



Percutaneous implantation of self-expandable aortic valve in high risk patients with severe aortic stenosis: The first experiences in Serbia

Perkutana implantacija samooslobađajuće aortne valvule kod visokorizičnih bolesnika sa teškom aortnom stenozom: prva iskustva u Srbiji

Milan A. Nedeljković*†, Branko Beleslin*†, Milorad Tešić*†, Vladan Vukčević*†, Goran Stanković*†, Siniša Stojković*†, Dejan Orlić*†, Ilija Bilbija‡, Miloš Matković‡, Tijana Simić§, Nemanja Menković||, Igor Mrdović*†, Gian Paolo Ussia¶, Zoran Perišić**, Momčilo Babić††

*Clinic for Cardiology, †Clinic for Cardiac Surgery, §Center for Anesthesiology and Reanimation, ||Clinic for Radiology, Clinical Center of Serbia, Belgrade, Serbia; ‡Faculty of Medicine, University of Belgrade, Belgrade, Serbia; ¶Department of Cardiovascular Disease, Tor Vergata University of Rome, Rome, Italy; **Clinic for Cardiovascular Diseases, Clinical Center Niš, Faculty of Medicine, University of Niš, Niš, Serbia; ††National Health Insurance Fund, Belgrade, Serbia;

Abstract

Background/Aim. Aortic stenosis (AS) is the most common valvular heart disease in elderly people, with rather poor prognosis in symptomatic patients. Surgical valve replacement is the therapy of choice, but a significant number of patients cannot undergo surgical procedure. We presented initial experience of transcatheter aortic valve implantation (TAVI) performed in Catheterization Laboratory of the Clinic for Cardiology, Clinical Center of Serbia. **Methods.** The procedures were performed in 5 patients (mean age 76 ± 6 years, 2 males, 3 female) with severe and symptomatic AS with contraindication to surgery or high surgical risk. The decision to perform TAVI was made by the heart team. Pre-procedure screening included detailed clinical and echocardiographic evaluation, coronary angiography and computed tomography scan. In all the patients we implanted a self-expandable aortic valve (Core Valve, Medtronic, USA). Six months follow-up was available for all the pa-

tients. **Results.** All interventions were successfully performed without significant periprocedural complications. Immediate hemodynamic improvement was obtained in all the patients (peak gradient 94.2 ± 27.6 to 17.6 ± 5.2 mmHg, $p < 0.001$, mean pressure gradient 52.8 ± 14.5 to 8.0 ± 2.1 mmHg, $p < 0.001$). None of the patients developed heart block, stroke, vascular complication or significant aortic regurgitation. After 6 months, the survival was 100% with New York Heart Association (NYHA) functional improvement in all the patients. **Conclusion.** This successful initial experience provides a solid basis to treat larger number of patients with symptomatic AS and high surgical risk who are left untreated.

Key words:

aortic valve stenosis; transcatheter aortic valve replacement; severity of illness index; risk factors; cardiac surgical procedures.

Apstrakt

Uvod/Cilj. Aortna stenoza (AS) je najčešća mana zaliska kod odraslih, sa prilično lošom prognozom kod simptomatskih bolesnika. Hirurška zamena aortnog zaliska je terapija izbora, ali kod značajnog broja bolesnika ona nije izvodljiva. Prikazali smo inicijalno iskustvo sa transkateterskom implantacijom aortnog zaliska *transcatheter aortic valve replacement* (TAVR) koja je izvedena u sali za kateterizaciju na Klinici za kardiologiju Kliničkog centra Srbije. **Metode.** Procedura je urađena kod 5 bolesnika (srednje godine starosti 76 ± 6 godina, 2 muškarca i 3 žene) kod bolesnika sa teškom i simp-

tomatskom AS koji su imali ili kontraindikacije za hiruršku zamenu aortnog zaliska ili visok rizik od hirurške procedure. Sve odluke o primeni TAVR doneo je kardiohirurški tim. Pregled bolesnika pre procedure obuhvatao je detaljni klinički i ehokardiografski pregled, koronarnu angiografiju i kompjuterizovanu tomografiju srca i vaskularnog sistema. Kod svih bolesnika implantiran je samooslobađajuć aortni zalistak (CoreValve, Medtronic, USA). Šestomesečno praćenje je sprovedeno kod svih bolesnika. **Rezultati.** Sve intervencije uspešno su izvedene, bez značajnih periproceduralnih komplikacija. Neposredno hemodinamsko poboljšanje postignuto je kod svih bolesnika (maksimalni gradijent priti-

