The acute effects of transcatheter aortic valve replacement on central aortic hemodynamics in patients with severe aortic stenosis

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ABSTRACT

Severe aortic stenosis (AS) induces abnormalities in central aortic pressure, with consequent impaired organ and tissue perfusion. Relief of AS by transcatheter aortic valve replacement (TAVR) is associated with both a short- and long-term hypertensive response. Counterintuitively, patients who are long-term normotensive post-TAVR have worsened prognosis compared with hypertensive patients, yet the underlying mechanisms are not understood. We investigated immediate changes in invasively measured left ventricular and central aortic pressure post-TAVR in patients with severe AS using aortic reservoir pressure (RP), wave intensity analysis (WIA) and indices of aortic function. 54 patients (mean age 83.6 ± 6.2 years, 50.0% female) undergoing TAVR were included. We performed RP and WIA on invasively acquired pressure waveforms from the ascending aorta and left ventricle immediately pre- and post-TAVR. Following TAVR, there were increases in systolic, diastolic, mean and pulse aortic pressures (all $p<0.05$). Post-TAVR reservoir pressure was unchanged (54.5±12.4 vs. 56.6±14.0 mmHg, $p= 0.30$) whereas excess pressure increased 47% (29.0±10.9 vs. 42.6±15.5 mmHg, $p<0.001$). WIA (arbitrary units, a.u.) demonstrated increased forward compression wave (64.9±35.5 vs. 124.4±58.9, $x10^3$ a.u., $p<0.001$), backward compression wave (11.6±5.5 vs. 14.4±6.9, $x10^3$ a.u., $p= 0.01$) and forward expansion wave energies (43.2±27.3 vs. 82.8±53.1, $x10^3$ a.u., $p<0.001$). Subendocardial viability ratio improved with aortic function effectively unchanged post-TAVR. Increased central aortic pressure following TAVR relates to increased transmitted power and energy to the proximal aorta with increased excess pressure but unchanged reservoir pressure. These changes provide a potential mechanism for the improved prognosis associated with relative hypertension post-TAVR.

Keywords.

Aortic blood pressure, aortic stenosis, reservoir pressure, wave intensity, TAVR.

INTRODUCTION

Degenerative aortic stenosis (AS) is the commonest form of aortic valve disease and is caused by progressive calcification of the valve leaflets, which impairs leaflet mobility and compromises valve orifice area.[1] This leads to restricted blood flow through the stenosed valve, typically leading to narrowed pulse pressure and a delay in peak aortic pressure.[2] Pathophysiological changes in central aortic pressure are known to adversely impact tissue and organ perfusion including that to the myocardium, which may contribute to ischaemia,[3] exertional symptoms and adverse outcomes.

Transcatheter aortic valve replacement (TAVR) is an established percutaneous therapy used to treat severe AS in patients at intermediate or high operative risk.[4] Relief of AS by TAVR has been shown to significantly elevate blood pressure both short- and long-term post-procedure.[5, 6] Counterintuitively, several studies have demonstrated that following TAVR, normotensive patients have worse clinical outcomes at short and longer term follow up than those with raised arterial blood pressure (BP)[5-7] however, the mechanisms are not understood.

Various models have been proposed to describe the ventriculo-arterial mechanisms responsible for the formation and distal propagation of the central aortic pressure, which is a fundamental prerequisite for the perfusion of tissue and key organs including the heart. Previous studies have demonstrated that the elasticity and compliance of the aorta are key in determining pressure waveform morphology during both systole and diastole.[8] One available approach for the evaluation of central aortic pressures is the ‘reservoir pressure model’ which proposes that aortic BP can be separated into components representing reservoir and excess pressures.[9] In systole, aortic reservoir pressure is characterized by cyclic volume-related

aortic distension (allowing blood storage with associated increase in potential energy) whilst in diastole, elastic recoil results in distal propagation of blood in association with decreased local aortic volume. In comparison, aortic root excess pressure is determined by volume inflow into the proximal aortic segment.[9] We have recently demonstrated that the shape of the excess pressure waveform in the proximal aorta is linearly related to the measured velocity profile as assessed by continuous Doppler imaging,[10] a finding which enables aortic WIA to be performed using aortic pressure-only waveforms. Insights into the hemodynamic changes in the aorta can also be obtained using wave intensity analysis (WIA), which provides a means for assessing the net influences of upstream (proximal) and downstream (distal) effects on arterial hemodynamics and this has been previously applied in the aorta and coronary arteries.[11, 12] This study presents results of aortic reservoir pressure and WIA immediately before and immediately after the deployment of a TAVR prosthesis, thus demonstrating the immediate impact of the relief of aortic valve obstruction upon central aortic hemodynamics.

We hypothesized that following TAVR, the main central hemodynamic changes would relate to the immediate alterations in the pattern of blood flow into the proximal aorta. This would manifest as an increase and change in the profile of excess pressure as well as increases in the energy and power of the WIA profiles. Conversely, we would expect to see minimal changes in reservoir pressure, which relates predominantly to the global arterial properties and would be expected to be unchanged immediately following valve deployment.

METHODS

Reservoir pressure analysis in this paper is based on source code available at http://www.bg.ic.ac.uk/research/k.parker/res_press_web/rp_download.html. In order to minimize the possibility of unintentionally sharing information that can be used to re-identify patient data, a subset of the data generated for this study are available from the corresponding author upon reasonable request.

