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Association between dicrotic notch and paravalvular regurgitation during the TAVI procedure

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NIEMINEN JENNY: Association between dicrotic notch and paravalvular regurgitation during the TAVI procedure

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Aorttaläppäahtauma on länsimaissa yleisin kajoavaa hoitoa vaativa läppäsairaus. TAVI:sta on tullut rutiinivaihtoehto etenkin suuren riskin potilaille ja sen tunnetuin komplikaatioriski on paravalvulaarinen vuoto (PVR), joka useiden tutkimusten mukaan korreloi negatiivisesti potilaan lyhyt- ja pitkäaikaisennusteeseen. Toimenpiteen aikana aortan painekäyrän kaksijakoisen pulssiaallon välissä voidaan havaita painauma (dicrotic notch, DN) aorttaläpän sulkeutuessa, jonka avulla paravalvulaariset vuodot voitaisiin löytää sydämen ultraäänitutkimusta luotettavammin ja tunnistaa potilaat, jotka tarvitsevat lisätoimia läppätoimenpiteen jälkeen. Myös aortan systolisen paineen merkittävä lasku läppärenkaan ympäryksen kontaktin jälkeen tiedetään viittaa parempaan hemodynaamiseen ennusteeseen ja se voisi tarjota kliinikolle yksinkertaisen ja nopean työkalun tekoläpän implantaation onnistumisen arvioimiseksi.

Tutkimuksen tavoitteena on ymmärtää hemodynaamisten muuttujien ja etenkin aortan painekäyrän dikroottisen painauman ennustevaikutusta suhteessa PVR:n esiintymiseen ja TAVI-läpän implantaation onnistumiseen, sekä mahdollisesti parantaa ja ohjata toimenpiteenaikaista päätöksen tekoa PVR:n suhteen.

Tutkimukseen sisältyi 101 vaikeaa aorttaläppäahtaumaa sairastavaa potilasta, joista kerättiin keskeiset kliiniset muuttujat ja toimenpiteen aikana monitoroitiin aortan painekäyrää. Välittömästi TAVI-läpän implantaation jälkeen tehtiin katetriteitse aortan varjoainekuvaus (aorttografia), jotka analysoitiin myöhemmin videodensitometrialla (VD). DN analysoitiin aortan painekäyristä kolmiportaista asteikkoa käyttäen. Näitä tuloksia verrattiin VD-analyysiin, joita edelleen potilaiden kliinisiin muuttujiin sekä sydämen ultraäänen ja aortan-TT:n kuvantamislöydöksiin.

Päätuloksena havaittiin, että DN:n esiintyminen liittyi merkitsevästi pienempään kliiniseen PVR:n esiintymiseen ($p=0.032$). Lisäksi potilaat, joilla esiintyi DN ja diastolinen verenpaine ylitti 40 mmHg, kliinisesti merkittävän paravalvulaarivuodon kehittyminen on erittäin epätodennäköistä. Tulokset viittaavat siihen, että DN:n esiintyminen läpän asennuksen jälkeen voisi toimia hemodynaamisena merkkinä potilaiden arvioinnissa aorttografian ja ultraäänen lisäksi.

ABSTRACT

Aims: Paravalvular regurgitation (PVR) after transcatheter aortic valve implantation (TAVI) is a well-known complication that is associated with increased mortality. Therefore, its prompt detection and effective management are crucial for improving patient outcomes. The aim of this study was to evaluate the presence of dicrotic notch (DN), defined as a small secondary upstroke in the descending phase of the arterial pressure waveform following the systolic peak and its association with PVR during TAVI.

Methods: In this retrospective singe-centre study, DN was assessed for its correlation with PVR during TAVI from a total of 101 patients. Patients were categorized into two groups based on the presence or absence of DN, which was determined from arterial pressure line recordings taken simultaneously with aortography. PVR was analysed from the left ventricular outflow tract (LVOT) using videodensitometry (VD) of aortography, with clinically significant PVR defined as LVOT-VD > 17%.

Results: DN was observed in 37 patients (36.6%) and clinically relevant PVR (LVOT-VD > 17%) was found in 24/101 patients (23.8%). The mean age of the notch cohort was 81.2 ± 6.6 years, with 54.5% being male. The mean gradient was 47.0 ± 14.1 mmHg, and the median aortic valve area (AVA) was 0.72 cm² (0.6–0.8).

Among patients with DN, 3/37 (8.1%) had an LVOT-VD > 17%, compared to 21/64 (32.8%) in patients without DN (AOR 0.14, 95% CI 0.02–0.84, p = 0.032). These results gave sensitivity (44.16%, 95% CI 32.84% to 55.93%), specificity (87.50%, 95% CI 67.64% to 97.34%), positive predictive value 91.9% (95% CI 79.3% to 97.1%) and negative predictive value 32.8% (95% CI 27.6% to 38.5%).

When considering diastolic pressure, patients with DN and diastolic pressure ≥ 40 mmHg had an incidence of significant PVR of 3.1%, while those without DN or with diastolic pressure < 40 mmHg had an incidence of 33.3% (AOR 0.067 95%CI 0.008-0.572, p=0.012). Balloon post-dilation was performed in 33 patients, with a lower incidence in patients with DN (40.6% vs. 18.9%; p = 0.025).

Conclusions: The presence of DN after valve deployment is associated with significantly lower rates of PVR. This finding suggests that DN may serve as a simple visual hemodynamic marker to guide decision-making during the TAVI procedure.

Key words: transcatheter aortic valve implantation, paravalvular regurgitation, dicrotic notch

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1. INTRODUCTION

1.1 Prevalence and risk factors

Aortic stenosis (AS) has become one of the most common valve diseases in developed countries along with mitral regurgitation. Its prevalence is expected to increase due to aging populations and its impact on healthcare resource consumptions is expanding.[1,2] Previous studies have estimated the clinically significant prevalence of aortic stenosis (AS) to range from 9,8% to 12,4% overall, with severe AS affecting approximately 3,4% to 4,3% of individuals over the age of 70 [3–5]. The incidence of severe AS has been estimated to be 52,5/100 000[6]. Given limited resources, it's crucial to focus on prevention and several risk factors has been identified that predispose to the development of AS. The most important of these include age, hypertension, hypercholesterolaemia, male gender, present smoking and diabetes [7–9]. From congenital abnormalities, bicuspid aortic valve is the most common and strongest predictor of severe AS with a prevalence estimated between 0,5-2,0% [10,11]. To date, no scientific evidence supports the notion that managing risk factors prevents the development of aortic stenosis.

