Early improvement of left ventricular function after implantation of a transcutaneous aortic valve: A tissue Doppler ultrasound study

Amélioration précoce de la fonction systolique après implantation d’une valve aortique transcutanée : étude échographique en mode doppler tissulaire

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Summary
Introduction. — The long-term effects of surgical treatment for aortic narrowing in left ventricular (LV) remodelling have been well described. The immediate benefit after release of obstruction is unknown.
Method and results. — Nineteen patients with significant and symptomatic aortic stenosis underwent transcutaneous implantation of an aortic valve. A conventional and tissue Doppler echocardiography was performed 48 hours before and 24 hours after the procedure. Apart from the dimensions, LV function and aortic haemodynamics, we measured systolic and diastolic myocardial velocities and systolic strain. The procedure resulted in a decrease to the mean transaortic gradient (from 43 ± 13 to 10 ± 3 mmHg, p = 0.001), an increase of the aortic surface area (from 0.6 ± 0.1 to 1.7 ± 0.1 cm², p = 0.001) and a reduction in the systolic LV volume (62 ± 27 to 48 ± 22, p = 0.04). We observed an improvement in the systolic radial and longitudinal strain of the posterior wall (p < 0.05), septal wall (p < 0.05) and lateral wall (p < 0.05). Improvement in systolic velocities on these walls and the inferior wall (p < 0.01) was also recorded. The regional diastolic velocity was significantly better on the posterior (p < 0.05) and septal (p < 0.05) walls.

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Conclusion. — The immediate drop in the transaortic gradient resulted in an improvement in myocardial velocities and strain, a sign of improvement in the regional systolic and diastolic regional function.

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Introduction

Aortic stenosis in adults has become the most common valvulopathy in the western world, mainly due to ageing of the population.

Left ventricular (LV) remodelling during aortic stenosis gradually leads to myocardial hypertrophy by cellular hypertrophy and collagen hyperplasia of the cellular matrix before systolic dysfunction occurs [1,2].

While conventional imaging tools are capable of easily identifying hypertrophy and altered LV ejection fraction, few are able to detect early remodelling of cardiomyopathies. They are tissue Doppler for subclinical contractile dysfunction and “integrated backscatter” for myocardial fibrosis. Both proved to be pathological in aortic stenosis [3,4]. In these works, tissue Doppler imaging was superior to any conventional ultrasound parameters, and detection of preclinical displacement or deformation abnormalities of movement was possible even if the LV EF was preserved.

To investigate acute change of global and regional LV function after overload release, both transcatheter aortic valvuloplasty and aortic valve implantation by cardiac catheterisation are good models [5], while aortic valve surgery is less appropriate due to the confounding factors influencing LV function, such as myocardial protection, extracorporeal circulation and the use of catecholamines.

In this work we seek to evaluate LV remodelling before and after transcatheter aortic valve implantation using tissue Doppler imaging, assuming its superiority to detect subclinical changes in segmental myocardial function compared to conventional ultrasound. By analyzing tissue Doppler imaging 24 hours after the procedure, we wanted to evaluate the role of the Frank-Starling relationship.

Method

All patients received written information and gave their written consent before participation in the study and the protocol was approved by the CCPRPB.

Population

Nineteen patients with an average age of 81 ± 7 years (from 62 to 92 years) and symptomatic aortic stenosis despite optimum medical treatment underwent implantation of the Cribier-Edwards percutaneous aortic valve. Inclusion and exclusion criteria were previously reported [5]. Vascular disease that precluded access, severe deformation of the chest, intracardiac thrombus, unprotected stenosis of the left main coronary artery not amenable to percutaneous intervention, myocardial infarction (MI) within 7 days, prosthetic heart valves, active infection, leukopenia (< 3000 white blood cells/mm²), coagulopathy, active bleeding, or acute anaemia (haemoglobin < 9 mg/dl) accounted for exclusion. Patients that could not be fully dilated with a 23 mm aortic valvuloplasty balloon (noteable waist) and patients with a native aortic valve annulus size greater than 24 mm or less than 19 mm were also excluded. All patients underwent a coronary angiogram before 1 week before implantation. Of the 19 patients, fourteen had an ischemic heart disease, revascularized if necessary, leaving five patients with a scar infarction (three anterior and two posterior infarction). Five
patients had no significant coronary lesions. Implantation of the valve took place under local anaesthesia. Implantation of a percutaneous aortic valve was always preceded by an aortic valvuloplasty. The procedure was anterograde (or transseptal) in 17 cases and was retrograde in two cases. A cardiac electrostimulation probe was also inserted. The aortic prosthesis was inserted and advanced on a guide wire into the stenotic native valve. Once optimal positioning was achieved, the artificial valve was deployed by inflating a 23 mm balloon around which the valve was crimped, while pacing the right ventricle at a rate around 220 beats per minute to ensure stability of the entire balloon catheter and artificial valve system during inflation.

