Left ventricular speckle tracking echocardiographic evaluation before and after TAVI

Vasiliki Tsampasian MSc MRCP, Vasileios Panoulas PhD FESC, Richard J Jabbour MBBS MRCP, Neil Ruparelia DPhil MRCP FESC, Iqbal S Malik PhD FRCP, Nearchos Hadjiloizou MBBS PhD, Angela Frame MSc, Sayan Sen MBBS PhD, Nilesh Sutaria MBChB MD, Ghada W Mikhail PhD FRCP FESC and Petros Nihoyannopoulos PhD FRCP FESC FACC

1Hammersmith Hospital, Imperial College Healthcare NHS Trust, London, UK
2Imperial College London, National Heart and Lung Institute, London, UK
3Harefield Hospital, Royal Brompton and Harefield NHS Foundation Trust, London, UK

Correspondence should be addressed to V Tsampasian: tsampasian@doctors.org.uk

Abstract

Aims: To assess left ventricular (LV) function before and after transcatheter aortic valve implantation (TAVI) using conventional echocardiographic parameters and global longitudinal LV strain (GLS) and compare outcomes between Edwards S3 and Evolut R valves.

Methods and results: Data were collected for consecutive patients undergoing TAVI at Hammersmith hospital between 2015 and 2018. Of the 303 patients, those with coronary artery disease and atrial fibrillation were excluded leading to a total of 85 patients, which constituted our study group. The mean follow-up was 49 ± 39 days. In total, 60% of patients were treated with Edwards S3 and 40% Evolut R. TAVI resulted in an early improvement of GLS (−13.96 to −15.25%, \(P = 0.01\)) but not ejection fraction (EF) (47.6 to 50.1%, \(P = 0.09\)). LV mass also improved, especially in patients with marked baseline LV hypertrophy (\(P < 0.001\)). There were no appreciable differences of LV function improvement and overall LV remodelling after TAVI between the two types of valves used (\(P = 0.14\)).

Conclusions: TAVI results in reverse remodelling and improvement of GLS, especially in patients with impaired baseline LV function. There were no differences in the extent of LV function improvement between Edwards S3 and Evolut R valves but there was a greater incidence of aortic regurgitation with Evolut R.

Key Words

- aortic stenosis
- transcatheter aortic valve implantation
- speckle tracking echocardiography
- global longitudinal strain

Introduction

Degenerative calcific aortic stenosis represents one of the commonest causes of valvular heart disease in developed countries (1). TAVI has emerged as a less invasive alternative treatment for the patients with high (2, 3), intermediate (4, 5, 6) and low (7, 8) surgical risk. With the advantages of faster recovery and reduced peri-operative mortality, TAVI offers a significant improvement in LV haemodynamics, symptoms and prognosis in those groups (8). In the current study, we investigated the impact of TAVI on GLS and further examined the potential interaction of valve type (Edwards S3 vs Medtronic Evolut R) using speckle tracking echocardiography.
Methods

Patient population

This is a prospective observational study that included consecutive patients from a single tertiary centre (Hammersmith Hospital, Imperial College Healthcare NHS Trust). Data were collected for all patients who underwent TAVI from April 2015 until May 2018. Exclusion criteria were patients with (1) coronary artery disease; (2) atrial fibrillation; (3) severe coexistent valve lesions, including severe aortic regurgitation (AR), mitral regurgitation (MR), mitral stenosis (MS); (4) valve-in-valve procedures (patients that had undergone previous SAVR) and patients with previous balloon aortic valvuloplasty (BAV); (5) severe aortic stenosis secondary to the bicuspid aortic valve and (6) poor quality echocardiographic images that did not allow speckle tracking echocardiographic analysis.

Of the 303 patients who underwent TAVI, 85 met our strict inclusion criteria and were included in the final study population.

TAVI procedure

All patients with severe symptomatic AS with high or intermediate risk for surgical aortic valve replacement were carefully evaluated by the multidisciplinary heart team. All patients underwent TAVI using the transfemoral approach. The devices used were the Evolut R self-expandable valve (26, 29 or 34 mm) or the Edwards Sapien 3 balloon-expandable valve (23, 26 or 29 mm), based on the operator’s preference.