1.2 Pathophysiology

AS is characterized by an inflammatory process driven by endothelial dysfunction from mechanical stress, lipoprotein and immune cell penetration leading to fibrosis, leaflet thickening and ultimately calcification. This calcification resembles the process seen in atherosclerosis and due to a progressive fibro-calcific remodelling and thickening of the cups leads to obstruction. The narrowed valve orifice results in a pressure gradient across the valve and with concomitant left ventricular pressure overload to LV hypertrophy but also to decreased coronary flow while the oxygen demand of the hypertrophic tissue has increased making the myocardium more susceptible to ischemia.[12–14] AS is a progressive disease with markedly increased all-cause mortality after symptom onset, with untreated symptomatic patients having an average life expectancy of two to five years after symptom onset.[15–17]

1.3 Clinical features and treatment

As previously described the pathophysiological mechanisms give rise to three cardinal symptoms: exertion-related angina, dyspnea due to the congestive heart failure and presyncope or syncope. Diagnosis primarily relays on transthoracic echocardiography to assess the severity of stenosis, as well as valve calcification and LV function. Additionally, CT and coronary angiography are essential for providing valuable information when planning the intervention and assessing prognosis. Currently, there are only invasive treatment options available but no effective medical therapy. Symptomatic AS is an indication for intervention while asymptomatic disease is typically recommended to treat if there's evidence of impaired LV function or if the patients develop symptoms during exercise training, but watchful waiting has been generally recommended with prompt intervention at symptom onset.[18,19] The use of SAVR and TAVI has increased overall survival and the choice of intervention modality is based on patient's characteristics and predicted life expectancy.

1.4 Transcatheter aortic valve implantation

Transcatheter aortic valve implantation (TAVI) has established its place in operatively treating patients with severe aortic stenosis possessing intermediate or major risk factors for surgical aortic valve replacement. Though advancements in valve design, image planning and increased operator experience have contributed to enhanced safety and reduction of procedural complications, paravalvular regurgitation (PVR) remains a major and well-known complication of TAVI[20,21]. Since the valve is implanted without sutures using oversizing to expand a stent, several etiologies for PVR have been proposed, such as an incomplete circumferential apposition of the prosthesis to the native annulus, suboptimal placement of the prosthesis or annulus-prosthesis-size mismatch. PVR is shown to be associated with poorer short- and long-term outcomes and increased mortality.[22,23] Therefore treatment of clinically relevant PVR immediately post-TAVI is recommended and may include balloon post-dilatation (BPD), valve retrieval and repositioning or valve-in-valve implantation[18,19].

1.5 Assessment of paravalvular regurgitation

Accurate grading of the severity of PVR is essential to guide interventions for prognostic and therapeutic purposes. There is evidence that patients with moderate or greater PVR have up to a threefold increase in mortality compared to those with none-trace and even mild-moderate PVR increased the 5-year overall mortality [24]. Previous studies have reported that the occurrence of moderate-to-severe PVR after TAVI can be as high as 7,4-17,2%[23,25,26]. The observed variability is likely due to differences in imaging modalities, timing of assessment, grading criteria and the types of prosthetic valves utilized.

The intraprocedural detection of PVR can be challenging due to constantly changing hemodynamic conditions and limitations in measurement technology. Transesophageal echocardiography (TEE) is impractical due to minimalist approach without. Transthoracic echocardiography (TTE) potentially under- or overestimates the true severity of PVR due to the nature of regurgitation mechanism in combination with regional calcification and additional signal artifacts. Despite these limitations, it remains together with aortography the mostly used method for detecting PVR. [27,28] Aortic root angiography is widely used it relies on reproducibility in classification through visual estimation is thus semi-quantitative and dependent on technical factors[29]. Therefore, invasive hemodynamic indices could offer a more precise method for accurate grading of PVR. [24,30]

Invasive hemodynamic indices and quantitative videodensitometry have emerged as a reproducible and more precise solutions for evaluating PVR. Quantitative videodensitometry enables an assessment of the regurgitant fraction (RF) using the final aortogram obtained after valve implantation. It has been validated in vitro with a mock circulation system[31] and in vivo using a porcine model[32]. It has demonstrated good correlation compared both to CMR and echocardiography. However its shortcomings are mainly limited yield, variabilities in angiographic acquisition standardization and its offline application requiring manual contour tracing. [30,33–35] To date, it has predominantly been utilized post-procedurally, with exception of a single study demonstrating its feasibility during the procedure as well[36].

1.6 Hemodynamic parameters predicting PVR

Previous studies have demonstrated the impact of LVOT, AVC (aortic valve cusp) and DLZ (device landing zone) calcification[37,38], larger annular dimensions[39] device under sizing and implantation depth[40] as risk factors for PVR after TAVI. Additional indexes to improve predictive values of hemodynamic parameters have been introduced such as ARI, DD, TIARI and DPTI.

The AR index has been demonstrated to decrease in parallel with increasing severity of PVR offering a precise judgement of the degree of PVR[41] whereas dicrotic AR index seems to be even more accurate than AR index[42]. Diastolic delta (DD) has shown the best correlation and predictive value for relevant PVR whereas ARI ratio is the strongest hemodynamic predictive value for 1-year mortality after TAVR[43]. Additionally it has been implied that DD ≤ 32 mmHg could guide the decision making to perform additional post-dilatation in order to reduce PVR[24]. Also time integrated aortic regurgitation index (TIARI) has been shown to associate with BDP after valve deployment however not being readily available during procedure[44]. Diastolic pressure-Time Index (DPTI) is significantly lower inpatients with relevant AR and predicts1-yearmortality after TAVI[45]. Despite the favourable preliminary findings, these methods require either intra-procedural left ventricular catheterization or complex integral calculations, which limit their practicality.

1.7 Dicrotic notch as an easily visualizable intraprocedural marker

Dicrotic notch (ND) is a small secondary upstroke in the descending phase of the arterial pressure waveform following the systolic peak[46]. A diminished notch magnitude is associated with significant aortic regurgitation, typically explained by increased pressure from stenosis, as well as inadequate filling of the sinuses and insufficient leaflet pliability for rapid closure, although several hypotheses on the mechanism of DN have been proposed[46,47]. In patients with severe calcified aortic stenosis as well as significant regurgitation DN occurs at a lower amplitude or is absent[48].