Ultrasound protocol

Ultrasound analysis was performed within 48 hours before inclusion of the patient and 24 hours after implantation of the valve. The ultrasound acquisition was performed on a General Electric Vivid7 equipped with a 1.7/3.4 MHz probe and receiving the second harmonic. The electrocardiogram was systematically displayed during ultrasound images acquisition. Dataset was recorded on a magneto-optical disk for offline analysis. The parasternal long-axis, apical four-chamber and five-chamber views were interrogated by M-mode, pulsed-wave Doppler and continuous-wave Doppler. Three additional tissue Doppler cardiac loops were acquired in the parasternal short-axis at papillary muscle level and in apical four- and two chamber views. The sample volume size for tissue Doppler interrogation was adjusted to 2 mm to avoid extra-anatomical information particularly in the parasternal short-axis view while preserving the quality of Doppler signal.

Ultrasound parameters

Each ultrasound parameter was averaged from three to five cardiac cycles. We measured LV systolic and diastolic diameter, ejection fraction, LV diastolic thickness, the transmitral peak early-diastolic velocity (E-wave), the transmitral peak late-diastolic velocity (A-wave), E-wave/A-wave ratio, the transmitral E-wave deceleration time, the cardiac output, the aortic valve area from the continuity equation, the transaortic peak and mean pressure gradient (G max and G mean, respectively) from the Bernoulli’s equation and the systolic pulmonary artery pressure (SPAP, the right atrial pressure was arbitrarily set at 10 mmHg).

In tissue Doppler imaging modality, the sample volume was placed within the posterior and the anterior wall in parasternal short-axis view and within the middle portion of the septal, lateral, anterior and posterior wall in the apical window. We measured the peak systolic velocity S, the peak early diastolic velocity E, the peak late diastolic velocity A, the peak strain rate imaging SRI and the peak systolic strain SI. Specifically, the peak systolic strain was measured during or after aortic valve closure. When two peaks were visible, only the closest to aortic valve closure was measured.

Statistics

All data were expressed as mean ± S.D. Given the amount of parameters, we did not test for normal distribution but com-

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic, aortic and conventional ultrasound data before and after implantation of the transcutaneous valve.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre implantation</td>
</tr>
<tr>
<td>Heart rate (beat/min)</td>
<td>73 ± 11</td>
</tr>
<tr>
<td>Syst blood pressure (mmHg)</td>
<td>112 ± 10</td>
</tr>
<tr>
<td>Aortic surface area (cm²)</td>
<td>0.6 ± 0.1</td>
</tr>
<tr>
<td>Maximum G (mmHg)</td>
<td>76 ± 16</td>
</tr>
<tr>
<td>Mean G (mmHg)</td>
<td>43 ± 13</td>
</tr>
<tr>
<td>IVSd (mm)</td>
<td>10 ± 2</td>
</tr>
<tr>
<td>LVED (mm)</td>
<td>53 ± 9</td>
</tr>
<tr>
<td>LVES (mm)</td>
<td>40 ± 10</td>
</tr>
<tr>
<td>LVPWd (mm)</td>
<td>10 ± 2</td>
</tr>
<tr>
<td>Teicholz EF (%)</td>
<td>48 ± 16</td>
</tr>
<tr>
<td>FS (%)</td>
<td>25 ± 10</td>
</tr>
<tr>
<td>LV systolic vol. (ml)</td>
<td>62 ± 27</td>
</tr>
<tr>
<td>LV diastolic vol. (ml)</td>
<td>114 ± 34</td>
</tr>
<tr>
<td>Simpson EF (%)</td>
<td>47 ± 16</td>
</tr>
<tr>
<td>E wave (m/s)</td>
<td>1.3 ± 0.3</td>
</tr>
<tr>
<td>A wave (m/s)</td>
<td>0.4 ± 0.2</td>
</tr>
<tr>
<td>E/A</td>
<td>3.9 ± 1.9</td>
</tr>
<tr>
<td>DT (ms)</td>
<td>143 ± 25</td>
</tr>
<tr>
<td>Flow (L/min)</td>
<td>4.6 ± 1.3</td>
</tr>
</tbody>
</table>