Two-dimensional echocardiographic analysis

All study participants underwent a comprehensive transthoracic echocardiographic study before and after TAVI using a standardised protocol. Two-dimensional echocardiographic measurements were obtained in each study, including LV dimensions, LV outflow tract diameter (LVOTd), transaortic mean and peak gradient, maximal transaortic velocity and LV outflow tract velocity. LV mass was calculated using the Devereux formula and indexed to body surface area. LV ejection fraction was calculated using the Simpson’s biplane method. The LVOT diameter before the TAVI procedure was measured from the parasternal long axis view (PLAX) in the zoomed image of the LVOT and the aortic valve in mid-systole. After TAVI, the LVOT diameter was measured from the zoomed image of the PLAX view in mid-systole. For the Edwards S3 valve, the measurement was performed at the end of the stent (pre-stent), while for the Evolut R, where the stent sits low in the LVOT, the diameter was measured within the stent (in-stent) and just proximal to the valve cusps. The effective orifice area of the aortic valve was calculated using the continuity equation and was indexed to the body surface area. Severe patient-prosthesis mismatch was defined as AVAi <0.65 cm²/m² (9).

After the TAVI procedure, the presence of paravalvular regurgitation (PVR) was assessed with the use of colour and continuous-wave Doppler. Very small jets were defined as trivial regurgitation. The circumferential extent of the AR jet was assessed to evaluate the degree of PVR. Mild PVR was defined when it was <10%, moderate when 10–30% and severe when the jet was ≥30%. The density of the AR jet in the continuous-wave Doppler was used to evaluate the severity of regurgitation, with faint jets indicating mild PVR and dense jets indicating severe PVR (10).

Strain analysis

Speckle tracking analysis was performed offline using a vendor-independent software (TomTec 2D Cardiac Performance Analysis, Munich, Germany). Global longitudinal strain (GLS) was assessed with the use of the speckle-tracking algorithm of the TomTec software (TomTec Imaging Systems GmbH, Unterschleissheim, Germany). The apical four-chamber, two-chamber and three-chamber views were analysed individually. For each of these images, the end-systolic and end-diastolic frames were selected by the user and the endocardial borders were traced manually. The software then calculated the regional and average longitudinal strain. The average endocardial longitudinal strain was recorded and documented for each study. Images with frame rate <50 were excluded.

Statistical analysis

Statistical analysis was performed using commercially available software STATA version 12 (Stata Corp., College Station, Texas). Continuous variables are presented as mean ± s.d. For the numerical paired and unpaired data variables, t-test and their non-parametric analogues were used as appropriate. When three independent groups were analysed, the ANOVA test or the Kruskal–Wallis test was used for parametric and non-parametric samples, respectively. For categorical variables, the chi-squared test and the McNemar’s test were used for unpaired and paired data, respectively. Regression analysis was performed to test causality between variables. Pearson correlation or
Spearman’s rank correlation were used as appropriate to assess the strength of association between the variables. Multiple regression analysis was performed to investigate possible factors impacting on the improvement of the systolic function after TAVI.

**Intra-observer and inter-observer variability**

Speckle tracking analysis of 20 studies was performed independently by two trained individuals blinded to the study data. The intraclass correlation coefficient for the GLS for the inter-observer variability was 0.93 (95% CI: 0.84, 1.02) suggestive of an excellent agreement between observers. The intraclass correlation coefficient for the GLS for the intra-observer variability was 0.92 (95% CI: 0.81, 1.02).

**Power calculations**

Power calculation was performed with the level of significance set at 0.05 and the power of the test at 0.8. The estimated sample size for a two-sample paired-means test was 16, assuming an improvement of the GLS of −3% (pre TAVI −12.2% post TAVI −15.2%) and a S.D. of the difference of 4% (Fig. 1). Our population included nearly four times more than the required sample (51 subjects in Edwards S3 group and 34 subjects in Evolut R group). Consequently, our sample size would be able to detect a true difference in GLS of 1.23% with a power of 0.8 and alpha 0.05.

**Results**

**Characteristics of entire study population**

The baseline characteristics of the entire study cohort are summarised in Table 1.

The mean interval time from the valve implantation to the follow-up echocardiographic study was 49 ± 39 days. All measurements for the study population before and after TAVI are presented in Table 2.

Multiple regression analysis was performed for all the baseline characteristics, including age, gender and all the various comorbidities (including LBBB) that the patients in this cohort had. None of these were found to be significant confounding factors on the improvement of the GLS post TAVI.

