



## Hemodynamic monitoring by pulse contour analysis during transcatheter aortic valve replacement: A fast and easy method to optimize procedure results☆☆☆



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### ABSTRACT

**Background:** Residual aortic regurgitation (AR) complicates a not negligible number of transcatheter aortic valve replacement (TAVR) procedures, and its entity is not always clear at intraprocedural angiographic and echocardiographic control. We applied a minimally invasive hemodynamic monitoring system (Pressure Recording Analytical Method, PRAM) in the setting of TAVR, with the aim of identifying parameters that may help in detection and quantification of residual AR.

**Methods:** We performed hemodynamic monitoring with PRAM in 43 patients undergoing trans-femoral TAVR. Investigated parameters were systolic (Psys, mm Hg), diastolic (Pdia, mm Hg), mean (MAP, mm Hg) and diastolic pressure (Pdic, mm Hg), cardiac output (CO, L/min), stroke volume (SV, mL), cardiac cycle efficiency (CCE, Units),  $dP/dt_{max\_rad}$  (mm Hg/ms), MAP-Pdic (mm Hg).

**Results:** Procedural success was achieved in 86% of the patients; vascular complications occurred in 3 (6.9%), death in 2 (4.7%). Twenty (46.5%) patients had at least mild residual AR. CO, SV, CCE and  $dP/dt_{max\_rad}$  changed significantly ( $p < 0.001$ ) between baseline and end of procedure in the overall population, with more evident modifications in the subgroup without residual AR. MAP-Pdic variations were statistically significant only in the subgroup without AR ( $p = 0.05$ ).

**Conclusions:** TAVR determined an improvement in hemodynamic parameters such as CO, SV, CCE,  $dP/dt_{max\_rad}$ . MAP-Pdic was able to discriminate patients with significant residual AR. Hemodynamic monitoring with PRAM system during TAVR is easy and fast to obtain and may help in clinical decision-making in controversial cases.

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### 1. Introduction

Trans-catheter aortic valve replacement (TAVR) is a minimally invasive alternative to conventional surgical aortic valve replacement and is currently applied to elderly patients with aortic valve stenosis at high to intermediate surgical operative risk [1,2]. The number of patients treated with this procedure worldwide is steadily rising along with the expertise gained in this field of cardiac structural interventions [3]. Improvements in procedure planning and technology allowed for an impressive decline in complications such as vascular damage, bleeding,

stroke, incorrect positioning, residual regurgitation, need for permanent pacemaker, etc.

One of the open issues in TAVR is the quantification of residual aortic regurgitation (AR) in the catheterization laboratory after valve implantation. Residual AR is mainly ascribed to paravalvular leak (PVL); it is one of the most relevant aspects impacting on long-term outcomes and its presence guides the need for additional procedural maneuvers (post-dilatation or implantation of a second prosthesis) [4–6]. Most diffuse tools to quantify residual AR are echocardiography and angiography, but these methodologies present intrinsic limitations (poor acoustic window, need for contrast dye administration) and may yield to controversial results.

We applied a pulse-contour analysis based hemodynamic monitoring system (PRAM, Pressure Recording Analytical Method) in patients undergoing TAVR in order to identify PRAM-derived parameters related to the presence of residual AR. The availability of a simple, easy to use parameter indicating the presence and the severity of residual AR may be useful in guiding procedural steps.

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PRAM technology has been validated in several settings, comprising critical care, general surgery and cardiac surgery [7,8], but little is known about its possible applications in patients presenting with severe aortic stenosis and undergoing percutaneous treatment. We attempted to identify baseline hemodynamic profile of severe aortic stenosis patients and the modifications occurring during a non-complicated procedure. The observation of PRAM parameters behavior during TAVR procedures allows us to timely identify abnormal modifications, leading to the early diagnosis of possibly severe complications such as acute bleeding.

