Am J Cardiovasc Dis 2021;11(2):203-211
www.AJCD.us /ISSN:2160-200X/AJCD0132724

Original Article

Improvements in global longitudinal strain after transcatheter aortic valve replacement according to race

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Received March 2, 2021; Accepted April 12, 2021; Epub April 15, 2021; Published April 30, 2021

Abstract: Objective: In the United States, racial minorities are underrepresented among patients receiving transcatheter aortic valve replacement (TAVR) and data regarding their outcomes is limited. Global longitudinal strain (GLS) is a measure left ventricular function and has independently predicted outcomes after TAVR. The aim of this study is to assess changes in GLS after TAVR according to race and factors predicting these changes. Methods: Electronic medical records of patients undergoing TAVR at the University of Illinois, Chicago and Jesse Brown Veteran's Administration Medical Center (Chicago, Illinois) from January 2017-February 2020 were reviewed retrospectively. The most recent transthoracic echocardiogram (TTE) prior to TAVR and the TTE 1-month post-procedure were used to determine GLS. Patients were included if both a pre- and post-procedure study were present and TTE images were of sufficient quality to process strain imaging. Results: A total of 103 patients (average age 76 ± 12 years, 80% male, 42% white) were included. At 1-month post-TAVR, GLS improved for all races: white (-2.7 ± 3.5%, P<0.001), African-American (-2.8 ± 3.3%, P<0.001), and Hispanic (-2.0 ± 2.1%, P<0.001). There were no differences in the degree of improvement among races (P=0.62). Baseline GLS was negatively correlated with changes in GLS overall (r=-0.44, P<0.001). Baseline aortic valve area (cm^2) was positively correlated with changes in GLS (r=0.2, P=0.036). Conclusions: This study demonstrated that GLS improved after TAVR independent of race with similar degrees of change across races. Baseline GLS and aortic valve area predicted strain improvement after TAVR, which suggests that those with more impaired LV function may benefit most from the procedure.

Keywords: Aortic valve stenosis, transcatheter aortic valve replacement, global longitudinal strain

Introduction

Speckle-tracking derived global longitudinal strain (GLS) is a novel parameter that has shown increasing utility in the evaluation of left ventricular (LV) function [1]. In contrast to left ventricular ejection fraction (EF) measured via two-dimensional (2D) echocardiography, GLS is able to quantify minute changes in myocardial deformation that may provide greater prognostic value in various pathologies [2, 3]. Specifically, baseline GLS independently predicts all-cause mortality in patients with aortic stenosis (AS) and in those who receive transcatheter aortic valve replacement (TAVR) for severe symptomatic AS, regardless of the approach [4-6]. In fact, pre-TAVR GLS provides greater sensitivity than traditional EF in predicting LV systolic function and myocardial recovery after aortic valve implantation [7, 8]. These relationships are particularly important, as TAVR has become one of the two therapeutic options for aortic valve replacement in patients with symptomatic AS from low to high risk for surgical aortic valve replacement, and the primary modality for the treatment of inoperable patients [9, 10]. AS is a common native valvular pathology and with TAVR being extended to lower surgical-risk populations with severe AS, adequately characterizing myocardial function before and after TAVR is of paramount importance [11, 12].

Despite TAVR's widespread application and increasing availability to those who meet criteria for intervention, significant barriers to access continue to exist for minority populations. From 2011 to 2016, African Americans were almost 10% less likely to receive TAVR for symptomatic severe AS in comparison to Whites [13]. Other registries have demonstrated discrepancies in access far greater, with African American, Hispanic, and Asian/Native American/Pacific Islanders comprising less than 10% of all TAVR cases [14]. To our knowledge, studies thus far analyzing GLS have included predominantly white populations and frequently do not depict racial breakdowns in their analyses. Given the increasing utility of using GLS to characterize LV function and the perceived limited benefit of TAVR in minorities, determining race-based improvements in GLS would add to the growing body of evidence that non-white patients benefit from TAVR. The purpose of this investigation is to compare changes in GLS after TAVR according to race.

