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# Special considerations on TAVI implanted in bicuspid aortic valves.

## Experience of Institute of Cardiology in Warsaw, Poland

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SOUHRN

Od té doby, co se začala provádět transkatétrová implantace aortální chlopně (TAVI), byly za relativní kontraindikaci provedení této metody považovány bikuspidální aortální chlopně (BAV). Pacienti s BAV byli vyřazeni z většiny velkých klinických studií TAVI. Rozvoj této implantační techniky a další studie však prokázaly, že tato metoda je schůdná a bezpečná také při BAV. V současné době někteří klinici prohlašují, že BAV již nemá být kontraindikací k provedené TAVI. Nicméně je třeba vzít v úvahu zvláštní aspekty jedinečné anatomie, když vybíráme pacienty vhodné pro tuto metodu. V našem centru od roku 2010 celkově 28 pacientů s bikuspidální aortální chlopní podstoupilo TAVI.



ABSTRACT

Since the advent of transcatheter aortic valve implantation (TAVI), bicuspid aortic valves (BAVs) have been considered relative contraindication for this procedure. Patients with BAVs were excluded from the majority of large clinical TAVI trials. However, the development of the implantation technique and further studies have proven this method feasible and safe also in BAVs. Nowadays some clinicians claim that BAV should no longer be a contraindication. Nevertheless special aspects of the unique anatomy need to be taken into consideration when qualifying patients for this procedure. In our center since 2010 a total number of 28 patients with bicuspid aortic valve stenosis underwent TAVI.

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Bicuspid aortic valve (BAV) is one of the most common congenital heart defects. It is recognized in about 0.8–2% of general population [1,2]. Among patients requiring treatment for aortic stenosis proportion of those with BAV may be as high as 20% [3]. Clinical characteristics of patients with BAV dysfunction relevantly differ from patients with tricuspid aortic valves.

Degeneration of BAVs occurs earlier in life and substantially higher percent of patients with BAV develops clinically significant stenosis, insufficiency or both through life. Traditionally patients with BAVs are primarily qualified for surgical aortic valve replacement or repair. It often occurs as soon as in third to fifth decade of life. Nevertheless, there is an increasing number of patients who require less invasive procedure due to severe comorbidities and/or advanced age. Many patients with BAVs disease stay symptomless until senility and clinically overt stenosis reveals so late (e.g. octogenerians) that surgical procedure risk is too high. Those may benefit from TAVI.

From anatomic point of view BAV is not a homogenous defect, but a spectrum of several developmental variants. In 2007 Sievers and Schmidtke published a classification of BAVs based on analysis of 304 surgical specimen. This classification was originally created for facilitation of surgical repair techniques; however, it may also be easily adapted for TAVI, as it gives a lot of essential information on structure of the valve. The main criterion is number of raphes, what determines one of the 3 following types: type 0 (no raphe); type 1 (1 raphe); and type 2 (2 raphes) [4]. Further, this implies the shape of annulus (round or elliptic/eccentric), predominating dysfunction (stenosis or insufficiency) and distribution of calcium. The most common type (88%) is Sievers 1 with raphe between left and right coronary cusps (71%) (Figs. 1 and 2). This type is particularly related to asymmetric annular geometry (oval shape of the annulus) and presents predominantly with stenosis (insufficiency in about 26–31% of specimen). On the other hand Sievers type 0 and type 2 which are quite rare (7% and 5 % respectively) present in similar proportion with stenosis and insufficiency. Type 2 often demonstrates extremely narrow orifices upon diagnosis.

In general BAV presents with stenosis in 75% and insufficiency in 15% of cases. It was documented that stenosis develops more rapidly if the aortic cusps are oriented asymmetrically or in the antero-posterior position. Calcific and fibrotic deposits are distributed mostly in raphes and at the base of the cusp. This process is age-dependent and occurs faster in BAVs than in patients with tricuspid aortic valves [5].

Bicuspid aortic valves cannot be fully understood without assessment of aortic root pathology. Coarctation of aorta, aortic dissection and aortic aneurysm frequently coexist with BAV [6]. Such pathology may indispensably eliminate patient from TAVI and impose surgical intervention [7]. Sievers type 1 LCC-RCC may be connected to aortic coarctation which is usually diagnosed in younger age [6].