S: systolic velocity; E: early diastolic velocity; A: late diastolic velocity; IVSd: inter-ventricular septum in diastole; LVED: left ventricular end-diastolic diameter; LVES: left ventricular end-systolic diameter; LVPWd: left ventricular posterior wall in diastole; EF: ejection fraction; FS: fractional shortening; DT: deceleration time.
Table 2  Velocities and strain of the anterior and posterior walls in the parasternal short-axis view.

<table>
<thead>
<tr>
<th>Parasternal short-axis view</th>
<th>Posterior wall</th>
<th>Anterior wall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Peak S (cm/s)</td>
<td>3.1 ± 1.8</td>
<td>4.9 ± 2.0</td>
</tr>
<tr>
<td>Peak E (cm/s)</td>
<td>3.3 ± 2.2</td>
<td>4.0 ± 2.6</td>
</tr>
<tr>
<td>Peak A (cm/s)</td>
<td>2.3 ± 1.4</td>
<td>3.3 ± 2.0</td>
</tr>
<tr>
<td>Peak SRI (/s)</td>
<td>1.3 ± 0.6</td>
<td>1.9 ± 0.6</td>
</tr>
<tr>
<td>Peak SI (%)</td>
<td>15 ± 10</td>
<td>24 ± 14</td>
</tr>
</tbody>
</table>

SRI: strain rate imaging; SI: strain; S: systolic velocity; E: early diastolic velocity; A: late diastolic velocity.

Table 3  Velocities and strain of the septal and lateral wall in the apical four-chamber view.

<table>
<thead>
<tr>
<th>Apical four-chamber view</th>
<th>Septal wall</th>
<th>Lateral wall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Peak S (cm/s)</td>
<td>2.3 ± 0.8</td>
<td>2.9 ± 1.2</td>
</tr>
<tr>
<td>Peak E (cm/s)</td>
<td>1.7 ± 0.9</td>
<td>2.6 ± 1.3</td>
</tr>
<tr>
<td>Peak A (cm/s)</td>
<td>3.4 ± 2.3</td>
<td>4.5 ± 2.6</td>
</tr>
<tr>
<td>Peak SRI (/s)</td>
<td>1.4 ± 0.8</td>
<td>3.7 ± 2.8</td>
</tr>
<tr>
<td>Peak SI (%)</td>
<td>15 ± 11</td>
<td>29 ± 13</td>
</tr>
</tbody>
</table>

SRI: strain rate imaging; SI: strain; S: systolic velocity; E: early diastolic velocity; A: late diastolic velocity.

Comparisons were made by Wilcoxon test with Bonferroni correction. Both inter- and intraobserver variabilities were analysed using Wilcoxon’s test. We used StatView (SAS Institute Corporation, Version 5.0). Significance was set at \( p < 0.05 \).

Results

Population

All patients were in NYHA functional class IV and two were in cardiogenic shock. Before procedure, aortic valve area averaged 0.6 ± 0.1 cm². The aortic peak pressure gradient was 76 ± 16 mmHg and the aortic mean pressure gradient was 43 ± 13 mmHg.

Conventional echocardiographic parameters after implantation

After the procedure aortic peak and mean pressure gradient decreased significantly while aortic valve area was statistically enlarged (Table 1). LV diameters tended to decrease after the procedure but only the end-diastolic volume was significantly reduced. Ejection fraction was unchanged after the implantation (Table 1).