Methods

Study population

All adult patients >18 years of age from the University of Illinois at Chicago and Jesse Brown Veteran's Administration Medical Center (JBVA, Chicago, Illinois) who underwent TAVR between February 2018 and July 2020 for severe AS were considered eligible for inclusion in the study. TAVRs were performed by the same operator for patients from either institution. Initial AS severity was determined by conventional 2D transthoracic echocardiography according to current guidelines, and TAVR candidacy was ultimately determined after a comprehensive evaluation by the institutional heart team. Exclusion criteria were met if patients lacked either a pre-procedure or post-procedure TTE. Additionally, patients were further excluded if their TTE was generally uninterpretable or not amenable to longitudinal strain measurements. Patients were categorized by race through self-reported data as White, African American, or Hispanic. Clinical and demographic data were obtained through retrospective chart review. IRB approval was obtained prior to initiation of data collection.

TTE analysis

Retrospective image analysis of transthoracic echocardiogram data was performed. For each TTE pre- and post-procedure, traditional echocardiographic indices of AS were measured, including the mean transvalvular gradient (mmHg) and peak transvalvular velocity (m/s). Aortic valve area (AVA, cm^2) was reported using the continuity equation via left ventricular outflow tract velocity time integral (LVOT VTI, cm) and the aortic valve velocity time integral (AV VTI, cm) measurements. The TTE obtained 30 days post procedure was used for analysis when available; otherwise, the earliest TTE after intervention was analyzed. Studies were performed either at UIC or JBVA by trained sonographers using a commercially available echocardiography system and analyzed by the same trained reader to allow for consistency among interpretations. A standardized imaging protocol that included detailed assessments of valvular and ventricular function was employed according to the American Society of Echocardiography guidelines [15].

Strain analysis

GLS and changes in GLS represented the primary outcomes of interest for this study. GLS was analyzed for each pre- and post-TAVR study using a commercially available software (Syngo Ultrasound Workplace, Siemens Medical Solutions, Mountain View, California USA). Strain values were obtained by tracing the left ventricular endocardial contour in the apical 2- and 4-chamber view of the left ventricle. An output strain value was generated by the software after analyzing 6 segments of myocardium in each view. Studies with at least 4 out of 6 segments needed adequate tracking to be considered viable. Three measurements were performed for each window with the resulting average retained so as to minimize variation secondary to software analysis. An average of both window values was utilized as the GLS. GLS itself is a negative value with less negative values corresponding to greater impairment in LV contractility. EF and changes in EF represented outcomes of interest as well. EF as calculated by the strain software was similarly recorded for each apical-4 and apical-2 cham-

Table 1. Baseline clinical and demographic characteristics stratified by race

	African American (n=34)	Hispanic (n=22)	White (n=43)	Total (n=103)	*p*-value
Age, years	75.5 ± 17.1	76.4 ± 10.2	76.2 ± 8.9	76 ± 12	0.96
Male	26 (76.5)	20 (90.9)	35 (81.4)	82 (79.6)	0.39
Smoking					
Former	13 (38.2)	8 (36.4)	22 (51.2)	44 (42.7)	0.39
Current	4 (11.8)	1 (4.6)	4 (9.3)	9 (8.7)	0.65
Coronary Artery Disease	16 (47.1)	16 (72.7)	28 (65.1)	60 (58.3)	0.11
Atrial Fibrillation	5 (14.7)	3 (13.6)	15 (34.9)	24 (23.3)	0.06
Chronic Obstructive Pulmonary Disease	8 (23.5)	2 (25.0)	11 (25.7)	22 (21.4)	0.28
Chronic Kidney Disease	16 (47.1)	4 (18.2)	8 (18.6)	29 (28.2)	0.01
Diabetes	13 (38.2)	8 (36.4)	12 (43.8)	35 (34.0)	0.60
Hyperlipidemia	22 (64.71)	13 (59.1)	28 (65.1)	66 (64.1)	0.88
Hypertension	28 (82.4)	15 (68.2)	37 (86.1)	84 (81.6)	0.22
Hypothyroidism	3 (8.8)	1 (4.6)	8 (18.6)	12 (11.7)	0.20

Continuous variables are represented as a mean ± SD; categorical variables are represented as n (%).

ber view. These values were averaged to yield an EF for each study analyzed.

