

# Nekoronarne kardiološke intervencije — pregled stanja u Hrvatskoj

## *Noncoronary cardiac interventions — an overview of the situation in Croatia*

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Perkutane koronarne intervencije već su dugo osnovno i ključno područje djelovanja intervencijskih kardiologa. Međutim, brzo širenje intervencijske kardiologije u posljednjih desetak godina dovelo je do revolucionarnih tehničkih dostignuća i uspješne provedbe brojnih intervencija izvan koronarnih arterija. Sukladno članku koji prati ovaj uvodnik, prikazujemo trenutnu situaciju u Hrvatskoj, uključujući perkutane intervencije na srčanim zaliscima, zatvaranje septalnih defekata i aurikule lijevog atrija, kao i liječenje arterijske hipertenzije renalnom denervacijom. Prikazujemo (prema našem najboljem znanju, pri čemu je većina informacija prikupljena iz osobne komunikacije) kratak pregled trenutne dostupnosti i učestalosti nekoronarnih intervencijskih postupaka u hrvatskim kardiološkim odjelima (**Tablica 1**).

Percutaneous coronary interventions have long been the mainstay and pivotal area of activity for the interventional cardiologist. However, rapid expansion of interventional cardiology within the past decade has led to revolutionary technical advances and successful clinical implementation of a number of interventions beyond coronary arteries. Pursuant to the article accompanying this editorial, this review of the current situation in Croatia includes percutaneous interventions on cardiac valves, closure of septal defects, and left atrial appendage, as well as treatment of arterial hypertension by means of renal denervation. We present (to the best of our knowledge, with most information being gathered from personal communication) a brief overview of the current availability and incidence of noncoronary interventional procedures in Croatian cardiology departments (**Table 1**).

**Table 1.** Overview of noncoronary cardiac interventions in Croatia.

Type of intervention	Number of patients treated to date	Hospitals performing interventions
Transcatheter aortic valve implantation	71	Dubrava University Hospital, Zagreb Magdalena Clinic, Krapinske Toplice University Hospital Centre Zagreb, Zagreb
Percutaneous patent foramen ovale or atrial septal defect closure in adults	225	Magdalena Clinic, Krapinske Toplice University Hospital Centre Rijeka, Rijeka University Hospital Centre Zagreb, Zagreb
Left atrial appendage closure	0	—
Renal denervation	29	Dubrava University Hospital, Zagreb Merkur University Hospital, Zagreb University Hospital Centre Rijeka, Rijeka University Hospital Centre Zagreb, Zagreb

## Transkateterska implantacija / zamjena aortnog zalistka (TAVI / TAVR)

Nakon prve TAVI u Hrvatskoj u siječnju 2011. godine, do danas je učinjen 71 zahvat. Ovaj postupak se trenutno provodi u tri klinike (Klinički bolnički centar Zagreb, Klinička bolnica Dubrava, Zagreb; Magdalena — Klinika za kardiovaskularne bolesti MF Osijek, Krapinske Toplice) sa značajnim zaostatom u broju potrebnih implantacija, prvenstveno zbog financijske situacije (ograničavajući čimbenik predstavlja trošak proteze). Objektivna procjena potrebe za TAVI u Hrvatskoj temelji se na učestalosti ove najčešće valvularne bolesti (što predstavlja procjenu prave simptomatske aortne stenoze) i iznosi između 200 i 250 slučajeva godišnje (Slika 1).

## Transcatheter aortic valve implantation / repair (TAVI / TAVR)

After the first TAVI in Croatia in January 2011, a total of 71 interventions have been carried out to date. This procedure is currently offered to patients in three clinics (Clinical Hospital Centre Zagreb, Zagreb; Dubrava Clinical Hospital, Zagreb; Magdalena Clinic, Krapinske Toplice), with the number of implantations lagging behind the needed, primarily due to the cumbersome financial environment (the cost of the prosthesis being the limiting factor). A fair estimation of the needs for TAVI in Croatia can be based on the prevalence of this most common valvular disease (accounting for the estimates of the true symptomatic aortic stenosis) and runs between 200 and 250 cases per year (Figure 1).

Figure 1. Projected number of patients per year in Croatia with indication for transcatheter aortic valve implantation.

