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Changes of left ventricular mechanics after trans-catheter aortic valve implantation and surgical aortic valve replacement for severe aortic stenosis: A tissue-tracking cardiac magnetic resonance study

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ABSTRACT

Background: Left ventricular (LV) mechanics are impaired in patients with severe aortic stenosis (AS). The aim of the present study was to assess their changes early and late after trans-catheter aortic valve implantation (TAVI) and surgical aortic valve replacement (AVR) using cardiac magnetic resonance (CMR) tissue-tracking imaging.
Methods: In 59 patients with severe AS undergoing either TAVI ($n = 35$) or surgical AVR ($n = 24$), CMR with late gadolinium enhancement (LGE) imaging was performed before and early post-procedure to evaluate LV function and mass, and presence/extent of LGE. A third CMR scan was performed in 29 patients after a mean follow-up of 15 ± 4 months. Tissue-tracking analysis was applied to cine CMR images, to assess LV global longitudinal (GLS), circumferential (GCS) and radial (GRS) strains.
Results: The TAVI and surgical AVR groups were similar with respect to baseline ($p = 0.14$) and early post-procedure ($p = 0.16$) LV ejection fraction. However, baseline LV GLS was significantly impaired in TAVI patients compared to surgical AVR patients ($p = 0.025$). Early post-procedure, TAVI resulted in a significant improvement of LV GLS ($p = 0.003$), while a significant worsening of LV GLS was observed early after surgical AVR ($p = 0.012$). At longer term follow-up, both TAVI and surgical AVR groups experienced a significant reduction of LV mass and a significant improvement of LV myocardial mechanics in all the three directions.
Conclusions: Treatment-specific differences in the changes of LV myocardial mechanics early after afterload release by TAVI and surgical AVR are present. Later, both interventions are associated with an improvement of LV myocardial deformation, alongside a regression of LV hypertrophy.

1. Introduction

Severe aortic stenosis (AS) is characterized by left ventricular (LV) geometry and functional changes, which are caused by long-lasting pressure overload [1,2]. In the earlier stage of the disease, increased LV wall thickness is able to counterbalance the high mid-wall stress and to maintain normal LV systolic function [1,2]. Later, when the LV pressure overload exceeds the LV hypertrophy, an impairment in LV performance is observed; of note, changes in LV mechanics commonly precede the decline of LV ejection fraction (EF), which can be preserved until end-stage disease; consequently, their identification, through the use of myocardial deformation imaging techniques, may be helpful for timely patient referral to aortic valve replacement (AVR).

Previous speckle-tracking echocardiography studies have consistently demonstrated a significant improvement of LV myocardial deformation parameters after surgical AVR among patients with severe AS and preserved LVEF [1,3,4]; however, this improvement is not observed immediately after surgery but usually lags behind until 6 months later [3,4]. While surgical AVR is considered the gold standard therapy for symptomatic severe AS, trans-catheter aortic valve implantation (TAVI) has emerged as a valid treatment option for those patients deemed at too high or prohibitive risk for conventional surgery [5,6]. Compared to surgical AVR, TAVI may represent a better model to investigate the acute changes of LV function after afterload release, because confounding factors influencing LV function related to the surgical intervention (such as the use of myocardial protection) and the post-operative period are not present [7].

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Our group recently reported on the early effects of TAVI and surgical AVR on myocardial function and aortic valve haemodynamics as assessed by cardiac magnetic resonance (CMR) imaging [8,9]; CMR provides indeed the unique opportunity to non-invasively evaluate LV volumes and mass, trans-valvular and trans-prosthetic flows and replacement fibrosis during a single examination with high accuracy and reproducibility. In our previous investigation, we did not observe any difference in early overt changes of LV systolic function, as assessed by LVEF, between TAVI and surgical AVR patients [8]. In the present study, we aim to investigate the subclinical changes of LV myocardial mechanics early and late after TAVI and to compare them with those observed early and late after surgical AVR in a cohort of consecutive patients with symptomatic severe AS. To this end, a recently introduced tissue-tracking CMR software system, which permits assessment of LV myocardial mechanics directly from cine CMR images without any need for a specific encoding pulse [10–13], was used.

2. Methods

2.1. Patient selection and study protocol

Patients with symptomatic severe AS referred for AVR were assessed by the heart team, taking into consideration age, comorbidities, risk scores, and frailty. A clinical decision then determined whether the individual proceeded to TAVI or surgical AVR. Patients undergoing TAVI who were included were all from the high-risk cohort. To limit bias, a high-risk cohort of patients referred to surgical AVR was selected for comparison purpose. Inclusion criteria were EuroSCORE > 12, age > 70 years, and subjective frailty assessment. Additionally, patients with a pre-procedure LV ejection fraction <45% were excluded to maintain homogeneity in peri-procedural functional assessment.