Aortic aneurysms are approximately 85 times more frequent in patients with BAVs than in the general population and account for 8 times higher incidence of dissection.

Furthermore BAV predisposes to some certain coronary anomalies. They also need to be taken into consideration when qualifying patients for TAVI [8]. For example type 0 BAV with vertically oriented orifice (lateral type with left and right coronary cusps) may have a narrow separation distance between the right and left main coronary ostia. Other anomalies of coronary arteries may involve their anomalous origin, shorter length of the main coronary arteries and a preponderance of left dominance [9].

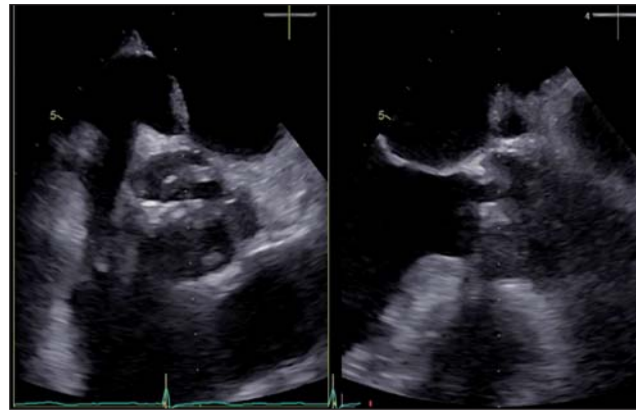

**Fig. 1 – An example of BAV type 1 RCC-LCC – TEE image – transverse and longitudinal projections.**

**Fig. 2 – BAV type Sievers 1 RCC-LCC presented in CT. Massive calcifications within raphe and cusps visible.**

BAVs, especially with bulky leaflets, enlarged aortic roots, dilated ascending aorta and significant aortic incompetence might cause difficulties with positioning and deploying a valve prosthesis [10]. All of this caused patients with BAVs to be excluded from major clinical trials with TAVI [11–13]. Consequently initial evidence on TAVI in BAV was collected owing to case reports and observational studies, mostly utilizing older generation devices [14–17].

Nevertheless multiple results show that TAVI is safe and effective in this group of patients. Initial concern about perivalvular leak seems to fade away with the advent of new generation devices [18].