ska: 94.2 ± 27.6 vs 17.6 ± 5.2 mmHg, $p < 0.001$; srednji gradijent pritiska: 52.8 ± 14.5 vs 8.0 ± 2.1 mmHg, $p < 0.001$). Nijedan bolesnik nije imao srčane blokove, moždani udar, vaskularne komplikacije ili značajnu aortnu regurgitaciju posle intervencije. Posle 6 meseci, preživljavanje je bilo 100%, a funkcionalno poboljšanje je postignuto kod svih bolesnika. **Zaključak.** Ovaj inicijalni uspeh predstavlja dobru osnovu za lečenje većeg broja bolesnika sa simptomatskom

AS koji imaju visok hirurški rizik, a do sada nisu bili adekvatno lečeni.

Ključne reči:

zalistak, aortni, stenoza; zalistak aorte, transkateterska zamena; bolest, indeks težine; faktori rizika; hirurgija, kardijalna, procedure.

Introduction

Aortic valve stenosis (AS) is becoming a common disease in elderly population. In patients with symptomatic severe AS there is unfavorable prognosis with survival rates of only 15–50% in 5 years¹. Surgical valve replacement is the therapy of choice in patients with symptomatic AS, but the mortality after isolated surgical procedures is 1–3% in patients under 70 years, and 4–8% above 70 years¹. In clinical practice at least 30% of patients with severe symptomatic AS do not undergo surgery for replacement of the aortic valve, due to advanced age, frequent comorbidities and frailty^{1,2}. An alternative and less invasive therapy – transcatheter aortic valve implantation (TAVI) was proposed and initiated in 2002³, and achieved in short period clinical acceptance, with more than 150,000 procedures done worldwide⁴. The initial experience demonstrated that TAVI has significant impact on prolongation and quality of life in inoperable and high risk patients with symptomatic AS, and as such, recognized by ESC guidelines for valve disease and recommended in high-risk surgical patients¹⁻³. Currently, we have the 2 valve modalities including self-expandable and balloon-expandable valve with similar performance and success rate^{2,5-7}. The first self-expanding CoreValve (Medtronic, USA) has been registered in Serbia and here we presented our initial experience of TAVI in first 5 patients performed in Catheterization Laboratory of the Clinic for Cardiology, Clinical Center of Serbia.

Methods

Study population

Implantation of CoreValve was performed between April and May 2014 in the first 5 patients (mean age 76 ± 6 years) with severe symptomatic AS, after evaluation by the heart team consisting of invasive cardiologist, cardiac surgeon and non-invasive cardiologist.

According to the current European guidelines for valvular heart disease¹, TAVI is recommended in patients with symptomatic severe AS with contraindication to surgical procedure or high surgical risk [Society of Thoracic Surgeons (STS) score $\geq 10\%$ and Logistic EuroSCORE $\geq 20\%$], without short life expectancy due to comorbidities or frailty. The decision for TAVI should always be provided by the heart team⁸, and currently performed in hospitals with surgical facilities. Exclusion criteria for TAVI included clinical (short life expectancy, significant comorbidities, as well as severe

coronary and other valvular heart disease that can be treated only by surgery) and anatomical (inappropriate size of the annulus and ascending aorta, thrombi in the left ventricle, active endocarditis, high risk of coronary artery obstruction, complex thrombotic plaques in the aorta, and unavailable adequate vascular access)¹.

All the patients were informed about the risks and benefits of the procedure and provided informed consent for TAVI. All the procedures were performed with the guidance of the experienced proctor for TAVI (GP.U).