Patients who met selection criteria had pre-procedural and post-procedural CMR with late gadolinium enhancement imaging (LGE) within 14 days of their procedure, to assess LV function and mass, trans-aortic valve and trans-prosthetic flow indices and presence/extent of LV scar/fibrosis; furthermore, tissue-tracking analysis was applied to cine CMR images to assess LV myocardial strain in the three directions (radial, circumferential, and longitudinal). A third CMR scan was also performed in consenting patients after a mean follow-up of 15 ± 4 months. All patients underwent pre-procedural coronary angiography.

The study was approved by the Human Research Ethics Committee and all patients gave written informed consent.

2.2. TAVI and surgical AVR techniques

All open surgery procedures were performed by experienced cardiothoracic surgeons. Techniques were similar, being standard median sternotomy and cardiopulmonary bypass with diastolic arrest achieved by antegrade tepid blood cardioplegia. Three tissue valve prostheses were used: Medtronic Mosaic (Medtronic Inc., Minneapolis, Minn), St Jude Medical Epic (St Jude Medical Inc., St Paul, Minn), and Trifecta (St Jude Medical Inc). Transcatheter valve procedures were performed by an interventional cardiologist and cardiac surgeon. All TAVIs were performed using combined angiography and transoesophageal echocardiography guidance. All procedures used the Edwards Sapien XT prosthesis (Edwards Lifesciences, Irvine, Calif) deployed transfemorally.

2.3. Coronary angiography analysis

Severity of coronary artery lesions was quantified using quantitative coronary angiography (QCA) by automated software and assessed visually when not suitable for QCA. A cutoff of >50% diameter stenosis was used to classify single, double, or triple vessel disease. Any lesion (>70% diameter stenosis by QCA) that was not revascularized was labelled incompletely revascularized.

2.4. CMR imaging protocol and data analysis

CMR studies were performed using a 1.5 Tesla scanner (Siemens Aera, Erlangen, Germany) and analysed using commercially available software (CMR^{42}, Circle Cardiovascular Imaging, Calgary, Canada). Cine images of vertical and horizontal long-axis and three-chamber slice and of a stack of contiguous short-axis slices from the atrioventricular ring to the apex were acquired using a steady-state free-precession pulse sequence (TE/TR 1.5/3.0 ms, flip angle 60°). Forward and regurgitant aortic flows were assessed using through-plane phase-contrast velocity mapping (free breathing, retrospective gating). The image plane was placed approximately 0.5 cm above the aortic valve at end-diastole, and maintained throughout the cardiac cycle. Commercially available gadolinium-based contrast agent (Gadovist 1.0, Gadobutrol; Bayer Healthcare, Berlin, Germany) was given to those patients with a glomerular filtration rate > 45 ml/min/m^2. Images were acquired after a 6-minute delay with the use of an inversion-recovery segmented gradient echo sequence. LGE images were acquired in identical long- and short-axis planes to the cine images, except for the most apical short-axis slice, which was excluded.

Biventricular volumes and function and LV mass were measured using standard volumetric technique from the cine short-axis images. Volume and mass measurements were indexed to body surface area. Trans-aortic valve and trans-prosthetic flow indices were quantified using cross-sectional phase contrast images with contouring of the aortic lumen to derive peak forward flow velocity (m/s), and forward and backward flow volumes (ml), for the calculation of transvalvular pressure gradient and regurgitant fraction (%).

Images were visually assessed for the presence of LGE areas; regions of elevated signal intensity had to be confirmed in two spatial orientations. The quantitative extent of LV LGE was determined. The LV myocardium was delimited by endocardial and epicardial contours, which were traced manually and a region of interest (ROI) was selected in effectively nulled myocardium. Mean signal intensity and SD of the ROI were measured. Enhanced myocardium was defined as myocardium with a signal intensity >5SD above the mean of the ROI. The extent of LGE was expressed as a percentage of the LV mass (%LV LGE).

2.5. Tissue-tracking analysis

Strain imaging was performed using a post-processing software (Tissue Tracking, CMR^{42}, Circle Cardiovascular Imaging, Calgary, Canada) that tracks every LV myocardial voxel through the cardiac cycle; its algorithm has been previously described [14]. Following uploading of the cine basal and apical short-axis images, the brightness was optimized to ensure optimal endocardial/blood pool discrimination; the mitral valve annular plane and the position of LV apex were then manually identified at end-diastole. The LV endocardial and epicardial borders (excluding papillary muscles and trabeculae) were then manually traced on the end-diastolic frame on long-axis and short-axis cine images; the software automatically propagated the contour and followed its features throughout the remainder of the cardiac cycle. Adjustment of contour tracking was done after visual assessment during cine loop playback to ensure that the LV segments were tracked appropriately. As the LV myocardial architecture consists of longitudinally and circumferentially orientated fibers located predominately in the epicardium/endocardium and mid-wall, respectively, longitudinal, circumferential, and radial strains are reflective of subendocardial, mid-wall, and transmural myocardial functions, respectively [15]. Global peak systolic longitudinal strain (GLS) was derived from the long-axis cine image analysis while global peak systolic circumferential (GCS) and radial (GRS) strains were derived from the short-axis cine image analysis (Fig. 1).

