ ) and TA ( $n = 11$ ) groups, TA patients showed persistently impaired apical longitudinal strain at the 1-mo follow-up ( $-15.9\%$  versus  $-22.3\%$ ,  $P < 0.05$ ). In terms of clinical outcomes, both groups ( $n = 131$  for TF,  $n = 53$  for TA) were similar in terms of 30-d mortality, readmission rate, and risk of post-TAVR acute kidney injury. However, TA patients experienced significantly longer length of hospitalization (7.58 versus 3.92 d,  $P = 0.02$ ), intensive care unit hours (105.4 versus 47.1 h,  $P = 0.02$ ), and were at a greater risk of long-term ( $>72$  h) intensive care unit stay (45% versus 25%,  $P = 0.01$ ). **Conclusions:** Patients undergoing TA-TAVR exhibit impaired apical longitudinal strain, although global myocardial function is similar to TF-TAVR otherwise. Myocardial strain measured by two-dimensional speckle tracking echocardiography appears to be a sensitive method to detect subtle cardiac remodeling after TAVR.

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## Introduction

Untreated severe aortic stenosis (AS) is characterized by a mortality of approximately 50% within 2 y of the onset of

symptoms and is the most common reason for hospitalization among all valvular pathologies.<sup>1–3</sup> While surgical aortic valve replacement remains the gold standard for the treatment of AS, encouraging results have been obtained using

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transcatheter aortic valve replacement (TAVR). The Placement of Aortic Transcatheter Valves (PARTNER) trial established that in patients at high surgical risk, TAVR significantly reduces mortality in AS patients and has outcomes superior to surgical aortic valve replacement.<sup>3,4</sup> While a transfemoral (TF) approach is typically used, in patients with limited peripheral vascular access due to factors such as vessel tortuosity, caliber, or atherosclerosis, a transapical (TA) route can be used. Interestingly, TA-TAVR is associated with higher overall periprocedural mortality but lower risk of cardiovascular death. Nonetheless, both TF and TA approaches have comparable mortality rates by 2 y after TAVR.<sup>5,6</sup>

While TAVR has widely been associated with acceptable clinical outcomes, few have examined acute changes in cardiac function with this procedure and reported conflicting results. Schattke et al. found immediate improvements in global left ventricular (LV) function after TAVR.<sup>7</sup> However, a study of 1661 TAVR patients using conventional echocardiographic parameters found no change in left ventricular ejection fraction (LVEF), a parameter that is commonly used to assess postprocedural outcomes in cardiac patients.<sup>8,9</sup> Interestingly, the validity of LVEF in predicting clinical outcomes has been recently challenged and supplanted with parameters obtained from speckle tracking echocardiography (STE). In particular, long-axis shortening of the LV chamber measured as global longitudinal strain (GLS) has garnered attention as a sensitive marker of cardiac performance. In the Phosphodiesterase-5 Inhibition to Improve Clinical Status and Exercise Capacity in Diastolic Heart Failure (RELAX) trial<sup>10</sup> which examined patients with heart failure and preserved ejection fraction, GLS was significantly reduced and associated with biomarkers of wall stress and collagen synthesis as well as diastolic function. Additionally, the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) study demonstrated that abnormal GLS had important prognostic implications in patients with an apparently normal ejection fraction.<sup>11</sup>

In the present study, we hypothesized that STE-derived GLS increases after TAVR before changes in LVEF, and we were interested in comparing differential changes in cardiac wall function between TF-TAVR and TA-TAVR. We utilized traditional echocardiographic methods as well as STE to better characterize the differences in cardiac functional changes after TF-TAVR and TA-TAVR. We further aimed to evaluate the preoperative characteristics and postoperative clinical outcomes of these groups.

