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Retrospective Study

Change and impact of left ventricular global longitudinal strain during transcatheter aortic valve implantation

Han Zhang, Jin-Jie Xie, Rong-Juan Li, Yue-Li Wang, Bao-Rong Niu, Li Song, Jing Li, Ya Yang

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Abstract

BACKGROUND

Although transcatheter aortic valve implantation (TAVI) is a safe and effective treatment for aortic stenosis, it still carries some risks, such as valve leaks, stroke, and even death. The left ventricular global longitudinal strain (LVGLS) measurement may be useful for the prediction of adverse events during this operation.

AIM

To explore the change of LVGLS during TAVI procedure and the relationship between LVGLS and perioperative adverse events.

METHODS

In this study, 61 patients who had undergone percutaneous transfemoral TAVI were evaluated by transthoracic echocardiography. Before surgery, data on left ventricular ejection fraction (LVEF) and LVGLS were collected separately following balloon expansion and stent implantation. Difference in values of LVGLS and LVEF during preoperative balloon expansion (pre-ex), preoperative stent implantation (pre-im) and balloon expansion-stent implantation (ex-im) were also examined. Adverse events were defined as perioperative death, cardiac rupture, heart arrest, moderate or severe perivalvular leakage, significant mitral regurgitation during TAVI, perioperative moderate or severe mitral regurgitation, perioperative left ventricular outflow tract obstruction, reoperation, and acute heart failure.

RESULTS

The occurrence of perioperative adverse events was associated with differences in pre-ex LVGLS, but not with difference in pre-ex LVEF. There were significant differences between pre-LVGLS and ex-LVGLS, and between pre-LVGLS and im-LVGLS ($P = 0.037$ and $P = 0.020$, respectively). However, differences in LVEF were not significant ($P = 0.358$, $P = 0.254$); however differences in pre-ex LVGLS were

associated with pre-LVGLS ($P = 0.045$). Compared to LVEF, LVGLS is more sensitive as a measure of left heart function during TAVI and the perioperative period. Moreover, the differences in LVGLS were associated with the occurrence of perioperative adverse events, and changes in LVGLS were apparent in patients with undesirable LVGLS before the surgery. Furthermore, LVGLS is useful to predict changes in cardiac function during TAVI.

CONCLUSION

Greater attention should be paid to the patients who plan to undergo TAVI with normal LVEF but poor LVGLS.

Key Words: Aortic stenosis; Ejection fraction; Longitudinal strain; Transcatheter aortic valve implantation; Left ventricular global longitudinal strain

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Core Tip: This study analyzed changes in left ventricular ejection fraction and left ventricular global longitudinal strain in patients with aortic stenosis undergoing transcatheter aortic valve implantation. Changes in left ventricular global longitudinal strain were significant in preoperative balloon expansion and stent implantation sections and it is sensitive to detect subtle change in left ventricle systolic function during the operation. It can also be used as a predictor of adverse events during the perioperative period.

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INTRODUCTION

As the prevalence of calcified aortic stenosis (AS) is increasing in aging societies[1], transcatheter aortic valve implantation (TAVI) provides an option for this population with intermediate-high surgical risks [2,3]. Recently studies have proved the feasibility and safety of this invasive method in short- and mid-term follow-up periods[4,5]. Echocardiography is the most widely used method to evaluate left ventricle (LV) function before and after the operation. Traditionally in echocardiographic measurements, LV systolic function is measured through left ventricular ejection fraction (LVEF) referring to the fraction of LV end-diastolic volume ejected during systole. LVEF is the most widely used measure for the assessment of LV systolic function and has been extensively used in clinical trials as well as in guidelines. Even so, LVEF is load dependent, and LVEF may thus be maintained despite reduced myocardial contractility using preload reserve or changes in LV geometry. In contrast, a decreased LVEF may be determined in spite of preserved contractility due to afterload mismatch, but could represent LV failure[6]. As to subclinical dysfunction, LVEF seems not to be an ideal indicator. Therefore, left ventricular global longitudinal strain (LVGLS), which is derived from speckle tracking echocardiography, is introduced to quantize subtle myocardial dysfunction. In valvular heart disease, LVGLS provides additional diagnostic and prognostic value. It has been demonstrated that LVGLS is depressed while LVEF is still preserved in AS patients[7], and recovery of LVEF and LVGLS after TAVI was also observed[8]. However, the impact of LVGLS and LVEF to TAVI operation procedure and perioperative adverse events is seldom noticed. The aim of the present study was to detect how the baseline and changes of LVGLS during operation affect the perioperative outcomes.