## 2. Methods

The study included symptomatic severe aortic stenosis patients undergoing TAVR at our institution between March 2016 and March 2017. Patients were prospectively enrolled in a database recording demographics, clinical and echocardiographic data, cardiovascular risk factors and cardiac and noncardiac comorbidities such as previous myocardial infarction, percutaneous coronary intervention (PCI), coronary artery by-pass grafting (CABG) or valve implantation, chronic obstructive pulmonary disease (COPD), renal failure, peripheral artery disease, cerebrovascular disease. Baseline echocardiographic evaluation was performed, including left ventricular ejection fraction (LVEF), mean aortic valve gradient and valve area, aortic and mitral regurgitation grading.

Every patient underwent surgical risk assessment with calculation of currently used risk scores (EuroSCORE II [9], STS-PROM [10]). Each patient's clinical history was discussed and the indication to TAVR confirmed by a multidisciplinary team. Every patient provided written informed consent to the procedure, including hemodynamic monitoring and the use of data for audit and research. Before performing TAVR, a thoracic-abdominal computed tomography (CT) angiography was obtained in every patient in order to select the best access route and, based on the annulus measurement and valve characteristics, the TAVR prosthesis type and size. Each patient underwent echocardiographic evaluation before hospital discharge with quantification of residual AR.

All data regarding TAVR procedure, intra-operative and periprocedural events as well as short-term outcomes were collected. Device success and adverse clinical events were defined following VARC-2 criteria [11].

During the interventional procedure all patients underwent hemodynamic monitoring with the PRAM system (MostCare, Vygon, Padova, IT). This monitoring system is based on the analysis of the pressure curve originating from an arterial source and has been validated in various settings and described in detail elsewhere [7,12].

All patients underwent 1-month follow-up including NYHA functional class evaluation, physical examination and echocardiography.

## 3. TAVI procedure

All the patients included in the study underwent TAVR by transfemoral route. The patients were implanted with either balloon-expandable (Sapien 3, Edwards Lifesciences, Irvine, CA, USA) or self-expanding (CoreValve Evolut R, Medtronic, Minneapolis, MN, USA) valves as appropriate based on clinical, echocardiographic and CT data.

The procedure was performed under local anesthesia (femoral nerve block with injection of 5 mL lidocaine 2% and 5 ml ropivacaine 0.5%) and mild sedation with fentanyl (0.5–1 µg/kg) in most of the patients; in a minority conscious sedation with fentanyl and propofol was the chosen anesthesiologic strategy. Balloon valvuloplasty was performed before the implantation of the prosthetic valve when indicated. After positioning of the valve, bedside echocardiographic evaluation and aortography with injection of at least 25 mL of contrast medium was performed to assess the presence and severity of aortic regurgitation. When moderate or severe residual aortic regurgitation (AR) was present and incomplete prosthesis expansion was evident, the valve was post-dilated during rapid ventricular pacing.

Before the procedure, radial artery cannulation was performed in every patient and hemodynamic monitoring with PRAM was started.

## 4. Pulse contour analysis with PRAM system

Pressure Recording Analytical Method (PRAM) is a minimally invasive monitoring system that derives multiple variables from beat-to-beat analysis of the arterial waveform. Data are recorded at 1000 Hz and stored electronically. The system requires neither calibration nor the introduction of patient's data such as age or gender as variables are not derived on the basis of pre-estimated parameters; only few anthropometric data are required (height and weight) to obtain indexed hemodynamic parameters.

The variables provided by the PRAM system comprise systolic arterial pressure (P<sub>sys</sub>, mm Hg), diastolic arterial pressure (P<sub>dia</sub>, mm Hg), dicrotic arterial pressure (P<sub>dic</sub>, mm Hg), mean arterial pressure (MAP, mm Hg), pulse rate (PR, bpm), cardiac output (CO, L/min), stroke volume (SV, mL), cardiac cycle efficiency (CCE, units) [12,13],  $dp/dt_{max,rad}$  (mm Hg/ms) (registered at radial artery level) [14], MAP-P<sub>dic</sub> [15] (Mean arterial pressure - dicrotic arterial pressure) (Fig. 1). Electronic storage of data was started in each patient following radial artery cannulation and went on throughout the procedure and it was stopped before the patient exited the operating room. During the registration, the morphology of arterial waves was continuously checked by a physician in order to detect over- or under-damping phenomenon and to optimize arterial waveform with correct positioning of the transducer and line extensions [16,17].

