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Review article

# The development of the TAVI program in Serbia – ten-years of experience

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**Abstract** Aortic stenosis (AS) is the most common valvular disease requiring surgical (SAVR) or transcatheter intervention (TAVI) in Europe and North America. The first TAVI was performed in 2002 in order to treat in-operable patients with AS, and the initial ESC guidelines recommended this procedure in patients with a high risk of SAVR. According to ESC guidelines for the treatment of valvular diseases from 2021, the decision on the treatment modality of AS is defined by the Heart team, and SAVR is recommended in younger patients with a low risk of surgery (<75 years STS-PROM/EuroScore II<4%), and TAVI is recommended in elderly patients ≥75 years or in patients with high operative risk (STS-PROM/EuroScore II>8%) or in patients not suitable for surgery. In addition, large randomized clinical studies (PARTNER 3, Evolut Low Risk and NOTION studies) showed that TAVI is also safe in patients with a low operative risk (STS-PROM/EuroScore II<4%), and not inferior to SAVR (UK TAVI trial). The first TAVI procedure in Republic of Serbia was performed on April 22, 2014 during BASIC 8+ congress. In the period of 2014-2023, 444 TAVI procedures were performed in Republic of Serbia, with exponential increase in in the last 2 years.

**Kew words** aortic stenosis, surgical aortic valve replacement (SAVR), transcatheter aortic valve intervention (TAVI)

## Introduction

Aortic stenosis (AS) is the most common primary valve lesion requiring surgery (SAVR) or transcatheter intervention (TAVI) in Europe and North America.[1,2] AS prevalence is rising rapidly as a consequence of the aging population.[3,4] SAVR was 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 years.[1,2] As an alternative of SAVR, transcatheter aortic valve implantation (TAVI) was proposed and initiated in 2002,[5] and in a short period achieved clinical acceptance and recommendations by the guidelines in the high-risk surgical patients.[1-6]

## Management of aortic stenosis according to ESC guidelines 2021

Use of SAVR and TAVI as complementary treatment options has allowed a substantial increase in the overall number of patients with aortic stenosis undergoing surgical or transcatheter intervention in the past decade.[6] ESC guidelines[1] suggested that randomized clinical trials (RCT) have assessed the two modes of intervention across the spectrum of surgical risk in predominantly elderly patients. These trials using surgical risk scores to govern patient selection demonstrated that TAVI is superior to medical therapy in extreme-risk patients and non-inferior to SAVR in high[7-11] and intermediate-risk patients at follow-up extending to 5 years.[12-17] In addition, PARTNER 3 and Evolut Low Risk trials demonstrated that TAVI is non-inferior to SAVR in low-risk patients at 2-year follow-up.[18-22] Rates of vascular complications, pacemaker implantation, and paravalvular regurgitation are consistently higher after TAVI, whereas a severe bleeding, acute kidney injury, and new-onset AF are more frequent after SAVR. Likelihood of paravalvular regurgitation has been reduced with newer transcatheter heart valve designs, but still pacemaker implantation (and new-onset left bundle branch block) may have long-term consequences[23-25] requiring further refine-

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**Table 1.** Number of TAVI procedures in Republic of Serbia since 2014

| Year | University Clinical Center of Serbia | Institute for CVD Dedinje | Institute for CVD Sremska Kamenica | Military Medical Academy | Total |
|---|---|---|---|---|---|
| 2014 | 5 | / | / | / | 5 |
| 2015 | 2 | 2 | 2 | / | 6 |
| 2016 | 1 | / | / | / | 1 |
| 2017 | / | / | / | 2 | 2 |
| 2018 | / | / | / | 2 | 2 |
| 2019 | / | 24 | / | 1 | 25 |
| 2020 | / | 9 | / | / | 9 |
| 2021 | / | 23 | / | / | 23 |
| 2022 | 30 | 166 | 24 | / | 220 |
| 2023 | 39 | 65 | 47 | / | 151 |

ments. Most patients undergoing TAVI have a swift recovery, short hospital stay, and rapidly return to normal activities. Despite these benefits, there is a wide variation in worldwide access to the procedure as a result of high device costs as well as different levels of health care resources[26].

In the summary the latest ESC guidelines form 2021 recommend that aortic valve intervention should be performed in Heart valve Centers (IC).[1] The choice between SAVR and TAVI must be based upon careful evaluation of Heart team (IC). SAVR is recommended in younger patients with low risk for surgery (<75 years STS-PROME/EuroScore II<4%) (IB), and TAVI is recommended in older patients ≥75 years or in patients with high surgery risk (STS-PROME/EuroScore II>8%) or in patients unsuitable for surgery (IA).[1]

## TAVI in clinical randomized trials

In the last fourteen yours,14 RCT for TAVI were published including more than 9000 patients. Initially TAVI was recommended for high-risk patients. From 2019, TAVI has been assessed in low and intermediate risk patient. The PARTNER 3[18,19] and Evolut Low Risk trials[20] demonstrated that TAVI is non-inferior SAVR in low-risk patients at 2-year follow-up. In the Partner 3 trial there were no significant between-group differences in major vascular complications, new permanent pacemaker insertions, or moderate or severe paravalvular regurgitation. Among patients with severe aortic stenosis who were at low surgical risk, the rate of the composite of death, stroke, or rehospitalization at 1 year was significantly lower with TAVI than with surgery. Importantly, patients in the low-risk trials were predominantly male and relatively elderly (e.g. PARTNER 3: mean age 73.4 years; <70 years 24%, 70-75 years 36%, >75 years 40%, >80 years 13%). Results of the Evolut Low Risk study[23] suggested that in the patients with severe aortic stenosis who were at low surgical risk, TAVI with a self-expanding supraannular bioprosthesis was noninferior to surgery with respect to the composite end point of death or disabling stroke at 24 months.[18,19]