## Methods

The institutional Transcatheter Valve Therapy database was used to identify all patients who underwent TAVR at Ronald Reagan UCLA Medical Center from 2012-2016. Patients were selected for TAVR based on criteria set forth by the Centers for Medicare and Medicaid services. Included patients had a Society of Thoracic Surgeons Predicted Risk of Mortality score >7% or had significant frailty or other conditions that raised operative risk. Patients who had

prior transplantation or those with incomplete data or unavailable echocardiograms were excluded. Patients were divided into the TF and TA cohorts based on procedural approach. Echocardiographic studies were evaluated in the preoperative, immediately postoperative, and short and/or intermediate follow-up time points. Parameters relevant to myocardial function included LVEF, left ventricular internal diameter (LVID), and parameters relating to ventricular mass regression: interventricular septal thickness at end-diastole (IVSd) and posterior wall thickness at end-diastole (PWd). Additionally, LV segmental longitudinal strains were measured using specialized 2D speckle tracking software (Philips QLAB v10.4, Philips Ultrasound, Bothell, WA). GLS was calculated as an average of longitudinal strains measured in the American Heart Association 17-segment model of the heart as assessed in the apical 2-chamber, 3-chamber and 4-chamber views. Clinical data were collected retrospectively from the institutional electronic health record. Statistical analysis was performed using Chi-square analysis of proportions, paired t-test and two-way repeated measures analysis of variance. Tabled results are presented in the format of patient count followed by percentage of total group size in parentheses or mean followed by 95% confidence interval in parentheses. This study was approved by the Institutional Review Board at the University of California, Los Angeles, and due to the retrospective nature of the study, an approved waiver of informed consent was also obtained.

## Results

A total of 216 patients were identified as having received TAVR during the study period. After application of exclusion criteria, 184 remained: 131 in TF and 53 in the TA groups. Clinical characteristics of the groups are shown in Table 1. Compared to TF, TA patients had a higher incidence of peripheral vascular disease (32% versus 7%,  $P < 0.001$ ). Despite this difference, both cohorts had similar surgical risk as predicted by the Society of Thoracic Surgeons Predicted Risk of Mortality (Table 1).

Various traditional echocardiographic parameters as well as myocardial strain via two-dimensional speckle tracking echocardiography (2D-STE) were recorded at three phases of the study: preoperative ( $20.1 \pm 6.2$  d), immediate postoperative ( $2.5 \pm 3.4$  d), and at a short and/or intermediate follow-up ( $32.7 \pm 11.3$  d) (Table 2). Comparing pre-TAVR and short and/or intermediate follow-up in patients with complete imaging at all three time points ( $n = 42$ , TF = 31, TA = 11): (i) there were no significant changes in LVEF, LVID, IVSd, or PWd ( $P > 0.05$ ); (ii) longitudinal strain significantly increased in magnitude for the anterior ( $-15.5\%$  to  $18.3\%$ ,  $P < 0.0001$ ), lateral ( $-14.0\%$  to  $-17.1\%$ ,  $P < 0.0001$ ), inferior ( $-14.9\%$  to  $-18.1\%$ ,  $P < 0.0003$ ), and septal segments ( $-14.2\%$  to  $-16.9\%$ ,  $P < 0.0002$ ); and (iii) GLS significantly increased over time ( $-15.6$  to  $-18.2\%$ ,  $P < 0.001$ ).

The TF and TA groups were similar with regards to postoperative LVEF, LVID, IVSd, PWd, GLS, and anterior, lateral, inferior, and septal segmental longitudinal strains ( $P > 0.05$ ) (Fig). However, there was a significantly worse longitudinal

**Table 1 – Demographic and comorbidity characteristics of patients undergoing TAVR.**

Characteristic	Transfemoral	Transapical	P value
Total	131	53	
Female	68 (52)	23 (43)	NS
Race			NS
Asian	7 (5)	5 (9)	
Black	8 (6)	1 (2)	
Caucasian	105 (80)	44 (83)	
Hispanic	10 (8)	2 (4)	
Age	84.0 (78.6-89.2)	87.6 (80.1-89.2)	NS
Creatinine	1.10 (0.9-1.5)	1.20 (0.9-1.5)	NS
Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) Score	6.0 (4.2-8.8)	7.1 (5.0-9.8)	NS
LVEF	60.0 (40.0-65.0)	60.0 (50.0-65.0)	NS
New York Heart Association (NYHA) class			NS
II	45 (34)	19 (36)	
III	61 (47)	23 (43)	
IV	24 (18)	11 (21)	
Atrial fibrillation	43 (33)	22 (42)	NS
Stroke	24 (18)	12 (23)	NS
Myocardial infarction	44 (34)	23 (43)	NS
Previous cardiac surgery	35 (27)	18 (34)	NS
Peripheral vascular disease	10 (7)	17 (32)	<0.001
Smoker/past-smoker	6 (5)	1 (2)	NS
Chronic lung disease	42 (32)	19 (36)	NS
Hypertension	102 (78)	45 (85)	NS
Diabetes	41 (31)	16 (30)	NS
Dialysis/renal failure	5 (4)	2 (4)	NS

NS = Not significant.

strain at the LV apex in the TA group versus the TF group at the 1-mo follow-up ( $-22.3 \pm 7.63\%$  versus  $-15.9 \pm 7.47\%$  for TF versus TA respectively,  $P < 0.05$ ).