Study procedures and the device

Preprocedure screening included detailed clinical examination, echocardiographic overview of the function and dimensions of the heart, function of the valves, dimensions of the aorta with evaluation of severity of aortic stenosis (Figure 1), coronary angiography with percutaneous coronary intervention (PCI) at least 1 month prior to TAVI, computed tomography (CT) scan for precise measurements of diameters of the left ventricular outflow tract, aortic annulus (Figure 2A), sinus Valsalva (Figure 2B), ascending aorta (Figure 2C), the distance from the annulus to the orifice of coronary arteries (Figure 2D), in addition to sinus Valsalva height. Also, vascular access including the dimensions and appearance of femoral and subclavian arteries was done with CT scan, as well as full anesthesiological work-up of the patient prior to the procedure.

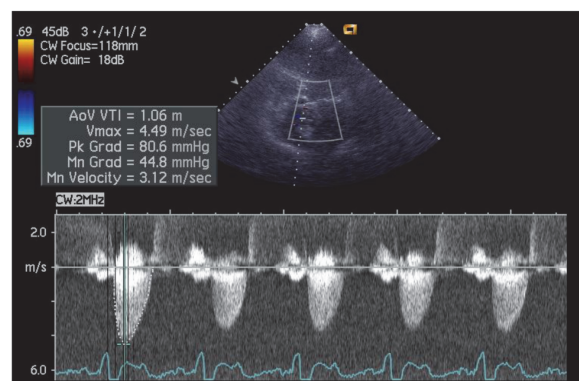


Fig. 1 – Transthoracic echocardiography – gradient across the aortic valve before transcatheter aortic valve implantation.

The CoreValve three leaflet bioprosthesis is made from porcine pericardium attached to nitinol frame (Figure 3). Nitinol frame allows crimping of the valve into the 18F profile loading system, which self expands into the full predesigned

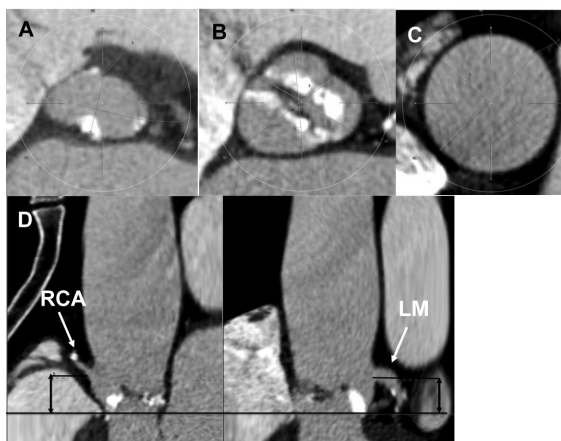


Fig. 2 – Computed tomography examination: A) Diameters of the aortic annulus; B) Diameters of the sinus Valsalva; C) Diameters of the ascending aorta; D) Distance from the annulus to orifice of the left main (LM) and right coronary artery (RCA).

form and after implantation extends from the left ventricular outflow tract across the aortic annulus into the aortic root. The valve is available in three dimensions of 26, 29 and 31 mm diameters, and valve size selection is based on the precise measurement of the aortic annulus and root by echocardiography and most importantly by CT. The procedure is performed in catheterization laboratory under deep analgesation or general anesthesia, either with pure percutaneous femoral approach or surgical incision of femoral artery. In cases in which femoral artery is too small or too tortuous, the procedure can be performed through subclavian artery. From the other inguinal groin femoral artery and vein, pigtail catheter is advanced into ascending aorta, whereas temporary pacemaker is placed into the right ventricle. After insertion of 18F sheath into right femoral or subclavian artery, left Amplatz catheter was advanced to aortic root to pass the aortic orifice first with soft wire and then exchanged for the Super Stiff Amplatz wire. Prior to implantation, a calcified valve is predilated with a large balloon under rapid ventricular pacing from right ventricle (Figure 4A). Aortic valve is then advanced and deployed under angiographic guidance from the pigtail catheter