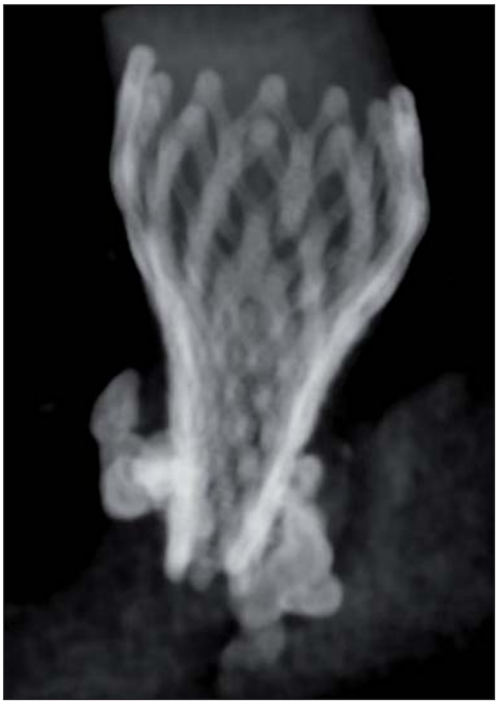

**Fig. 3 – A visualization (CT) of elliptic distortion of CoreValve implanted in BAV.**

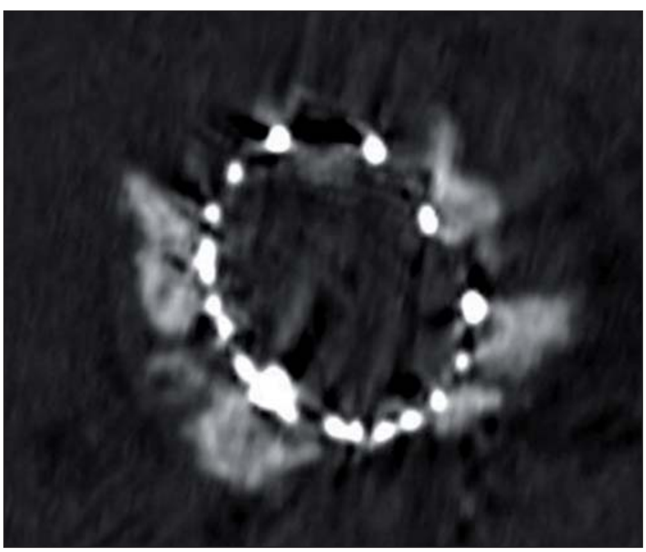

**Fig. 4 – CT scan (cross-section) of Sapien valve implanted in massively calcified bicuspid aortic valve. The mass of calcium pushed aside, but the prosthesis is well aligned.**

**Fig. 5 – Two stents of prosthetic aortic valves visible upon TEE in the ascending aorta.**

Diagnostic procedures for qualification for TAVI do not differ between patients with BAVs and tricuspid aortic valves. All commercially available prostheses may be theoretically implanted in BAVs. Widespread utilization of angio-CT helped to improve proper device selection and sizing in process of minimizing risk of aortic annulus rupture and perivalvular leakage [19]. Recent studies enlighten annulus eccentricity issue. Surprisingly, in a large study comparing CT scans of bicuspid (n = 200) and tricuspid (n = 200) aortic valves ellipticity index turned out to be smaller in patients with bicuspid aortic valves (1.24 vs. 1.29) while annular area was larger (5.21 vs 4.63 $cm^2$) than in tricuspid valves [20]. Unfortunately eccentric leaflet and annulus calcifications are more common in BAVs. They may impose non-circular expansion of transcatheter heart valve (THV), higher grade of paravalvular leakage and increased risk of pacemaker implantation after TAVI [21].

Procedural technique for THV implantation in BAV requires some extra attention compared to tricuspid AV – angiographic visualization of annulus level and selection of proper projection for implantation may be more difficult due to asymmetric shape of Valsalva sinuses and irregular appearance of the cusps [22].

The risk of elliptic distortion or non-circular expansion seems to be smaller if the prosthesis is implanted deeper below the annular level rather than at exactly the annular level [23]. Non-circular expansion seems to be more

**Table 1 – Baseline clinical characteristics of patients with BAVs qualified for TAVI in Institute of Cardiology, Warsaw, Poland in 2010–2016**

| Risk factor | CAD | PCI | CABG | MI | Stroke/ TIA | DM2 | Obesity/ met. syndrome | Ex-card. art.-path. | Onc. | AF | COPD | Osteop. | Ren. Ins. | PH | EF <50% |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of pts | 16 | 8 | 6 | 10 | 6 | 12 | 7 | 11 | 4 | 7 | 7 | 3 | 8 | 9 | 10 |

AF – atrial fibrillation of any kind; CABG – previous coronary artery by-pass grafting; CAD – coronary artery disease; COPD – chronic obstructive pulmonary disease; DM2 – diabetes mellitus type 2; EF < 50% – left ventricle ejection fraction < 50% at baseline ex-card. art.-path. – extracardiac arteriopathy including carotid stenosis, limb arteries atherosclerosis, aortic aneurysm; MI – previous myocardial infarction; No of pts – number of patients with given risk factor; obesity/met. syndrome – BMI >30 $kg/m^2$ and/or metabolic syndrome; onc. – history of cancer or hematologic disease; osteop. – osteoporosis; PCI – previous percutaneus coronary interventions; PH – pulmonary hypertension with pulmonary artery systolic pressure at least 50 mmHg; ren. ins. – renal insufficiency understood as eGFR < 50 ml/kg/min; stroke/TIA – cerebral stroke or transient ischemic attack in the past.

| Table 2 – Direct outcomes in terms of perivalvular leak grade (PVL). Total number of patients, who undergone successful THV deployment = 27 | |
|---|---|
| No PVL detected | 2 |
| Trivial | 3 |
| Small | 10 |
| More than small but less than moderate | 4 |
| Moderate | 7 |
| More than moderate | 1 |
| Severe | 0 |

