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Effects of transcatheter aortic valve implantation on ascending aorta wall elastic properties: Tissue Doppler imaging and strain Doppler echocardiography study☆

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A R T I C L E I N F O

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Background: Aortic elastic properties are determinants of left ventricular function by means of ventriculo-arterial coupling and indicators of cardiovascular risk. Aortic valve stenosis surgical replacement temporary reduces aortic function damaging vasa vasorum, while transcatheter aortic valve implantation (TAVI) does not influence it in the short term. We studied aortic distensibility, stiffness, M-mode strain and tissue strain after 6 and 12 months from TAVI.
Methods: We enrolled 15 patients with symptomatic severe aortic stenosis who underwent CoreValve prosthesis (Medtronic, Minneapolis, MN) implantation. Everyone had blood pressure measurement and echocardiography registration before TAVI and after 6 and 12 months.
Results: After TAVI NYHA class ($p = 0.016$), peak and mean aortic valve gradients ($p < 0.001$ for both) improved. Aortic distensibility increased ($p = 0.032$ in the first 6 months, $p = 0.005$ in the second 6 months, and $p = 0.003$ from baseline to 12 months), as well as stiffness decreased ($p = 0.034$; 0.090; 0.001), M-mode strain and tissue strain ameliorated ($p = 0.041$; 0.004; 0.004; and $p = 0.013$; 0.002; 0.001, respectively), tissue Doppler imaging improved (S′ wave: $p = 0.289$; 0.347; 0.018. E′ wave: $p = 0.018$; 0.113; 0.007. A′ wave: $p = 0.002$; 0.532; 0.001). Moreover, some left ventricular parameters improved at 6 months, such as ejection fraction (from 49 ± 16 to 57 ± 11%; $p = 0.044$) and diastolic interventricular septum thickness (from 14 ± 2 to 12 ± 2 mm; $p = 0.010$). Even systolic pulmonary artery pressure ($p = 0.019$) and left diastolic dysfunction grade ameliorated ($p = 0.042$).
Conclusions: For the first time we demonstrated that aortic elastic properties improve at 6 and 12 months after TAVI, thus influencing ventriculo-arterial coupling and ameliorating left ventricular function.

1. Introduction

Aortic elastic properties are important determinant of left ventricular function by means of ventriculo-arterial coupling. They also influence coronary blood flow and are independent prognostic factors of cardiovascular risk [1,2]. Geometry of aorta, qualities of its wall, pressure in it, autonomic nervous system and perfusion via vasa vasorum flow: all determine aortic elastic properties [3–5]. Therefore, they are altered in several pathologic conditions involving aorta and aortic valve [6–10]. Aortic valve stenosis is a quite frequent valvular disease which could require a surgical treatment [11,12]. It could be done in open or transcatheter. Open chest surgery is still considered the gold standard for symptomatic patients, but recently transcatheter aortic valve implantation (TAVI) is an option for patients at high surgical risk [13–18]. After open surgery vasa vasorum are removed or damaged, so that various studies reported a reduction of aortic elastic properties; vice versa TAVI do not alter them [19–21]. Insofar, it is reasonable to hypothesize that elastic aortic properties may remain stable or improve after the procedure. A recent work by Vavuranakis M et al. in fact found that seven days after TAVI aortic distensibility and stiffness do not change [22]. However, to date, no studies have been published with a longer follow-up (for example 6 or 12 months). In addition, none have evaluated TAVI effects on aortic elastic properties by means of M-mode strain and tissue strain of aortic wall. The aim of the present

☆ Every author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.
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study was to evaluate aortic distensibility, stiffness, M-mode strain and tissue strain 6 and 12 months after TAVI compared with pre-procedural ones.

2. Methods

2.1. Subjects

From January 2011 to August 2011 we consecutively enrolled 15 patients with symptomatic severe aortic stenosis and left ventricular ejection fraction >45% who underwent successful TAVI at the Cardiologic Unit of University Civil Hospital of Brescia, Italy.