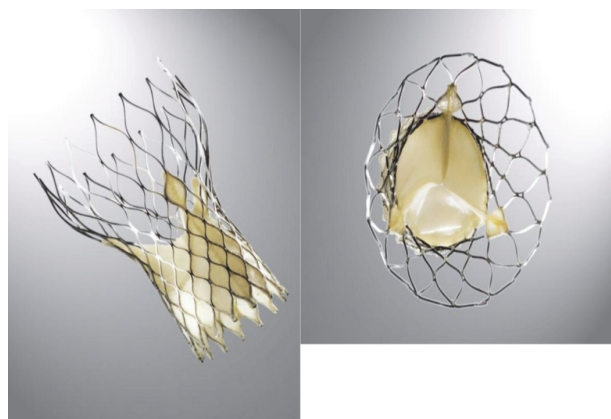


Fig. 3 – The CoreValve three leaflet bioprosthesis – porcine pericardium attached to nitinol frame. Courtesy of Medtronic.

ter positioned in the aortic root (Figure 4B). After successful aortic prosthesis implantation, aortography was performed for evaluation of aortic regurgitation along with assessment of left ventricular pressures and curves (Figure 4C). All cases were finished by femoral suture performed by the surgeons, and transthoracic echocardiographic evaluation of position and function of aortic valve, residual aortic regurgitation and right ventricle pressures (Figure 5). Immediately after the procedure, all the patients were transferred to cardiac care unit for close clinical and hemodynamic monitoring for the next 2 to 3 days. The premedication included aspirin and clopidogrel for few days prior to the intervention, with continuation for the next 3–6 months.

Statistical analysis

Continuous variables were presented as mean \pm standard deviation. Categorical variables were presented as frequencies in percentages. Statistical significance was calculated by Student's *t*-test, or χ^2 for categorical variables. $p < 0.05$ was considered statistically significant.

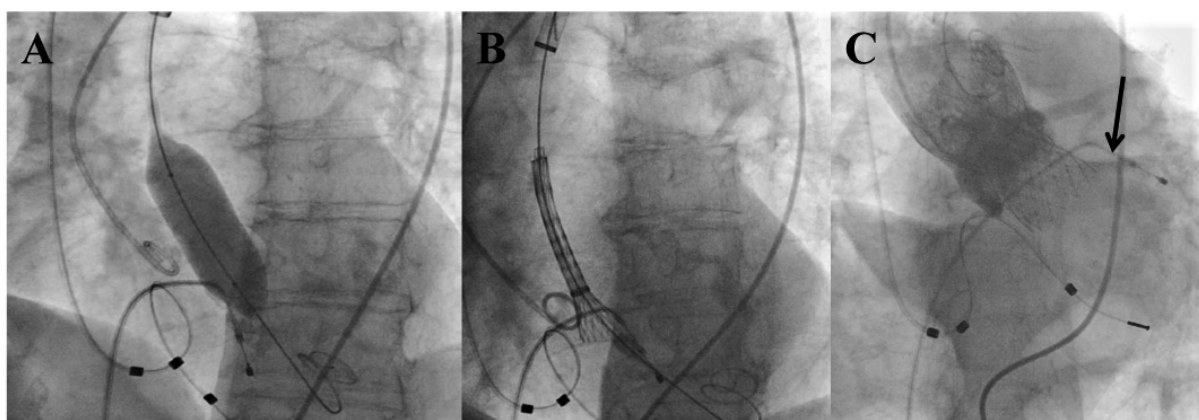


Fig. 4 – A) Predilatation of the native aortic valve with a balloon; B) Deployment of the CoreValve under angiographic guidance from the pigtail catheter positioned in the aortic root; C) Final aortography, with mild paravalvular aortic regurgitation (arrow).

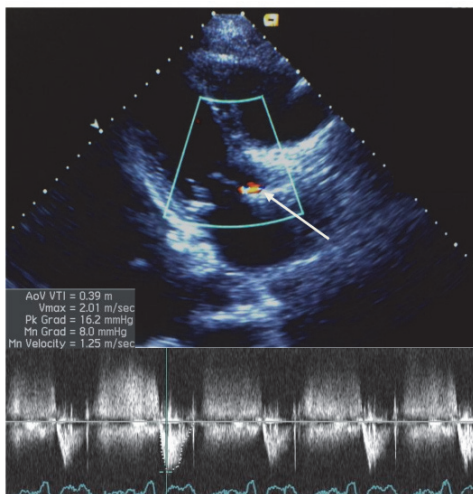


Fig. 5 – Transthoracic echocardiography – gradient across the CoreValve and trivial paravalvular regurgitation (arrow) after the transcatheter aortic valve implantation procedure.