Data was extracted retrospectively from our catheterization hemodynamic recording system in patients who underwent TAVR at MonashHeart (Monash Health, Melbourne, Australia) using either self-expandable, balloon expandable or mechanically expandable valves. Simultaneous left ventricular and aortic pressures were acquired using 6Fr pigtail catheters with aortic measurements taken approximately 5 cm above the aortic annulus. Measurements were performed at baseline before balloon aortic valvuloplasty (if required) and were repeated typically within five minutes after valve deployment (**Figure 1A and 1B**). Signals were transduced via a Philips Xper Cardio Physiomonitoring System (Andover, MA, USA). Signals were sampled at 500 Hz with data exported and analyzed offline using MATLAB (MathWorks, Inc, Natick, Massachusetts, USA). Two hundred patients were randomly selected for this analysis. Patients were considered for inclusion if their pre- and post-TAVR recorded tracings demonstrated regular R-R intervals and those without significant peri-valve implant hypotension (<90mmHg). Resultant pressure waveforms were carefully evaluated with pressure-damped traces excluded by observers blinded to all other data. The flow chart for patient selection is given in **Figure S1 in Supplemental Materials**. The aortic pressure waveforms were ensembled using 5-10 consecutive beats (**Figure 1C and 1D**), following which, reservoir pressure (**Figures 1E and 1F)** and wave intensity analysis was performed.

Reservoir pressure analysis

Reservoir pressure analyses were performed using previously described methods from ensembled-averaged pressure waveforms.[9] To calculate reservoir pressure, it is assumed that P_r satisfies overall conservation of mass

$$\frac{dP_r}{dt} + k_d(P_r - P_\infty) = \frac{Q_{in}}{C} \quad (1)$$

Where k_d is the diastolic rate constant (the reciprocal of the diastolic time constant $\tau = RC$, R is the net resistance to flow through the microcirculation and C is the net compliance of the arteries). Q_{in} is the volume flow rate into the aortic root and P_∞ is the asymptote of the diastolic pressure run-off. It is assumed that $Q_{in} = \zeta P_x$, where ζ is a constant related to and of the same units as the characteristic impedance of the aortic root and P_x is excess pressure.

Under these conditions Equation 1 can be written

$$\frac{dP_r}{dt} + k_d(P_r - P_\infty) = k_s(P - P_r) \quad (2)$$

where k_s is the systolic rate constant (the reciprocal of ζC). In this approach the proportionality of P_x to Q is a fundamental requirement.

This first-order linear differential equation can be solved as:

$$P_r = e^{-(k_s+k_d)t} \int_0^t P(t')e^{(k_s+k_d)t'}dt' + \frac{k_d}{k_s + k_d}\left(1 - e^{-(k_s+k_d)t}\right)P_\infty \quad (3)$$

where the diastolic parameters k_d and P_∞ are obtained first by fitting an exponential curve to P during diastole and k_s is obtained by minimizing the square error between P and P_r obtained over diastole. All indices of reservoir pressure are reported above the diastolic.

Wave Intensity Analysis

WIA was performed using previously validated methods.[13] Given the previously demonstrated close correlation between the waveform profile of excess pressure and the

envelope of Doppler flow velocity in the proximal aorta, this was substituted for the flow waveform in the calculation of wave intensity profiles.[10] The peak wave intensity values represent the peak power density in the wave whilst the area of the waveform represents the energy flux of the wave (energy per unit cross-section of the artery). As excess pressure was used as a surrogate for flow velocity, the units of wave intensity are reported in arbitrary units (a.u., dimensionally equal to pressure squared). We identified the three main waves occurring during the cardiac cycle (**Figure S2 in Supplemental Materials**)[14, 15] being a systolic forward compression wave (FCW) occurring when blood is ejected into the aorta with the rising aortic pressures, followed by a backward compression wave (BCW), caused by reflection of the FCW from sites of higher impedance, and a late systolic forward expansion wave (FEW) representing the separation tensions within the column of blood.

Pressure waveforms were separated into forward (Pf) and reverse going (Pb) components as previously described.[16] Reflection ratio, Pb_{max}/Pf_{max}, was calculated along with the time to peak forward and reverse pressures. Aortic characteristic impendence was calculated from WIA as the initial slope of pressure/flow loop as previously described.[17]

Left ventricular energy balance was estimated using Buckberg's subendocardial viability ratio (SEVR), defined as aortic diastolic pressure-time integral (DPTI) divided by the left ventricular systolic tension time index (TTI, the integral of left ventricular pressure between aortic start systole and start diastole). This represents the ratio between myocardial oxygen demand and supply. In this estimation we have not allowed for left ventricular diastolic pressure and have used directly measured left ventricular systolic pressure rather than the usual surrogate of aortic systolic pressure. This is appropriate in view of the large pressure drop across the aortic valve in the pre-TAVR situation.

Statistical analysis

Data analysis was performed using PRISM (GraphPad Software, Inc., La Jolla, CA, USA). The changes in hemodynamic indices, separated wave pressure parameters and wave intensity were compared using a two-way Student's t-test; non-normally distributed continuous data were tested with a paired Wilcoxon test. Chi-squared tests were used to compare categorical variables. A p value <0.05 was considered statistically significant. All data are presented as pre-TAVR vs. post-TAVR unless specifically stated.

RESULTS

Of the initial 200 selected patients, 71 did not meet the inclusion criteria. Of the remaining, 75 were excluded due to dampened pressure tracings, inadequate ECG recording prohibiting automated wave-ensembling, or the lack of required identifiable fiducial points for determination of reservoir pressure (**Figure S1 in Supplemental Materials**). 54 patients were included in the final analysis. The mean age of those with analyzable data was 83.6 ± 6.2 years and 50% were female. There were no significant differences between the baseline clinical and demographic data of the 75 excluded and the 54 included patients (**Table S1 in Supplemental Materials**). All patients underwent TAVR via femoral arterial access and all patients had balloon aortic valvuloplasty prior to valve deployment. The patient baseline and procedural characteristics are presented in **Table 1**. The echocardiographic and invasive hemodynamic indices before and after the procedure are presented in **Table 2**.