Tissue Doppler imaging parameters after implantation

The reproducibility of conventional echocardiography has not been tested (same operator). Intraobserver variability
was 4 ± 3% for velocities and 6 ± 6% for the strain. Interobserver variability was 5 ± 3% for velocities and 10 ± 9% for the strain.

While there was no change in EF after implantation of the transcutaneous aortic valve, both systolic and end-diastolic peak velocities were significantly increased in the posterior wall after the procedure (Table 2) in short-axis view, while peak early diastolic velocity tended to increase without however reaching a statistically significant value. Similarly, both peak SRI and SI were statistically improved. Fig. 1 showed improvement in posterior wall peak velocities and strain. Aortic valve implantation enhanced anterior wall peak SRI and SI but did not modify peak velocities.

In the apical four-chamber view, both systolic and diastolic velocities were significantly improved in the septum at 24 hours follow-up (Table 3), while no changes were observed in the anterior wall. Furthermore, the benefit of valve implantation in the inferior and lateral wall concerned the peak systolic velocity with no effect on the peak diastolic velocity (Table 4). Improvement of SRI and SI was not uniform. A statistical increase in the strain was only observed on the septal and lateral wall.

Figure 1. The figure illustrates the myocardial velocities (top), the strain (middle), and the strain integral (bottom) before (left images) and after (right images) implantation of a transcutaneous aortic valve. There is an increase to all ultrasound parameters after the procedure in this example.
Discussion

Left ventricular remodelling and aortic narrowing

LV remodelling is the process by which the myocardium adapts in response to a stress. In case of aortic stenosis, the remodelling trigger is the gradual increase in parietal pressure secondary to afterload rise. A number of haemodynamic, endothelial and neurohormonal changes are activated. Both activation of the renin-angiotensin-aldosterone and sympathetic systems has been implicated in histological modification [6]. Myocytes and nuclei hypertrophy, fibroblasts proliferation occur at early stage. Macroscopically, this is characterized by anatomical hypertrophy which is said to be initially compensatory. This tissue remodelling leads to isolated abnormal relaxation that is slightly or not symptomatic. Although systolic function throughout EF measurement is apparently normal, tissue Doppler imaging demonstrates abnormal velocities and strain at this pre-clinical stage. In patients with aortic stenosis and normal EF, Bruch et al. showed significant reduction in the longitudinal systolic and early diastolic velocities compared with control subjects [7]. Similarly, Kowalski et al. reported a deterioration in the radial and longitudinal strain proportional to the severity of the aortic valve area [4].

At a more advanced stage of the disease, histological abnormalities are more severe with cardiomyocytes death and apoptosis replaced by fibrosis that creates a typical disarray [8,9]. This phenomenon is accelerated by capillary rarefaction and coronary hypoperfusion [10]. Functionally, relaxation abnormalities are completed by altered tissue remodelling. Aortic valve replacement operates through aortic narrowing [11]. This benefit has been reported in the literature after aortic valvuloplasty [16]. The lack of publication within 24 hours after surgical aortic valve replacement is due to the fact that EF is not reasonably interpretable after myocardial protection, extracorporeal circulation, positive inotropic drugs administration, variations in preload or even the bi-ventricular interdependence under assisted ventilation, apt to excessive variability. Moreover, the presence of a paradoxical septum contributes to the difficulties in measuring the perioperative EF. Nevertheless, Sutton et al. reported a perioperative fall in the systolic circumferential and meridional wall stress related to a decrease in afterload [12].

Regression of LV hypertrophy starts from seven day post-operative while EF continues to improve [13]. At long-term follow-up, the benefit of the stenosis relief is observed on EF, volumes and hypertrophy [14]. It is related both to the renin-angiotensin-aldosterone and adrenergic system deactivation. On the histological level, reverse remodelling is much slower. For Krayenbuehl et al., regression of cardiomyocytes hypertrophy and decline of myocardial fibrosis is only detectable 70 months after the surgical procedure [15].