Only one study has demonstrated that dicrotic notch index (DNI) defined as the difference between SBP and dicrotic notch divided by pulse pressure, suggest that a lower DNI is observed in patients with hemodynamically significant aortic regurgitation. Statistical difference has been found in DNI between patients with ≥ moderate PVL and those with ≤ mild PVL, although there were only five patients in the former study group.[49] Another study suggest that the dicrotic AR index reflecting the actual pressure drop by the regurgitant flow occurring during the diastolic phase after aortic valve closure and dicrotic notch, decreases proportionately according to the PVR grade[42].

Interpretation of dicrotic notch could offer a useful addition in evaluation of PVR intraoperatively during TAVI without the need of LV pressure measurement of advanced integral calculations. Also, DN is a specific point on the waveform reflecting aortic valve closure whereas the other indices (ARI, DD, TIARI, DPTI) are derived from different parameters of arterial pressure dynamics.

In this study, we aimed to assess the predictive value of the dicrotic notch (DN) for identifying clinically significant paravalvular regurgitation (PVR) and predicting implantation success to support and guide early decision-making regarding PVR.

METHODS

2.1 Patients and study design

In this retrospective single-centre study all consecutive patients (between 29.11.2021 – 19.9.2022) with severe aortic stenosis referred for TAVI to Turku University hospital Heart Center were evaluated for this study. After excluding 22 patients due to missing or non-analysable hemodynamic tracings and videodensiometric data, 101 patients were included in the final analysis. Patient demographics and procedural data were collected from medical records and the TAVI registry.

All patients were treated with either self-expandable valve (Acurate Neo 2 ®; Boston Scientific, Marlborough, Massachusetts, USA or Evolut Pro ®; Medtronic, Dublin, Ireland) or balloon expandable valve (Sapien Ultra ®; Edwards Lifesciences, Irvine, California, USA) using full range of all available valve sizes.

The study has been approved by the Ethics Committee of the University of Turku and all patients has provided written informed consent in accordance with the Declaration of Helsinki between January 2022 and September 2022.

2.2 TAVR procedure

For all patients the procedure was performed via the transfemoral approach under local anaesthesia. Aortography and transthoracic echocardiography were utilized to assess the procedural outcome. The decision for post-dilatation due to clinically relevant PVR or an insufficiently expanded valve was assessed based on clinical indications by the primary operator. All safety endpoints were reported according to the VARC-3 criteria[50]. Aortography was performed with pigtail catheter using 20ml and 15ml/s contrast dye in all cases.

2.3 Hemodynamic parameters and videodensiometric analysis

Hemodynamic tracings were captured as a snapshot simultaneously with aortography from the patient's hemodynamic monitor during the procedure. These tracings were collected from the arterial line in the radial artery, with at least three representative cardiac cycles recorded.

In previous studies, dicrotic notches have been categorized into four types (Type I to IV) [47]. In Type I, there is a clear incisura in the downward slope of the wave before the DN, which then makes an upward motion in the pressure curve. To simplify visual assessment and to identify an accessible periprocedural hemodynamic marker, we classified patients with Type I as the DN group. All other types (Types II–IV), which show horizontal, slurred, or diminished waves, were categorized as the no-DN group. In this study, analysis of arterial pressure waveforms and

classification into DN and no-DN groups were performed by an experienced senior TAVI operator in a blinded manner. An example of DN characterization is presented in Figure 1.

Figure 1

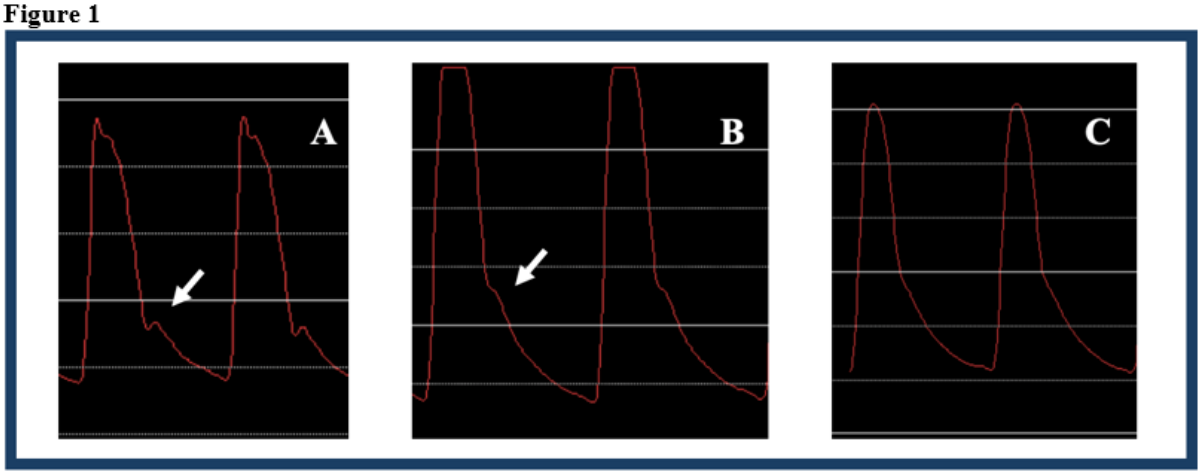

Figure 1. Examples of DN types in blood pressure tracings. (A) The DN is clearly visible with a prominent upstroke (arrow). (B) The DN in distinguishable and lacking the upstroke component. (C) The DN is absent altogether. Example A was categorized as the DN group, while B and C were classified into the no-DN group.

Quantitative assessment of PVR using videodensitometry was conducted with CAAS A-Valve (version 2.0.2, Pie Medical Imaging, Maastricht, The Netherlands). This software generated time-density curves in the aortic root and left ventricular outflow tract (LVOT). In this study, we applied a clinically relevant cutoff value of LVOT-AR > 17%, as established in several recent studies[51,52]. Videodensitometric analysis was performed independently and blinded to the hemodynamic analysis post-procedural.

2.4 Statistical analysis

The data was analysed using JMP® Pro (version 17.0.0, SAS Institute Inc., Cary, NC) and is presented as mean ± SD if normally distributed, and as median with interquartile range (25th – 75th percentile) if not. Normal distribution assumption was evaluated both visually and checked with Shapiro-Wilk's test. Evaluation of p-values for continuous variable was performed using either Student's t-test or the Wilcoxon rank sum test, while categorical variables were analysed using the Chi-square test or Fisher's exact test. Levene's test was conducted to assess the equality of variances.