MATERIALS AND METHODS

Study population

From November 2019 to November 2020, we retrospectively studied patients who had undergone transfemoral TAVI. Inclusion criteria for TAVI were the following: (1) 2D echocardiography showed severe native AS with peak aortic valve (AV) velocity ≥ 400 cm/s or mean AV gradient ≥ 40 mmHg or AV area < 1 cm²; (2) 70 years of age or at high surgical risks; and (3) Severe AS with relevant symptoms and above New York Heart Association functional classification class II.

Transthoracic echocardiography (TTE) was performed before, during, and immediately after the operation using EPIQ7C ultrasound machines (Philips Healthcare, Bothell, WA, United States). In total, 98 patients underwent TAVI, and 37 patients were excluded due to incomplete image collection or unanalyzable poor trace or TEE performance. From the original set of patients, 61 patients with AS were included in the study. **Table 1** presents the clinical characteristics of the study subjects. These patients were divided into two groups, a normal LVEF group and a reduced LVEF group based on a threshold of 50% for normal LVEF. With a threshold of -20% for LVGLS[9], the normal LVEF group was further stratified into a normal LVGLS subgroup and an increased LVGLS subgroup.

Definitions of perioperative adverse events

Perioperative adverse events were pre-specified as following: perioperative death, cardiac rupture, heart arrest, moderate or severe perivalvular leakage (PVL), significant mitral regurgitation (MR) during TAVI and moderate or severe postoperative residual MR, perioperative residual ventricular outflow tract obstruction, perioperative reoperation, and perioperative acute heart failure. The observation period was from the initiation of TAVI to hospital discharge.

Echocardiography

Patients included in the study underwent standard echocardiography using EPIQ7C ultrasound system (Philips Healthcare). Offline analyses were performed for LV measurements using TomTec software (GE Healthcare, Chicago, IL, United States). The mean transvalvular gradient was calculated using the Bernoulli formula. The AV area was measured using the continuity equation. LVEF was obtained using Biplane Simpson methods. Short axis view at AV level was used to observe morphological characteristics. The global 2D LVGLS was acquired in the apical long axis view, in apical four chamber, and in apical two chamber view. The speckle-tracking echocardiography-derived measurements were performed with software package (TomTec Imaging Systems, Unterschleissheim, Germany). For speckle tracking analysis, 3 cycles were recorded at a frame rate between 40 and 80 frames per second and were averaged for strain analysis. LVGLS was defined as the peak negative value from the strain curve at end-systole. From 3 manually selected landmark points (lateral and septal mitral annulus and LV apex) in apical views, LV endocardial borders were automatically detected by the software. Automatic tracking of myocardial speckles was performed in the cardiac cycle, manually correction was performed if automatic tracing was not appropriate. LVEF and LVGLS data were collected preoperatively immediately after anesthesia introduction, following balloon expansion and following stent implantation respectively. Value variant of LVGLS and LVEF during preoperative balloon expansion (pre-ex), preoperative stent implantation (pre-im) and balloon expansion-stent implantation (ex-im) were then calculated.

Statistical analysis

All results are expressed as mean \pm SD. Student's *t* test was used to compare echocardiographic data between baseline and values during and after the operation. Linear regression analysis was conducted to test the correlation among the variations before, during, and after the procedure of LVEF, LVGLS and perioperative adverse events. Differences were considered statistically significant if the *P* value was less than 0.05. All statistical analyses were performed with SPSS version 24.0 statistical analysis software (IBM Corp., Armonk, NY, United States).