Table 3 – Periprocedural complications after TAVI implanted in BAVs

| Complication | Number of patients affected |
|---|---|
| Death within 30 days | 0 |
| In-hospital death | 2 |
| Access site complications | 6 |
| Pacemaker implantation | 7 |
| Bleeding (clinically significant) | 3 |
| Conversion to surgery | 1 |
| Malfunction of prosthesis – need for another device | 2 |
| More than moderate regurgitation | 1 |
| Stroke/TIA | 1 |
| Periprocedural MI | 0 |

probable with self-expanding valves compared to balloon mounted prostheses (Fig. 3) [21].

Previous studies documented higher grade of perivalvular leakage in patients with BAVs compared to tricuspid AVs [14,15,24], however, newer devices with extra sealing skirt offer excellent result [18,25]. Still further research is needed.

Furthermore, there is a persistent concern about relatively high proportion of pacemaker implantation in BAV-patients after TAVI. According to available data it is as high as 17–29% [14–16,18,26]. It seems to be correlated with the depth of THV implantation in left ventricle outflow tract as well as with difficulty setting exact annulus plane on angiography. The fact that the majority of BAVs is type 1 R-L with bulky calcifications within the raphe might also be an important matter – such anatomical configuration may cause protrusion of calcific mass into proximity of membranous part of interventricular septum promoting atrioventricular and/or intraventricular conduction block (see Fig. 4).

## Experience of Institute of Cardiology in Warsaw

In our center among all 354 patients, who had undergone TAVI between January 2010 and October 2016, 28 presented with BAVs (7.9%), 15 females. Mean age of the patients was 76.6 years. 13 patients were 80 years old or more at the time of the procedure. Basic clinical characteristics was not different compared to patients with tricuspid aortic valves (Table 1). All of the patients suffered from severe symptomatic aortic valve stenosis (functional NYHA class from 2 to 4) with mean aortic valve area of 0.56 $cm^2$ (0.36–0.9 $cm^2$) calculated by continuity equation and transaortic mean pressure gradient of 63.2 mmHg (40–94 mmHg) as measured in TTE or TEE. They were considered high surgical risk with an average calculated logistic EuroSCORE 1 of 18.59% (4.38–33.09%) and had been previously disqualified from surgical aortic valve replacement (SAVR) by institutional Heart Team. Every patient routinely underwent pre-procedural diagnostic evaluation, including angio-CT scan.

Written informed consent was given and signed by every patient and an operator. Twenty-three self-expandable and 5 balloon-mounted valves were used. Twelve THVs were newer generation valves. The majority of patients (20) received Medtronic devices (Medtronic, Inc., Minneapolis, MN, USA) including CoreValve (12 patients) and Evolut R (8 patients) systems. 5 patients received Edwards devices (Edwards Life Sciences, Inc., Irvine, CA, USA) –2 patients – Edwards Sapien, 2 patients – Sapien XT and 1 patient – Sapien 3. Another 3 patients received Lotus Valve (Boston Scientific Corporation, Marlborough, MA, USA).

Transfemoral access was utilized in 23 patients, whereas the remaining 5 needed transapical (2 patients) or transsubclavian (3 patients) approach.

Twenty-seven out of 28 patients had their prostheses implanted successfully. One patient required conversion to surgical aortic valve replacement due to pop-up of the self-expandable prosthesis to the ascending aorta. Two patients needed implantation of another prosthesis (valve-in-valve) immediately after the first one due to severe perivalvular leaks (Fig. 5).

Seven patients needed pacemaker implantation due to persistent grade 2 or 3 atrioventricular block after TAVI. Six patients experienced some access site complications and required either surgical intervention or percutaneous angioplasty techniques.