Patients were treated with TAVI if the aortic valve area was <1 cm^2, if the European System for Cardiac Operative Risk Evaluation Score (EuroSCORE) [23] was >20% or if ≥1 of the following criteria was met: contraindication for surgery, severely reduced pulmonary function, liver cirrhosis, or metastatic cancer.

All patients underwent TAVI procedure with a third-generation self-expanding CoreValve prosthesis (Medtronic, Minneapolis, MN). The procedure was performed at the catheterization laboratory under local anesthesia and mild sedation with fluoroscopy guidance. The prosthesis was implanted via the transfemoral approach [13]. Procedural success was defined as implantation of a functioning aortic prosthesis valve without intraprocedural mortality and with a paravalvular leak <2.

Written informed consent was obtained from each patient after the explanation of rationale and study protocol. The investigational protocol was conformed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments and was approved by the institutional committee.

The pre-procedural echocardiography acquisition was performed the same day of the procedure.

2.2. Blood pressure measurement

Blood pressure was assessed using a standard, calibrated sphygmomanometer. The mean of three sitting and standing blood pressures was recorded. The arm in which the highest sitting diastolic pressures found was the arm used for all subsequent readings throughout the study. Every effort was made to have the same staff member obtain blood pressure measurements in each individual patient, at the same time of day, using the same equipment. Systolic pressure was recorded when the initial sound is heard (Phase I of the Korotkoff sound), while diastolic pressure at the disappearance of the sound (Phase V of the Korotkoff sound). The cuff was deflated at a rate not greater than 2 mm Hg/s.

2.3. Echocardiography

Echocardiograms were done using Vivid 7 (General Electric Medical Systems, Milwaukee, WI, USA) equipment with a 3.5 MHz transducer, with the patients in the left lateral decubitus position, in accordance with the standardization of the American Society of Echocardiography [24]. Digital loops were stored on the hard disk of the echocardiograph for on-line and off-line analyses and transferred to a workstation (EchoPac; GE Health-care, Waukesha, WI, USA) for off-line analysis. Left ventricular volumes and ejection fraction were obtained by the modified biplane Simpson method. Aortic valve parameters and left ventricular diastolic function were also evaluated. All these parameters were analyzed the day of the procedure before it and 6 months later, while aortic elastic properties were evaluated even 12 months after TAVI.

All conventional and tissue Doppler imaging (TDI) measurements were taken in five consecutive cycles and the means were used for statistical comparison. Aortic size was assessed at four levels: Valsalva sinuses, sinotubular junction, tubular tract, and aortic arch at the end of diastole. Aortic elastic indexes: distensibility, and stiffness index were calculated from the echocardiographically-derived thoracic aortic diameters (mm/m^2). Aortic elasticity was assessed on the basis of a 2D guided M-mode recording of systolic (AoS) and diastolic (AoD) aortic diameters, 3 cm above the aortic valve. AoD was obtained at the peak of the R wave at the simultaneously recorded ECG, and AoS was measured at the maximal anterior motion of the aortic wall. The following indexes of aortic elasticity were calculated: aortic distensibility $= [2 \times (AoS - AoD) / (AoD \times PP)]\ (10^{-6} \times cm^2 \times dyn^{-1})$; aortic stiffness index $= \ln(SBP / DBP) / [(AoS - AoD) / AoD]$ (pure number) where SBP and DBP refer to brachial systolic and diastolic blood pressure respectively, in mm Hg; pulse pressure (PP) was calculated as SBP–DBP, and ln(SBP / DBP) refers to the natural logarithm of the relative pressure [25]. Parasternal long-axis recordings of the aortic anterior wall were done with activated TDI. Two-dimensional tissue velocity images of the aortic wall were obtained at 130 ± 15 frames/s, which implies a temporal resolution of approximately 16 ms. The velocity scale was modified to avoid aliasing. A sample volume was placed in the region of interest on the anterior aortic wall (3 cm above the aortic valve at the same position as in M-mode measurements). TDI wall velocities during systole (S′), early relaxation (E′) and atrial systole (A′) were measured. Velocity data sets were analyzed off-line using dedicated software (EchoPac; GE Health-care, Waukesha, WI, USA), and peak systolic strain was measured from the resulting deformation curves.