RESULTS

3.1 Baseline characteristics

The baseline features of the 101 patients divided in no-notch (37) and notch (64) groups are presented in Table 1. The mean age of the cohort was 81.2 ± 6.6, with 54.5% being male. Average EuroSCORE II was 3.9 (1.5–4.4) and majority of the patients presented *NYHA II*

(57,4%) or *NYHA III* (37,6%) class. On preoperative echocardiography, the mean left ventricular ejection fraction (EF) was 56% (51-61.5), mean aortic valve area (AVA) 0.72 (0.6-0.8) cm^2 and mean gradient 47.0 (± 14.1) mmHg. Bicuspid valve was seen in 16% of patients and valve-in-valve procedure was performed in 6% of cases. There were no statistically significant differences between the two group in any baseline characteristics.

Table 1

Variable	All patients	Notch	No Notch	p-value
Demographics				
Age	79.7 ± 6.6	79.3 ± 5.96	79.9 ± 6.97	0.68
Sex				
Male	55 (54.5)	23 (62.2)	32 (50)	
Female	46 (45.5)	14 (37.8)	32 (50)	0.24
BMI (kg/m2)	27.6 ± 5.4	28.2 ± 5.6	27.3 ± 5.2	0.66
Prior medical history				
EuroSCORE II	3.9 (1.5–4.4)	4.7 (1.4–5.4)	3.4 (1.5–4.2)	0.86
NYHA class				
NYHA I	1 (1.0)	1 (2.7)	0	
NYHA II	58 (57.4)	17 (45.9)	41 (64.0)	
NYHA III	38 (37.6)	17 (45.9)	21 (32.8)	
NYHA IV	4 (0.4)	2 (5.4)	2 (3.1)	0.22
DM	30 (29.7)	13 (35.1)	17 (26.6)	0.36
CAD	49 (48.5)	21 (56.8)	28 (43.8)	0.21
Prior CAGB	13 (12.9)	5 (13.5)	8 (12.5)	0.88
COPD	7 (6.9)	3 (8.1)	4 (6.3)	0.72
AF	42 (41.6)	20 (54.1)	22 (34.4)	0.053
Hypertension	71 (70.3)	24 (64.9)	47 (73.4)	0.36
Prior PM	7 (6.9)	2 (5.4)	5 (7.8)	0.65
AR severity				
mild	26 (25.7)	8 (21.6)	18 (28.1)	
moderate	9 (8.9)	4 (10.8)	5 (7.8)	
severe	3 (3.0)	1 (2.7)	2 (3.1)	0.87
Bicuspid valve	16 (15.8)	4 (10.8)	12 (18.8)	
Valve-in-valve	6 (5.9)	1 (2.7)	5 (7.8)	0.30
Preoperative echocardiography				
EF%	56 ± 11.2	53.1± 14.3	57.7 ± 8.6	0.25
AVA cm2	0.72 ± 0.13	0.73 ± 0.11	0.72 ± 0.15	0.97
Peak gradient mmHg	76.5 ± 21.7	71.9 ± 15.7	79.1 ± 24.2	0.12
Mean gradient mmHg	47.0 ± 14.1	43.2 ± 10.4	48.9 ± 15.3	0.07

Values are presented as number with/without the mean ± standard deviation (SD), or the median with the interquartile range (IQR) or the percentage. BMI body mass index, Euroscore II European System for Cardiac Operative Risk Evaluation, NYHA New York Heart Association, DM diabetes mellitus, CAD coronary artery disease, CAGB coronary artery bypass graft, COPD chronic obstructive pulmonary disease, AF atrial fibrillation,

HTN hypertension, PM pacemaker, AR aortic regurgitation, EF ejection fraction, AVA aortic valve area.

3.2 Procedural characteristics and clinical outcomes

Details of the procedural characteristic are provided in Table 2. DN was found in 37/101 patients (36.7%) in intraprocedural hemodynamic tracings taken immediately after valve deployment. The median LVOT-VD was 7% (2-17%) and there was a difference in patients with DN and patients without (5% (1.5-9%) vs. 10% (3-19%); p=0.006) (Figure 2). Clinically relevant PVR (LVOT-VD > 17%) was found in 24/101 patients (23.8%). Among patients with DN, 3/37 (8.1%) had an LVOT-VD > 17%, compared to 21/64 (32.8%) in patients without DN (AOR 0.14, 95% CI 0.02–0.84, p = 0.032). These results gave sensitivity (44.16%, 95% CI 32.84% to 55.93%), specificity (87.50%, 95% CI 67.64% to 97.34%), PPV 91.9% (95% CI 79.3% to 97.1%) and NPV 32.8% (95% CI 27.6% to 38.5%).

Figure 2

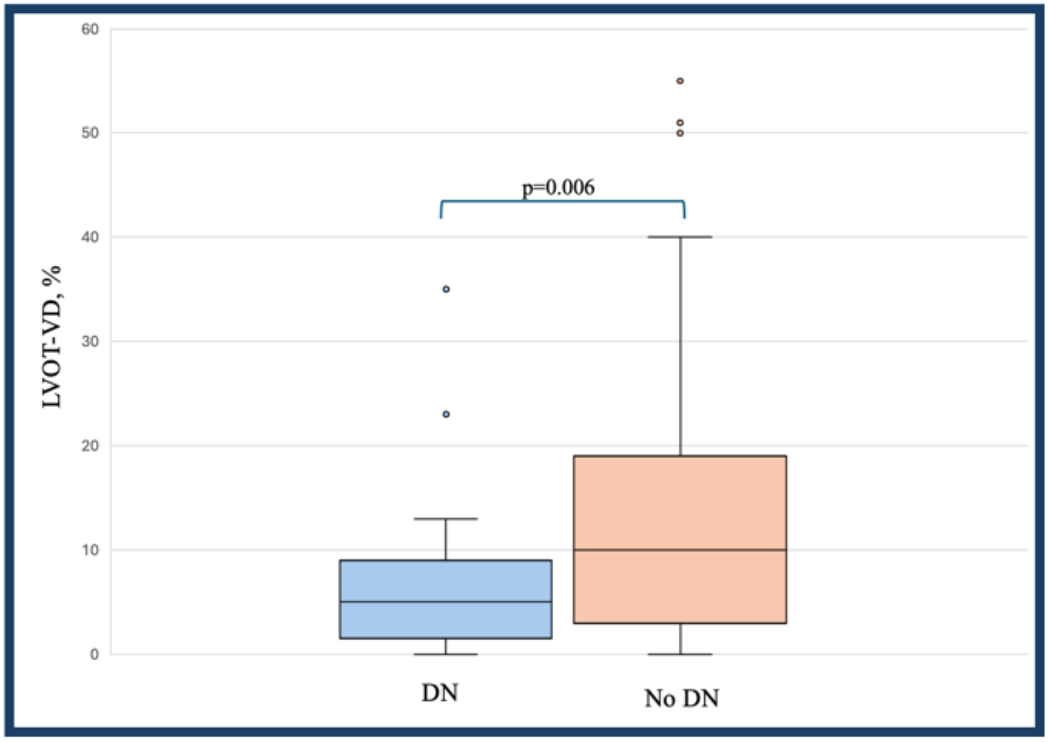

Figure 2. The difference between groups regarding median LVOT-VD was statistically significant; 5% in the DN group (1.5-9%) vs. 10% in the No DN group (3-19%), p=0.006.