### Indications for TAVI in Croatia

- ▶ **Croatia: 4,3 million**
- ▶ **20.000 with AS (0.5%)**
- ▶ **3200 severe AS (16%)**
- ▶ **1600 symptomatic (50%)**
- ▶ **480 do not undergo AVR (30%)**
- ▶ **~ 200-250 TAVI candidates (60%)**



Kliničke karakteristike liječenih bolesnika trebaju biti u skladu s pravom indikacijom za ovim postupkom — teška simptomatska aortna stenoza u visokorizičnih ili inoperabilnih bolesnika. Uglavnom su to su stariji bolesnici s brojnim komorbiditetima, često s prethodnom operacijom srca i u životnoj dobi višoj od 90 godina. Postupak se obavlja ili u općoj anesteziji ili u dubokoj sedaciji s lokalnom anestezijom, ovisno o mjestu krvožilnog pristupa. U većine bolesnika, arterijskom sustavu se pristupa transfemoralnim putem, a kod manjeg broja slučajeva odabire se pristup alternativnim putem — potključna arterija, transapikalno, izravno aortno i transabdominalno. Oslikavanje prije samog zahvata je bitno za potvrđivanje indikacije za implantacijom aortne valvule, kao i za uspješno planiranje (prvenstveno za određivanje odgovarajuće veličine valvule i pristupnog puta). Tri modaliteta oslikavanja uključena u većini slučajeva su transtorakalna i transezofagealna ehokardiografija (TTE, TEE), klasična koronarna angiografija i aortografija (CA) i višeslojna kompjutorizirana tomografija (MSCT). Rutinska primjena TAVI postupka svakako je usporena zbog visokog troška i nepostojanja paušalne cijene zahvata (DTS).

The clinical characteristics of the patients treated should be in accordance with the true indication for this procedure — severe symptomatic aortic stenosis in patients with a high risk for surgery or deemed inoperable. Typically, these are older patients with numerous comorbidities, often with prior cardiac surgery and aged over 90. The procedure is performed either in general anaesthesia or deep sedation with local anaesthesia, depending on the vascular access site. In the majority of patients, the arterial system is accessed via the transfemoral route, with a small number of cases performed through the subclavian, transapical, direct aortic or transabdominal access points. Preprocedural imaging is essential for confirming the indication for aortic valve implantation, as well as for successful planning (primarily for determining the appropriate size of the valve and access route). Three imaging modalities are included in the majority of cases, transthoracic and transesophageal echocardiography, classic coronary angiography and aortography, and multislice computed tomography. The implementation of TAVI in routine practice is certainly slowed by the high cost of the procedure and current lack of proper reimbursement.

## Perkutane intervencije na mitralnom zalisku

Stariji srčani bolesnici nerijetko imaju tešku mitralnu regurgitaciju, koja ima lošu prognozu. Ovi bolesnici imaju povećanu učestalost od komorbiditeta s neprihvatljivim rizikom za kardiokirurški zahvat bolesti mitralnog zaliska. Zbog toga su razvijene i ispitane perkutane metode za rekonstrukciju mitralnog zaliska. MitraClip sustav je najopsežnije proučen i odobren za uporabu u Europskoj Uniji. Načelo rekonstrukcije oponaša kiruršku tehniku — Alfierijev šavom (Alfieri stitch, rekonstrukcija edge-to-edge). To je vrlo komplicirana intervencijska tehnika koja zahtijeva opsežno i precizno predproceduralno i postproceduralno oslikavanje, uključujući i 3D transezofagijsku ehokardiografiju. Podaci o uspješnosti i koristi od postupka proizlaze prije svega iz EVEREST studije, koja je u značajnoj mjeri opterećena metodološkim pitanjima. Jedna zamjerka je da se uspjeh u ovoj studiji temeljio na mitralnoj regurgitaciji koja je bila manja ili do 2+, što u uobičajenim okolnostima ne bi bio prihvatljiv kirurški rezultat. Iako se čini da se postupkom može postići korist u bolesnika kod kojih postoji visok rizik od operacije mitralnog zaliska, potrebni su i drugi podaci kako bismo potvrdili da li ova tehnika koja imitira rekonstrukciju, a koja je zapravo već odavno napuštena od strane kirurga, predstavlja doista izvediv izbor za liječenje mitralne regurgitacije. Postavljanje MitraClip ili sličnih naprava u Hrvatskoj će vjerojatno biti odgođeno zbog vrlo velikog troška.

## Perkutano zatvaranje atrijskog septalnog defekta ili otvorenog foramena ovale

Nekirurško zatvaranje prirodnih septalnih defekata u pedijatrijskoj i odrasloj populaciji hrvatskim je bolesnicima dostupno već više od deset godina. Prikazani podaci (225 bolesnika liječenih ovom metodom do danas) se odnose samo na odrasle bolesnike liječene u tri centra.