The Nordic Aortic Valve Intervention (NOTION trial)[16] was designed to compare transcatheter aortic valve replacement (TAVI) to surgical aortic valve replacement (SAVR) in patients 70 years or older with isolated severe aortic valve stenosis. NOTION trial demonstrated that there was no statistical difference for major clinical outcomes 5 years after TAVI with a self-expanding prosthesis compared to SAVR. Higher rates of prosthetic regurgitation and pacemaker implantation were seen after TAVI.[16]

The latest published study for TAVI in low risk-patients was UK TAVI trial[27]. In this randomized clinical trial conducted at 34 UK centers, 913 patients aged 70 years or older with severe, symptomatic aortic stenosis and moderately increased operative risk due to age or comorbidity were enrolled. This study proved that in patients aged 70 years or older with severe, symptomatic aortic stenosis and moderately increased operative risk, TAVI was non inferior to surgery with respect to all-cause mortality at 1 year.

There is some new potential indication fields for TAVI, which include asymptomatic severe aortic stenosis (RECOVERY, AVATAR, ENVOLVED and EARLY TAVR trials) and moderate AS “at risk“ (UNLOAD, PROGRESS, EXPAND TAVR II trials).

## Implementation of TAVI in Republic of Serbia

From 2014-2023 year in Republic of Serbia (RS) 444 TAVI procedures was performed. The first TAVI procedure in Republic of Serbia was performed on April 22, 2014 during BASIC 8+ congress. In the 2014 year 5 TAVI procedures was done in University Clinical Center of Serbia, next 6 TAVI procedures was done during 2015 (two TAVI during BASIC 9+), after that TAVI was done sporadically until 2019, when Institute for cardiovascular disease Dedinje started with commercial TAVI program and number of TAVI procedures in RS raised (Table 1). In 2022, Republic Fund for Health insurance started with noncommercial TAVI program and provided 141 self-expandable valves including 111 Evolute (Medtronic) and 30 Portico (Abbot) valves. For 2023 and 2024, 300 valves will be provided including 225 Evolute (Medtronic), 45 Portico (Abbot), and 30 balloon-expandable Myval (Meril Lifesciencies).

The first results of TAVI procedures in Serbia was published 2016[28] demonstrating all successful interventions

without significant periprocedural complications. In this initial group of patients, immediate hemodynamic improvement was obtained in all 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[28]. All the initial results are encouraging, and the new data with much higher number of patients will be soon available.

## Conclusion

Percutaneous treatment of aortic stenosis with TAVI in patients over 75 years is challenging procedure and requires careful discussion and selection of the patients by the Heart team, detailed planning and preparation of the procedure taking into account all potential pitfalls, full engagement of the team performing the procedure, and careful observation of the in-hospital clinical course. Selection of the most appropriate mode of intervention should be considered in the light of comorbidities (including frailty and overall quality of life), anatomical and procedural characteristics, the relative risks of SAVR and TAVI, and long-term outcome.

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## *Sažetak*

## *Razvoj TAVI programa u Srbiji – desetogodišnje iskustvo*

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*Aortna stenoza (AS) je najčešće valvularno oboljenja koje zahteva hirurško (SAVR) ili transkatetersku intervenciju (TAVI). Prva TAVI urađena je 2002. godine kod hirurški inoperabilnog pacijenta, da bi u kratkom vremenskom periodu našla kliničku primenu tako da su inicijalne ESC preporuke ovu proceduru preporučivale kod pacijenata sa visokim rizikom za SAVR. Prema ESC preporukama za lečenje valvularnih mana iz 2021.godine odluku o modalitetu lečenja AS definiše Heart team, a SAVR se preporučuje kod mlađih pacijenata sa niskim rizikom od operacije (<75 godina STS-PROM/EuroScore II<4%), a TAVI se preporučuje kod starijih pacijenata ≥75 godina ili kod pacijenata sa visokim operativnim rizikom (STS-PROM/EuroScore II>8%) ili kod pacijenata koji nisu pogodni za operaciju. Sa druge strane velike randomizovane kliničke studije (PARTNER 3, Evolut Low Risk and NOTION studije) su pokazale da je TAVI bezbedna i ne-inferiorna u odnosu na SAVR i za pacijente sa niskim operativnim rizikom (STS-PROM/EuroScore II<4%)(UK TAVI trial). Prva TAVI procedura u Srbiji je urađena 22.04.2014. godine tokom BASIC 8+ kongresa. Od 2014-2023 godine u našoj zemlji je urađena 444 TAVI procedura sa eksponencijlanim rastom u poslednje 2 godine..*

***Ključne reči:*** *aortna stenoza, hirurška zamena aortne valvule (SAVR), transkateterska zamena aortne valvule (TAVI)*