Following TAVR, there was the expected significant reduction in invasive mean transvalvular gradient (52.0 ± 14.2 vs. 10.5 ± 14.2 mmHg, $p < 0.001$), with a concomitant reduction in peak left ventricular pressure (176.3 ± 25.5 vs. 151.2 ± 28.0 mmHg, $p < 0.001$). There were significant increases in all measures of aortic BP including systolic (128.4 ± 22.0 vs. 144.9 ± 26.6 mmHg, $p < 0.001$), diastolic (52.9 ± 9.8 vs. 56.8 ± 11.2 mmHg, $p = 0.03$), mean (81.1 ± 13.7 vs. 88.9 ± 15.8 mmHg, $p < 0.002$) and pulse (75.6 ± 18.1 vs. 88.1 ± 20.2 mmHg, $p < 0.001$) pressures. Mean heart rate trended towards an increase (63.6 ± 10.8 vs. 66.4 ± 10.1 beats/min, $p = 0.07$) whilst diastolic time fraction remained unchanged following valve deployment (0.625 ± 0.057 vs. 0.633 ± 0.047, $p = 0.31$). The time to peak systolic LV pressure (expressed as a fraction of the cardiac cycle) was unchanged post-TAVR (0.293 ± 0.136 vs. 0.315 ± 0.132, $p = 0.39$) whilst the time to peak systolic aortic pressure decreased (0.288 ± 0.048 vs. 0.248 ± 0.032, $p < 0.001$).

Subendocardial Viability Ratio

DPTI was unchanged post TAVR (42.2 ± 11.4 vs. 42.0 ± 10.7 mmHg.sec, p= 0.91). SEVR was increased post-TAVR (0.97 ± 0.32 vs. 1.25 ± 0.35, p<0.001) predominantly due to decreased LV pressure and consequent TTI (45.1 ± 9.8 vs. 35.0 ± 8.8 mmHg.sec, p< 0.001).

Reservoir pressure analysis

Analysis demonstrated no changes in the aortic reservoir pressure following TAVR (54.5 ± 12.4 vs. 56.6 ± 14.0 mmHg, p = 0.30; **Table 3, Figure 2 [GRAPHIC ABSTRACT]**). However, excess pressure increased by 47% following TAVR (29.0 ± 10.9 vs. 42.6 ± 15.5 mmHg, p <0.001). Further analysis demonstrated that the integral of excess pressure – which relates to the total flow during the cardiac cycle[10] – was significantly greater following TAVR (6.66 ± 2.76 vs. 9.36 ± 3.73 mmHg·s, p <0.001). The time to peak reservoir and excess pressure both decreased post-TAVR (p <0.001 for both). There were no differences in the diastolic (18.0±9.6 vs. 14.5±11.6 sec^{-1}, p = 0.052) or systolic (3.9±1.1 vs. 4.2±1.1 sec^{-1}, p = 0.18) rate constants following TAVR.

Aortic wave intensity analysis

Following TAVR, WIA demonstrated large increases in the peak FCW (1016.3 ± 684.0 vs 2431.1 ± 1304.6 $x10^3$ a.u., p <0.001; **Table 3**; **Figure 3**) and FCW energy (64.9 ± 35.5 vs. 124.4 ± 58.9 $x10^3$ a.u., p<0.001). This was associated with an intensification in the peak BCW (-92.5 ± 52.7 vs. -125.5 ± 76.9 $x10^3$ a.u, p = 0.01) and increase in BCW energy (11.6 ± 5.5 vs. 14.4 ± 6.9 $x10^3$ a.u., p = 0.01). Post-TAVR, peak FEW increased (956.0 ± 589.9 vs. 1473.2 ± 1071.9, $x10^3$ a.u., p <0.001) as did the FEW energy (43.2 ± 27.3 vs. 82.8 ± 53.1 $x10^3$ a.u., p<0.001).

Aortic function

There were no changes in aortic characteristic impedance following TAVR (1.01 ± 0.13 vs 1.04 ± 0.10, p= 0.27). Reflection ratio decreased following TAVR (0.56 ± 0.10 vs 0.47 ± 0.13, p<0.001) predominantly driven by an increase in the magnitude of the Pf wave (50.3 ± 13.7 vs 62.8 ± 16.9 mmHg, p <0.001) with no change in the magnitude of the Pb wave (27.2 ± 5.9 vs 28.2 ± 6.9 mmHg, p = 0.64). The time between the peak forward and backward pressures increased following TAVR (0.064 ± 0.019 vs 0.077 ± 0.025 seconds, p<0.001).

DISCUSSION

This study presents new insights into the immediate physiological changes within the ventriculo-aortic complex in patients with severe AS treated with TAVR. Following TAVR, greater systolic, diastolic, mean and pulse arterial pressures were immediately observed, consistent with previous studies that have shown both immediate and long term increases in aortic BP in patients following TAVR.[5-7, 11] Aortic reservoir pressure analysis demonstrates that the increase in total aortic pressure is related to increases in excess pressure without appreciable change in reservoir pressure. Reservoir pressure is recognized to be predominantly dependent on arterial wall properties which is unlikely to change immediately following aortic valve intervention. Left ventricular energetics also improved post-TAVR with increase in energy suppy:demand balance.

Excess pressure, which relates to inflow to the proximal aorta demonstrated significant increases following TAVR. Besides changes in the blood flow profile, this may also be attributable to increased systemic vascular resistance, an observation which has previously been documented post-TAVR.[11] Following TAVR, the prosthetic valve will not only open more briskly, but will have a greater effective orifice area, thus allowing the discharge of greater volume of blood into the aorta earlier in the cardiac cycle, with greater volumetric flow and thus greater momentum. The summation of excess pressure across the full cardiac cycle – a surrogate of the total volumetric flow across the cardiac cycle[10] – increases considerably following TAVR suggesting a potential for increase in stroke volume. The immediate and delayed effects of TAVR on stroke volume however remain unclear,[5, 6, 11] and our echocardiographic data at a mean of 3.0 days post-TAVR in fact demonstrates a reduction in stroke volume. The immediate changes in excess pressures therefore likely represent changes in the patterns of flow and physiology that would potentially facilitate the

upregulation of stroke volume with increasing physiological demands, partially mediated through a combination of reduction of systemic vascular resistance in addition to greater ventricular contractility.