Statistics

Categorical variables were presented as numbers (%) and compared using Pearson's Chi-squared analysis. Continuous data were reported using mean ± SD with independent samples' t-test or ANOVA used to test for significance when appropriate. Patient demographics and baseline clinical data were described using frequency tables and compared via univariate analysis. Echocardiographic parameters and GLS were compared via univariate analysis as well. Pearson's correlation coefficient was used to test the relationship between continuous variables as a component of a linear model. A *p*-value <0.05 was considered statistically significant. Analyses were performed using IBM SPSS Statistics for Windows, Version 26 (Armonk, NY: IBM Corp).

Results

Population characteristics

103 patients met the final inclusion criteria of having an adequate pre- and post-procedure TTE amenable to strain analysis within the prespecified team period. The average time to TAVR from pre-procedural TTE was 107.6 ± 104.1 days and the average time to the first out-of-hospital post-procedural TTE after TAVR was 35.1 ± 44.8 days. The study population was predominantly male (80%) with an average age of 76 ± 12 years. The male predilection was largely driven by the veteran component of the cohort. Baseline demographic and clinical characteristics of the overall cohort are shown in **Table 1**. White Americans comprised 42%, African Americans 33%, Hispanics 21%, and other 4% of the group. The age at time of TAVR was similar among races (76.2 ± 8.9 White, 76.4 ± 10.2 Hispanic, 75.5 ± 17.1 African American years, P=0.96) with a disproportionate male representation (81% White, 91% Hispanic, 77% African American, P=0.39). No significant differences in baseline comorbidities existed with respect to race with the exception that atrial fibrillation was more prevalent in Whites (35% White, 14% Hispanic, 15% African American, P=0.06) and chronic kidney disease that was more prevalent in African Americans (19% White, 18% Hispanic, 47% African American, P=0.01) (**Table 1**).

Changes in TTE parameters

Baseline echocardiographic parameters according to race are shown in **Table 2**. Aortic Valve V_{max} (cm/s) was similar at baseline among the three groups (369.5 ± 72.0 cm/s White, 351.01.2 ± 62.8 cm/s Hispanic, and 383.2 ± 66.7 cm/s African American, P=0.23). Mean aortic valve area was lower in Whites (1.0 ± 0.3 cm^2) compared to African Americans (1.2 ± 0.5 cm^2) and Hispanics (1.2 ± 0.5 cm^2), but this did

Table 2. Baseline 2D TTE parameters stratified by race

	African American (n=34)	Hispanic (n=22)	White (n=43)	*p*-value
Interventricular Septal Wall Thickness, End-Diastole (cm)	1.4 ± 0.2	1.3 ± 0.3	1.2 ± 0.2	0.17
LV Internal Dimension, End-Diastole (cm)	4.7 ± 1.0	4.6 ± 0.5	4.7 ± 0.7	0.81
LV Posterior Wall Thickness, End-Diastole (cm)	1.3 ± 0.2	1.3 ± 0.2	1.2 ± 0.2	0.16
Aortic Valve Area (cm^2)	1.2 ± 0.5	1.2 ± 0.5	1.0 ± 0.3	0.06
Aortic Transvalvular V_{max} (cm/s)	383.2 ± 66.7	351.0 ± 62.8	369.5 ± 72.0	0.23
AV Mean Pressure Gradient (mmHg)	34.6 ± 12.4	29.2 ± 9.5	32.7 ± 13.2	0.27
Ejection Fraction, %	38.9 ± 12.1	35.3 ± 11.6	40.8 ± 9.3	0.16
Global Longitudinal Strain, %	-11.2 ± 4.1	-11.0 ± 4.0	-11.4 ± 3.5	0.94

2D: two-dimensional; TTE: transthoracic echocardiogram; LV: left ventricular; AV: aortic valve. Continuous variables are represented as a mean ± SD.