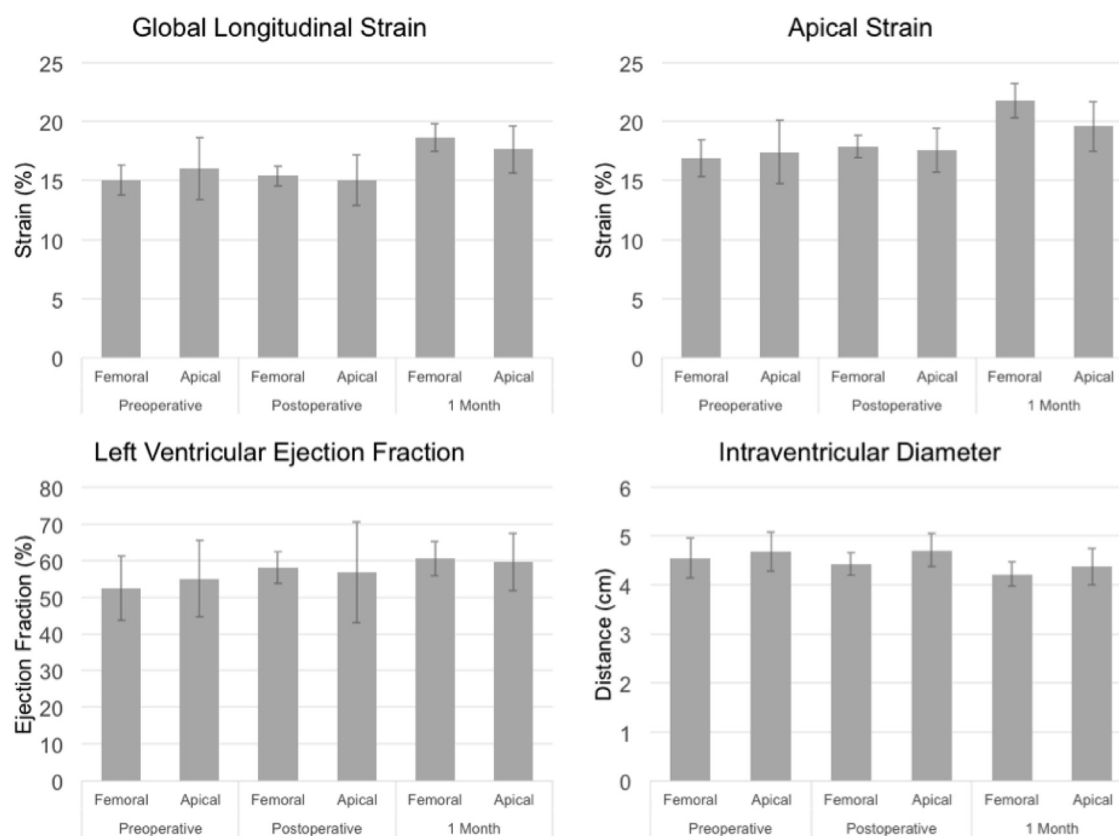
There were a number of significant differences in clinical outcomes between the TF versus TA groups as shown in Table 3. Both groups had similar 30-d mortality, readmission

rate, and risk of post-TAVR acute kidney injury. However, TA patients experienced significantly longer length of hospitalization (7.58 versus 3.92 d,  $P = 0.02$ ), more intensive care unit (ICU) hours (105.4 versus 47.1 h,  $P = 0.02$ ), and were at a greater risk of prolonged (>72 h) ICU stay (44% versus 25%,  $P = 0.01$ ).