2.6. Statistical analysis

Continuous variables are expressed as mean and SD. Categorical data are presented as absolute numbers and percentages. Differences in continuous variables between two groups were assessed with the Student *t*-test or the Mann–Whitney *U* test, where appropriate. Chi-square or Fisher's exact test, where appropriate, was computed to assess differences in categorical variables. Comparisons between baseline and follow-up were performed with the Student *t*-test or the Wilcoxon signed rank test for paired continuous data, where appropriate, and the McNemar test for paired categorical data. Linear regression analyses were performed to determine the relations between pre-intervention LV myocardial mechanics and the following variables: 1) logistic EuroSCORE, 2) pre-intervention LV mass index, 3) pre-intervention aortic regurgitation and 4) pre-intervention %LV LGE. Furthermore, linear regression analyses were performed to determine the relations between early and late post-intervention changes (Δ) of LV myocardial mechanics and the following variables, respectively: 1) early and late Δ of LV mass index, 2) early and late Δ of aortic regurgitation and 3) early and late Δ of %LV LGE. Two-tailed tests were considered statistically significant at the 0.05 level. Statistical analysis was performed using the SPSS (SPSS 22; SPSS Inc., Chicago, IL) software package.

3. Results

3.1. Clinical characteristics of the patient population

A total of 59 patients were included in the study; 35 patients underwent TAVI while 24 patients underwent surgical AVR. The pre-operative clinical characteristics of the two groups are presented in Table 1. Patients in the TAVI group were significantly older ($p = 0.001$), had a higher rate of previous cardiac surgery ($p < 0.001$), higher plasmatic value of pre-operative brain natriuretic peptide ($p = 0.050$), and a higher prevalence of previous cerebrovascular accident ($p = 0.009$); overall, the TAVI group had a higher logistic EuroSCORE ($p = 0.006$). All patients with prior cardiac surgery had previously undergone coronary artery bypass surgery, with coronary angiography demonstrating patent mammary artery grafts in each. There was no significant difference between groups when comparing incompletely revascularized coronary territories (TAVI, 8 out of 105 vs. surgical AVR, 3 out of 72; $p = 0.36$). All patients successfully proceeded as clinically indicated to TAVI or surgical AVR intended group, without no procedure-related mortality in either group. Mean prosthetic valve size was larger in the TAVI group (25 ± 2 mm vs. 23 ± 2 mm; $p < 0.001$). In the surgical group, the mean cardiopulmonary