Table 3. Net improvements in EF and GLS after TAVR stratified by race

	African American	*p*-value	Hispanic	*p*-value	White	*p*-value
ΔEF, %	5.8 ± 8.4	<0.001	5.4 ± 6.8	0.001	3.5 ± 8.1	0.007
ΔGLS, %	-2.8 ± 3.3	<0.001	-2.0 ± 2.1	<0.001	-2.7 ± 3.5	<0.001

EF: ejection fraction; GLS: global longitudinal strain; TAVR: transcatheter aortic valve replacement. Continuous variables are represented as a mean ± *SD*.

not reach statistical significance (P=0.06). No significant differences in aortic valve mean pressure gradient or 2D echocardiographic parameters were found across races. EF as determined by the average value of the 4-chamber and 2-chamber EF calculations was reduced and similar among races, although numerically lowest for the Hispanic group (40.8 ± 9.3% White, 35.3 ± 11.6% Hispanic, 38.9 ± 12.1% African Americans, P=0.16).

Changes in GLS

GLS was similar among races at baseline and reduced (-11.4 ± 3.5% White, -11.0 ± 4.0% Hispanic, -11.2 ± 4.1% African Americans, P=0.94). GLS improved after TAVR for each race as compared to pre-TAVR values (-2.7 ± 3.5% White, P<0.001; -2.0 ± 2.1% Hispanic, P<0.001; -2.8 ± 3.3% African American, P<0.001) (**Table 3**). EF as measured by the strain software similarly improved for each race compared to pre-TAVR values (White 3.5 ± 8.1%, P=0.007; Hispanic 5.4 ± 6.8%, P=0.001; African American 5.8 ± 8.4%, P<0.001). No significant differences were noted in the degree of GLS improvement after TAVR across the three races (P=0.62), in EF as determined by the strain software (P=0.44), or 2D TTE parameters (**Table 4**).

Baseline GLS was inversely correlated with improvements in GLS. Specifically, greater severity in GLS values was correlated with larger net changes in GLS (r=-0.43, P<0.001) (**Figure 1**). Baseline aortic valve area (cm^2) was also correlated with improvements in GLS (r=0.2, P=0.036) with smaller baseline aortic valve areas correlating with larger improvements. This relationship was driven primarily by patients who were non-white (r=0.3, P=0.021) as compared to those who were white (r=0.07, P=0.68).

Discussion

Our results demonstrate that LV function improved after TAVR as defined by GLS and EF for severe AS at 1-month follow-up for the overall study population and by race. Each race showed improvement in strain parameters as compared to baseline, and no significant differences were demonstrated in the degree of strain improvement across races. Our results also showed that greater severity in baseline GLS correlated with larger improvements in strain after TAVR. This relationship was also true for baseline aortic valve area, with smaller areas correlating to larger strain improvements. Our cohort represented a unique subset of TAVR patients, as it comprised a relatively uniform distribution of different races that were all derived from a single operator database. To our knowledge, no studies have explicitly compared changes in strain parameters according to race.

Improvements in GLS overall after TAVR as demonstrated here have been described previ-

Table 4. Comparisons in net changes in 2D TTE and GLS values among races after TAVR

	African American (n=34)	Hispanic (n=22)	White (n=43)	*p*-value
Interventricular Septal Wall Thickness, End-Diastole (cm)	-0.1 ± 0.2	-0.1 ± 0.2	-0.03 ± 0.2	0.57
LV Internal Dimension, End-Diastole (cm)	-0.03 ± 0.4	0.1 ± 0.5	0.05 ± 0.35	0.54
LV Posterior Wall Thickness, End-Diastole (cm)	.002 ± .02	-0.1 ± 0.2	0.01 ± 0.16	0.01
LV Outflow Tract Velocity Time Integral (cm)	-1.6 ± 8.7	-2.4 ± 8.1	-0.4 ± 7.4	0.63
LV Outflow Tract Velocity Max (cm/s)	15.0 ± 50.2	7.0 ± 40.5	13.9 ± 31.5	0.75
AV Velocity Time Integral (cm)	-44.1 ± 16.8	-40.5 ± 24.7	-43.1 ± 20.5	0.81
Aortic Valve Area (cm^2)	1.1 ± 1.0	1.0 ± 0.9	1.2 ± 0.6	0.77
AV Transvalvular V_{max} (cm/s)	-170.9 ± 61.4	-139.4 ± 76.8	-176.3 ± 75.0	0.13
AV Mean Pressure Gradient (mmHg)	-23.9 ± 11.3	-18.7 ± 10.6	-23.9 ± 12.3	0.19
EF, %	5.6 ± 8.6	5.4 ± 6.8	3.4 ± 8.2	0.44
GLS, %	-2.8 ± 3.3	-2.0 ± 2.1	-2.7 ± 3.5	0.62

2D: two-dimensional; TTE: transthoracic echocardiogram; EF: ejection fraction; GLS: global longitudinal strain; TAVR: transcatheter aortic valve replacement; LV: left ventricular; AV: aortic valve. Continuous variables are represented as a mean ± SD; categorical variables are represented as n (%).