## 5. Statistical methods

Data have been stored in a dedicated database and analyzed with SPSS 20 for Windows (IBM-SPSS Inc., Chicago, IL). Data are reported as frequencies (%) or means ± SD.

Comparisons were made between baseline and end of procedure values by means of Student's *t*-test for paired data. Statistical significance was set for  $p \leq 0.05$ . Receiver operating characteristic (ROC) curves [95% confidence interval (CI)] were constructed for comparison between MAP-P<sub>dic</sub> and residual aortic regurgitation (detected at pre-discharge echocardiography). Linear regression analysis was performed between NYHA class variation at 1-month follow-up and intraprocedural variations in CCE and  $dp/dt_{max,rad}$ . Linear regression analysis was performed between NYHA class variation at 1-month follow-up and MAP-P<sub>dic</sub> measurement at the end of the procedure.

## 6. Results

Baseline demographic and echocardiographic characteristics of the 43 patients included in this study, as well as clinical outcomes following TAVR, are shown in Table 1. Mean age was 86 years (range 71–96), with 26 females (60.5%). Mean EuroSCORE II was 4.06 (range 1.1–20.82), mean STS-PROM was 6.22 (range 1.16–22.89).

Balloon valvuloplasty was performed before implantation of the valve in 34 out of 43 patients (79.1%). Thirty-seven out of 43 patients (86%) reached procedural success according to VARC-2 criteria. In 3 patients (6.9%) moderate AR persisted at the end of the procedure despite post-dilatation. In one patient implantation of a second prosthesis was required because of migration of the first prosthesis towards the ascending aorta. Two patients died before discharge; in one case, death occurred after surgical treatment of procedure-related papillary muscle rupture determining severe mitral regurgitation with cardiogenic shock. In the other patient, cardiac tamponade due to left ventricular outflow tract rupture occurred, with prompt but unsuccessful surgical correction.

Three patients (6.9%) experienced vascular access related complications. One superficial femoral artery occlusion required balloon



**Fig. 1.** PRAM monitoring system provides several classical and specific hemodynamic parameters, based on the arterial pressure waveform and on the identification of diastolic pressure. ABP = arterial blood pressure; PR = pulse rate; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; CVP = central venous pressure; PPV = pulse pressure variation; CCE = cardiac cycle efficiency; Ea = arterial elastance.

angioplasty, one common iliac artery dissection and partial rupture was treated with covered stent implantation, one access site bleeding was corrected surgically.

**Table 1**

Baseline demographic, clinical and echocardiographic characteristics of study population and procedural outcomes.

Variable	All patients (n = 43)
Age (years), mean ± SD (range)	86 ± 4 (71–96)
Female, n (%)	26 (60.5%)
BSA (m <sup>2</sup> ), median (IQR)	1.68 (1.24–2.11)
EuroSCORE II, mean ± SD (range)	4.06 ± 3.9 (1.1–20.82)
STS-PROM, mean ± SD (range)	6.22 ± 4.6 (1.16–22.89)
Hypertension, n (%)	33 (76.7%)
Diabetes, n (%)	11 (25.6%)
Atrial fibrillation, n (%)	7 (16.3%)
Chronic lung disease, n (%)	4 (9.3%)
Renal failure (eGFR < 60 mL/min), n (%)	19 (44.2%)
Peripheral vascular disease, n (%)	3 (6.9%)
Cerebrovascular disease, n (%)	1 (2.3%)
Previous CABG, n (%)	4 (9.3%)
Previous PCI, n (%)	19 (44.2%)
NYHA class II, n (%)	16 (37.2%)
NYHA class III, n (%)	24 (55.8%)
NYHA class IV, n (%)	2 (4.7%)
LVEF (%), mean ± SD (range)	53 ± 9.7 (29–68)
AVA index (cm <sup>2</sup> /m <sup>2</sup> ), mean ± SD (range)	0.41 ± 0.13 (0.24–0.73)
Mean pressure gradient (mm Hg), mean ± SD (range)	51 ± 16.02 (20–84)
Procedural success (VARC-2 criteria), n (%)	37 (86%)
At least mild AR, n (%)	20 (46.5%)
Moderate AR, n (%)	3 (6.9%)
Vascular complications, n (%)	3 (6.9%)
Cerebrovascular complications, n (%)	0 (0%)
Permanent pacemaker implantation, n (%)	4 (9.3%)
Peri-procedural death, n (%)	2 (4.7%)