Postoje dvije glavne indikacije za perkutano zatvaranje septalnog defekta. Neosporna indikacija postoji kod bolesnika s hemodinamski značajnim atrijskim septalnim defektom (ASD). Perkutano zatvaranje ASD može se sigurno izvesti samo kod defekta tipa secundum s odgovarajućim anatomskim svojstvima. Položaj, veličina i oblik kao i prisutnost odgovarajućih rubova se dijagnosticira transezofagijskom ehokardiografijom (TEE), što je bitno i za planiranje kao i za vođenje postupka. Sinus venosus i defekti tipa primum nisu pogodni za perkutano zatvaranje te se liječe kirurškim putem. Druga manje jasna indikacija za zatvaranje septalnog defekta postoji kod bolesnika (obično mlađih) s kriptogenim moždanim udarom i otvorenim foramenom ovale, pri čemu se dijagnoza i indikacija postavljaju u suradnji s neurolozima te ponovno potvrđuje TEE-om. Korist od ovog postupka nije sa sigurnošću potvrđena, budući da novije studije nisu uvjerljivo potvrdile superiornost ovog postupka u odnosu na medikamentoznu terapiju. Stoga je odluku potrebno donositi na pojedinačnoj osnovi, u uskoj suradnji s neurolozima. Ovaj postupak je redovito dostupan hrvatskim bolesnicima, iako je s vremena na vrijeme onemogućen zbog financijskih razloga.

## Zatvaranje aurikule lijevog atrija (LAA)

Glavni rizik povezan s fibrilacijom atrija predstavlja tromboembolijski moždani udar s embolusom koji potječe iz aurikule lijevog atrija (LAA). Postoji značajan broj bolesnika koji nisu u mogućnosti nastaviti s prvom linijom liječenja s oral-

## Percutaneous interventions on mitral valve

The ageing cardiac patients often present with severe mitral regurgitation, which carries a poor prognosis. These patients have an increased incidence of comorbidities with unacceptable risk for cardiac surgery for their mitral valve disease. On this background, percutaneous methods for mitral valve repair have been developed and tested. The MitraClip system is one system, which has been studied most extensively and has also been approved for the use in the European Union. The principle of the repair mimics the surgical Alfieri stitch technique (edge-to-edge repair). This is a highly complicated interventional technique, which requires extensive and precise preprocedural and periprocedural imaging, including 3D transesophageal echocardiography. The data on success rates and benefit of this procedure primarily stem from the EVEREST trial, which is a study plagued by methodological issues. One objection is that the success in this study was based on a mitral regurgitation smaller or equal to 2+, which under normal circumstances would not be a surgically acceptable result. While it seems that the procedure may convey benefit particularly to patients who are at high risk for mitral valve surgery, further data are needed to confirm if this technique, which imitates the repair, which has actually long been abandoned by the surgeons, represents a truly viable option for the treatment of mitral regurgitation. The implementation of MitraClip or similar devices in Croatia is most probably going to be delayed due to its enormous cost.

## Percutaneous atrial septal defect or patent foramen ovale closure

The nonsurgical closure of congenital septal defects in paediatric and adult population has been offered to Croatian patients for well over a decade. The data shown here (225 patients treated with this method to date) refer to adult patients only, treated in three centres.

There are two main indications for percutaneous septal defect closure. The undisputed indication is given in a patient with haemodynamically significant atrial septal defect (ASD). Percutaneous closure of ASD can safely be performed only in secundum type defects with appropriate anatomical properties. The position, size and shape as well as the presence of adequate rims is diagnosed with transesophageal echocardiography, which is essential both for planning and for the periprocedural guidance. Sinus venosus and primum type defects are not suitable for percutaneous closure and should be treated surgically. Another, less clear indication for septal defect closure is given in patients (typically younger) with cryptogenic stroke and patent foramen ovale, which is diagnosed in collaboration with neurologists and again confirmed by transesophageal echocardiography. The benefit of this procedure remains elusive, as recent studies have not convincingly confirmed the superiority of the procedure over medical treatment. The decision should be made on an individual basis and in close collaboration with neurologists. This procedure is available to Croatian patients on a regular basis, although at times hampered by financial aspects.

## Left atrial appendage (LAA) closure

The main risk related to atrial fibrillation is the thromboembolic stroke, with emboli originating from left atrial appenda-

nim antikoagulansima. Kirurška ligacija koja se uvijek obavlja kao dio nekog drugog postupka rutinski se izvodi ukoliko je indicirana, npr. tijekom operacije mitralnog zaliska. Perkutane naprave su razvijene za liječenje ove skupine bolesnika. Ove naprave postavljaju se transseptalnim putem u aurikulu lijevog atrija (LAA). Nekoliko studija je ukazalo na moguću dobrobit ovog pristupa. Definitivna uloga ovog postupka još nije utvrđena osobito obzirom na rastuću primjenu novih oralnih antikoagulansa (koji tipično imaju manje krvarenja s istom ili boljom učinkovitošću u usporedbi s varfarinom). Ovaj postupak još nije izveden u Hrvatskoj prvenstveno zbog svoje relativno visoke cijene.