Self-expandable valves were used in 75.3% of patients, while 24.8% received balloon-expandable valves. Valve utilization differed between patients with and without DN (56.8% vs. 43.2% and 79.7% vs. 20.3%, respectively; p = 0.0011). The DN was more frequently absent with self-expanding valves compared to balloon-expandable suggesting an increased incidence

of PVR. This is consistent with similar findings reported in other studies where self-expanding prosthesis have been shown to be associated with a higher risk of PVR[53,54].

Patients with DN had larger annulus perimeters and areas (81.6 mm [76–87.5] vs. 76.2 mm [72–80.1]; p = 0.0004, and 518.9 mm² [447–590] vs. 450.6 mm² [400–500]; p = 0.0003). Additionally, mean cover index was 8.6 ± 7.5 overall, with a significantly higher value in no DN group compared to the DN group (9.8 ± 7.4 vs 6.4 ± 7.1 p=0.024).

Predilatation was performed in 73.3% of patients without difference in patients with or without DN. Balloon post-dilatation (BPD) was performed in 32.7% of patients of which 18.9% in patients with DN and 40.6% without (p=0.025). 20 patients out of 33 BPD were performed due to significant PVL. Among these 20 patients, only 3/20 (15%) had DN before BPD. However, after BDP, DN was present in 13/20 patients (65%). VD analysis showed a significant difference between pre- and post-BPD values (20% [10.75–20.75%] vs. 3.5% [2–12%], p = 0.004)

Postoperative echocardiography showed a mean AVA of 2.1 ± 0.43 cm², a median mean gradient of 5 (4–7) mmHg, and mild-or-more PVL in 10.9% of patients, with no significant difference between those with or without DN. In hemodynamic tracings immediately after valve deployment, mean SBP, MAP, and PP were higher in patients with DN compared to those without DN: SBP (159.7 ± 24.6 mmHg vs. 146.9 ± 23.0 mmHg; p = 0.0115), MAP (91 ± 14.4 mmHg vs. 84.1 ± 15.6 mmHg; p = 0.027), and PP (103.1 ± 21.3 mmHg vs. 94.2 ± 18.1 mmHg; p = 0.036). Diastolic pressure was not statistically different between the two groups.

Procedural complications were evaluated within 30 days of the procedure. Access-site related vascular complications occurred in 7 patients, from which 4 were major (4.0%) and 3 minor (3.0%). Non disabling stroke occurred in 3 patients (3.0%), disabling stroke in 1 (1.0%). The occurrence rates were similar between groups.

Table 2.

Variable	All patients	Notch	No Notch	p-value
CT annulus, mm	78.2 ± 7.5	81.6 ± 8.3	76.2 ± 6.2	0.001*
CT annulus area, cm2	475.6 ± 89.4	518.9 ± 100.5	450.6 ± 72.0	0.0006*
Cover index, %	8.6 ± 7.5	6.4 ± 7.1	9.8 ± 7.4	0.024*
Predilatation	74 (73.3)	26 (70.3)	48 (75.0)	0.60
Postdilatation	33 (32.7)	7 (18.9)	26 (40.6)	0.025*
Valve type				
Self-expanding	76 (75.3)	21 (56.8)	55 (79.7)	
Balloon-expanding	25 (24.8)	16 (43.2)	9 (20.3)	0.0011*
Stroke, all	4 (4.0)	2 (5.4)	2 (3.1)	
non disabling	3 (3.0)	1 (2.7)	2 (3.1)	
disabling	1 (1.0)	1 (2.7)	0	0.59
PPI	9 (8.9)	3 (8.1)	6 (9.4)	0.83
Vascular complications	7 (6.9)	1 (1.0)	6 (0.06)	0.42
major	4 (4.0)	0	4 (4.0)	
minor	3 (3.0)	1 (1.0	2 (2.0)	0.33
Postoperative echocardiography				
AVA, cm2	2.1 ± 0.43	2.2 ± 0.47	2.1 ± 0.40	0.24
Peak gradient mmHg	10 (8–13)	10 (8–12.5)	10 (8–13)	0.56

Mean gradient mmHg	5 (4–7)	5 (4–7)	5 (4–7)	0.99
PVL≥ mild	11 (10.9)	3 (8.1)	8 (12.5)	0.30
LVOT-VD, %	7 (2–17)	5 (1.5–9)	10 (3–19)	0.006*
LVOT-VD > 17%	24 (23.8)	3 (8.1)	21 (32.8)	0.032*
Hemodynamics				
systolic pressure	151 ± 24.3	159.7 ± 24.6	146.9 ± 23.0	0.0115*
diastolic pressure	54.1 ± 13.9	56.6 ± 12.6	52.7 ± 14.5	0.17
mean arterial pressure	86.6 ± 15.5	91 ± 14.4	84.1 ± 15.6	0.027*
pulse pressure	97.5 ± 19.7	103.1 ± 21.3	94.2 ± 18.1	0.036*

Values are presented as number with/without the mean ± standard deviation (SD), or the median with the interquartile range (IQR) or the percentage. CT computer tomography, PPI permanent pacemaker implantation, AVA aortic valve area, PVL paravalvular leak, LVOT-VD left ventricle outflow track videodensitometry

3.4 Hemodynamic results and videodensitometry

The results from intraprocedural hemodynamic tracings are presented in Table 3. Assessed by videodensitometry using an LVOT-VD cutoff of > 17%, patients were divided into two groups based on PVR severity to identify patient- and procedure-related factors associated with higher PVR rates. Significant PVR was observed in 24/101 patients (23.8%) in VD analysis of aortography performed immediately after valve deployment. Advanced age and higher EuroSCORE II were associated with an increased risk of PVR, while aortic annulus size (area or perimeter), cover index, bicuspid valve morphology, and THV type showed no significant association. Intraprocedural PVR led to a numerically higher, but not statistically significant, occurrence of mild-or-more PVR in postprocedural echocardiography (9.1% vs. 16.7%; p = 0.24). In multivariate analysis, only DP (p=0.0099) and the presence of DN (p=0.02) were significantly associated with higher rates of PVR.