In addition to increases in excess pressure, improvements in flow following TAVR are evidenced by the changes in wave intensity profiles. We observe significant increases in aortic FCW power and energy following TAVR, consistent with previous data[11] suggesting improvement in the transvalvular energy profile following TAVR. Aortic BCW power and energy resulting from reflection of a FCW arriving at sites of impedance mismatch were also greater following TAVR. Contrary to previous findings,[11] our analysis demonstrates increasing aortic FEW power and energy following relief of valvular obstruction.

As hypothesized there were no changes of note in aortic function post-TAVR, as illustrated by no change in characteristic impedance or reservoir pressure (an index of global arterial function) parameters. Additionally, there was no increase in magnitude of any reflected pressure wave, which consequently implies a decreased contribution of aortic impedance to overall increase in central blood pressure post-TAVR. This was predominantly due to an increase in left ventricular-generated forward pressure wave. The slight increase in delay of the backward going pressure wave is consistent with either, or combination of, a pressure-dependent increase in proximal aortic stiffness and/or a peripheral vasodilatation leading to a consequent reduction in, or distal displacement of, any significant impedance mismatch.

Further changes that suggest restoration in central aortic pressure towards premorbid physiology relate to relative timing within the cardiac cycle. Thickened and calcified valves in AS lead to restricted and delayed valvular opening, which manifests clinically with the

pathognomonic *pulsus tardus*. It has been demonstrated that the invasively-derived time between the left ventricular and aortic systolic peaks is associated with the severity of AS.[18] Our data shows that following TAVR, there is a decrease in the time to peak systolic aortic, reservoir and excess pressures, which suggests earlier delivery of blood volume into the aorta and partial normalization of aortic flow patterns.

Elevated aortic BP following TAVR can have immediate and long-term implications for patients. Following valve deployment, hypertensive patients pose greater challenges relating to access site hemostasis. Additionally, significant BP surges can lead to neurological events and acute pulmonary oedema.[6] The long-term impact of hypertension following TAVR continues to intrigue clinicians. In non-AS patients, hypertension is typically associated with increased vascular stiffness, altered global arterial properties and poorer prognosis.[19] Conversely, several studies have shown that increased arterial BP (systolic BP thresholds greater than 130 and 140 mmHg) in patients following TAVR paradoxically confers better outcomes compared to lower arterial BP.[5-7] Findings from this study suggest that increases in aortic BP following TAVR relate to improved excess pressure and transvalvular wave energy profiles. The basic mechanism of elevation of central BP post-TAVR is a reduction in the energy loss associated with blood transiting a stenotic aortic valve and therefore this energy is retained to generate increased contained BP in a proximal aortic vessel of unchanged impedance. These hemodynamic changes facilitate improved physiological states at rest and during upregulation for myocardial, cerebral and other organ demand. Maintenance of relatively elevated BP may also indicate an underlying preservation of cardiac function in a proportion of TAVR patients with potential for improvement in symptoms and prognosis in comparison to non-hypertensive post-TAVR patients. It is possible to hypothesis that hypertension post-TAVR is a less deleterious state than underlying poor cardiac function and

hence imparts an apparent protective state. Whilst lower BP targets remains desirable in the normal population, optimal thresholds remain unknown in the post-TAVR patient cohort. Further research is required to elucidate the mechanisms, pathophysiology and consequences of hypertension following TAVR to better understand its relationship with improved outcomes.

Limitations of this study include it being a retrospective analysis of data from a single center. Pressure measurements were acquired from fluid-filled rather than solid state catheters, which can be prone to pressure-dampening, signal attenuation and high frequency information loss. However, potential error was minimized by blinded adjudication of all pressure traces and there were no differences between the baseline clinical and demographic data for the included and excluded patients. Finally, the rapid ventricular pacing used for balloon aortic valvuloplasty and valve deployment may result in ventricular stunning and has potential to affect immediate post-TAVR aortic pressure readings.[20]

PERSPECTIVES

In summary, the relief of aortic valvular obstruction following TAVR results in the immediate elevation of central aortic pressure due to increased excess pressure and improved transvalvular energy profiles without changes in reservoir pressure. Persistently higher blood pressure post-TAVR is an apparently protective state. We have shown that acute increases in BP post-TAVR relate to measurable increases in transmitted power and energy to the proximal aorta. If borne out in future studies and shown to predict long-term BP post-procedural, WIA may provide an easily assessable and potentially modifiable biomarker to stratify prognosis post-TAVR.

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DISCLOSURES:

None.

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NOVELTY AND SIGNIFICANCE

What is New?

- This in vivo in human study is the first that uses reservoir pressure analysis to examine the impact of transcatheter aortic valve replacement (TAVR) upon aortic haemodynamics. It has shown that increases in aortic blood pressure (BP) post-TAVR are predominantly attributable to increases in aortic excess pressure and not reservoir pressure.
- Additionally, aortic wave intensity analysis (WIA) increases the energies in the three main waves post-TAVR, in keeping with an improvement in the transvalvular energy profile.

What is Relevant?

- Treatment of severe aortic stenosis (AS) with TAVR has been shown to elevate blood pressure, both short- and long-term post-procedure.
- Emerging evidence suggests that patients who are subsequently normotensive post-TAVR have worse clinical outcomes than hypertensive patients. The mechanisms of this are not understood.

Summary

This study uses invasively-derived data from patients undergoing TAVR immediately pre- and post-valve deployment. The results demonstrate that increased BP post-TAVR is predominantly due to increased excess pressure and improvement in transvalvular energy profiles. This suggests that acutely elevated aortic pressures post-TAVR are due to alterations in blood flow patterns in aortic inflow in contrast to the changes in global arterial properties that occur with hypertension in a non-AS population. Such alterations in blood flow and improvements in ventricular-arterial coupling are likely to be responsible for enhanced tissue and organ perfusion post-TAVR.

FIGURE LEGENDS

Figure 1: Left ventricular and aortic pressures before and after transcatheter aortic valve replacement (TAVR). Panels (A) and (B) presents aortic (red) and ventricular (blue) pressure signals before and after TAVR, respectively. Panels (C) and (D) presents the ensembled pressure signals with the dotted line representing their standard deviation. Panels (E) and (F) presents the ensembled aortic pressure (red), excess pressure (yellow) and reservoir pressure (green).