LV mass improved after TAVI for the total population (209.7 ± 72.8 to 194.7 ± 55.4, P=0.0009) reflecting regression of LV hypertrophy. The baseline LV mass was strongly correlated with the rate of the LV mass reduction after TAVI (r=−0.65, 95% CI: −0.60, −0.38, P < 0.0001). This remained significant even after adjustment for age, gender and baseline LV function. Patients with marked hypertrophy at baseline showed a greater reduction in LV mass after TAVI compared with subjects who did not have a significant degree of LV hypertrophy at baseline (Fig. 2). Additionally, there was a significant correlation between the improvement in the LV mass and the improvement of the EF after TAVI (P=0.02).

GLS significantly improved after TAVI −13.96 ± 5.1 vs −15.25 ± 4.2, P=0.011 (Figs 2 and 3). The EF, however, failed to demonstrate such a difference (P=0.09) (Fig. 4). The baseline LV systolic function had a significant effect on the outcome. Patients with impaired LV function at baseline had a greater improvement of both the EF and the GLS after TAVI compared to patients with preserved baseline LV function (Figs 5 and 6).

Regarding pulmonary hypertension, in the baseline study, 49 patients (58.33%) had no pulmonary hypertension (PASP of less than 30 mmHg), 28 patients (33.33%) had moderately elevated pulmonary pressures (PASP 31–55 mmHg) and 7 patients (8.33%) had severely elevated pulmonary pressures (PASP >55 mmHg). After TAVI, 56 patients had normal pulmonary pressures, 25 patients had moderate pulmonary hypertension and 4 patients had severely elevated pulmonary pressures of >55 mmHg. Overall, the incidence of the three groups of pulmonary hypertension did not show statistically significant improvement after TAVI (P=0.32, 95% CI: 0.87, 1.67).

Regression analysis revealed no significant correlation between the incidence and stage of pulmonary hypertension at baseline and the improvement of GLS (P=0.259, 95% CI: −0.025, 0.006).
The diastolic function and the LV filling pressure did not demonstrate significant change after TAVI in this cohort (\(P=0.741\), \(P=0.98\), respectively).

**Comparison between Edwards S3 and Evolut R**

Patients were categorised into two groups according to the type of TAVI valve implanted (Edwards S3 or Evolut R). The baseline characteristics and echocardiographic parameters of each group are presented in Table 3. Of the 85 patients of the study group, 51 (60%) had the self-expandable valve (Evolut R) and 34 (40%) had the balloon-expandable valve (Edwards S3).

We found that the type of valve used had no significant impact on the difference of the GLS after TAVI (95% CI: 0.24, 1.37, \(P=0.214\), Table 4). This was confirmed when the GLS difference (GLS after TAVI – GLS before TAVI) was compared between the two groups (\(P=0.136\)) (Fig. 7). Similarly, there was no difference in the other echocardiographic parameters between the two types of valves (Table 4).

With regards to paravalvular regurgitation after TAVI, the incidence of paravalvular regurgitation overall was higher with the Evolut R (85.29% compared to 68.62% with the Edwards S3), however, this did not reach the level of statistical significance (\(P=0.117\)).

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### Table 2  Echocardiographic data at baseline and after the TAVI for the entire study group.

| Echocardiographic data | Study before TAVI | Study after TAVI | \(P\)-value |
|------------------------|------------------|-----------------|-------------|
| Days of echocardiogram | 59 ± 74          | 49 ± 39         | <0.0001     |
| AV peak velocity (m/s) | 4.41 ± 0.77      | 2.20 ± 0.50     | <0.0001     |
| AV peak gradient (mmHg)| 80 ± 27          | 20.4 ± 8.68     | <0.0001     |
| AV mean gradient (mmHg)| 44.7 ± 15.7      | 9.9 ± 4.3       | <0.0001     |
| AV orifice area (cm²)  | 0.69 ± 0.18      | 1.28 ± 0.52     | <0.0001     |
| LVEDD (cm)             | 4.44 ± 0.62      | 4.44 ± 0.65     | 0.921       |
| IVS (cm)               | 1.29 ± 0.29      | 1.22 ± 0.22     | 0.004       |
| PWT (cm)               | 1.21 ± 0.25      | 1.15 ± 0.19     | 0.0006      |
| LVESD (cm)             | 3.01 ± 0.73      | 2.93 ± 0.69     | 0.448       |
| RWT                    | 0.56 ± 0.17      | 0.53 ± 0.12     | 0.043       |
| LVMi (g/m²)            | 120 ± 39.2       | 111.1 ± 28.05   | 0.0009      |
| SV (mL)                | 70.09 ± 19.1     | 66.25 ± 19.64   | 0.149       |
| E/A                    | 0.89 ± 0.57      | 0.76 ± 0.28     | 0.741       |
| E/e’                   | 16.1 ± 7.7       | 15.9 ± 7.0      | 0.98        |
| EF (%)                 | 47.6 ± 15.1      | 50.1 ± 12.7     | 0.09        |
| GLS (%)                | −13.96 ± 5.1     | −15.25 ± 4.2    | 0.011       |