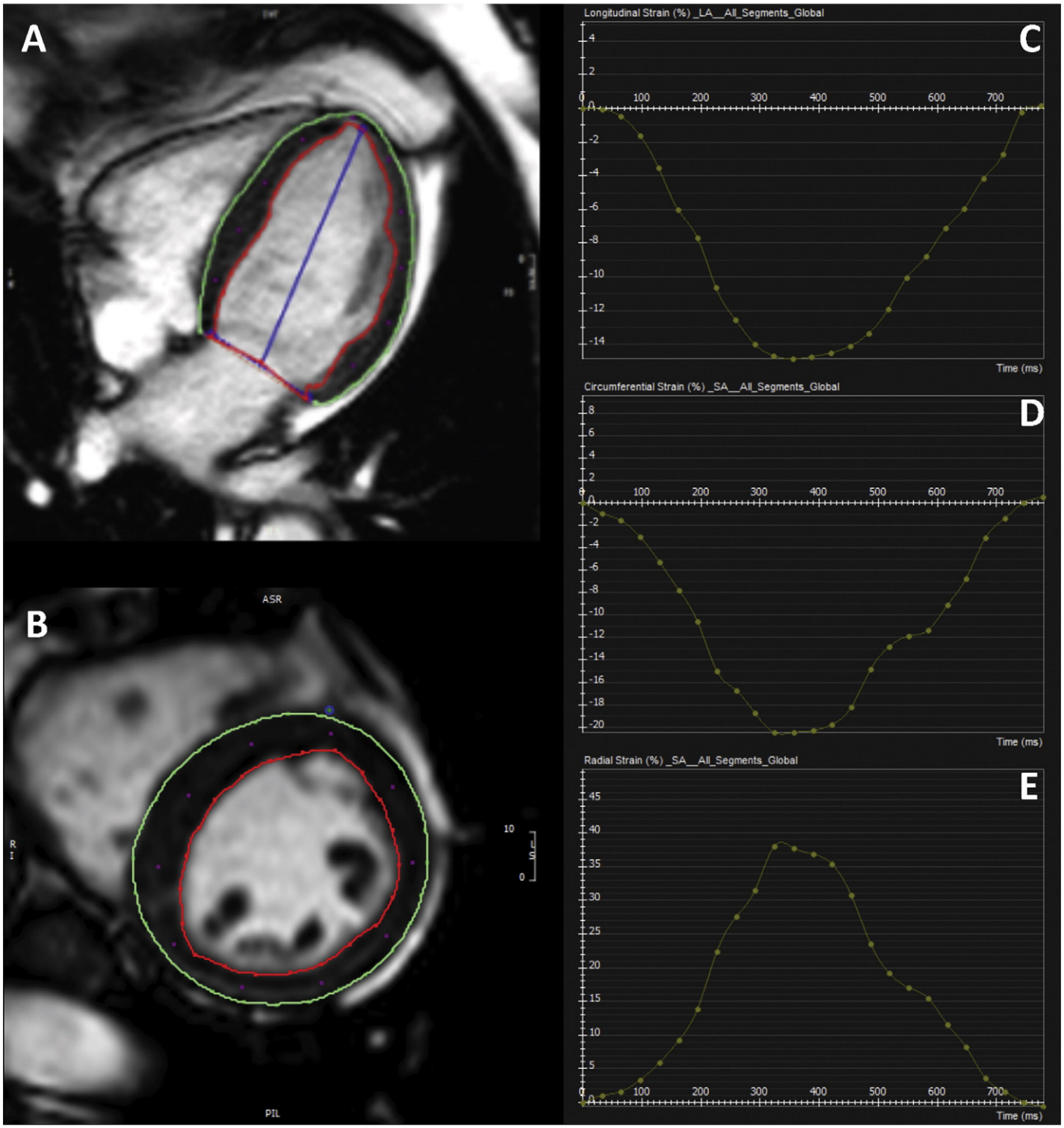

Fig. 1. Tracking of the endocardial and the epicardial border of the left ventricle on a 4-chamber steady-state free precession image (panel A) and on the mid-section of a short-axis view (panel B) using tissue-tracking software. The global left ventricular longitudinal (panel C), circumferential (panel D), and radial (panel E) strain patterns of a patient with severe aortic stenosis are also shown.

bypass and cross-clamp times were 65 ± 13 min and 50 ± 11 min, respectively.

3.2. CMR imaging results

3.2.1. Pre-operative vs. early post-operative changes

Table 2 presents the pre-operative and early post-operative CMR characteristics of the patient population. Mean time to postoperative scan was 4.7 ± 4 days vs. 5.8 ± 2 days for TAVI and AVR patients, respectively ($p = 0.22$). Pre-operatively, LV end-diastolic volume (EDV) and LV end-systolic volume (ESV) were within normal limits and LVEF was preserved in both groups. Post-operatively, no significant change in LVEF was observed in both groups (TAVI: $p = 0.63$; surgical AVR: $p = 0.83$), while a significant reduction of both LVEDV and LVESV was observed among patients referred to surgical AVR ($p < 0.001$ and $p = 0.008$, respectively). No significant change in LV mass index was observed early after intervention in both groups (TAVI: $p = 0.27$; surgical AVR: $p = 0.55$). Post-intervention, a similar

significant reduction of peak trans-aortic velocity was observed in both groups ($p < 0.001$ for both). Aortic regurgitant fraction remained unchanged in the TAVI group ($p = 0.32$) while it significantly decreased in the surgical AVR group ($p = 0.025$); consequently, while no significant difference in aortic regurgitant fraction was observed preoperatively between the two groups ($p = 0.22$), post-intervention aortic regurgitant fraction was significantly greater in the TAVI cohort compared to the surgical AVR group ($p < 0.001$).

Pre-procedure and post-procedure assessment of LV scar/fibrosis by LGE imaging was performed in 43 patients (26 patients in the TAVI group and 17 in the surgical AVR group) and 44 patients (27 patients in the TAVI group and 17 in the surgical AVR group), respectively. At baseline, LV LGE, expression of scar/fibrosis, was observed in 73% and 59% of patients referred to TAVI and surgical AVR, respectively ($p = 0.51$); %LV LGE was similar between the two groups ($p = 0.41$). Post-operatively, no significant change in the prevalence of LV LGE compared to baseline was observed in both groups ($p = 1.0$ and $p = 0.50$, respectively); however, %LV LGE significantly increased in both groups ($p = 0.023$ in the TAVI group and $p = 0.020$ in the surgical AVR group). The magnitude of increase of %LV LGE was similar between the two groups ($p = 0.36$).

3.2.2. Late post-operative changes

After a mean follow-up of 15 ± 4 months, a third CMR scan was performed in 29 consenting patients (17 in the TAVI group and 12 in the surgical AVR group). Both LVEDVi (77 ± 21 ml/m^2) and LVESVi (25 ± 18 ml/m^2) significantly decreased in the TAVI cohort, when compared to those observed at post-intervention ($p = 0.040$ and $p = 0.010$, respectively); in the surgical AVR group, no significant changes in LVEDVi (59 ± 13 ml/m^2) and LVESVi (14 ± 7 ml/m^2) were conversely observed ($p = 0.95$ and $p = 0.77$, respectively). LVEF did not change compared to post-intervention in both groups (TAVI: 70 ± 14%, $p = 0.11$; surgical AVR: 78 ± 8%, $p = 0.40$, respectively), while a significant reduction in LV mass index was observed in both cohorts (TAVI: 67 ± 20 g/m^2, $p = 0.012$; surgical AVR: 51 ± 8; $p = 0.009$). The magnitude of decrease of LV mass index was similar between the two groups (ΔLV mass index = −5.8 ± 8.4 g/m^2 in the TAVI group vs. −13 ± 14 g/m^2 in the surgical AVR group; $p = 0.14$). Peak trans-aortic velocity significantly decreased in the surgical AVR group compared to post-intervention (2.42 ± 0.51 m/s; $p = 0.015$), while it did not change significantly in the TAVI cohort (2.16 ± 0.33 m/s; $p = 0.50$). Aortic regurgitant fraction did not significantly change in both groups compared to post-intervention (TAVI: 14 ± 13%; $p = 0.23$; surgical AVR: 5.1 ± 3.2%; $p = 0.20$).