2.4. Statistical analysis

All analyses were carried out using IBM SPSS Statistics 20 for Windows (SPSS, Inc., Chicago, IL). Continuous variables were tested for normality with Kolmogorov–Smirnov test and represented by mean ± standard deviation, while categorical variables as frequency (n) and percentage of the sample. Paired-samples *t* test was performed to analyze the difference between means for continuous variables between baseline, 6 months and 12 months follow-up, and χ^2 test for the difference between proportions for categorical ones. For all statistical tests, probability values <0.05 were considered significant.

3. Results

The characteristics at baseline are summarized in Tables 1 and 2. The mean age was 83 ± 5 years, 6 patients were male (40.0%) and the Logistic EuroSCORE was 28.1 ± 20.8%. Mean Body Mass Index (BMI) was 25.86 ± 4.24 kg/m^2. All patients were symptomatic: 5 in New York Heart Association (NYHA) class II (33.3%), 8 in NYHA class III (53.3%) and 2 in NYHA class IV (13.4%). The peak and mean baseline transvalvular gradient were 83 ± 28 mm Hg and 49 ± 19 mm Hg, respectively. Calculated indexed aortic valve area at baseline was 0.33 ± 0.15 cm^2/m^2 and maximal aortic flow velocity was 4.7 ± 0.6 m/s^2. Baseline dimensions of aorta were: Valsalva sinus diameter of 35 ± 4 mm, sinotubular

Table 1
Baseline characteristics of study populations.

Variable	Value
Age (years)	83 ± 5
Sex (n and % of males)	6/15 (40.0%)
BMI (kg/m^2)	25.86 ± 4.24
BSA (m^2)	1.79 ± 0.14
Logistic EuroSCORE (%)	28.1 ± 20.8
Valsalva sinuses diameter (mm)	35 ± 4
Sinotubular junction diameter (mm)	27 ± 4
Tubular tract diameter (mm)	35 ± 5
Aortic arch diameter (mm)	24 ± 3
Indexed aortic valve area (cm^2/m^2)	0.33 ± 0.15
Maximal aortic flow velocity (m/s)	4.7 ± 0.6

BMI = Body Mass Index; BSA = Body Surface Area; EuroSCORE = European System for Cardiac Operative Risk Evaluation Score.

Table 2
Blood pressure, heart rate and NYHA class.

Variable	0 months	6 months	p
SBP (mm Hg)	121 ± 10	120 ± 9	0.096
DBP (mm Hg)	71 ± 8	70 ± 9	0.164
HR (bpm)	74 ± 11	75 ± 11	0.670
NYHA class	I: 0/15 (0.0%) II: 5/15 (33.3%) III: 8/15 (53.3%) IV: 2/15 (13.4%)	I: 3/15 (20.0%) II: 10/15 (66.7%) III: 2/15 (13.3%) IV: 0/15 (0.0%)	0.016

SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; HR = Heart Rate; NYHA = New York Heart Association.

junction diameter of 27 ± 4 mm, tubular tract diameter of 35 ± 5 mm, and aortic arch diameter of 24 ± 3 mm. At 6 months of follow-up NYHA class improved to 3 patients in NYHA class I (20.0%), 10 in NYHA class II (66.7%), and 2 in NYHA class III (13.3%) ($p = 0.016$), while systolic and diastolic blood pressures and heart rate remained unchanged.