Figure 2: Violin plot demonstrating reservoir and excess pressure before and after transcatheter aortic valve replacement (TAVR).

Figure 3: Density cloud plots representing the distribution of magnitudes of wave power and energy in the aortic root before and after transcatheter aortic valve replacement (TAVR). Following TAVR there are clear increases (shift to the right) in the distribution of forward compression wave (FCW), backward compression wave (BCW) and forward expansion wave (FEW) indicating improved trans-valvular energetics.

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TABLE 1 | Patient baseline and procedural characteristics (n = 54)	
Patient demographic data	
Age (years)	83.6 ± 6.2
Female	27 (50.0%)
BMI (kg/m^2)	27.4 ± 4.9
Hypertension	40 (74.1%)
Diabetes mellitus	14 (25.9%)
Dyslipidaemia	34 (63.0%)
Smoker or ex-smoker	27 (50%)
Previous MI	6 (11.1%)
Previous PCI	11 (20.3%)
Previous CABG	10 (18.5%)
Previous stroke	3 (5.6%)
Peripheral vascular disease	7 (13.0%)
Chronic kidney disease (eGFR<45)	17 (31.5%)
Cardiovascular drug therapy	
Statin	38 (70.3%)
ACE or ARB	28 (51.9%)
ß-blocker	25 (46.3%)
α-blocker	0 (0%)
Calcium channel blocker	14 (25.9%)
Diuretics	20 (37.0%)
Procedural characteristics	

General anesthesia	12 (22.2%)
Access	
Femoral	54 (100%)
BAV	54 (100%)
Valve type	
CoreValve	4 (7.4%)
Evolut R	23 (42.6%)
Lotus	16 (29.6%)
Edwards S3	9 (16.7%)
Acurate Neo	2 (3.7%)
Mean valve size, mm	26.9 ± 2.6

Values are mean ± SD or n (%). BAV indicates balloon aortic valvuloplasty; BMI, body mass index; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass surgery; ACE, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

TABLE 2 | Echocardiographic and invasive hemodynamic indices pre- and post-TAVR			
Variables	**Pre-TAVR**	**Post-TAVR**	**p value**
Echocardiographic indices			
Peak velocity, ms^{-1}	4.4 ± 0.5	2.2 ± 0.6	<0.0001
Mean gradient, mmHg	47.8 ± 12.8	11.0 ± 6.1	<0.0001
Peak gradient, mmHg	79.0 ± 20.6	20.2 ± 12.03	<0.0001
Aortic valve area, cm^2	0.8 ± 0.2	1.9 ± 0.5	<0.0001
Stroke volume, ml	85.3 ± 18.3	76.4 ± 17.2	0.008
Ejection fraction, %	59.2 ± 14.0	59.8 ± 13.8	0.7
Aortic regurgitation		(valvular/paravalvular)	
Mild	17 (31.5%)	5/11 (9.3% / 20.4%)	
Moderate	10 (18.5%)	0/5 (0% / 9.3%)	
Severe	0 (0%)	0 (0% / 0%)	
Intraprocedural invasive indices			
Heart rate, beats/min	63.6 ± 10.8	66.4 ± 10.1	0.07
Systolic aortic BP, mmHg	128.4 ± 22.0	144.9 ± 26.6	<0.001
Diastolic aortic BP, mmHg	52.9 ± 9.8	56.8 ± 11.2	0.03
Mean aortic BP, mmHg	81.1 ± 13.7	88.9 ± 15.8	0.002
Pulse aortic pressure, mmHg	75.6 ± 18.1	88.1 ± 20.2	<0.001
Mean transvalvular gradient, mmHg	52.0 ± 14.2	10.5 ± 5.6	<0.001
Peak left ventricular pressure, mmHg	176.3 ± 25.5	151.2 ± 28.0	<0.001
Diastolic time fraction	0.625 ± 0.057	0.633 ± 0.047	0.31
Time to peak systolic left ventricular pressure as a fraction of the cardiac	0.293 ± 0.136	0.315 ± 0.132	0.39