SD = standard deviation, BSA = body surface area; IQR (interquartile range), STS-PROM = society of thoracic surgeons predicted risk of mortality; eGFR = estimated glomerular filtration rate (MDRD formula); CABG = coronary artery by-pass grafting; PCI = percutaneous coronary intervention; NYHA = New York Heart Association; LVEF = left ventricle ejection fraction; AVA = aortic valve area; VARC = valve academic research consortium; AR = aortic regurgitation.

Based on pre-discharge echocardiographic evaluation, at least mild AR was observed in 20 patients (46.5%); 12 (60%) received a self-expanding valve and 8 (40%) a balloon-expandable valve. Fig. 2 shows the result of hemodynamic monitoring in a case of moderate AR.

Results of comparisons between PRAM parameters registered at baseline and at the end of the procedure are summarized in Table 2. These comparisons are also presented separately for the two subgroups with no residual AR (23 patients) and with mild/moderate AR (20 patients).

There was no statistically significant difference between baseline and post-procedure measurements for Psys, Pdia, MAP, Pdic in the overall population.

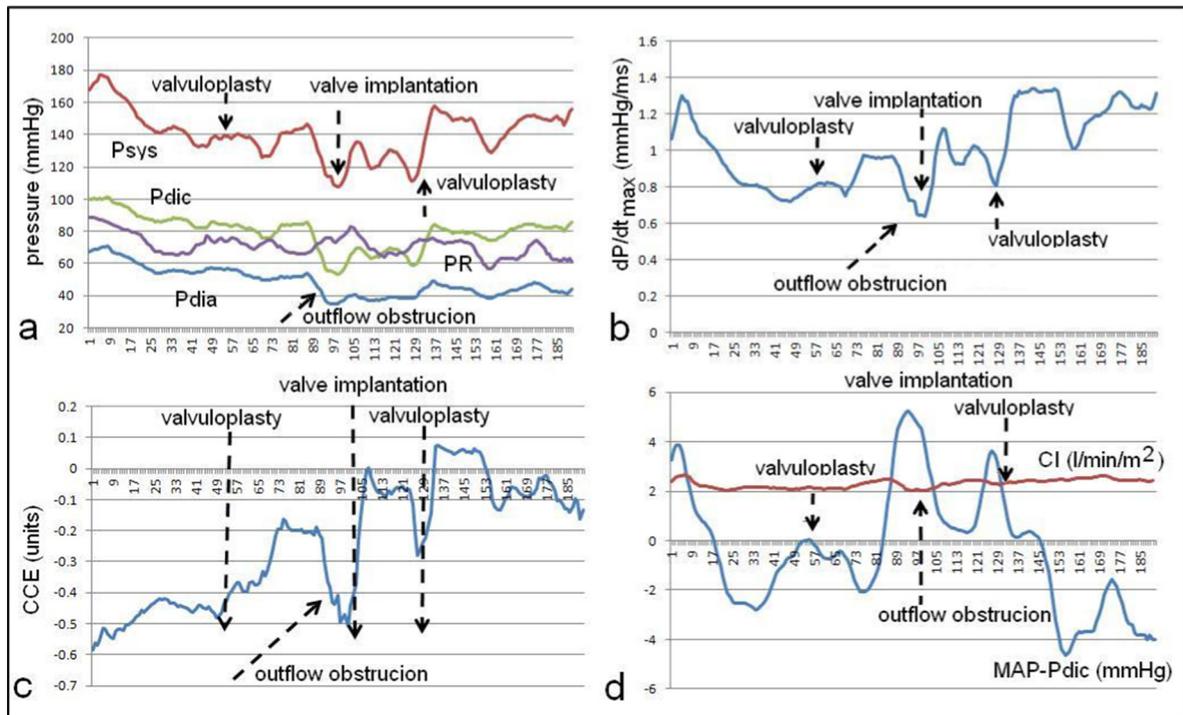
CO, SV and CCE significantly increased post-procedurally in the overall population and in both subgroups (with/without residual AR). dP/dt<sub>max,rad</sub> increased significantly from baseline to post-procedure in the overall population, but failed to demonstrate significant improvement in the subgroup with at least mild AR.