A complete study dataset was available in all patients: the echocardiographic parameters evaluated at baseline and during follow-up of 6 months are summarized in Table 3. There were significant periprocedural reductions in peak (to 19 ± 8 mm Hg; $p < 0.001$) and mean (to 10 ± 5 mm Hg; $p < 0.001$) transvalvular gradients. Left ventricular ejection fraction improved from 49 ± 16% to 57 ± 11% ($p = 0.044$), while end-diastolic and end-systolic volumes not significantly decreased (from 112 ± 45 to 108 ± 39 mL, $p = 0.530$; from 59 ± 43 to 45 ± 19 mL, $p = 0.167$; respectively). Indexed left ventricular mass decreased from 181.8 ± 38.4 to 166.4 ± 38.7 g/m^2 without reaching statistical significance ($p = 0.202$), as well as telediastolic diameter, systolic and diastolic posterior wall thickness and systolic interventricular septum thickness not significantly improved. Only diastolic intraventricular septum thickness significantly decreases after 6 months (from 14 ± 2 to 12 ± 2 mm, $p = 0.010$). Finally, systolic pulmonary artery pressure was significantly reduced by the procedure (from 40 ± 12 to 28 ± 9 mm Hg, $p = 0.019$), but S wave on left ventricular lateral wall increased without statistical significance.

Patients who underwent TAVI showed an improvement in left ventricular diastolic function during 6 months follow-up (see Table 3). In fact, at baseline 9 patients had grade I (60.0%), 5 grade II (33.3%), and 1 grade III (6.7%), while after 6 months from TAVI procedure 3 had normal diastolic function (20.0%), 11 grade I (73.3%), and 1 grade III (6.7%) ($p = 0.042$). Nevertheless, mitral flow and left ventricular TDI parameters did not show statistically significant changes from baseline.

In Table 4 and Fig. 1 aortic elastic properties are resumed, reporting baseline, 6 and 12 months of follow-up parameters. TDI S′ wave significantly improved after 12 months, changing from 5.17 ± 1.37 at baseline to 5.68 ± 1.18 cm/s ($p = 0.018$), but not after 6 months (9.77 ± 16.70 cm/s; p value from baseline to 6 months: 0.289; p value from 6 to 12 months: 0.347). TDI E′ and A′ waves significantly improved only in the first 6 months, respectively moving from −4.42 ± 2.55 to −5.57 ± 2.37 cm/s ($p = 0.018$) and from −6.28 ± 2.27 to −4.76 ± 1.89 cm/s (0.002); vice versa, changes in from 6 to 12 months did not reach significance, being 12-month E′ value −5.68 ± 2.20 cm/s ($p = 0.113$) and A′ value −4.72 ± 1.78 (0.532). Therefore, TDI E′ and A′ waves improvement from baseline to 12 months was statistically significant ($p = 0.007$ and 0.001 respectively). Moreover, aortic distensibility showed an improvement from 2.24 ± 1.69 at baseline to 3.46 ± 3.03 at 6 months ($p = 0.032$) to 4.14 ± 2.96 $10^{-6} \times cm^2 \times dyn^{-1}$ at 12 months (p from 6 to 12 months = 0.005; p from baseline to 12 months = 0.018) and aortic stiffness decreased from 14.05 ± 7.13 at baseline to 10.30 ± 6.99 at 6 months ($p = 0.034$) and to 7.31 ± 4.55 at 12 months (p from 6 to 12 months = 0.090; p from baseline to 12 months = 0.001). In conclusion, aortic strain values significantly improved after 6 and 12 months. In particular, M-mode strain moved from 5.50 ± 4.12 at baseline to 8.67 ± 8.16 at 6 months ($p = 0.041$) and to 10.41 ± 8.03% at 12 months (p from 6 to 12 months and from baseline to 12 months = 0.004), while tissue strain from −14.0 ± 9.2 at baseline to −17.2 ± 7.5 at 6 months ($p = 0.013$) and to −19.9 ± 6.3% at 12 months (p from 6 to 12 months = 0.002; p from baseline to 12 months = 0.001).