**IVS**, interventricular septum; **LVEDD**, LV end-diastolic diameter; **LVESD**, LV end-systolic diameter; **LVMi**, LV mass indexed to body surface area; **PWT**, posterior wall thickness; **RWT**, relative wall thickness; **SV**, stroke volume. Bold indicates statistical significance.

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**Figure 1**

Correlation of improvement in LV mass with baseline LV mass. Patients with greater baseline LV mass had a more significant reduction of the LV mass regression (\(P < 0.001, r = −0.65\)).

**Figure 2**

GLS before and after TAVI. GLS before and after TAVI for the total study population. There was a statistically significant improvement of the GLS after TAVI (\(P = 0.01\)).
Figure 3
Case example of GLS improvement before and after TAVI. Speckle tracking analysis of the LV function of a patient with severe AS before (A) and after (B) TAVI.
Nevertheless, when analysing the degree of regurgitation, there was a significantly increased incidence of moderate paravalvular regurgitation in the Evolut R group (14.7% vs 3.9% \( P = 0.019 \)) (Fig. 8). The presence of any degree of paravalvular regurgitation did not affect significantly the GLS after TAVI (\( P = 0.711, 95\% \) CI: 0.84, 1.28).

Additionally, there were 23 patients who developed new LBBB and required PPM implantation post TAVI (13 patients with Edwards S3 and 10 patients with Evolut R). Although the percentage of new pacemaker implantation in the immediate post-TAVI period was higher in the Evolut R group, this difference was not found to be of statistical significance (\( P = 0.69 \)). Logistic regression analysis showed that the incidence of a new pacemaker after TAVI was not found to have a significant impact on the outcome (GLS change) after TAVI (\( P = 0.886, 95\% \) CI: −0.024, 0.02).

**Discussion**

The main findings of this study were as follows: (1) in patients with severe AS undergoing TAVI, there is an early improvement in LV systolic function as detected by GLS but not with EF; and (2) the type of valve used did not influence the outcome, as LV function and LV mass improved to the same extent in both groups.

**GLS vs EF**

Several studies have shown that TAVI induces early improvement of the LV function that is detected only by strain parameters (11, 12, 13). Similarly, in our study, we found that GLS significantly improved in the total population, while EF failed to show a significant improvement. This may have significant clinical implications as such an improvement in GLS may be of prognostic relevance. Recent studies have shown that the improvement in GLS after TAVI is correlated with symptomatic improvement, better prognosis and lower mortality rate (12, 14, 15). The ejection fraction, on the other hand, remains a debated issue, as there is conflicting evidence as to whether it improves after TAVI. This controversial finding is most likely related with the time of the echocardiographic examination after TAVI.
Table 3  Baseline characteristics and echocardiographic parameters of the patients according to the type of valve used in the TAVI procedure.