The MAP-Pdic measurements showed significant modifications only in the subgroup without residual AR (from a negative average measurement of  $-1.57 \pm 4.61$  at baseline to positive measurements of  $0.92 \pm 6.46$  post-TAVR,  $p = 0.005$ ).

NYHA functional class significantly improved from  $2.65 \pm 0.57$  at baseline to  $1.41 \pm 0.49$  at 1-month follow-up ( $p < 0.0001$ ). SV and CO variations did not correlate with NYHA improvement; on the contrary, CCE and dP/dt<sub>max,rad</sub> intra-procedural variations correlated significantly with NYHA class variation ( $r^2 = 0.21$  and  $p = 0.024$ ;  $r^2 = 0.31$  and  $p = 0.0001$ , respectively). MAP-Pdic measurement at the end of the procedure correlated with NYHA class improvement at 1-month follow-up ( $r^2 = 0.25$ ,  $p = 0.0007$ ) (Fig. 3).

In order to identify a cut-off threshold able to discriminate patients presenting with at least mild residual AR, we analyzed by means of receiver operating characteristic (ROC) curve both MAP-Pdic delta (end minus baseline) and absolute MAP-Pdic at the end of the procedure.

For delta, we found an area under the curve (AUC) of 0.69 (95%CI 0.53 to 0.84,  $p = 0.037$ ). This analysis found a cut-off of 4.8 mm Hg



**Fig. 2.** Hemodynamic monitoring in a patient presenting with moderate residual AR at end of procedure. a) Systemic variables showing minor fluctuations during the procedure. b)  $dP/dt_{max\_rad}$  decreasing during the initial part of the procedure, possibly due to administration of anesthesiologic drugs, with step-wise increases after each valve-related maneuver (balloon valvuloplasty, valve release, post-dilatation). c) Initial CCE values are very low, present step-like increases after balloon valvuloplasty, a temporary decrease with positioning of the prosthetic valve within the stenotic valve orifice (probably due to mechanical obstruction to outflow and to rapid ventricular pacing) and a second, consistent, step-wise increase after valve deployment. After the decision to post-dilate, we can observe a second drop in CCE corresponding to positioning of the valvuloplasty balloon within the prosthesis and to rapid ventricular pacing, followed by a marked increase to positive values after post-dilatation. d) MAP-Pdic initial values are slightly positive, after fluctuations corresponding to procedural maneuvers shows negative values at the end of the procedure, consistent with the presence of significant residual regurgitation; in this situation, not all of ventricular work is used to maintain systemic perfusion and the reflow of part of systolic output towards the left ventricle makes aortic valve closure to occur earlier than in standard conditions because of rapid raising of ventricular pressure. As a consequence, Pdic values are higher than MAP and MAP-Pdic shows negative values. In this case, angiography and echocardiography confirmed the persistence of moderate AR. AR = aortic regurgitation; CCE = cardiac cycle efficiency; Pdic = diastolic pressure; MAP = mean arterial pressure. On horizontal axis: time (30 s steps).

using the Youden's method with a sensitivity of 90%, a specificity of 43% and a correct classification rate (efficiency) of 65%.

When absolute MAP-Pdic value was considered, an AUC of 0.75 was obtained, and a cut-off of  $-1.93$  mm Hg had a sensitivity of 85%, a specificity of 65% and an efficiency of 74%.