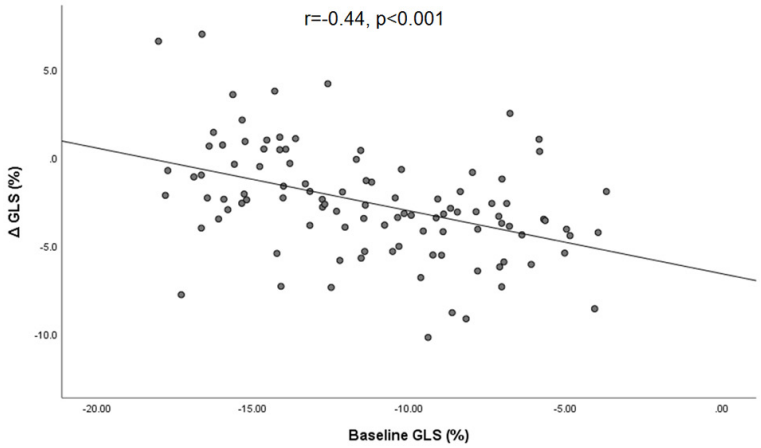

Figure 1. Net changes in GLS 1-month post-TAVR vs. baseline GLS. GLS: global longitudinal strain; TAVR: transcatheter aortic valve replacement.

ously for all-comers. Giannini et al., for example, showed that strain improved after TAVR at the level of the septal and lateral myocardial walls as early as 72 hours after intervention [16]. These improvements appeared to persist beyond this time period, as Corrigan et al. showed that the reversal of GLS impairments after TAVR were present at 1-year follow-up and were further predicted by baseline mean aortic valve pressure gradients [17]. Kamperidis et al. showed that GLS improved after TAVR for those with low-flow, low-gradient phenotypes of AS regardless of EF with LV functional recovery and mass reduction most prominent 6 months after procedure [18]. However, these improvements were not stratified by race and the composition of these studies were overwhelmingly white, giving little insight into the improvements in GLS realized by minority populations.

Concomitant increases in EF alongside strain have also been demonstrated. Corrigan et al. noted a 3% increase at LVEF after TAVR with changes driven predominantly by those with reduced EF [17]. Logstrup et al. noted improvements in EF in addition to longitudinal systolic deformation after TAVR independent of access approach and also showed that those with greatest strain and EF improvements had overall lower mortality [19]. In another study, Gegenava et al. similarly noted improvements in both EF and GLS at 3, 6, and 12 months that were driven in part by decreasing levels of thoracic aortic calcification [8].

Etiologies for the improvement in strain and EF after TAVR are likely based on improved ventricular hemodynamics from reductions in afterload after valve implantation [8]. In severe AS, left ventricular contraction against persistently elevated pressures overtime leads to increased left ventricular wall stress that results in remodeling in the deleterious forms of concentric hypertrophy and myocardial fibrosis [20-22]. In certain cases, LV adaptation to minimize this heightened wall stress eventually becomes

overrun by this chronically elevated afterload and varying degrees of systolic and diastolic dysfunction occur [23]. Even when overt systolic dysfunction is absent, subtle changes as detected by strain analysis can suggest LV impairment [22]. After valve replacement, this afterload pressure is drastically reduced [24]. As a result, wall stress is diminished and overtime this results in the regression of noted hypertrophy and improvement in contractility as well [25]. For example, Logstrup et al. noted regression of LV hypertrophy at 1-year follow-up [19]. Biederman et al. noted decreases in both LV mass index and improvements in circumferential strain via cardiac magnetic resonance imaging (CMR) soon after aortic valve replacement [25].