Assessment of LV scar/fibrosis by LGE imaging was performed in 17 patients (9 patients in the TAVI group and 8 in the surgical AVR group). The prevalence of LV LGE was similar to that observed post-intervention in both groups (89% in the TAVI group and 71% in the surgical AVR group; $p = 1.0$ for both) and the %LV LGE did not significantly change in both groups compared to post-intervention (TAVI: 10 ± 11%, $p = 0.39$; surgical AVR: 3.9 ± 6.5%, $p = 0.38$, respectively).

Table 1
Preoperative clinical characteristics of patient population.

	TAVI ($n = 35$)	Surgical AVR ($n = 24$)	p value
Age (years)	85 ± 6	80 ± 4	0.001
Male gender	22 (63%)	9 (38%)	0.068
Diabetes	12 (34%)	11 (46%)	0.42
Hypertension	31 (89%)	21 (88%)	1.00
Hypercholesterolemia	29 (83%)	17 (71%)	0.34
Previous myocardial infarction	7 (20%)	3 (13%)	0.51
Previous percutaneous coronary intervention	11 (31%)	3 (13%)	0.13
Redo	14 (40%)	0 (0%)	<0.001
Atrial fibrillation	10 (29%)	6 (25%)	0.78
Pulmonary arterial hypertension	6 (17%)	9 (38%)	0.13
Logistic EuroSCORE	28 ± 13	21 ± 7	0.006
Brain natriuretic peptide (pg/ml)	1525 (657–2337)	834 (313–1088)	0.050
Chronic obstructive pulmonary disease	13 (37%)	11 (46%)	0.59
Renal impairment	11 (31%)	9 (38%)	0.78
Previous cerebrovascular accident (stroke or transient ischemic attack)	12 (34%)	1 (4%)	0.009

Data are expressed as mean ± standard deviation or median (interquartile range) and n (%).
Abbreviations: AVR: aortic valve replacement; TAVI: trans-catheter aortic valve implantation.

Table 2
Pre-operative and early post-operative cardiac magnetic resonance characteristics of patient population.

	TAVI	Surgical AVR	p value
Left ventricular end-diastolic volume index (ml/m^2)			
- Pre-operative	80 ± 21	71 ± 18	0.11
- Post-operative	81 ± 21*	59 ± 13∫	<0.001
- Δ post-operative vs. pre-operative	0.91 ± 11	−12 ± 12	<0.001
Left ventricular end-systolic volume index (ml/m^2)			
- Pre-operative	28 ± 21	20 ± 11	0.062
- Post-operative	27 ± 19*	16 ± 8¶	0.002
- Δ post-operative vs. pre-operative	−0.31 ± 6.5	−4.1 ± 6.9	0.036
Left ventricular ejection fraction (%)			
- Pre-operative	68 ± 16	73 ± 10	0.14
- Post-operative	69 ± 14*	74 ± 10*	0.16
- Δ post-operative vs. pre-operative	0.54 ± 6.6	0.38 ± 8.4	0.93
Left ventricular mass index (g/m^2)			
- Pre-operative	77 ± 19	69 ± 20	0.14
- Post-operative	76 ± 19*	69 ± 21*	0.17
- Δ post-operative vs. pre-operative	−0.80 ± 4.2	−0.29 ± 2.3	0.55
Peak trans-aortic valve velocity (m/s)			
- Pre-operative	3.44 ± 0.85	3.54 ± 0.75	0.64
- Post-operative	2.26 ± 0.40∫	2.52 ± 0.61∫	0.076
- Δ post-operative vs. pre-operative	−1.21 ± 0.88	−0.98 ± 0.71	0.33
Aortic regurgitant fraction (%)			
- Pre-operative	17 ± 15	12 ± 15	0.22
- Post-operative	16 ± 11*	5 ± 3†	<0.001
- Δ post-operative vs. pre-operative	−2.7 ± 16	−7.5 ± 14	0.26
LV LGE			
- Pre-operative	19/26 (73%)	10/17 (59%)	0.51
- Post-operative	20/27 (74%)*	12/17 (71%)*	1.0
%LV LGE			
- Pre-operative	7.4 ± 9.2	4.2 ± 7.3	0.23
- Post-operative	8.1 ± 8.8†	5.0 ± 7.8†	0.24
- Δ post-operative vs. pre-operative	1.7 ± 3.4	0.83 ± 1.3	0.36

Data are expressed as mean ± standard deviation and n (%).
Abbreviations: AVR: aortic valve replacement; LGE: late gadolinium enhancement; TAVI: trans-catheter aortic valve implantation.
* $p > 0.05$ vs. pre-operative.
¶ $p < 0.01$ vs. pre-operative.
∫ $p < 0.001$ vs. pre-operative.
† $p < 0.05$.