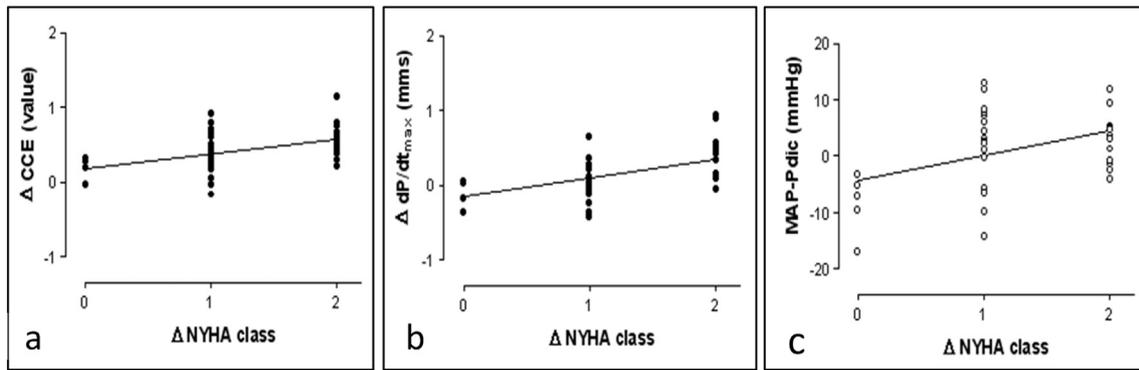
**7. Discussion**

Hemodynamic monitoring with the PRAM system consists in continuous monitoring of both classical hemodynamic parameters and more sophisticated indices of ventriculo-arterial coupling. While the

**Table 2**  
Results of PRAM measurement at baseline and end of procedure.

	Base (n = 43)	End (n = 43)	p-Value	Base No/trivial AR (n = 23)	End No/trivial AR (n = 23)	p-Value	Base Mild/moderate AR (n = 20)	End Mild/moderate AR (n = 20)	p-Value
Psys (mm Hg), mean ± SD	147.8 28.8	153.9 22.8	0.703	146.1 31.2	152.2 19.6	0.965	152.6 28.1	155.8 26.7	0.784
Pdia (mm Hg), mean ± SD	60.9 11.8	62.4 11.2	0.595	59.8 11.2	65.5 11.5	0.789	62.5 12.4	58.9 10.1	0.207
MAP (mm Hg), mean ± SD	89.9 15.3	92.9 13.2	0.857	88.6 15.6	94.4 13.3	0.938	92.6 15.3	91.2 13.7	0.507
Pdic (mm Hg), mean ± SD	92.4 17.3	94.1 14.8	0.419	90.3 18.3	93.4 15.0	0.366	95.9 15.9	94.7 15.2	0.649
PR (bpm), mean ± SD	69.1 9.1	67.5 10.5	<b>0.012</b>	69.2 7.9	66.5 10.8	0.224	69.6 10.8	68.6 10.5	<b>0.004</b>
CO (L/min), mean ± SD	4.38 0.53	4.95 0.69	<b>&lt;0.001</b>	4.38 0.52	5.08 0.71	<b>0.003</b>	4.36 0.55	4.80 0.67	<b>&lt;0.001</b>
SV (mL), mean ± SD	66.5 13.5	76.3 13.9	<b>&lt;0.001</b>	65.8 10.9	79.4 13.0	<b>0.001</b>	66.5 16.4	72.8 14.7	<b>&lt;0.001</b>
CCE (units), mean ± SD	-0.330 0.341	0.058 0.244	<b>&lt;0.001</b>	-0.316 0.282	0.100 0.177	<b>&lt;0.001</b>	-0.345 0.401	0.012 0.302	<b>&lt;0.001</b>
$dP/dt_{max\_rad}$ (mm Hg/ms), mean ± SD	0.983 0.368	1.187 0.305	<b>&lt;0.001</b>	0.984 0.413	1.209 0.295	<b>0.004</b>	1.030 0.374	1.162 0.329	0.053
MAP-Pdic (mm Hg), mean ± SD	-2.30 5.62	-1.07 6.43	0.105	-1.57 4.61	0.92 6.46	<b>0.005</b>	-3.10 6.56	-3.92 5.47	0.564 0.012*

Psys = systolic pressure; Pdia = diastolic pressure; MAP = mean arterial pressure; Pdic = diastolic pressure; PR = pulse rate; CO = cardiac output; SV = stroke volume; CCE = cardiac cycle efficiency. Statistical significance set for  $p < 0.05$ .