**Table 2 – Echocardiographic and 2D-STE outcomes between patients undergoing TF-TAVR versus TA-TAVR.**

Parameter	Pre-TAVR		Postoperative		1-mo		P value	
	TF	TA	TF	TA	TF	TA	Postoperative	TF versus TA
LVEF	51.3	54.9	58.3	55.6	60.5	59.5	NS	NS
GLS	-15.1	-16.0	-15.4	-15.0	-18.7	-17.6	<0.001	NS
Anterior	-15.4	-15.6	-16.3	-16.3	-19.4	-17.1	<0.0001	NS
Lateral	-13.8	-14.2	-14.6	-14.6	-17.3	-16.9	<0.0001	NS
Inferior	-15.0	-14.8	-15.1	-14.7	-18.7	-17.5	<0.0003	NS
Septal	-13.3	-15.1	-14.7	-16.1	-17.2	-16.5	<0.002	NS
Apex	-17.4	-15.6	-18.0	-17.5	-22.3	-15.9	<0.0001 (TF) 0.06 (TA)	<0.05
LVID	4.47	4.64	4.40	4.68	4.22	4.36	NS	NS
IVSd	1.31	1.27	1.22	1.23	1.21	1.15	NS	NS
PWd	1.31	1.27	1.22	1.23	1.21	1.15	NS	NS

NS = Not significant.



**Fig – Postoperative changes in strain, ejection fraction, and ventricular diameter after TAVR.**

## Discussion

GLS obtained from STE is becoming increasingly validated in the literature as a valuable prognostic marker of adverse clinical events. Compared to strain imaging by tissue Doppler echocardiography, STE has been found to have better reproducibility and sensitivity.<sup>12-14</sup> In the case of AS, GLS has been found to have prognostic value as a predictor of all-cause and cardiovascular mortality.<sup>15-17</sup> Additionally, worsening of GLS has been associated with adverse clinical outcomes in a wide variety of settings including diabetic heart disease,<sup>18</sup> congestive heart failure,<sup>19</sup> and chronic kidney disease.<sup>20</sup> Furthermore, GLS has been found to be a more sensitive indicator of early stage hypertrophic cardiomyopathy compared to LVEF.<sup>13</sup> Moreover, in a meta-analysis of 5721 patients with underlying cardiac diseases including heart failure, myocardial infarction, and valvular heart disease, GLS was a stronger predictor of all-cause mortality compared to LVEF.<sup>21</sup> However, literature utilizing GLS to grade functional recovery following percutaneous cardiac interventions such as TAVR remains limited.<sup>22</sup> Moreover, research utilizing STE specifically to compare TF-TAVR to TA-TAVR approaches has been sparse and produced mixed results thus far. In a study of 26 TAVR patients, Bochenek *et al.* found that in contrast to the TF approach, TA patients showed no significant improvement in peak systolic longitudinal strain at a 1-y follow-up.<sup>23</sup> Yet, Ando *et al.* reported no significant differences in the immediate post-TAVR GLS between TF and TA groups using transesophageal

echocardiograms.<sup>24</sup> In the present study, we found that TA-TAVR and TF-TAVR patients had similar increases in GLS, readmissions risk, and cardiovascular mortality. However, TA-TAVR was associated with worsening apical longitudinal strain (ALS), as well as longer ICU and hospital stays when compared to TF-TAVR.

Several of our echocardiographic findings deserve further discussion. Given the need to introduce a large-bore cannula into the apex of the heart with large concentric purse strings for TA access with possible associated myocardial injury, our group was interested in examining regional and global myocardial function after TA-TAVR. Despite differing risk profiles, we found post-TAVR GLS to be similar between the TF and TA groups at the 1-mo follow-up. However, we found significantly reduced ALS in the TA group, which persisted at the 1-mo follow-up. Similarly, Meyer *et al.* found unique impairment in ALS using cardiac magnetic resonance feature tracking in TA patients at a 3-mo follow-up.<sup>25</sup>

This lack of functional recovery in the LV apex of TA patients may be due to the greater degree of myocardial injury experienced by TA patients, likely related to the surgical approach. All major TAVR approaches have been documented to yield finite amounts of myocardial injury, evidenced by elevations in markers of myocardial necrosis such as cardiac troponin I and creatine kinase-MB.<sup>26-29</sup> However, myocardial necrosis markers following TA-TAVR have been found to be significantly higher when compared to both TF and trans-aortic approaches.<sup>26,29</sup> This may be attributable to the large pledgeted pursestring sutures that are currently placed at the