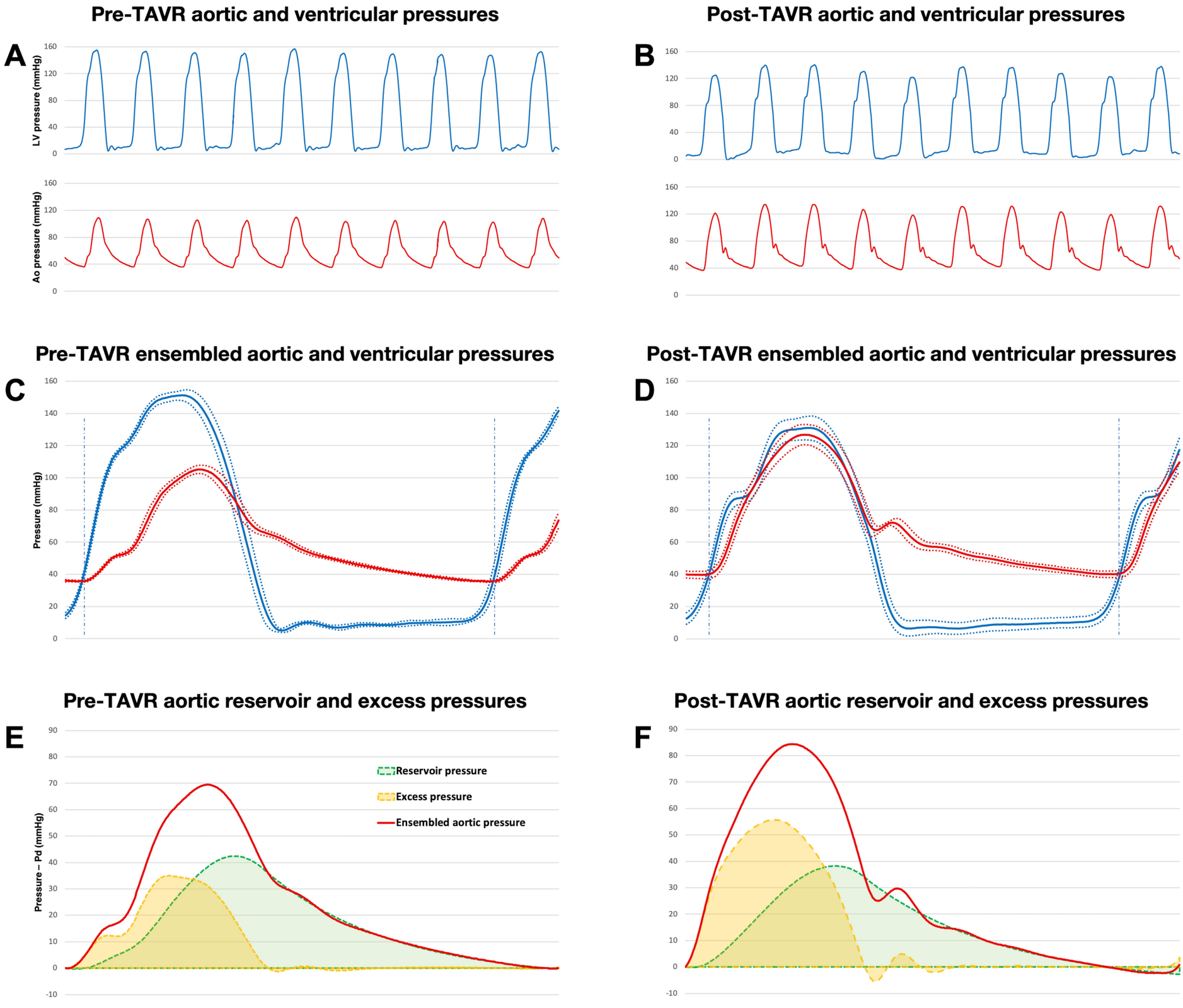
period			
Time to peak systolic aortic pressure as a fraction of the cardiac period	0.288 ± 0.048	0.248 ± 0.032	<0.001

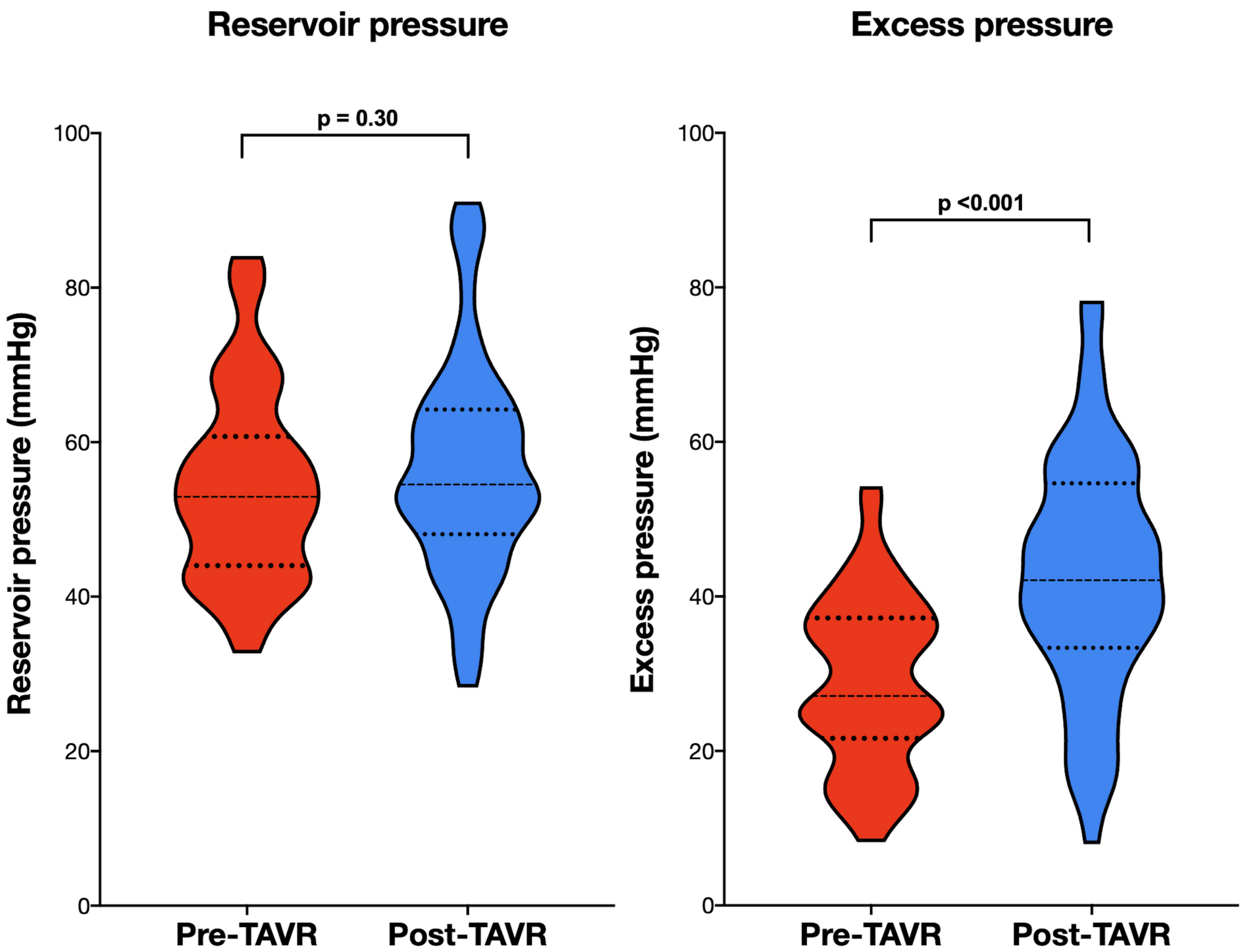
Values are mean ± SD. TAVR indicates transcatheter aortic valve replacement; BP, blood pressure.