**Fig. 3.** Linear regression analysis between NYHA class variation at 1 month follow-up and intraprocedural variations in CCE (a), intraprocedural variations in  $dP/dt_{\max\_rad}$  (b), and end of procedure MAP-Pdic (c).

improvement in cardiac efficiency indexes and ventricular contractility indexes were expected and in line with previous reports post TAVR and AVR, a PRAM-specific parameter, MAP-Pdic, showed a different behavior at post-procedural evaluation in patients with or without residual AR. Residual AR is still an open issue after TAVR. Despite technological improvements aimed at obtaining optimal valve positioning and complete sealing on aortic annulus, at least mild AR is observed in a consistent proportion of patients and its prognostic significance is still under debate. Most studies have shown worse long term prognosis in the presence of moderate to severe residual AR but some studies suggested a higher mortality even with mild AR [18–21]. In the PARTNER trials and registries, one-year mortality was higher both in patients with moderate/severe residual AR and with mild residual AR compared to patients with none/trace paravalvular leak [22]. Some recent studies failed to demonstrate higher mortality in patients with mild/moderate AR, but observed higher incidence of progression to grade  $\geq 3$  AR [23]. Part of these discrepancies can be caused by the lack of reliability of the diagnostic techniques used for assessment of aortic regurgitation. Of course transthoracic echocardiography remains the most widely used and readily available method but the assessment of paravalvular regurgitation is suboptimal. Contrast injection in the ascending aorta is recommended in all cases post-TAVR, also to confirm coronary patency, but results are critically dependent from rate and amount of contrast injected and the position of the pig-tail catheter. The aortic regurgitation index [(aortic diastolic blood pressure – left ventricular end-diastolic pressure)/systolic blood pressure  $\times 100$ ] is a generally accepted parameter, with values  $< 25$  considered as an index of significant AR [24]. Still this is an invasive method requiring the crossing of the prosthesis after deployment to obtain intraventricular pressures; moreover, AR seems not to be the only determinant of ARI, which can be influenced by several factors such as heart rate, increased aortic stiffness, diastolic dysfunction causing LV end diastolic pressure elevation. Transesophageal echocardiography is certainly more reliable in the evaluation of paravalvular regurgitation circumferential extension, but this method is not in practical use in the vast majority of the transfemoral TAVR performed under local anesthesia. AR measured with cardiac magnetic resonance (CMR) has been claimed to have the greatest accuracy but this method is cumbersome, not always applicable to frail not fully cooperative elderly patients and anyway this assessment is not widely available.

MAP-Pdic (difference between mean arterial pressure and dirotic pressure) is an expression of the interaction between LV contractility and a given afterload. In normal conditions, dirotic pressure (corresponding to aortic pressure at the time of aortic valve closure) is similar to MAP, and MAP-Pdic values approach 0. In the presence of aortic regurgitation, aortic valve closure occurs earlier within the cardiac cycle, shifting the dirotic pressure to higher levels so that the difference between MAP and Pdic tends to become negative. In our study, MAP-Pdic variations in the subgroup without residual AR were statistically significant, with positive end of procedure measurements, while in the

subgroup with at least mild AR MAP-Pdic remained negative. Low baseline values ( $-2.3 \pm 5.6$  mm Hg) suggest the presence of increased Pdic measurements in most patients, possibly related to some degree of AR in the context of aortic stenosis; MAP-Pdic variations during the procedure, and specifically after valve deployment, appear to be closely related to variations in AR severity.

If validated with further studies and within larger populations, this parameter may be useful in identifying the presence and hemodynamic relevance of residual AR, and it could have a role in decision making about valve post-dilatation or, in extreme cases, implantation of a second valve.

We also evaluated the behavior of other hemodynamic parameters in relation to the presence or absence of residual AR.

CCE, the ratio between hemodynamic work performed by the heart and energy expenditure [13], increased significantly in the overall population and in the two subgroups, possibly indicating an improved ventriculo-arterial coupling after relieving the aortic stenosis. This was observed in the overall population, but crude values were higher in the subgroup without residual AR. Also CO and SV showed a significant increase at the end of the procedure in all subgroups, with higher measurements in the subgroup without residual AR.