Table 3.

Variable	All Patients n=101	VD ≤ 17 n=77	VD > 17 n=24	p-value
Age	79.7 ± 6.6	78.9 ±6.6	82.1 ± 6.2	0.037*
EuroSCORE II	3.9 (1.5–4.4)	2.12 (1.48–4.43)	4.13 (3.11–4.81)	0.045*
Predilatation	74 (73.3)	57 (74.0)	17 (70.1)	0.79
Post Dilatation	33 (33.3)	20 (26.7)	13 (54.2)	0.01*
CT annulus perimeter, mm	78.2 ± 7.5	78.1 ± 7.7	78.4 ± 6.8	0.86
CT annulus area, mm^2	475.6 ± 89.4	473.9 ± 93.2	481.3 ± 77.5	0.70
Cover Index, %	8.5 (7.5)	7.9 (7.3)	10.8 (7.8)	0.10
PVL post procedure ≥ mild	11 (10.9)	7 (9.1))	4 (16.7)	0.24
Bicuspid valve	16 (15.8)	13 (16.8)	3 (12.5)	0.44
DP, mmHg	54.1 (13.9)	57.0 (13.2)	45.0 (11.9)	0.0002*
DP < 40 mmHg	16 (15.8)	6 (7.8)	10 (41.7)	0.0003*
Systolic pressure mmHg		154.4 ± 22.2	142.6 ± 28.7	0.076
Pulse pressure mmHg		97.6 ± 18.7	97.6 ± 23.1	0.96
Mean artery pressure mmHg		89.4 ± 14.3	77.6 ± 15.8	0.0024*

Notch	37 (36.7)	34 (44.2)	3(12.5)	
and DP > 40 mmHg	32 (31.7)	31 (40.2)	1 (4.2)	0.0049*
				0.0004*
No Notch *or* DP < 40 mmHg	69	46 (59.7)	23 (95.8)	0.0001*
Balloon expandable valve	25	21	4	
Self-expandable valve	76	56	20	0.29

Values are presented as number with/without the mean ± standard deviation (SD), or the median with the interquartile range (IQR) or the percentage. BMI body mass index, Euroscore II European System for Cardiac Operative Risk Evaluation, CT computed tomography, PVL paravalvular leak, DP diastolic pressure. Multivariable analysis was performed in variables with statistical significance in univariate model. Similar variables, variables with strong correlation or no causation to LVOT-VD were excluded in multivariable model.

When DP values were categorized into three groups (<40 mmHg, ≥40 to <60 mmHg, and ≥60 mmHg), patients with DP <40 mmHg had higher LVOT-VD values compared to those with DP ≥40 to <60 mmHg (22% [6–23.75%] vs. 7% [2–16%], p = 0.006) and those with DP ≥60 mmHg (22% [6–23.75%] vs. 6% [1–11%], p = 0.002) (Figure 3). There was no statistically significant difference in VD values between patients with DP ≥40 to <60 mmHg and those with DP ≥60 mmHg. The ROC analysis predicting the outcome using the LVOT-VD > 17% and the DP yielded an AUC of 0.76 (95% CI: 0.71-0.81) (Figure 4).

When a DP cutoff of ≥ 40 mmHg was applied to patients with DN, 32/101 patients met both criteria, of whom 1/32 (3.1%) had LVOT-VD >17% and among patients without DN or with DP ≤40 mmHg, 23/69 (33.3%) had VD >17% (AOR 0.067 95%CI 0.008-0.572, p=0.012). These results gave sensitivity of 40.3% (95% CI 29.2% to 52.1%), specificity of 95.5% (95% CI 78.9% to 99.9%), PPV of 96.9% (95% CI 81.7% to 99.5%) and NPV of 33.3 (95% CI 29.0% to 38.0%). Patients with or without DN in relation to LVOT-VD and DP are demonstrated in Figure 5.

Figure 3.

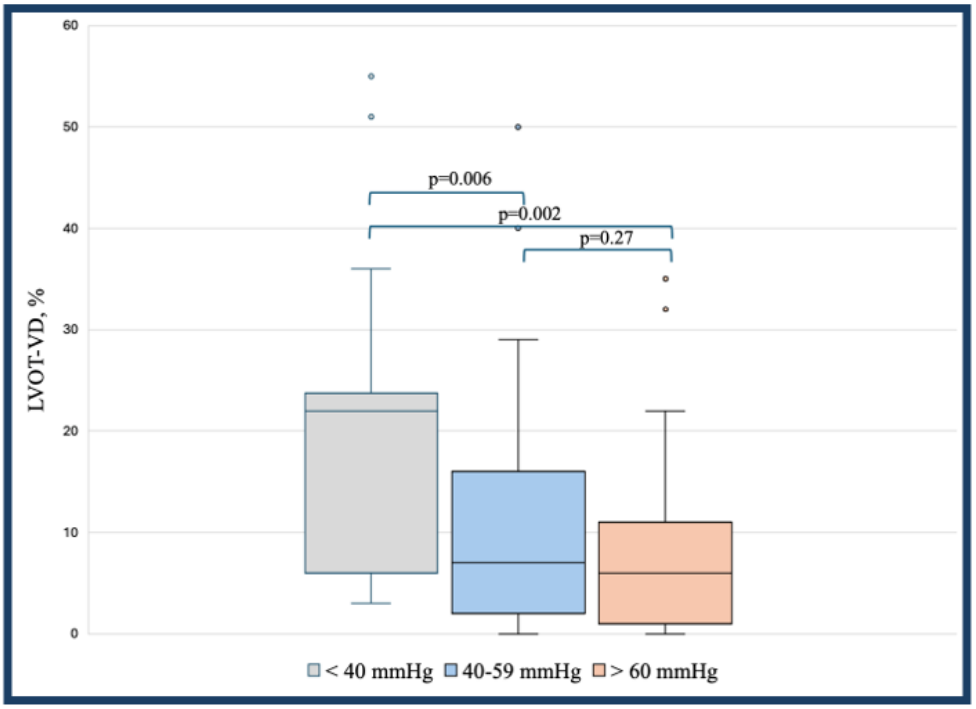

Figure 3. Patients with DP <40 mmHg exhibited higher LVOT-VD values compared to those with a DP 40-59 mmHg as well as those with a DP >60mmHg.