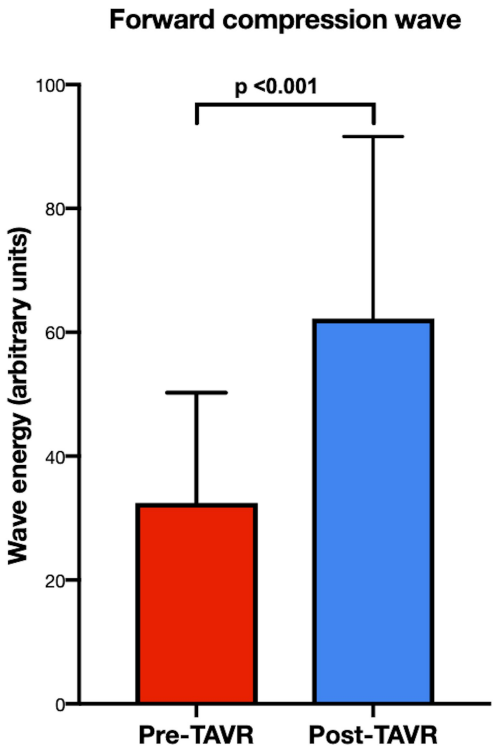
TABLE 3 | Reservoir and wave intensity analysis pre- and post-TAVR			
Variables	**Pre-TAVR**	**Post-TAVR**	**p value**
Reservoir pressure analysis			
Reservoir pressure (peak), mmHg	54.5 ± 12.4	56.6 ± 14.0	0.30
Excess pressure (peak), mmHg	29.0 ± 10.9	42.6 ± 15.5	<0.001
Excess pressure integral, mmHg.s	6.66 ± 2.76	9.36 ± 3.73	<0.001
Rate constant of systolic aortic filling (k_s), per second	18.0 ± 9.6	14.5 ± 11.6	0.052
Rate constant of diastolic aortic emptying (k_d), per second	3.9 ± 1.1	4.2 ± 1.1	0.18
Time to peak reservoir pressure as a fraction of the cardiac period	0.335 ± 0.052	0.309 ± 0.039	<0.001
Time to peak excess pressure as a fraction of the cardiac period	0.219 ± 0.053	0.169 ± 0.044	<0.001
Aortic characteristic impedance, a.u.	1.01 ± 0.13	1.04 ± 0.10	0.27
Pf_{max}, mmHg	50.3 ± 13.7	62.8 ± 16.9	<0.001
Pb_{max}, mmHg	27.2 ± 5.9	28.2 ± 6.9	0.64
Pb_{max}/Pf_{max}, reflection ratio	0.56 ± 0.10	0.47 ± 0.13	<0.001
Time between Pf_{max} and Pb_{max} waves, seconds	0.064 ± 0.019	0.077 ± 0.025	<0.001
Subendocardial viability ratio			
DPTI, mmHg.sec	42.2±11.4	42.0±10.7	0.91
TTI, mmHg.sec	45.1±9.8	35.0±8.8	<0.001

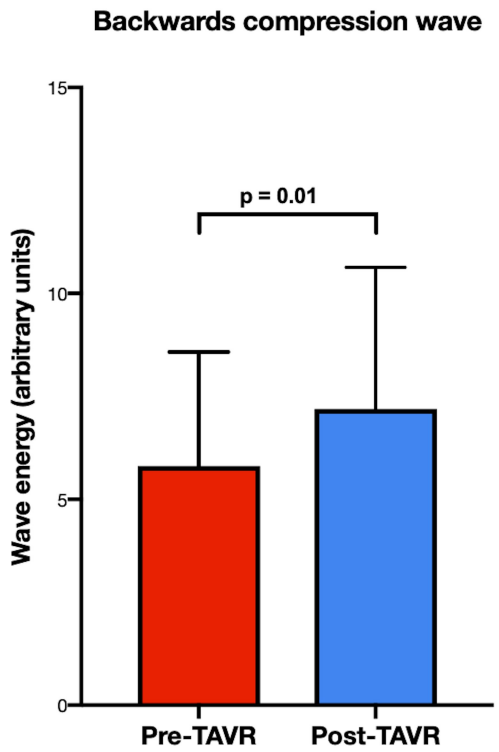
SEVR	0.97±0.32	1.25±0.35	<0.001
Wave intensity analysis			
FCW energy, $x10^{-3}$, a.u.	64.9 ± 35.5	124.4 ± 58.9	<0.001
FCW (peak), $x10^{-3}$, a.u.	1016.3 ± 684.0	2431.1 ± 1304.6	<0.001
BCW energy, $x10^{-3}$, a.u.	11.6 ± 5.5	14.4 ± 6.9	0.01
BCW (peak), $x10^{-3}$, a.u.	-92.5 ± 52.7	-125.5 ± 76.9	0.01
FEW energy, $x10^{-3}$, a.u.	43.2 ± 27.3	82.8 ± 53.1	<0.001
FEW (peak), $x10^{-3}$, a.u.	956.0 ± 589.9	1473.2 ± 1071.9	<0.001

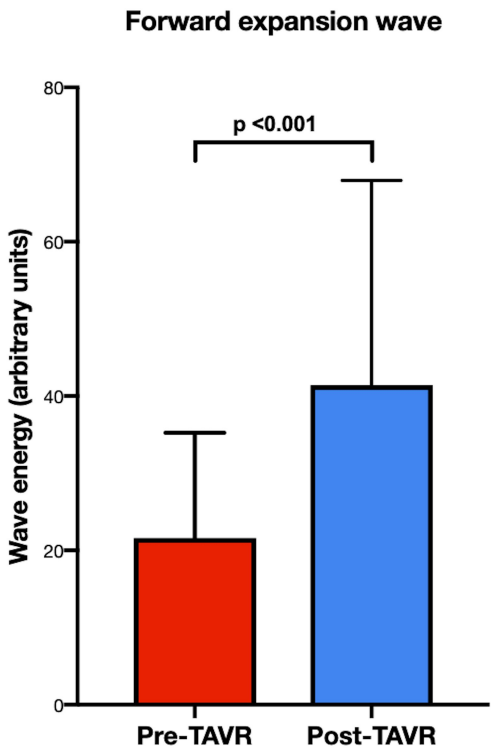
Values are mean ± SD or n (%). TAVR indicates transcatheter aortic valve replacement; Pf, forward going pressure; Pb, reverse going pressure; FCW, forward compression wave; BCW, backward compression wave; FEW, forward expansion wave; a.u., arbitrary units; SEVR, subendocardial viability ratio; DPTI, diastolic pressure-time integral; TTI, left ventricular systolic tension time index.