$dP/dt_{\max\_rad}$  is a descriptor of pressure wave profile, expressed as the variation in pressure (p) over time (t) during systole; a high  $dP/dt$  ratio indicates an improved LV contractility, while a low  $dP/dt$  ratio indicates reduced cardiac contractility [25,26]. In our study  $dP/dt_{\max\_rad}$  changed significantly between baseline and end of procedure in the overall population but this was mainly due to significant improvement in the subgroup without residual AR; in the group with at least mild AR,  $dP/dt_{\max\_rad}$  variations did not reach statistical significance ( $p = 0.53$ ). Taken together, these results suggest that even a mild degree of residual AR impairs the optimal performance of the implanted valve.

	No AR	Mild/moderate AR	Bleeding
CO (L/min)	↑	↑	↑
SV (mL)	↑	↑	↑
CCE (units)	↑	↑	↓
$dP/dt_{\max\_rad}$ (mmHg/ms)	↑	=	↑
MAP-Pdic (mmHg)	↑	↓	↑

**Fig. 4.** Summary of main PRAM parameters modifications in patients presenting without significant residual AR, with mild/moderate AR or with periprocedural bleeding after TAVR. CO = cardiac output; SV = stroke volume; CCE = cardiac cycle efficiency; AR = aortic regurgitation.

In Fig. 4 we summarize the modifications in main PRAM parameters following aortic valve implantation without residual AR, with at least mild AR or in case of significant bleeding. A sudden hypotension during TAVR occurs in some cases and the identification of its cause is not always immediate (e.g.: bleeding, pericardial effusion, coronary occlusion, pump failure). The implementation of PRAM parameters allows an easy and fast detection of bleeding; in this case we observe a preserved  $dp/dt_{\max\_rad}$  along with a sudden reduction in CCE.

One of the strengths of this study is the inclusion of patients treated without general anesthesia (GA), minimizing the hemodynamic influence of anesthesiologic drugs. This allowed a fair comparison of indexes of myocardial efficiency and ventriculo-arterial coupling, without the confounding changes induced by GA. We are aware that most studies dealing with PRAM methodology validation did not include patients presenting with severe aortic stenosis, a condition that may alter pressure wave transmission at the peripheral level.

However, a recent multicentric study successfully demonstrated a good correlation between echocardiographic and PRAM-derived cardiac output in a population of ICU patients with a large spectrum of clinical conditions [7]. Other authors have evaluated the performance of PRAM methodology in the setting of unstable patients after cardiac surgery, including single valve intervention, demonstrating good agreement between PRAM and thermodilution measurements [8]. In the setting of severe aortic stenosis patients undergoing TAVR, PRAM technology, not needing calibration nor pre-estimated parameters insertion, could be particularly useful in determining the effectiveness of the treatment based on pressure waveform modifications after prosthesis positioning.

## 8. Study limitations

The main limitation of the present study is that the study population was consecutive but small. Fortunately modern prostheses have greatly diminished the amount of residual AR. This explains why moderate residual AR was present in only 3/43 patients precluding the possibility of a separate statistical analysis for patients presenting with mild and moderate residual AR. This could be very useful because in most studies, the negative prognostic significance of AR seems to be limited to moderate AR. Moreover, if conducted within a larger population and with a greater number of moderate residual AR, the analysis could lead to the identification of a threshold value for MAP-Pdic identifying moderate AR.

## 9. Conclusions

TAVR determined an improvement in hemodynamic parameters such as CO, SV, CCE,  $dp/dt_{\max\_rad}$ ; which was more evident in the absence of residual AR. A PRAM-specific hemodynamic parameter, MAP-Pdic, showed significant modifications after prosthesis deployment only in the subgroup of patients who did not present significant residual AR, and appeared to be useful in discriminating patients with even mild AR. If this observation was confirmed within larger populations, and possibly after the identification of a threshold value defining moderate AR, MAP-Pdic could become an immediate tool to guide intraprocedural decision-making in controversial cases.

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