RESULTS

Baseline patient characteristics

Sixty-one patients underwent transfemoral TAVI and TTE tests. Self-expanding prosthetic valves were used in this operation. **Table 1** presented the clinical characteristics of participants in the study. Twenty patients were female. The mean age of the participants was 73.42 ± 7.60 years. Based on the results of echocardiographic tests, all patients had AS, with an average AV area of 0.66 ± 0.29 cm². Peak flow velocity of aortic flow was 478.21 ± 103.36 cm/s, and pressure gradient across AV was 56.47 ± 22.33 mmHg. Thirty patients had more than moderate aortic regurgitation simultaneously. 2D echocardiography was used to assess the valve morphology at the short axis view. Among all the participants, 28 patients (45.9%) had bicuspid aortic valve (BAV) and 33 patients (54.1%) had tricuspid aortic valve (TAV). Complications included hypertension (32 patients, 52.5%), coronary heart disease (18 patients, 29.5%), diabetes (14 patients, 23%), impaired pulmonary function (11 patients, 18%) and stroke (11 patients, 18%).

Clinical events during TAVI

Totally perioperative adverse events occurred in 16 patients during the observation. Neither aortic dissection nor procedural coronary flow impairment was observed in the entire study population. Details of the events are listed in **Table 2**. The most common adverse event was moderate or severe PVL

Table 1 Clinical characteristics of participants undergoing transcatheter aortic valve implantation

Characteristics	<i>n</i> = 61
Female (<i>n</i>)	28
Age (yr)	73.42 ± 7.60
Height (cm)	164.67 ± 7.05
Weight (kg)	65.88 ± 10.61
NYHA class III/IV (<i>n</i>)	43/5
Other diseases	
Hypertension	32
Diabetes	14
Hyperlipemia	8
Coronary heart diseases	18
Impaired pulmonary function	11
Stroke	11

NYHA: New York Heart Association functional classification.

Table 2 Adverse events during the perioperative period

Perioperative adverse events	<i>n</i>
Cardiac rupture	2
Heart arrest	1
Perioperative death	2
Perioperative reoperation	2
Perioperative acute heart failure	1
Moderate or severe perivalvular leakage	5
Perioperative LVOTO	1
Significant mitral regurgitation	2

LVOTO: Left ventricular outflow tract obstruction.

(5 patients, including 3 patients with BAV and 2 patients with TAV). No evidence showed the development of PVLs was related to the morphology of AV (OR = 1.008, 95%CI: 0.582-1.745, *P* = 0.978). During liner regression analyses, only deviation of pre-ex LVGLS was associated with perioperative adverse events (OR = 1.384, 95%CI: 1.030-1.861, *P* = 0.031). Other factors that might have effects on the occurrence of adverse events but showed no statistical significance are listed in [Table 3](#).

Effects of TAVI on echocardiographic parameters

Both peak AV velocity (478.21 ± 103.36 cm/s *vs* 232.77 ± 56.03 cm/s; *P* = 0.000) and mean pressure gradient (56.47 ± 22.33 mmHg *vs* 11.95 ± 5.48 mmHg; *P* = 0.000) significantly decreased after TAVI. Concomitant AR decreased from 30 to 5 cases. However, AV area increased evidently (0.66 ± 0.29 cm² *vs* 1.78 ± 0.3 cm²).

The TAVI procedure was divided into three sections in the study: preoperatively after the induction of anesthesia, following balloon expansion and following stent implantation. LVEF and LVGLS at the three sections and the deviations of LVEF and LVGLS over the three sections were calculated. There was a decline in LVEF over the three sections, but the decrease was not statistically significant. There was also declining trend in LVGLS and the pre-ex and pre-im mean values of LVGLS increased significantly (*P* = 0.037 and *P* = 0.020, respectively) while no significant increase was noted in the ex-im mean value (*P* = 0.835). Some patients' LVGLS became better (18 patients, -15.00 ± 4.92) after prosthesis implantation, while some others became worse (43 patients, -12.36 ± 4.62). By comparing the baseline LVGLS between these 2 types of patients, it was found that the patients whose LVGLS increased had worse baseline