3.3. Strain analysis

3.3.1. Pre-operative vs. early post-operative changes

Fig. 2 shows the pre-intervention and post-intervention values of LV GLS, GCS and GRS in the two groups. Pre-operatively, significantly lower values of LV GLS and GRS were observed in the TAVI group, compared to the surgical AVR cohort ($p = 0.025$ and $p = 0.046$, respectively). Early post-operatively, GLS significantly improved in the TAVI group ($p = 0.003$), while it significantly worsened in the surgical AVR cohort ($p = 0.012$). Overall, the post-intervention changes of GLS and GCS were significantly different between the two groups (ΔGLS: −1.16 ± 2.12% in the TAVI group vs. 1.95 ± 3.52% in the surgical AVR group; $p < 0.001$; ΔGCS: −0.53 ± 2.83% in the TAVI group vs. 1.59 ± 4.51% in the surgical AVR group; $p = 0.032$), while the change of GRS was

not significantly different (1.13 ± 7.9% in the TAVI group vs. −3.29 ± 11% in the surgical AVR group; $p = 0.081$).

At linear regression analysis (Table 3), pre-intervention LV myocardial mechanics were significantly related to logistic EuroSCORE, pre-intervention LV mass index and pre-intervention %LV LGE; however, no significant relation was observed between pre-intervention LV myocardial mechanics and pre-intervention aortic regurgitant fraction, as well as between early Δ of LV myocardial mechanics and early Δ of LV mass index, early Δ of aortic regurgitant fraction and early Δ of %LV LGE.

3.3.2. Late post-operative changes

In the late post-operative scan, a significant improvement of LV myocardial strains in the three directions was observed in both groups compared to the early post-intervention scan (TAVI group: GLS −16.0 ± 4.1%, $p = 0.006$; GCS: −19.1 ± 3.9, p 0.014; GRS: 36.4 ± 10.7%, $p = 0.019$; surgical AVR group: GLS −18.4 ± 2.2%, $p = 0.018$; GCS: −21.2 ± 2.8, p 0.032; GRS: 43.8 ± 8.9%, $p = 0.035$), in keeping with an enhancement of global LV function. The magnitude of improvement of LV myocardial strains was not statistically different between the two groups (ΔGLS: −0.88 ± 1.16% in the TAVI vs. −3.1 ± 3.8% in surgical AVR group; $p = 0.077$; ΔGCS: −0.96 ± 1.44% in the TAVI vs. −2.2 ± 3.1% in surgical AVR group; $p = 0.22$; ΔGRS: 2.92 ± 4.6% in the TAVI vs. 6.4 ± 9.3% in surgical AVR group; $p = 0.25$).

At linear regression analysis (Table 3), late Δ of LV myocardial mechanics were significantly related to late Δ of LV mass index, while they were not related to late Δ of aortic regurgitant fraction and late Δ of %LV LGE.

4. Discussion

The results of the present study can be summarized as follows: 1) AS patients referred to TAVI have reduced LV myocardial mechanics compared to AS patients referred to surgical AVR; 2) LV myocardial mechanics in AS patients are significantly related to the cardiac surgery risk profile, the extent of LV hypertrophy and the extent of LV scar/fibrosis; 3) TAVI results in an immediate improvement of LV GLS, while a significant worsening of LV GLS is observed early after surgical AVR; 4) post-intervention changes of LV myocardial mechanics are not related to the post-intervention change of aortic regurgitation and the post-intervention change of LV scar/fibrosis; 5) at longer term follow-up, both TAVI and surgical AVR groups experience a significant improvement of myocardial mechanics in all the three directions, consistent with an improvement in global LV function; and 6) the improvement of LV myocardial mechanics observed long-term is significantly related to the reduction LV hypertrophy.