Tissue Doppler imaging and early left ventricular remodelling after transcutaneous aortic valve replacement

Transcutaneous aortic valve replacement leads to immediate and persistent decrease in transaortic pressure gradient that improves global and segmental LV function. The existence of coronary artery disease has certainly influenced the velocities analysis, but this was significantly attenuated by any systematic coronary revascularization before implantation and the patient was his own witness.

Peak systolic velocities are improved in all segments explored except in LV anterior wall short-axis view and inferior wall apical two-chamber view. These results are consistent with those reported in the literature. In a preliminary study, Bauer et al. showed early improvement in radial velocity and strain after transcutaneous aortic valve implantation [16]. The lack of improvement in peak velocities within anterior wall may be explained by the poor resolution of tissue Doppler imaging in the near field or the limited velocities in this region of interest. The lack of improvement in peak velocities within the inferior wall may be explained by the predominant effect of the Frank-Starling relationship on radial rather than longitudinal function, by an irreversible process, by a methodological problem or the limited number of patients in the present study.

Peak diastolic velocities are variably affected by transcutaneous aortic valve implantation. Despite a global tendency to increase in all segments, peak early diastolic are significantly increased in the septal wall from the four-chamber view. Those are unexpected results since
diastolic early function is linked to systolic function due to the coexisting contraction-relaxation coupling mechanism [17]. However aortic stenosis is a particular model in which diastolic function paradoxically normalises long after systolic function. In his follow-up study on patients after aortic valve replacement, Villari et al. found that LV relaxation and LV stiffness normalised at 22-month and 81-month follow-up, respectively [18]. In another study, they concluded that persistent postoperative hypertrophy maintains LV relaxation abnormalities, creates LV diastolic dysynchrony that promotes functional disorders [19]. Our results are consistent with these findings and a longer follow-up should demonstrate normalization of diastolic function.

Strain is more specific to contraction than velocity. In the present study, there was improvement both in strain rate imaging and strain 24-hours after implantation of the transcutaneous valve [20,21]. Again, this is related to the instantaneous drop in LV afterload which enhances LV function through the Frank-Starling relationship. Similar observations were reported in rat model of aortic banding. The instantaneous banding relief was accompanied by an improvement in regional LV contractility [22]. However, aortic debanding after 2 months led to a full recovery of contractility, whereas contractility remained decreased when debanding was performed after 9 months, due to excessive fibrosis [22]. The unexpected results observed on the anterior wall both in short-axis and apical two-chamber views were methodological. Although useful, the measurement of myocardial velocities does not necessarily reflect the regional function. Many pathophysiological situations are characterized by passive displacement detectable in tissue Doppler, i.e. MI. Reflecting the velocity gradient between two points, both strain and strain rate imaging are surrogate for myocardial contraction. Thus, in our work, the deformation increase after valve implantation demonstrates that systolic velocity enhancement is attributable to the Frank-Starling relationship. Without strain analysis, the velocity changes might be attributable to translational motion twisting of the myocardium. In the absence of diastolic strain analysis, it is difficult to understand the mechanism that leads to higher early-diastolic velocities but we can assume a similar effect due the natural link between contraction and relaxation known as the contraction/relaxation coupling. Regarding the late-diastolic velocity, improvement is certainly attributed to better atrial contraction in response to the decrease in ventricular preload, as indirectly suggested by E/A decrease in the present work.

Limitations

The first limitation of this study is the short-term follow-up. Mild- and long-term follow-up should specify the magnitude of reverse remodelling independent to afterload correction. Nevertheless, it should be reminded that, to the best of our knowledge, this is the first study demonstrating the recovery of LV global and segmental contractile function immediately after stenosis relief that is not affected by the surgical perioperative environment.

Another limitation is the limited number of patients and the absence of controls. However, this is a new technique in which the rate of inclusion directly meets with a strict control. This pitfall will gradually be overcome.

Conclusion

At 24-hour postoperative, implantation of a transcutaneous aortic valve in patient with aortic stenosis improved both global and regional systolic and diastolic function which in relation to the Frank-Starling relationship. This immediate benefit should contribute to improve myocardial performance irrespective of EF and patient condition.

References