Figure 4

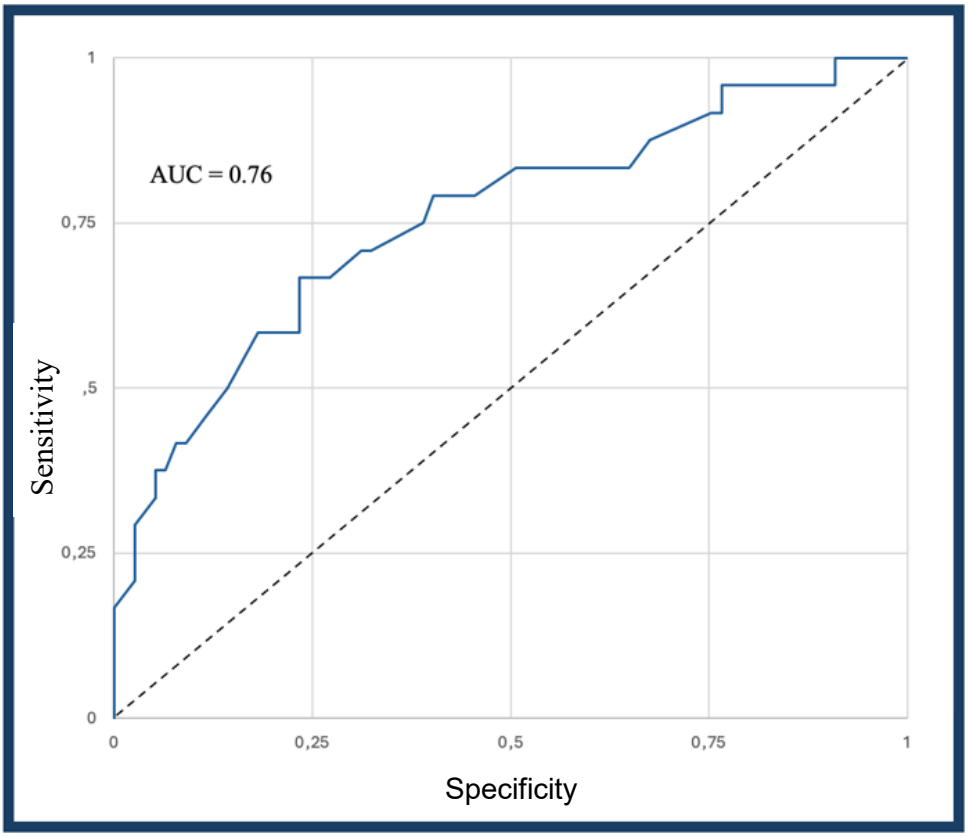

Figure 4. The ROC analysis showing the predictive value for diastolic blood pressure and the LVOT-VD for relevant PVL (LVOT-VD >17%). AUC indicates area under the curve; ROC receiver operating characteristics; LVOD-VD left ventricle outflow track videodensitometry.

Figure 5

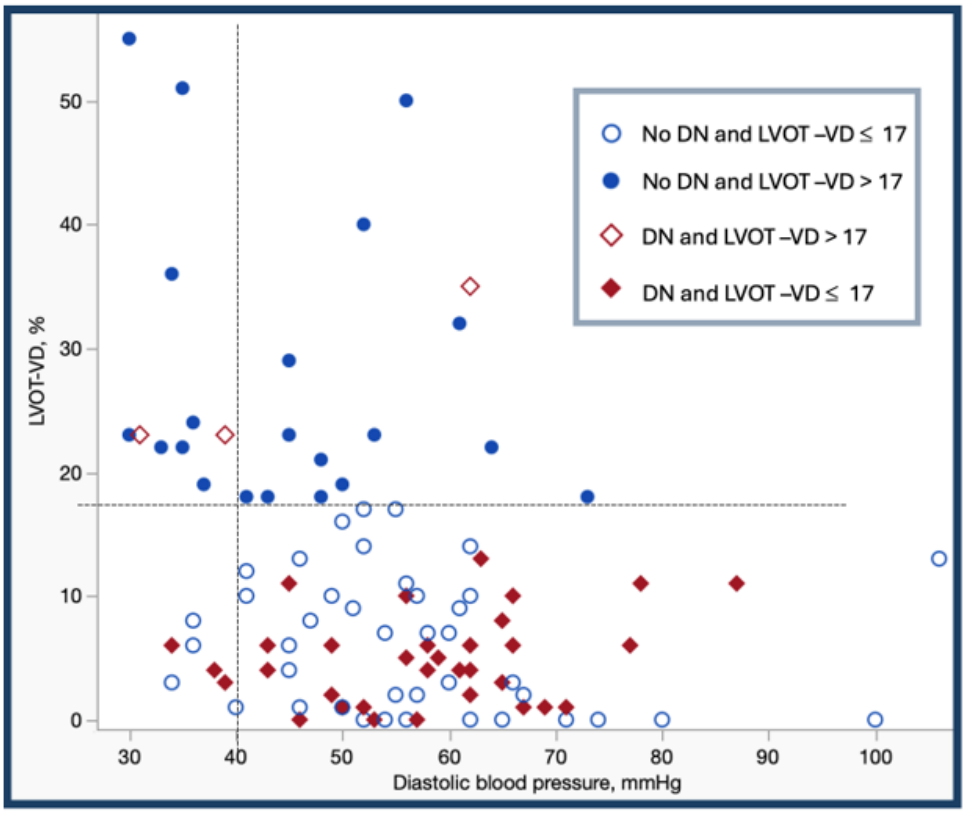

Figure 5. Patients with or without DN in relation to LVOT-VD and DP. Only three patients exhibited notch in aortography and still had a LVOT-VD > 17 indicating PVR. When adding a DP cutoff only one patient exhibited PVR compared to patients without DN or DP ≤40 mmHg, 33,3% had VD >17, with a statistically significant difference. Most patients with absence of notch still didn't have significant PVR.