Table 3 Factors influencing perioperative adverse events

	OR	95%CI	P value
Sex	0.089	0.003-2.425	0.152
Age	1.141	0.974-1.335	0.102
Weight	0.929	0.823-1.048	0.228
Height	1.233	0.942-1.615	0.127
Hypertension	2.579	0.309-21.515	0.381
Diabetes	5.512	0.398-76.356	0.203
Hyperlipemia	0.721	0.027-19.079	0.845
Coronary heart diseases	1.919	0.218-16.924	0.557
Impaired pulmonary function	2.656	0.154-45.870	0.502
Stroke	2.290	0.240-21.846	0.472

CI: Confidence interval; OR: Odds ratio.

LVGLS ($P = 0.049$).

When the threshold for LVEF was set at $\geq 50\%$, patients were divided into a preserved LVEF group (39 patients) and a decreased LVEF group (22 patients). In the preserved LVEF group, changes in LVGLS were greater than in LVEF. The mean pre-ex and pre-im LVGLS values decreased obviously. In total, 13 adverse events occurred in this group. In the decreased LVEF group, neither LVEF nor LVGLS displayed significant changes and 3 adverse events occurred. Details for the two groups are showed in [Table 4](#) and [Table 5](#).

We further subdivided the normal LVEF group into a normal LVGLS group (11 patients) and an increased LVGLS group (28 patients) with a threshold $\leq -20\%$ for LVGLS. An increasing trend can be observed in LVGLS in both groups. Adverse events occurred 10 times in the increased LVGLS group and 3 times in the normal LVGLS group. When comparing difference in the values of LVGLS between pre-ex and pre-im sections, it revealed that rise in the mean values of LVGLS was more significantly in the increased group than in the normal group ($P = 0.039$, $P = 0.015$).

DISCUSSION

TAVI is a guideline recommended as an alternative treatment in AS patients with or without AR who deemed to have moderate or severe surgical risk[10]. As reported previously, these patients can benefit from the operation with decreased peak velocity, pressure gradient, and degree of AR and increased AV area. It has been demonstrated that TAVI resulted in continued beneficial changes in LVEF and LVGLS [11,12]. However, the change in LV function during the procedure has seldom been noted. The present study revealed that (1) The baseline LV function could have effect on the change in subtle LV function during TAVI procedure; (2) LVGLS was more sensitive than LVEF to reflect the changes in subtle LV function during the operation; and (3) The changes in LVGLS during TAVI may have an influence on the occurrence of perioperative adverse events.

We categorized the TAVI procedure into three sections based on balloon expansion and rapid pacing. Balloon expansion would do obstruction in left ventricular outflow tract within a short time, and rapid pacing was needed to bring down the blood pressure. These actions may be exerted several times if necessary; however, both manipulations might do harm to the LV function in case of improper actions or taking too much time. We collected TTE images immediately after anesthesia introduction, balloon expansion, and protheses implantation in consideration of the possible injuries.

All the patients in the study suffered from AS. Although LVEF exceeded 50% in the preserved LVEF group (39 patients), the mean value of LVGLS had declined in severe AS patients, which was consistent with the previous studies[13,14]. Conventional LVEF is useful in detecting global LV dysfunction, but it is not sensitive enough. As reported earlier, our data also suggest that the myocardium of patients with severe AS is intrinsically dysfunctional despite preserved LV function based on the level of LVEF. The subtle injury of LV function might lead to a downtrend in the tolerance to manipulations during TAVI procedure. It should be noted that strain is load dependent, and the reduction in LVGLS may be partially explained by an increase in LV afterload pressure[12,15].