Finally, we compared aortic distensibility, stiffness, M-mode strain and tissue strain variations from baseline to 6 months with them from 6 to 12 months of follow-up (Table 5). We found that there were no statistical differences between them.

4. Discussion

This study confirms data reported by Vizzardi E et al. in 2012 regarding left ventricular diastolic function and mass [26]. However, to our knowledge, this is the first study considering mid-term follow-up aortic elastic properties changes (6 and 12 months) after a TAVI, and the first using M-mode strain and tissue strain of aortic wall. Recently, Vavuranakis M et al. demonstrated that 7 days after the procedure aortic distensibility and stiffness remain unchanged [22], in contrast with the early post-surgical period (open chest) in which aortic vasa vasorum are

Table 3
Echocardiographic parameters.

Variable	0 months	6 months	p
Diastolic IVST (mm)	14 ± 2	12 ± 2	0.010
Systolic IVST (mm)	16 ± 4	17 ± 3	0.812
Diastolic PWT (mm)	14 ± 3	12 ± 3	0.127
Systolic PWT (mm)	18 ± 3	19 ± 4	0.565
End-diastolic diameter (mm)	56 ± 8	58 ± 9	0.131
Indexed left ventricular mass (g/m^2)	181.8 ± 38.4	166.4 ± 38.7	0.202
End-diastolic volume (mL)	112 ± 45	108 ± 39	0.530
End-systolic volume (mL)	59 ± 43	45 ± 19	0.167
Ejection fraction (%)	49 ± 16	57 ± 11	0.044
Peak aortic valve gradient (mm Hg)	83 ± 28	19 ± 8	<0.001
Mean aortic valve gradient (mm Hg)	49 ± 19	10 ± 5	<0.001
E wave	0.93 ± 0.33	0.82 ± 0.38	0.390
A wave	0.79 ± 0.40	0.88 ± 0.42	0.513
E/A	1.41 ± 0.95	1.28 ± 1.10	0.678
Deceleration time	217 ± 67	215 ± 39	0.911
E′ wave	3.00 ± 1.29	3.43 ± 1.40	0.356
A′ wave	5.64 ± 0.75	5.21 ± 1.58	0.356
S′ wave	5.67 ± 1.62	6.15 ± 0.76	0.364
E/E′	41.81 ± 30.68	22.02 ± 5.28	0.134
Systolic pulmonary artery pressure (mm Hg)	40 ± 12	28 ± 9	0.019

IVST = InterVentricular Septum Thickness; PWT = Posterior Wall Thickness.

Table 4
Aortic elastic properties.

Variable	0 months	p (0–6 months)	6 months	p (6–12 months)	12 months	p (0–12 months)
S′ wave (cm/s)	5.17 ± 1.37	0.289	9.77 ± 16.70	0.347	5.68 ± 1.18	0.018
E′ wave (cm/s)	−4.42 ± 2.55	0.018	−5.57 ± 2.37	0.113	−5.68 ± 2.20	0.007
A′ wave (cm/s)	−6.28 ± 2.27	0.002	−4.76 ± 1.89	0.532	−4.72 ± 1.78	0.001
Distensibility ($10^{-6} \times cm^2 \times dyn^{-1}$)	2.24 ± 1.69	0.032	3.46 ± 3.03	0.005	4.14 ± 2.96	0.003
Stiffness	14.05 ± 7.13	0.034	10.30 ± 6.99	0.090	7.31 ± 4.55	0.001
M-mode strain (%)	5.50 ± 4.12	0.041	8.67 ± 8.16	0.004	10.41 ± 8.03	0.004
Tissue strain (%)	−14.0 ± 9.2	0.013	−17.2 ± 7.5	0.002	−19.9 ± 6.3	0.001