**Table 3 – Clinical outcomes among patients undergoing TAVR approach.**

Outcome	Transfemoral	Transapical	P value
<b>Primary clinical outcomes</b>			
Length of stay	7.58	3.92	<0.05
Readmission	23 (17.6)	11 (20.8)	NS
<b>Mortality</b>			
Index admission	1 (0.8)	0	NS
< 30-d discharge	3 (2.3)	0	NS
ICU hours	47.1	105.4	<0.05
Prolonged ICU stay (>72 h)	24 (45.2)	33 (25.1)	<0.05
<b>Postoperative complications</b>			
<b>Major adverse event</b>			
Atrial fibrillation	11 (8.4)	7 (13.2)	NS
Cardiac arrest	4 (3.1)	0	NS
Coronary obstruction	1 (0.8)	0	NS
Device-related embolism	1 (0.8)	0	NS
<b>Hemorrhage</b>			
Access site bleed	6 (4.6)	0	NS
Access site hematoma	2 (1.5)	1 (1.9)	NS
Gastrointestinal	0	2 (3.8)	NS
Genitourinary	0	1 (1.9)	NS
Other	5 (3.8)	2 (3.8)	NS
Ischemic stroke	2 (1.5)	1 (1.9)	NS
Transient ischemic attack	1 (0.8)	0	NS
Vascular compromise	2 (1.5)	1 (1.9)	NS
Myocardial infarction	1 (0.8)	0	NS
Acute kidney injury	24 (18.3)	15 (28.3%)	NS
Renal failure and dialysis	3 (2.3)	1 (1.9)	NS
Perforation	1 (0.8)	0	NS
<b>Unplanned surgical procedures</b>			
Percutaneous coronary intervention	1 (0.8)	0	NS
Vascular surgery	2 (1.5)	1 (1.9)	NS
Pacemaker implantation	19 (14.5)	8 (15.1)	NS

NS = Not significant.

apex of the left ventricle to reapproximate the myocardium at the site of direct cannulation. In other studies, higher levels of myocardial necrosis markers and TA-TAVR are both independently associated with greater risk of acute kidney injury,<sup>30-32</sup> less improvement in LVEF,<sup>24</sup> and higher in-hospital, 30-d, and 1-y overall mortality.<sup>26,30-32</sup> It has also been hypothesized that TA-TAVR may be associated with an elevated risk of cholesterol embolization to the renal vascular bed, and thus potentially may be an additional risk factor for acute kidney injury.<sup>32,33</sup> It should also be noted that even when levels of baseline comorbidities between TF and TA groups are controlled for using propensity matching statistical methods, TA-TAVR is still independently associated with higher risk of acute kidney injury.<sup>34-36</sup> The association between the TA approach and acute kidney injury may be critical in explaining why TA-TAVR has a significantly higher mortality rate and length of stay compared to TF in the early postprocedural period (0-6 mo) but has comparable mortality at the 2-y follow-up time point.

In congruence with previous work, we also found the myocardial strains measured by STE were more sensitive in assessing post-TAVR functional LV recovery for the entire cohort when compared to traditional echocardiographic parameters such as LVEF. Customary measures of cardiac remodeling and function such as LVEF, LVID, IVSd, and PWd did not significantly change by the 1-mo follow-up, whereas longitudinal strains and GLS measured by 2D-STE did. Thus, using markers of subclinical cardiac function such as GLS could have utility in early detection of postoperative functional changes in patients with AS and perhaps other conditions.

The present study has several limitations including those inherent to its retrospective nature. The limited number of patients in the study may impact the statistical significance of our findings. Nonetheless, this is one of the largest series examining the evolution of STE and clinical parameters post-TAVR. We did not report long-term changes in such parameters due to the paucity of available echocardiographic data, an area that deserves further investigation.

## Conclusion

Patients who underwent a TF approach showed significantly greater increases in post-TAVR LV ALS, although global myocardial functional recovery did not significantly differ between TF and TA groups. TA-TAVR may be offered to patients without concern for reduction in global myocardial function. Additionally, it appears that myocardial strain measured by 2D-STE is more sensitive than traditional measures in detecting subtle cardiac remodeling after TAVR. Further investigation to ascertain long-term clinical outcomes and changes in GLS is warranted and may provide insights into late cardiac events in this population.

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## Disclosure

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this manuscript.

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