4.1. Myocardial mechanics in AS

Even though commonly used in clinical practice, LVEF is an insensitive and often misleading index of the contractile properties of LV myocardium [2]. Non-invasive imaging techniques aiming to directly assess LV myocardial deformation (such as speckle-tracking echocardiography) have indeed demonstrated an impairment of myocardial contractility in AS patients despite the presence of normal LVEF; alterations in myocardial perfusion and metabolism and the development of ischemia and fibrosis have been advocated as possible explanations for this finding [16–21]. Impaired coronary flow reserve, which occurs because of reduced myocardial supply related to both decreased coronary perfusion pressure and increased myocardial metabolic demand due to increased LV workload, may lead to repetitive episodes of myocardial ischemic injury [16,17]. As a consequence of continued ischemia and myocardial hibernation, fibrotic tissue replacement may eventually occur [22], negatively influencing LV myocardial mechanics [18,20,21]. Altered myocardial substrate utilization, with a preference to glucose metabolism and down-regulation of fatty acid oxidation, and consequent excessive myocardial triglyceride accumulation (steatosis), has also been demonstrated to be independently linked to the degree of LV strain impairment in patients with severe AS [19]. The higher susceptibility of subendocardial fibers to increased wall stress and reduced myocardial perfusion explains the progressive subendocardial to transmural impairment of myocardial function observed with increasing AS severity and chronic pressure overload [2,18]. Mild AS is indeed characterized by an impairment of GLS, which is reflective of subendocardial myocardial function, while GCS and GRS, reflective of midwall and transmural myocardial functions respectively, are still preserved [1]. The development of severe AS is conversely associated with a significant impairment of LV myocardial deformation in all the three directions (i.e. longitudinal, circumferential and radial), even if LVEF is still preserved [1,2].

In the present study, a significant inverse relation between LV strain parameters and the cardiac surgery risk profile was found, partially explaining the lower LV strain value observed in AS patients referred to TAVI (which were older and with a higher logistic EuroSCORE) compared to those referred to surgical AVR. In addition, a significant inverse

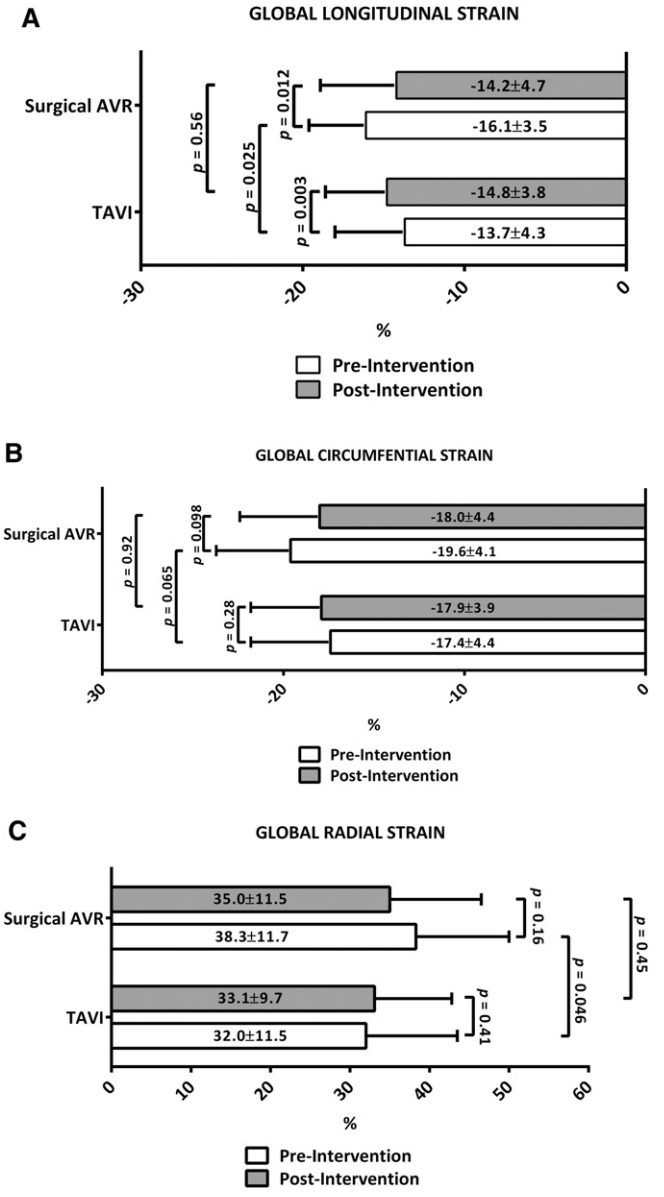

Fig. 2. Pre-intervention and post-intervention left ventricular myocardial strains in the three directions (longitudinal, panel A, circumferential, panel B, and radial, panel C) in the trans-catheter aortic valve implantation (TAVI) and surgical aortic valve replacement (AVR) groups.

Table 3
Results of linear regression analyses performed to determine significant correlates of pre-intervention LV myocardial mechanics as well as their early and late post-intervention changes (Δ).