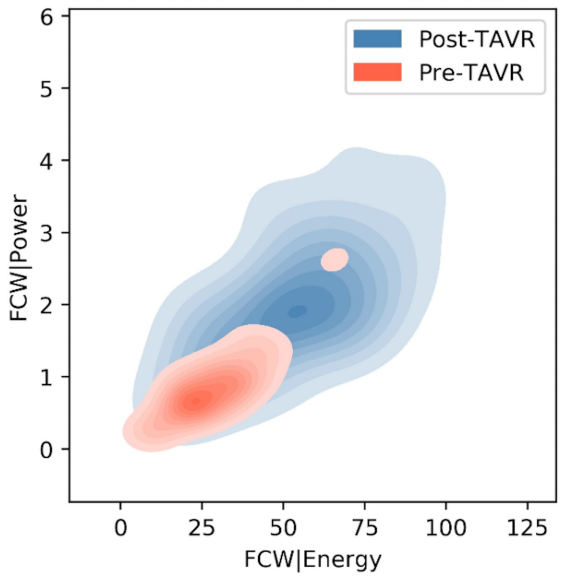

Pre-TAVR aortic and ventricular pressures
A
LV pressure (mmHg)
Ao pressure (mmHg)
Post-TAVR aortic and ventricular pressures
B
Pre-TAVR ensembled aortic and ventricular pressures
C
Pressure (mmHg)
Post-TAVR ensembled aortic and ventricular pressures
D
Pre-TAVR aortic reservoir and excess pressures
E
Pressure – Pd (mmHg)
Reservoir pressure
Excess pressure
Ensembled aortic pressure
Post-TAVR aortic reservoir and excess pressures
F

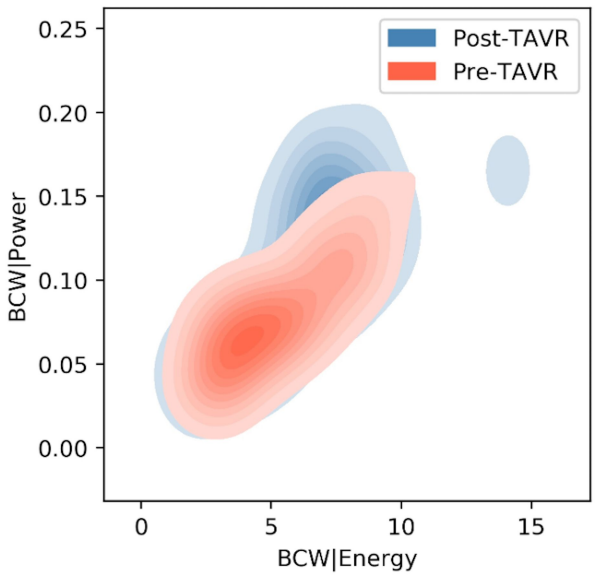

Reservoir pressure
p = 0.30
Reservoir pressure (mmHg)
100
80
60
40
20
0
Pre-TAVR
Post-TAVR
Excess pressure
p <0.001
Excess pressure (mmHg)
100
80
60
40
20
0
Pre-TAVR
Post-TAVR

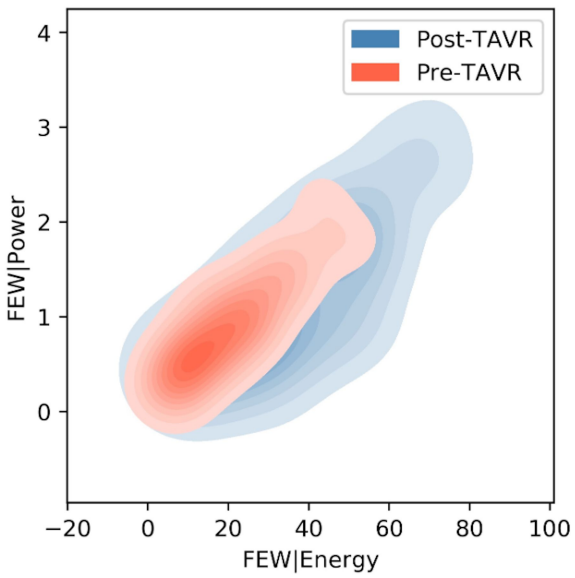

Forward compression wave
p <0.001
Wave energy (arbitrary units)
100
80
60
40
20
0
Pre-TAVR
Post-TAVR


Backwards compression wave
p = 0.01
Wave energy (arbitrary units)
15
10
5
0
Pre-TAVR
Post-TAVR


Forward expansion wave
p <0.001
Wave energy (arbitrary units)
80
60
40
20
0
Pre-TAVR
Post-TAVR


Post-TAVR
Pre-TAVR
FCW|Power
6
5
4
3
2
1
0
0
25
50
75
100
125
FCW|Energy


Post-TAVR
Pre-TAVR
BCW|Power
0.25
0.20
0.15
0.10
0.05
0.00
0
5
10
15
BCW|Energy


Post-TAVR
Pre-TAVR
FEW|Power
4
3
2
1
0
−20
0
20
40
60
80
100
FEW|Energy