4. DISCUSSION

4.1 Challenges in the evaluation and quantification of PVR

Accurate grading of PVR remains essential even though the incidence of PVR is decreasing due to newer generation TAVI devices and improved operator skills. There's increased evidence that even mild to moderate PVR is associated to adverse outcomes[55–58], highlighting the importance of proper assessment. Still, some studies have failed to demonstrate a clear association[40,59], which may be to a certain extent explained by difficulty in accurately assessing none/trace or mild PVR, potentially leading to underestimation of its true severity.

With the growing acceptance of the minimalist approach there is an increased demand for new solutions to evaluate PVR since there is now longer use of TEE due to requirements of anaesthesia and patient compliance. The minimalist approach yields equal mortality outcomes compared to the conventional approach, and it is associated with shorter hospitalization and lower resource utilization. However, the prevalence of PVR appears to be marginally higher, especially since TEE

is now rarely utilized.[60,61] Quantitative videodensitometry has emerged as a novel method for assessing PVR as it can be performed from routine aortography without additional procedural manipulation. However, its current application remains limited to offline analysis but nonetheless defining VD-AR cutoff values are crucial to detect device success. Abdel-Wahab et al. have reported that a VD-AR ≥10% corresponded to >mild PVR ($p > 0.001$; sensitivity 100%, specificity 83%) whereas a VD-AR ≥25% corresponded to moderate-to-severe PVR ($p = 0.004$; sensitivity 100%, specificity 98%).[34] Other studies suggest that LVOT-AR values >17% correspond to clinically-relevant greater than mild AR post- TAVR and significantly increased one-year all-cause mortality compared to patients LVOT-AR values ≤0.17.[51,52] Our findings are consistent with the hypothesis that a VD-AR cut-off >17% corresponds to clinically relevant moderate-severe PVR.

Previous studies have identified hemodynamic markers predicting PVR development, however, their applicability is limited by the need of additional resources which may be considered suboptimal within the framework of minimalist procedural approach. Roijaakkers et al. reported that DD and VD had a weak but significant correlation but also when used together it had a higher positive predictive value (PPV) for PVR compared to when either one was used alone[30]. Only one study has been conducted to measure DNI intraoperatively. Mohaney et al. demonstrated that DNI, defined as as the difference between SBP and DN height divided by pulse pressure, could be used onsite without advanced calculations or LV catheterization. They observed that lower DNI correlated to hemodynamically significant AR, hence the difference in DNI between AR ≥mild and AR < mild was not statistically significant. However, DNI exhibited a good PPV for detecting significant AR with an AUC of 0.8. A cutoff value < 0.63 provided 100% sensitivity, effectively identifying true positives, while a cutoff of < 0.5 provided 95,5% specificity, accurately identifying true negatives.[49] Another study associated DBP to aortic PVR severity and clinical outcome after PVR. Although there were various causes for intraprocedural low BP, their data suggested that very low BP (<40mmHg) had high incidence of PVR. [62]

4.2 Relation between DN and PVR

The dicrotic notch is readily available during the TAVI procedure and doesn't require any additional conditions or equipment for identification. Our findings demonstrate that the combined evaluation of DN along with VD yields promising results in analysing this issue. The main finding of this study was that the presence of a dicrotic notch in intraprocedural hemodynamic tracings after valve deployment was associated with significantly lower rates of clinically relevant PVR (LVOT-VD > 17%) compared to patients without DN (8.1% vs. 32.8%; AOR 0.14, 95% CI 0.02–0.84, $p = 0.032$). Although DN appears to be a great addition to the evaluation of clinically relevant PVR with a high PPV and specificity, its negative predictive value (NPV) and sensitivity remains poor, meaning a significant proportion of individuals with a negative result indeed do not exhibit clinically relevant PVR requiring management. The second significant finding was that patients with very low DBP (<40 mmHg) had a high incidence of PVR. The PPV and specificity were increased while sensitivity decreased when the presence of a DN was combined with DBP (≥ 40 mmHg) compared to patients without DN or DBP < 40mmHg ($p=0.012$, PPV 96.6%, specificity 95.5%, NPV 33.3%, sensitivity 40.3%). These results support the notion that patients exhibiting both DN and DBP > 40mmHg are very unlikely to develop a clinically relevant PVR.

These findings suggest that the presence of DN after valve deployment could be used as an additional hemodynamic marker in excluding clinically significant PVR along with aortography and

echocardiography during the TAVI procedure. Since the treatment of clinically relevant PVR immediately post-TAVR is recommended, the presence of a DN may also serve as a useful indicator when evaluating the effectiveness of post-dilatation. Additionally, the presence of both DN and DBP > 40mmHg suggests a favourable outcome, although further research need to be conducted to support this finding.

4.3 Limitations

Several limitations should be considered when interpreting the results of this study. The retrospective design may introduce selection bias and data from 22 patients were non-analysable. While the overall sample size was modest, subgroups were relatively small. The primary aim was to assess whether DN could be a useful tool for evaluating hemodynamic outcomes in a periprocedural setting; however, no definitive DN cutoff could be established due to the subjective nature of visual evaluation. Additionally, despite blinded assessment, the evaluation was performed by a single operator, which may limit the results' interpretation and validity.

4.4 Future prospects

As the number of TAVI procedures is increasing and indications expanding the need to prevent complications, particularly PVR, has become increasingly evident. Future studies should be conducted to prospectively and more precisely assess the cutoff values for VD in larger cohorts. Also, dicrotic notch should be evaluated in comparison with other hemodynamic parameters and methods to determine its positive predictive value for clinically relevant PVR as well as its intra-procedural utility enhancing PVR prediction, particularly when used alongside with other modalities, especially in cases where conventional methods are limited or yield inconclusive results. Together, hemodynamic parameters and aortography could guide the operator’s decision making regarding additional actions. Since the DN is assessed before the prosthetic valve is released from the catheter it provides the operator with an opportunity to optimize the placement with certain valve types. Additionally, DN could be used assessing outcomes of post-dilatation performed due to PVR. Notably, the dicrotic notch (DN) is the only marker identifiable through visual inspection alone. Further research should be carried out to evaluate the association between DBP and PVR, as well as to assess the potential value of combining DBP with the presence of DN in clinical evaluation.

5. CONCLUSION

In this retrospective study, we evaluated the presence of DN in intraprocedural hemodynamic tracings in patients undergoing TAVI procedure and its association with PVR assessed quantitively by videodensiometric analysis. The presence of DN following valve deployment is associated with lower rates of significant PVR, suggesting that it could be used as easy and straightforward visual hemodynamic marker to evaluate procedural success during TAVI.

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