## Renalna denervacija

Medikamentno liječenje arterijske hipertenzije vrlo je učinkovito u većine bolesnika, o čemu postoji mnogo podataka, kako o smanjenju smrtnosti, tako i pobola povezanih s ovim širom svijeta najčešćim kardiovaskularnim stanjem. Međutim, postoji značajna manjina bolesnika s takozvanom rezistentnom hipertenzijom. Ovisno o vrsti definicije i intenzitetom dijagnostičkih postupaka (pri čemu je nužno isključiti lošu suradljivost), učestalost rezistentne hipertenzije se može kretati u rasponu od 5 do 15% populacije bolesnika s arterijskom hipertenzijom. Ovo stanje je definirano kao rezistentno povišenje arterijskog tlaka iznad ciljnih vrijednosti uz istovremeno liječenje s tri ili više antihipertenziva različitih klasa, uključujući i diuretik.

Renalna denervacija temelji se na načelu modifikacije simpatičkog živčanog sustava bilateralnom destrukcijom inervacije renalne arterije, uglavnom pomoću radiofrekvencijske ablacije, koristeći klasičnu kateterizaciju kroz femoralnu arteriju. Postupak dovodi do promjena renalne vaskularne rezistencije, djelovanja renina, kao i simpatičkog tonusa bubrege i drugih organa. Istraživanja su dokumentirala značajno neposredno i održano (do tri godine) smanjenje vrijednosti arterijskog tlaka.

Najnovije ESC/ESH smjernicama za liječenje arterijske hipertenzije navode da je ova metoda obećavajuća, ali još uvijek postoji potreba za više podataka iz pravilno provedenih istraživanja kako bismo bili u mogućnosti odrediti dugoročnu učinkovitost i sigurnost renalne denervacije, posebice u usporedbi s najboljom mogućom medikamentoznom terapijom.

Ova se tehnika koristi u nekoliko hrvatskih centara od početka 2012. godine. S obzirom na učestalost hipertenzije, broj bolesnika liječenih dosada je ostao vrlo malen. Ponovno, primjena renalne denervacije je daleko ispod mogućih ciljeva, obzirom na trošak katetera.

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ge (LAA). There are a significant number of patients who are not able to continue the first-line treatment with oral anticoagulation. Surgical ligation, which is always performed as a part of another procedure, is routinely carried out if indicated, e.g. during mitral valve surgery. However, percutaneous devices have been developed to treat such patients. These devices use the transseptal route to reach the left atrium, where specially designed occluders are implanted in the LAA. Several studies have demonstrated possible benefit from this approach. The definite role of this procedure is yet to be established, especially with respect to the continuously growing use of novel oral anticoagulants (which show typically less bleeding with same or superior efficacy compared to warfarin). This procedure has not yet been performed in Croatia, primarily due to its relatively high cost.

## Renal denervation

Medical treatment of arterial hypertension is extremely effective in the majority of patients, with a vast body of data on reduction of both mortality and morbidity associated with this worldwide most prevalent cardiovascular condition. However, there is a significant minority of patients who have the so-called resistant hypertension. Depending on its definition and the vigour with which it is diagnosed (and poor compliance is excluded), the incidence of resistant hypertension may range from 5 to over 15% of hypertensive population. It is defined by persistent elevation of blood pressure above the target values while treating the patient with three or more antihypertensives of different classes, including a diuretic.

The principle of this intervention lies in targeting the sympathetic nervous system by bilateral destruction of the renal artery innervation, mostly by means of radiofrequency ablation using classic catheterization through the femoral artery. This in turn influences renal vascular resistance, renin activity, as well as sympathetic tone to the kidney and other organs. Studies have documented significant immediate and sustained (up to three years) blood pressure reduction.

The most recent ESC/ESH Guidelines for the management of arterial hypertension conclude that this method is promising, but still more data are needed from properly designed trials to determine the long-term efficacy and safety of renal denervation, especially in comparison with the best possible medical therapy.

This technique has been used in several Croatian centres since the beginning of 2012. In view of the prevalence of arterial hypertension, the number of patients treated so far has remained very low. Again, the use of renal denervation is far under the possible target numbers due to the cost of the catheters.

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**Organizator/Organizer**



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## 15. hrvatski simpozij o aritmijama i elektrostimulaciji srca

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### Kotizacija/Registration fee

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