Compared with baseline data, both LVEF and LVGLS became worse over the operation. The manipulation of TAVI was presumed when the LV function had already been injured. However, LVEF only showed obvious change in pre-ex section, while LVGLS changed significantly in both pre-ex and pre-im

Table 4 Changing trend in left ventricular ejection fraction and left ventricular global longitudinal strain in the preserved left ventricular ejection fraction group

	Preserved LVEF group	Pre-ex	Pre-im	Di-im	Inter-group
Baseline LVEF	64.57 ± 7.63				
LVEF after expansion	60.17 ± 9.73				
LVEF after implantation	58.38 ± 11.39				
<i>P</i> value		0.081	0.013	0.432	0.040
Baseline LVGLS	-18.09 ± 3.30				
LVGLS after expansion	-13.99 ± 4.22				
LVGLS after implantation	-12.94 ± 5.59				
<i>P</i> value		0.003	0.000	0.309	0.000
PAEs	13				

Ex-im: Balloon expansion-stent implantation; LVEF: Left ventricular ejection fraction; LVGLS: Left ventricular global longitudinal strain; PAEs: Perioperative adverse events; Pre-ex: Preoperative balloon expansion; Pre-im: Preoperative stent implantation.

Table 5 Changing trend in left ventricular ejection fraction and left ventricular global longitudinal strain in the decreased left ventricular ejection fraction group

	Decreased LVEF group	Pre-di	Pre-im	Di-im	Inter-group
Baseline LVEF	34.34 ± 9.74				
LVEF after expansion	35.23 ± 9.98				
LVEF after implantation	35.91 ± 11.52				
<i>P</i> value		0.780	0.623	0.833	0.884
Baseline LVGLS	-9.07 ± 3.31				
LVGLS after expansion	-7.72 ± 4.09				
LVGLS after implantation	-8.24 ± 4.00				
<i>P</i> value		0.245	0.472	0.654	0.500
PAEs	3				

Ex-im: Balloon expansion-stent implantation; Pre-ex: Preoperative-balloon expansion; Pre-im: Preoperative-stent implantation; LVEF: Left ventricular ejection fraction; LVGLS: Left ventricular global longitudinal strain; PAEs: Perioperative adverse events.

sections. The LVGLS changed less if the baseline LVGLS was in normal range, while normal baseline LVEF could not guarantee the change during the operation. This again showed that while subtle variations in baseline LV function could affect the degree of tolerance to the manipulation of TAVI to some extent, LVGLS was a more sensitive index.

Some LVGLS became worse in patients during TAVI after prostheses implantation compared with the baseline data, while some LVGLS would improve in others. Patients with declined LVGLS had worse baseline LVGLS ($-15.00 \pm 4.92\%$ vs $-12.36 \pm 4.62\%$; $P = 0.049$) compared to those with normal LVGLS. This implied that the patients with better baseline LV function may be more tolerable to the procedure and could restore better after the overload of LV had been resolved.

According to the statistical data of present study, the deviation of pre-ex LVGLS was associated with the happening of clinical events. It may demonstrate the dysfunction occurring during the procedure could result in complications in some circumstances. When comparing the normal LVGLS subgroup and increased LVGLS subgroup in the preserved LVEF group, there were totally 13 clinical events in the normal LVEF group with 10 events occurring in 28 patients in the increased LVGLS subgroup and 3 events occurring in 11 patients in the normal LVGLS subgroup. Fewer events were observed in the relatively good LVGLS subgroup. In both pre-ex and pre-im sections, the mean value of deviations in the increased subgroup changed more significantly than that of normal LVGLS subgroup. Previous studies have suggested the presence of ischemia and myocardial fibrosis in the endocardium from sustained pressure loading in severe AS. The biopsy results proving myocardial fibrosis in aortic

stenosis is directly related to the reduction in GLS[16,17]. In this study, the different levels in LVGLS change in the three sections during TAVI may be explained by the fibrosis in endocardium. LVGLS variation could reflect the change of LV function in a certain range, and the variation may have implications for the outcome of TAVI in the perioperative period. However, if low enough, neither LVEF nor LVGLS could be reflective of the change of subtle LV function. As many of this group showed eccentric hypertrophy, it was assumed that the fibrosis and myocardial apoptosis were too severe to react with operation in a short time[18-20]. We did not find additional adverse clinical events in the declined LVEF group, which may be due to more protective measures carried out in this group. Other factors, such as advanced age, low weight, hypertension, diabetes, coronary heart disease and stroke, might also slightly stimulate the occurrence of clinical events.