	β value	p value
Pre-intervention global longitudinal strain		
Logistic EuroSCORE	0.45	<0.001
Pre-intervention LV mass index	0.46	<0.001
Pre-intervention aortic regurgitant fraction	0.073	0.60
Pre-intervention %LV LGE	0.38	0.011
Pre-intervention global circumferential strain		
Logistic EuroSCORE	0.44	0.001
Pre-intervention LV mass index	0.38	0.003
Pre-intervention aortic regurgitant fraction	0.032	0.82
Pre-intervention %LV LGE	0.50	0.001
Pre-intervention global radial strain		
Logistic EuroSCORE	−0.43	0.001
Pre-intervention LV mass index	−0.40	0.002
Pre-intervention aortic regurgitant fraction	−0.066	0.63
Pre-intervention %LV LGE	−0.45	0.003
Early Δ global longitudinal strain		
Early Δ LV mass index	−0.071	0.59
Early Δ aortic regurgitant fraction	−0.25	0.068
Early Δ %LV LGE	−0.17	0.28
Early Δ global circumferential strain		
Early Δ LV mass index	−0.10	0.44
Early Δ aortic regurgitant fraction	0.033	0.81
Early Δ %LV LGE	−0.059	0.72
Early Δ global radial strain		
Early Δ LV mass index	0.14	0.31
Early Δ aortic regurgitant fraction	−0.042	0.76
Early Δ %LV LGE	0.002	0.99
Late Δ global longitudinal strain		
Late Δ LV mass index	0.49	0.007
Late Δ aortic regurgitant fraction	−0.24	0.23
Late Δ %LV LGE	0.035	0.88
Late Δ global circumferential strain		
Late Δ LV mass index	0.45	0.014
Late Δ aortic regurgitant fraction	−0.24	0.23
Late Δ %LV LGE	0.12	0.66
Late Δ global radial strain		
Late Δ LV mass index	−0.50	0.006
Late Δ aortic regurgitant fraction	0.31	0.13
Late Δ %LV LGE	−0.10	0.71

Abbreviations: LGE: late gadolinium enhancement.

relation between LV strain parameters and the extent of LV hypertrophy (i.e. LV mass index) and the extent of LV scar/fibrosis (i.e. %LV LGE) was observed, confirming previous observations [1,2,18,20,21,23].

4.2. Changes of LV myocardial mechanics after TAVI and surgical AVR

Previous studies have investigated the changes of LV myocardial deformation late after surgical AVR, consistently demonstrating an improvement of LV strain in all the three directions after a period of at least 6 months [1,3,24]. However, fewer data are available regarding the changes of LV strain early after surgical AVR. Lindqvist et al. have shown a lack of improvement of lateral LV longitudinal strain 1 week after surgical AVR [4]; similarly, Rost and colleagues did not observe any significant change of LV strain values within 1 week after surgical AVR [3]. The assessment of changes in LV myocardial deformation early after surgical AVR is however limited by several confounding factors associated with the surgical procedure itself and the post-operative period (i.e. use of myocardial protection, cardiopulmonary bypass and inotropic agents); conversely, the isolated removal of LV pressure overload due to TAVI may represent a better model to investigate the acute changes of LV function in AS patients [7,25].

In the present study, treatment-specific differences in the changes of LV myocardial mechanics early after afterload release by TAVI and surgical AVR were observed. AS patients referred to surgical AVR experienced a significant decline of LV GLS early after intervention; this finding is likely explained by the stunning of the subendocardial longitudinally oriented myocardial fibers (which are more vulnerable than the circumferentially oriented mid-wall fibers) due to the ischemia-reperfusion injury and marked activation of systemic inflammatory response facilitated by cardioplegia and the use of cardiopulmonary bypass [26–28]. Conversely, a significant improvement of LV GLS was observed early after intervention in AS patients referred to TAVI, likely related to the beneficial effect of pure pressure unloading on subendocardial layer, through an improvement of coronary flow reserve and myocardial arterial supply [1,16,29]. At longer term follow-up, an improvement of LV myocardial deformation in all the three directions was observed in both groups; the regression of LV hypertrophy related to LV unloading at early stage and correction of neurohormonal imbalances later helped to further improve LV performance, by improving the transmural myocardial perfusion [1,29,30].

4.3. Study limitations

This study has some limitations that should be acknowledged. First, this trial lacked a randomized design; however, TAVI remains utilized largely in the inoperable cohort, limiting randomization. As expected, patients in the TAVI group were significantly older because they consisted of both technically and medically high-risk patients, with a higher rate of redo cases. Second, the study population was relatively small and only a minority of patients underwent a long-term follow-up CMR examination; consequently, our results need to be confirmed by further prospective studies with larger sample size. Third, LGE imaging, which allows detection of LV scar and replacement fibrosis, was not performed in all patients, and T1 mapping, which allows detection of extracellular volume expansion because of interstitial fibrosis, was not part of the CMR protocol. Fourth, clinical follow-up data were not available; consequently, no information can be provided about the prognostic role of LV deformation parameters and their post-intervention changes in severe AS patients. To this end, larger studies with long-term follow-up are necessary.

5. Conclusions

Myocardial deformation analysis by tissue-tracking CMR demonstrates treatment-specific differences in the changes of LV myocardial mechanics early after afterload release by TAVI and surgical AVR; TAVI is able to immediately determine an improvement of LV GLS, while a transient reduction of LV GLS is observed early after surgical AVR. At longer-term follow-up, both interventions are associated with an improvement of LV myocardial deformation in all the three directions.

Disclosures

No conflicts of interest, financial or otherwise, are declared by the authors.

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