All of the TAVI procedures brought significant reduction in transaortic gradient (drop of peak gradient from 102.2 mmHg to 17.6 mmHg approximately). Fifteen patients achieved excellent result with no, trivial or small perivalvular regurgitation, 11 had more than small, but less than moderate, or moderate regurgitation, and one patient had more than moderate regurgitation (Table 2). The latter died in hospital later on from multi-organ failure. One patient, who ended up with moderate regurgitation, required re-TAVI after 2 years, because of worsening of heart failure symptoms to NYHA III and progress of regurgitation to severe. The second TAVI procedure brought him an excellent result with no more than small aortic insufficiency. This time new generation device was used (Evolut R).

Table 3 sets together periprocedural complications and number of patients who were affected with them in our cohort.

There were no deaths within 30 days after the procedure, but 2 patients died in hospital due to time-distant complications after the TAVI (infective endocarditis and multi-organ failure). Six-month follow-up of 13 patients is available – except those 2 deaths, all remained in good clinical condition demonstrating heart failure symptoms of class I or II according to New York Heart Association (NYHA). We also have 1-year data of 9 of them – all still remaining in good clinical condition. Six of them survived more than 2 years, but no detailed clinical data is available.

Our results are similar to those achieved in major clinical registries, although the sample size is relatively small.[26]

## Conclusion

There is an increasing volume of data proving TAVI in BAV stenosis feasible and safe for patients with high surgical risk. There is still a need for large prospective trials to fully evaluate effectiveness of this procedure in a population of patients with BAVs. Some special aspects must be taken into consideration when qualifying patients with BAV stenosis for TAVI. New generation devices compared to older ones bring consistently better outcomes not only in patients with tricuspid aortic valve disease, but also with bicuspid valve disease. BAV should no longer be considered contraindication for TAVI, but through clinical assessment, including CT scan, should be performed in every patient so that an individualized (heart team discussed) decision could be taken.