Results

Baseline clinical and echocardiographic characteristics of the patients are presented in Table 1. All the patients were symptomatic prior to intervention with 80% of the patients in New York Heart Association (NYHA) class II-III. Common comorbidities were present in all the patients including

mostly moderate to severe impairment of renal function, as well as previous cerebrovascular events, diabetes, previous thoracotomy and porcelain aorta in individual patients. High surgical risk that precluded cardiac surgery was estimated as a STS score of 16.3 ± 1.4 and LogEuroScore of 21.98 ± 9.87 . All the patients had preserved left ventricular dimensions and function with the mean aortic valve area of $0.71 \pm 0.12 \text{ cm}^2$.

Three of the patients had coronary artery disease, successfully treated previously with stenting. Control angiography demonstrated patent coronary arteries without significant new lesions or restenosis in all the three patients. There were no significant coronary artery stenosis in the other two patients.

In three patients procedure was performed through femoral artery, and in two patients left subclavian artery was used as entry site. Immediate hemodynamic improvement was achieved in all the patients, with decrease of peak pressure gradient from $94.2 \pm 27.6 \text{ mmHg}$ to 17.6 ± 5.2 ($p = 0.003$), and mean pressure gradient from $52.8 \pm 14.5 \text{ mmHg}$ to $8.0 \pm 2.1 \text{ mmHg}$ ($p = 0.002$). As indirectly measured from transthoracic echocardiography immediately after the procedure inside catheterization laboratory, systolic right ventricle pressure also decreased from 63 ± 15 to $40 \pm 7.3 \text{ mmHg}$ ($p = 0.020$) (Table 2). After the procedure all the patients had only mild aortic regurgitation. None of the patients suffered from any severe vascular complications, stroke,

Table 1

Clinical and echocardiographic characteristics of the patients (n = 5)

Variable	Value
Age (years), $\bar{x} \pm \text{SD}$	76 ± 6
Male/female, n (%)	2/3 (40/60)
Atrial fibrillation, n (%)	1 (20)
Left bundle branch block, n (%)	0
Chronic obstructive pulmonary disease, n (%)	0
Previous thoracotomy, n (%)	1 (20)
Chronic renal failure, n (%)	
none	1 (20)
moderate	3 (60)
severe	1 (20)
Previous cerebrovascular event, n (%)	1 (20)
Hypertension, n (%)	5 (100)
Diabetes, n (%)	2 (40)
Porcelain aorta, n (%)	1 (20)
Peripheral vascular disease, n (%)	2 (40)
Previous coronary artery disease, n (%)	3 (60)
Syncope, n (%)	1 (20)
Previous pacemaker, n (%)	2 (40)
STS score, $\bar{x} \pm \text{SD}$	16.3 ± 1.4
LogEuroScore, $\bar{x} \pm \text{SD}$	21.98 ± 9.87
Aortic area (cm^2), $\bar{x} \pm \text{SD}$	0.71 ± 0.12
LV end-diastolic dimension (mm), $\bar{x} \pm \text{SD}$	54 ± 5
LV systolic dimension (mm), $\bar{x} \pm \text{SD}$	33 ± 7
Ejection fraction (%), $\bar{x} \pm \text{SD}$	65 ± 5

STS – Society of Thoracic Surgeon; LV – left ventricle; \bar{x} – mean value; SD – standard deviation.

Table 2

Clinical and echocardiographic characteristics of the patients – before the intervention and 30 days follow-up

Variable	Before intervention	After	<i>p</i>
NYHA Class, n (%)			
I-II	1 (20)	4 (80)	0.058
III-IV	4 (80)	1 (20)	
Peak pressure gradient (mmHg), $\bar{x} \pm \text{SD}$	94.2 ± 27.6	17.6 ± 5.2	0.003
Mean pressure gradient (mmHg), $\bar{x} \pm \text{SD}$	52.8 ± 14.5	8.0 ± 2.1	0.002
Systolic right ventricle pressure (mmHg), $\bar{x} \pm \text{SD}$	63 ± 15	40 ± 7.3	0.020

NYHA – New York Heart Association; \bar{x} – mean value; SD – standard deviation.

transient ischemic attacks, heart block or other procedure complications, except for the one patient who developed in-hospital gastrointestinal bleeding due to erosive gastroduodenitis which was successfully treated with blood transfusion and proton pump inhibitors. The mean hospital stay was 14 ± 10 days. None of the patient died within 30 days and 6 months follow-up, and symptoms and quality of life improved in all the patients.

