International Journal of Cardiology 228 (2017) 184–190

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

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

Gaetano Nucifora [a,c,*], John-Paul Tantiongco [a,b,c], Gareth Crouch [b,c], Jayme Bennetts [b,c], Ajay Sinhal [b,c], Phillip J. Tully [b,c], Craig Bradbrook [b], Robert A. Baker [b,c], Joseph B. Selvanayagam [a,b,c]

[a] *Department of Hearth Health, South Australian Health & Medical Research Institute, Adelaide, Australia*
[b] *Department of Cardiovascular Medicine, Flinders Medical Centre, Bedford Park, Adelaide, Australia*
[c] *Flinders University, Bedford Park, Adelaide, Australia*

ARTICLE INFO

Article history:
Received 31 August 2016
Accepted 6 November 2016
Available online 09 November 2016

Keywords:
Aortic stenosis
Cardiac magnetic resonance
Fibrosis
Hypertrophy
Myocardial mechanics
Tissue-tracking

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].

---

* Corresponding author at: Department of Heart Health, South Australian Health & Medical Research Institute (SAHMRI), North Terrace, Adelaide, 5000, SA, Australia and Flinders University, Bedford Park, Adelaide, 5047, SA, Australia.
E-mail address: gaetano.nucifora@sahmri.com (G. Nucifora).

http://dx.doi.org/10.1016/j.ijcard.2016.11.200
0167-5273/© 2016 Elsevier Ireland Ltd. All rights reserved.

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 preoperative 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