| Characteristics and parameters | Edwards S3 | Evolut R | P-value |
|--------------------------------|------------|----------|---------|
| n (%)                          | 51 (60%)   | 34 (40%) | 0.291   |
| Euroscore (%)                  | 8.04 ± 4.4 | 9.5 ± 5.7| 0.291   |
| Age (years)                    | 81.29 ± 6.21| 79.67 ± 8.29 | 0.246 |
| Female, n (%)                  | 29 (64.4)  | 16 (35.5)| 0.291   |
| BSA (m²)                       | 1.72 ± 0.15| 1.77 ± 0.14| 0.128  |
| Bundle branch block, n (%)     | 8 (15.7)   | 8 (23.5) | 0.823   |
| Pacemaker, n (%)               | 5 (9.8)    | 4 (11.8) | 0.521   |
| Hypertension, n (%)            | 31 (60.8)  | 22 (64.7)| 0.715   |
| Lung disease, n (%)            | 18 (35.3)  | 11 (32.4)| 0.779   |
| CKD, n (%)                     | 12 (23.5)  | 9 (26.5) | 0.758   |
| Diabetes mellitus, n (%)       | 8 (15.7)   | 6 (17.7) | 0.518   |
| Hyperlipidemia, n (%)          | 16 (55.7)  | 13 (44.8)| 0.513   |
| AVA (cm²)                      | 0.67 ± 0.19| 0.72 ± 0.16| 0.407  |
| MG (mmHg)                      | 45.16 ± 15.63| 44.18 ± 16.06 | 0.781 |
| PG (mmHg)                      | 81.22 ± 26.94| 79.33 ± 28.98| 0.756 |
| LVEDD (cm)                     | 4.46 ± 0.62| 4.43 ± 0.63| 0.499  |
| IVSD (cm)                      | 1.3 ± 0.29 | 1.26 ± 0.29| 0.327  |
| PWT (cm)                       | 1.23 ± 0.23| 1.19 ± 0.27| 0.186  |
| LVESD (cm)                     | 3.03 ± 0.70| 2.98 ± 0.79| 0.577  |
| FS (%)                         | 32.4 ± 8.8 | 33.2 ± 1.01| 0.449  |
| RWT                            | 0.57 ± 0.16| 0.55 ± 0.19| 0.584  |
| SV (mL)                        | 67.94 ± 19.27| 73.24 ± 18.78| 0.147 |
| LVMI (g/m²)                    | 124.4 ± 43.3| 113.4 ± 31.6| 0.184 |
| EF (%)                         | 47.5 ± 15.2| 47.8 ± 15.2| 0.523  |
| E/A ratio                      | 0.86 ± 0.60| 0.88 ± 0.43| 0.120  |
| E/e’ ratio                     | 14.68 ± 7.77| 15.62 ± 7.94| 0.465 |
| GLS (%)                        | -13.08 ± 4.85| -15.26 ± 5.26| 0.07   |

AVA, AV area; BSA, body surface area; CKD, chronic kidney disease; FS, fractional shortening; IVSD, interventricular septum diameter; LVEDD, LV end-diastolic diameter; LVESD, LV end-systolic diameter; LVMI, LV mass indexed to body surface area; MG, mean gradient; PG, peak gradient; PWT, posterior wall thickness; RWT, relative wall thickness; SV, stroke volume.

There are few studies to support that only strain analysis post TAVI reflects the outcome. Several studies have shown that patients with severely reduced baseline EF and GLS have the most significant improvement in both the EF and the GLS in the group of patients with severely reduced baseline EF and GLS. There is so far no clear explanation for this phenomenon. Some suggest that this may represent a physiological reaction of the LV after resolution of the high gradient through the aortic valve (16). This study is the first to our knowledge that patients with coexistent comorbidities, such as coronary artery disease and atrial fibrillation, were excluded as they may have an impact on the outcome. Therefore, these factors can be safely ruled out as possible confounding factors and cannot explain the differences noted in the degree of improvement between patients with reduced and preserved baseline LV function.

**Regression of the LV hypertrophy after TAVI**

There was significant regression of the LV mass after TAVI. The regression of the LV hypertrophy was strongly affected by the baseline LV mass, as patients with more significantly hypertrophied LV walls were noted to have the more notable improvement. Given the negative prognostic implications of LV hypertrophy, its regression is undoubtedly a desirable goal (19). Early LV mass regression after TAVI, is thought to be due to the rapid regression of myocyte hypertrophy, whereas a late regression occurs as a consequence of fibrosis remodelling, which may take place over months or years (19, 20).

**Diastolic function**

The impact of TAVI on the LV diastolic function seems to be rather controversial with conflicting results (11, 16, 20, 21, 22). However, all previous studies have included patients with atrial fibrillation and coronary artery disease. Conversely, in our study patients with coronary artery disease, concomitant significant valvular pathology and atrial fibrillation were excluded, giving a better picture of LV remodelling after TAVI. Consequently, we found no appreciable improvement in diastolic function after TAVI. This could be a result of the transient increase of diastolic myocardial stiffness that occurs early after valve replacement, followed by regression of fibrosis and reversal of diastolic dysfunction (19, 23).

**Comparison between the two types of valves**

A few studies have compared the Edwards S3 and the Evolut R valves. Most have focused on the safety
profile of the valves, including pre- and post-procedural complications and mortality, which were similar in both (24, 25). These TAVI valves are more advanced compared to their forerunners in that they reduce the incidence of paravalvular regurgitation and procedural clinical complications. To our knowledge, this is the first study that compared the LV response between these two valves using GLS. We demonstrated that LV systolic and diastolic function and LV mass were similar between the two valves and that the rate of improvement was similar.