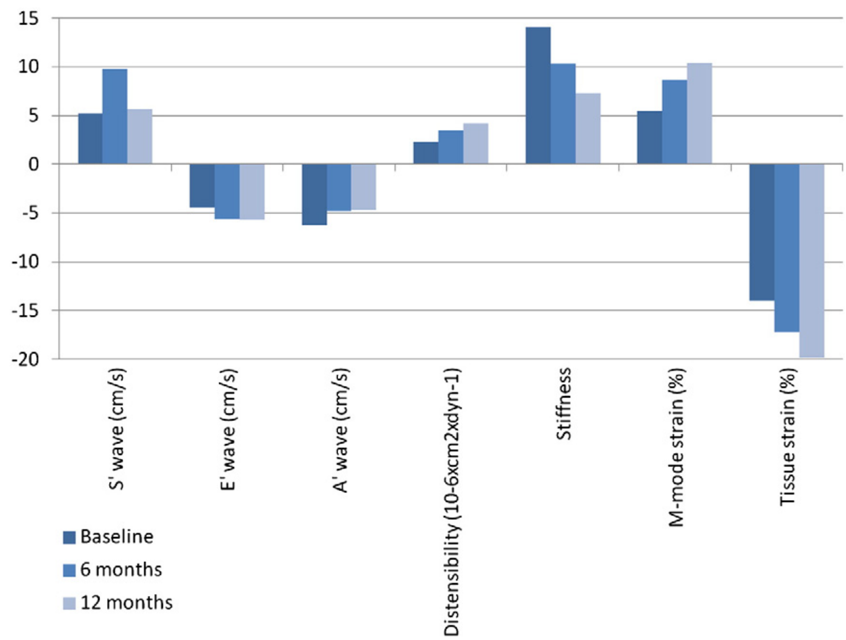

Fig. 1. Aortic elastic properties (p values reported in Table 4).

damaged and/or removed with the periaortic fat tissue and aortic function decreases [19–21]. Albeit our study enrolled only 15 people with severe symptomatic aortic stenosis, it interestingly seems to demonstrate that aortic function really improves after TAVI at 6 and 12-month follow-up. In fact, distensibility increases, stiffness reduces and M-Mode and tissue strains ameliorate. These data are very useful in understanding how aortic function may influence ventriculo-arterial coupling and so cardiovascular risk. In fact, although our study seems underpowered to detect statistically significant differences in left ventricular morphology and function, some parameters instead significantly improved 6 months after TAVI, such as diastolic interventricular septum thickness, ejection fraction, systolic pulmonary artery pressure and diastolic dysfunction grade. We think that these mid-term changes could be almost partly attributed to the improving of aortic elastic properties. Further studies are needed to test this hypothesis. In fact, if why aortic function decreases after open chest surgery is easy to understand, vice versa why it improves after TAVI is really unclear. Perhaps the normalization of wall stress upon the proximal aortic root due to the drastic reduction of transvalvular gradient could be responsible of the recovery of aortic elastic properties.

Table 5
Aortic elastic properties variations in the first and in the second 6 months.

Variable	Delta 0–6 months	Delta 6–12 months	p
Distensibility ($10^{-6} \times cm^2 \times dyn^{-1}$)	−1.22 ± 1.98	−0.68 ± 0.79	0.369
Stiffness	3.75 ± 6.19	2.99 ± 6.36	0.793
M-mode strain (%)	−3.17 ± 5.47	−1.74 ± 1.95	0.373
Tissue strain (%)	3.2 ± 4.4	2.7 ± 2.7	0.694

The present study shows some limitations of note. First is the small number of patients, which limits the possibility of a more robust statistical analysis. Second, improved aortic elastic properties may partly reflect the improved flow across the aortic valve, and by itself, not really be at all a marker for improved cardiovascular risk.

In conclusion, what prognostic role this phenomenon could have is difficult to be explored because open chest surgery is still considered the gold standard and TAVI is only an alternative to high surgical risk patients. These findings suggest a further advantage of TAVI respect conventional surgery.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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