Our study additionally demonstrated that greater baseline GLS severity and smaller aortic valve areas correlated with larger strain improvements after TAVR. Al-Rashid et al. demonstrated that baseline global radial strain and global circumferential strain predicted improvements in GLS [26]. Schueler et al. was able to similarly show that improvements in 3-dimensional functional strain were driven by baseline depression in LV function and suggested that those with greater LV impairment stood to benefit most from TAVR from a hemodynamic perspective [27]. This was supported by corresponding decreasing levels of NT-proBNP 6 months after procedure and clinical improvement in patients with those characteristics. Gotzmann et al. noted that improvements in LV function by traditional 2D EF measurements after TAVR were also only demonstrated in those with lower EF pre-TAVR [24]. Explanations for these phenomena are also likely due to the relief of chronic increased afterload. In those with severely reduced function or smaller valve area, it is reasonable to infer that this effect is most pronounced. All of this suggests that those with greater LV impairment at baseline may still stand to benefit from TAVR [4].

Although GLS improved after TAVR for each race independently, there were no significant differences in the degrees of improvement among races. To our knowledge, this has not been reported previously. Among studies that have analyzed GLS, one stratified results by race and observed GLS to be lower overall in African Americans (-16.5 ± 3.5%) as compared to whites (-17.5 ± 3.0%) and Hispanics (-17.3 ± 2.9%) in patients with normal left ventricular function [28]. However, no GLS assessments have been reported thus far in response to TAVR. Given this, our findings suggest that minorities are likely to benefit from potential improvements in left ventricular function after TAVR despite known discrepancies in access to the procedure. Alkhouli et al. noted in a large 2011-2016 registry that TAVR use was significantly lower in minorities in the United States [14]. This is true despite their analysis showing no differences in adjusted in-hospital or 1-year mortality, myocardial infarction, or stroke across race. The explanations for these findings were complex with one etiology possibly being related to the genetic predisposition favoring Caucasian heritage for the development and worsening of AS in comparison to minorities [29]. Evidence supporting this assertion include studies that show African Americans have a lower baseline prevalence of AS and may also experience fewer AS-related hospitalizations in comparison to White counterparts [29, 30]. Hispanics may also experience a diminished severity of valvular disease, as one study by Sashida et al. found that Hispanic heritage was protective against aortic valve thickness [31].

Despite these baseline genetic differences, there are likely other unaccounted for factors that explain the discrepancy in TAVR access among races. Alkhouli's analysis suggested that regions in the US with the greater race-based discrepancies had numerically longer driving distances to TAVR centers [14]. Lack of sufficient trust in the medical system, differing levels of health literacy, individual patient refusal, and provider bias may have also contributed as well [32, 33]. Brennan et al. examined patients with severe, symptomatic AS from 2007-2017 and found that African American patients were disproportionately still less likely to receive TAVR even after adjusting for census-based and patient-level differences than their white counterparts [13]. Although unidentified, treatment bias at varying levels may have been responsible for these findings even beyond socioeconomic differences. Given these factors, the improvement in GLS across all races offers echocardiographic evidence of improved LV function to support TAVR access for minorities.

This study was not without limitations, of which the most prominent was the sample size, which if larger may have detected a stronger difference in the various relationships tested here. A larger sample size for each race would have allowed for more definitive conclusions to be drawn. However, the sample size was sufficient to reach statistically significant results and form reasonable conclusions. Another limitation was that our studies were all analyzed 1-month post TAVR. It is possible that the effects we observed differed at varying lengths of time after procedure. Finally, our analysis was based solely on GLS and was performed using specific software derived from traditional 2D transthoracic echocardiography. Alternative means for strain analysis using different software elements exist, and as such, consideration of these additional methods may reinforce results found here.

Conclusion

This study demonstrated that GLS improved after TAVR independent of race and confirms the findings of several studies prior demonstrating this result. Additionally, the magnitude of GLS improvement was similar across races. These results contribute to the body of evidence that minorities are likely to show improvements in LV function despite AS traditionally being associated with Caucasian ancestry. Finally, baseline GLS and aortic valve area predicted the degree of strain improvement after TAVR, which suggests that those with more impaired LV function may benefit most from the procedure. Further studies are necessary to confirm these findings.

Disclosure of conflict of interest

None.

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