The incidence of paravalvular regurgitation and the incidence of severe patient-prosthesis mismatch were compared between the two groups. While the rate of new pacemaker implantation and patient-prosthesis mismatch was similar, a higher incidence of more than mild paravalvular regurgitation was demonstrated with the self-expandable Evolut R valve. This finding is significant, as more than mild paravalvular regurgitation after TAVI is associated with higher mortality rates (3, 26).

Limitations

The main limitation of this study is the relatively small sample size but was sufficiently powered to detect a true difference in GLS of 1.23% with a power of 0.8 and alpha 0.05. The length of time between the TAVI and follow-up varied among patients. However, the number

### Table 4

| Echocardiographic parameters | Edwards S3 | Evolut R | P-value |
|-----------------------------|------------|----------|---------|
| Days of echocardiographic study after TAVI | 51.05 ± 45 | 49.7 ± 27.5 | 0.603 |
| AVA (cm²) | 0.53 ± 0.31 | 0.71 ± 0.6 | 0.186 |
| MG (mmHg) | 33.89 ± 15.38 | 36.15 ± 15.25 | 0.509 |
| PG (mmHg) | 58.25 ± 26.11 | 62.76 ± 27.77 | 0.444 |
| LVEDD (cm) | 0.09 ± 0.06 | 0.15 ± 0.47 | 0.041 |
| LVESE SD (cm) | 0.09 ± 0.58 | 0.06 ± 0.21 | 0.725 |
| IVS (cm) | 0.06 ± 0.16 | 0.08 ± 0.19 | 0.629 |
| PWT (cm) | 0.02 ± 0.13 | 0.06 ± 0.13 | 0.187 |
| LVMI (g/m²) | 10.84 ± 30.5 | -5.98 ± 23.38 | 0.440 |
| E/A ratio | -0.13 ± 0.56 | -0.04 ± 0.49 | 0.358 |
| E/e' | 1.52 ± 7.56 | 1.67 ± 8.49 | 0.06 |
| LVEF (%) | 3.36 ± 11.6 | 1.41 ± 12.9 | 0.651 |
| GLS (%) | -1.95 ± 4.01 | -0.30 ± 5.02 | 0.136 |

AVA, AV area; IVS, interventricular septum; LVEDD, LV end-diastolic diameter; LVESE SD, LV end-systolic diameter; LVMI, LV mass indexed to body surface area; MG, mean gradient; PG, peak gradient; PWT, posterior wall thickness; RWT, relative wall thickness.

Figure 7

Improvement in GLS according to type of valve. The change in the left ventricular global longitudinal strain after TAVI was not found to be significantly affected by the type of valve used in the procedure, as there were similar changes in the two groups (P = 0.136).

Figure 8

Paravalvular Regurgitation after TAVI according to the type of valve used. Percentage of patients with various degrees of paravalvular regurgitation after TAVI. A significantly higher proportion of patients treated with the Evolut R had moderate paravalvular regurgitation (P = 0.019).
of days between the echocardiographic studies and the procedure was similar between the groups and did not have an impact on the results. Additionally, patients who did not survive the procedure or up to the follow-up echocardiogram were not included in the study. All subjects are from a single tertiary centre and all echocardiograms were performed by accredited echocardiographers (blinded).

Conclusions

TAVI in patients without significant coronary artery disease, AF or other valvular lesions results in significant improvement of the LV systolic function as assessed by GLS. This improvement is more pronounced in patients with more severe baseline LV systolic function. The difference in GLS before and after TAVI was similar between the Edwards S3 and Evolut R valves. Therefore, the type of valve did not influence the remodelling of LV after TAVI. However, patients with Evolut R had a higher rate of moderate paravalvular leak, which could potentially have an impact on the LV function in the long-term. The findings of this study suggest that GLS might be a more sensitive method of left ventricular assessment after TAVI compared to the EF, as it can potentially detect changes of the left ventricular function even in the short-term follow-up. Further studies should be considered to expand the current work and identify the potential role of GLS in patients with aortic stenosis being considered for TAVI.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding

This review did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

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Received in final form 18 July 2020
Accepted 28 July 2020
Accepted Manuscript published online 29 July 2020