In line with previous reports, there was an improvement in LVGLS both at septal and lateral level as early as 72 h after the procedure, and constant beneficial could also be observed in early and late periods [5,21]. Although the benefits are obvious, the subtle change during operation should not be ignored, which may influence the perioperative clinical events.

Limitations

The following are several limitations of this study. Firstly, this was a single center retrospective study, the follow-up period is limited to perioperative time, and this study was designed to assess the acute effects of the procedure on LV strain. A long-term study is necessary to observe whether any alteration of the changes in myocardial strain and clinical outcomes. Secondly, we excluded many patients due to the poor imaging or the failure in collecting all the needed images. That maybe lead to the bias of the results. Thirdly, LVGLS was affected by arrhythmia, and the results would be influenced to some degree. However, it was unavoidable when images collected after balloon expansion and stent implantation. Finally, all the data in the present study were collected under anesthesia. It may be different with the results in normal physiological conditions, and LV function could be affected by cardiotoxic agents. Further and detailed research is needed.

CONCLUSION

In conclusion, LVGLS is more sensitive than conventional LVEF to detect subtle change in LV systolic function during TAVI operation in patients with severe AS. The change ranges of LVGLS during the procedure were associated with the baseline LVGLS and can affect the perioperative outcomes of TAVI. More attention should be paid to patients who had preserved LVEF with increased LVGLS and who had a wide variation in LVGLS during the operation. These findings can provide new insights into the understanding of LV mechanics and pathophysiology in patient with sever AS and play an important role in intraoperative monitoring.

ARTICLE HIGHLIGHTS

Research background

The efficacy of transcatheter aortic valve implantation (TAVI) and prognosis of aortic stenosis (AS) is usually restricted by perioperative adverse events. Global longitudinal strain is a commonly used echocardiographic parameter for the detection of left ventricular function. Whether there is an association between the changes in global longitudinal strain and the occurrence of perioperative adverse events during TAVI remains unknown.

Research motivation

If global longitudinal strain is useful for the predication of perioperative adverse events, monitoring of global longitudinal strain can be carried out before the operation and corresponding measures can be taken to reduce the operational risk.

Research objectives

To assess changes in left ventricular global longitudinal strain (LVGLS) during the surgery of TAVI and the association between LVGLS and perioperative adverse events in patients with calcified aortic stenosis.

Research methods

A retrospective study was carried in 61 patients with calcified AS undergoing TAVI. These patients underwent standard echocardiography examination. LVEF and LVGLS data were collected during preoperative balloon expansion, preoperative stent implantation, and balloon expansion-stent implantation. The patients were categorized into a normal left ventricular ejection fraction (LVEF) group

and a reduced LVEF group, and the normal LVEF group was further stratified into a normal LVGLS subgroup and an increased LVGLS subgroup. The association between changes in LVEF and LVGLS and the occurrence of perioperative adverse events were analyzed.

Research results

In the preserved LVEF group, LVEF only showed obvious change in preoperative balloon expansion section, while LVGLS declined significantly in both preoperative balloon expansion and preoperative stent implantation sections. In the decreased LVEF group, neither LVEF nor LVGLS displayed significant changes. Changes in LVGLS in preoperative balloon expansion section and preoperative stent implantation section were associated with perioperative adverse events which indicating changes in LVGLS during TAVI may have an influence on the occurrence of perioperative adverse events.

Research conclusions

In the preserved LVEF group, changes in LVGLS were greater than in LVEF. LVGLS can be a marker to be used for the prediction of changes in cardiac function during TAVI.

Research perspectives

The optimal cut-off value for LVGLS and timing for measurement of LVGLS still needs to be guaranteed by large scale multi-center studies.

FOOTNOTES

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