Discussion

Initial results with percutaneous implantation of self-expandable aortic valve in patients with symptomatic aortic stenosis with high surgical risk are promising and confirm previous excellent experience and data on TAVI^{9,10}. The technique appeared to be safe, feasible, effective and successful in reducing large pressure gradient and symptoms in patients with severe AS^{11,12}. Our initial results on survival are excellent, with complication of gastrointestinal bleeding occurring only in one patient. However, this complication was associated with concomitant antithrombotic and anticoagulant therapy and not to procedure *per se*. Of course, the initial results need to be extended with consistent application and performance as this highly sophisticated procedure requires considerable experience and learning curve. The other point is that the prevalence of degenerative AS is linked to aging population, and as such is expected to represent an increasingly important public health problem in our country. Thus, support from the national health authorities and national health funding system is essential in wider application of this novel technique, as TAVI is therapeutic option that has demonstrated improved survival and quality of life. Target population for TAVR includes symptomatic patients with severe aortic stenosis who are refused by the surgeons due to high surgical risk, and the estimated percentage is around 0.02% of the whole population¹. Thus, for the population of our country the estimate would be around 150 patients *per* year which is far more than initially expected but appeared to be quite true as the number of patients with AS are either not diagnosed at all or underdiagnosed and poorly referred to the surgeons. Thus, with initiation of TAVI program in other countries, the number of surgical procedures for aortic valve replacement did not decrease, but on the contrary increased due to higher awareness of this severe disease and better referral for the treatment.

Complications of TAVI include stroke in 1–5% of the patients^{1–4}, onset of new left bundle branch block (in 7–18% with balloon-expanding valves and in 30–80% of patients with self-

expanding valves)¹³, need for new pacemaker (in 7–17.3% for the balloon expanding valves and in 37–40% for the self-expanding valves)^{2, 14, 15}, and vascular complications up to 20%,^{2,3,16}. Also, trace or mild paravalvular regurgitation is a common finding in the majority of the patients after TAVI procedure¹. However more than a mild paravalvular regurgitation may have an impact on long-term survival of the patients^{17,18}. None of our first 5 patients developed any of the common TAVI complications.

The first mechanical heart valve on mitral position was surgically implanted in March 1960¹⁹. Next year Harken et al.²⁰ reported a small series with caged-ball prosthesis in the aortic position, and 40 years later Alain Cribier implanted first transcatheter aortic valve by anterograde approach^{2, 21}. In 2004, the first pure retrograde approach was performed, and the first complete percutaneous retrograde implantation of CoreValve (Medtronic, USA) was done in 2006^{2,21}. Until today, more than 90% of cases were performed either with self-expandable CoreValve (Medtronic) or balloon-expandable Edwards/Sapien aortic valve, but more than 10 different aortic valves with different technical characteristics and designs are under clinical investigations. Survival rates after CoreValve implantation is excellent and range from 71–84% after 1 year in more than 500 patients^{5, 16, 17}. Similarly, PARTNER trial, the first randomized trial on AS in non-surgical candidates, demonstrated significant reduction in all cause and cardiovascular death in patients treated with TAVI in comparison to the standard therapy^{2, 22}. In addition, excellent worldwide experience and safety profile with TAVI in high risk patients, in 2014 further lowers the threshold for this procedure to patients with moderate surgical risk²³.

Conclusion

Our initial results with CoreValve transcatheter aortic valve implantation (TAVI) is promising and encouraging, improvement of symptoms and hemodynamics excellent, and this initial experience opens the therapeutic door to treat a large number of patients who remain to be treated.

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