**Conflict of interest**
None declared.

**Funding body**
None.

**Ethical statement**
Authors state that the research was conducted according to ethical standards.

**Informed consent**
Written informed consent was signed by every patient and the operator.

### References

[1] W.C. Roberts, The congenitally bicuspid aortic valve. A study of 85 autopsy cases, American Journal of Cardiology 26 (1970) 72–83.
[2] M. Campbel, Calcific aortic stenosis and congenital bicuspid aortic valves, British Heart Journal 30 (1968) 606–616.
[3] W.C. Roberts, K.G. Janning, J.M. Ko, et al., Frequency of congenitally bicuspid aortic valves in patients ≥80 years of age undergoing aortic valve replacement for aortic stenosis (with or without aortic regurgitation) and implications for transcatheter aortic valve implantation, American Journal of Cardiology 109 (2012) 1632–1636.
[4] H.H. Sievers, C. Schmidtke, A classification system for the bicuspid aortic valve from 304 surgical specimens, Journal of Thoracic and Cardiovascular Surgery 133 (2007) 1228–1233.
[5] F.Y. Sabet, W.D. Edwards, H.D. Tuzelaar, et al., Congenitally bicuspid aortic valves: A surgical pathology study of 542 cases (1991 through 1996) and a literature review of 2715 additional cases, Mayo Clin Proc 74 (1999) 14–26.
[6] A.C. Braverman, H. Guven, M.A. Beardslee, et al., The bicuspid aortic valve, Current Problems in Cardiology 30 (2005) 470–522.
[7] R. Erbel, V. Aboyans, C. Boleau, et al., 2014 ESC guidelines on the diagnosis and treatment of aortic diseases, European Heart Journal 35 (2014) 2873–2926.
[8] P.A. Patel, J.T. Gutsche, W.J. Vernick, et al., The functional aortic annulus in the 3D era: Focus on transcatheter aortic valve replacement for the perioperative echocardiographer, Journal of Cardiothoracic and Vascular Anesthesia 29 (2015) 240–245.
[9] J.M. Perez-Ponares, J.L. de la Pompa, D. Franco, et al., Congenital coronary artery anomalies: a bridge from embryology to anatomy and pathophysiology – a position statement of the development, anatomy, and pathology ESC Working Group, Cardiovascular Research 109 (2016) 204–216.
[10] M. Napodano, G. Tarantini, A. Ramondo, Is it reasonable to treat all calcified stenotic aortic valves with a valved stent? Probably yes if we get a full stent expansion, Journal of the American College of Cardiology 53 (2009) 219.
[11] M.B. Leon, C.R. Smith, M. Mack, et al.; PARTNER Trial Investigators, Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery, New England Journal of Medicine 363 (2010) 1597–1607.
[12] M.B. Leon, C.R. Smith, M.J. Mack, et al.; PARTNER 2 Investigators, Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients, New England Journal of Medicine 374 (2016) 1609–1620.
[13] D.H. Adams, J.J. Popma, M.J. Reardon, et al.; U.S. CoreValve Clinical Investigators, Transcatheter aortic-valve replacement with a self-expanding prosthesis, New England Journal of Medicine 370 (2014) 1790–1798.
[14] D. Mylotte, T. Lefevre, L. Søndergaard, et al., Transcatheter aortic valve replacement in bicuspid aortic valve disease, Journal of the American College of Cardiology 64 (2014) 2330–2339.
[15] A. Yousef, T. Simard, J. Webb, et al., Transcatheter aortic valve implantation in patients with bicuspid aortic valve: a patient level multi-center analysis, International Journal of Cardiology 189 (2015) 282–288.
[16] J. Kochman, Z. Huczek, P. Scisło, et al., Comparison of one- and 12-month outcomes of transcatheter aortic valve replacement in patients with severely stenotic bicuspid versus tricuspid aortic valves (results from a multicenter registry), American Journal of Cardiology 114 (2014): 757–762.
[17] M. Kosek, A. Witkowski, M. Dąbrowski, et al., Transcatheter aortic valve implantation in patients with bicuspid aortic valve: a series of cases, Kardiologia Polska 73 (2015) 627–636.
[18] G.Y. Perlman, P. Blanke, D. Dvir, et al., Bicuspid Aortic Valve Stenosis: Favorable Early Outcomes With a Next-Generation Transcatheter Heart Valve in a Multicenter Study, JACC. Cardiovascular Interventions 9 (2016) 817–824.
[19] A.B. Willson, J.G. Webb, T.M. Labounty, et al., 3-dimensional aortic annular assessment by multidetector computed tomography predicts moderate or severe paravalvular regurgitation after transcatheter aortic valve replacement: a multicenter retrospective analysis, Journal of American College of Cardiology 59 (2012) 1287–1294.
[20] F. Philip, N.N. Faza, P. Schoenhagen, et al., Aortic annulus and root characteristics in severe aortic stenosis due to bicuspid aortic valve and tricuspid aortic valves: implications for transcatheter aortic valve therapies, Catheterization and Cardiovascular Interventions 86 (2015) E88–E98.
[21] K. Hayashida, E. Bouvier, T. Lefèvre, et al., Transcatheter aortic valve implantation for patients with severe bicuspid aortic valve stenosis, Circulation. Cardiovascular Interventions 6 (2013) 284–291.
[22] G.Y. Perlman, P. Blanke, J.G. Webb, Transcatheter aortic valve implantation in bicuspid aortic valve stenosis, EuroIntervention 12 (Y) (2016) Y42–Y45.
[23] D. Himbert, F. Pontnau, D. Messika-Zeitoun, et al., Feasibility and outcomes of transcatheter aortic valve implantation in high-risk patients with stenotic bicuspid aortic valves, American Journal of Cardiology 110 (2012) 877–883.
[24] Z.G. Zhao, H. Jilaihawi, Y. Feng, M. Chen, Transcatheter aortic valve implantation in bicuspid anatomy, Nature Reviews. Cardiology 12 (2015) 123–128.
[25] A.W. Chan, D. Wong, J. Charania, Transcatheter Aortic Valve Replacement in Bicuspid Aortic Stenosis Using Lotus Valve System, Catheterization and Cardiovascular Interventions 2016 Mar 31. doi: 10.1002/ccd.26506. [Epub ahead of print]
[26] T. Bauer, A. Linke, H. Sievert, et al., Comparison of the effectiveness of transcatheter aortic valve implantation in patients with stenotic bicuspid versus tricuspid aortic valves (from the German TAVI Registry), American Journal of Cardiology 113 (2014) 518–521.