

# Bolesti srčanih zalistaka u Hrvatskoj u 2011. godini

## *Valvular heart diseases in Croatia in 2011*

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Stečene greške srčanih zalistaka rjeđe su zastupljene nego koronarna bolest srca (KBS), srčana dekompenzacija i hipertenzija<sup>1</sup>. Međutim, u pojavljivanju stečenih grešaka srčanih zalistaka dogodile su se značajne promjene tijekom nekoliko posljednjih desetljeća. Dva su vanjska čimbenika na to imala važan utjecaj. Prvi je široka primjena antibiotika u liječenju streptokoknih infekcija koje su bile i još su uvijek jedan od glavnih uzroka stečenih srčanih grešaka, posebice u nerazvijenim zemljama i zemljama u razvoju. Drugi je čimbenik produžen životni vijek stanovništva s višim standardom i boljom medicinskom skrbi, s posljedičnim pojavom patologija svojstvenih starijim dobnim skupinama, ponajprije entiteta vezanih uz degenerativne procese. Ne ulazeći u dublju analizu tih dvaju fenomena, koji obilježavaju medicinu našeg doba, možemo se ograničiti samo na praktične posljedice s kojima se osjetno susrećemo u svakodnevnoj kliničkoj praksi te na dostupne epidemiološke podatke<sup>2</sup>.

Regionalne posebnosti stečenih grešaka srčanih zalistaka uočavaju se u različitim područjima svijeta i Europe. Podaci koji proizlaze iz Euro Heart Survey iz 2001. godine ukazuju na te regionalne razlike u Europi<sup>1</sup>. Može se uočiti češće pojavljivanje mitralne stenoze u istočnoj Europi, zatim nešto rjeđe u mediteranskim zemljama i mnogo rjeđe u zemljama zapadne Europe te posebno u sjevernoeuropskim, nordijskim zemljama. Socioekonomski čimbenici svakako se nameću pri objašnjavanju tih razlika. Mogu se, stoga, s vremenom očekivati daljnje promjene u smjeru smanjivanja tih regionalnih razlika, paralelno sa smanjivanjem socioekonomskih razlika<sup>2</sup>.

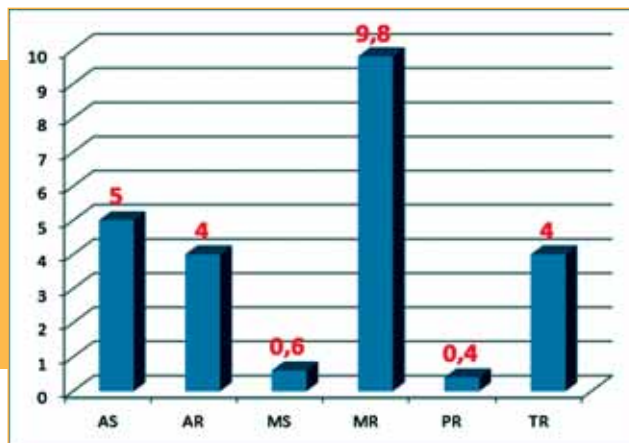
Nepostojanje nacionalnog registra za bolesti srčanih zalistaka potaklo nas je na jedno malo retrogradno ispitivanje u Zavodu za kardiovaskularne bolesti Kliničke bolnice Sveti Duh Zagreb u kojem smo pokazali pojavnost pojedinih grešaka srčanih zalistaka kod svih hospitaliziranih bolesnika u 2011. godini. Također smo pretražili komorbiditet kod istih bolesnika: postojanje KBS, preboljelog infarkta miokarda, angine pectoris, operacija aortokoronarnog premoštenja, perkutanih koronarnih intervencija i srčanih elektrostimulatora. Cilj ovog ispitivanja bio je odrediti važnost ove patologije u sveukupnom pojavljivanju te njeno preklapanje s ostalim kardiološkim patologijama u formi komorbiditeta (**Slika 1 i 2**).

Acquired valvular heart diseases are less common than coronary artery disease (CAD), heart failure and hypertension<sup>1</sup>. However, significant changes in occurrence of acquired heart valve diseases have occurred over the past few decades. There are two external factors that influenced that phenomenon. The first is the wide use of antibiotics in the treatment of streptococcal infections, which were and still are a major cause of acquired heart diseases, especially in underdeveloped countries and developing countries as well. The second factor is the prolonged life expectancy of people with higher living standard and better medical care, with the consequent occurrence of pathologies typical for the older age groups, primarily the entities associated with degenerative processes. Without going into a deeper analysis of these two phenomena, which characterize the medicine of our times, we can only focus on the practical consequences that we largely encounter in daily clinical practice and the available epidemiologic data<sup>2</sup>.

Regional characteristics of acquired heart valve diseases are observed in different regions in the world and Europe. The data resulting from the 2001 Euro Heart Survey indicate those regional differences in Europe<sup>1</sup>. We can observe more frequent occurrence of mitral stenosis in Eastern Europe, then slightly less frequent occurrence of mitral stenosis in the Mediterranean countries and much less frequent mitral stenosis in Western Europe, especially in the northern, Nordic countries. Socioeconomic factors are certainly to be borne in mind when explaining these differences. We can, therefore, with time expect further changes in terms of reducing such further regional changes, simultaneously with a decrease in socio-economic differences<sup>2</sup>.

The lack of a national registry for heart valve diseases prompted us to conduct a small-scale retrograde trial at the Institute of Cardiovascular Diseases of the Sveti Duh Clinical Hospital in Zagreb, which demonstrated the incidence of certain heart valve diseases in all hospitalized patients in 2011. We also searched for the comorbidity with same patients: the existence of CAD, history of myocardial infarction, angina pectoris, coronary artery bypass graft surgery, percutaneous coronary interventions and heart electrostimulators. The aim of this study was to determine the importance of this pathology in the overall incidence and its overlapping with other heart pathologies in the form of comorbidity (**Figure 1 and 2**).

**Figure 1.** Incidence of specific valvular diseases (%) among all patients hospitalized in Clinical Hospital Sveti Duh, Department for Cardiovascular Diseases in 2011.



AS — aortic stenosis; AR — aortic regurgitation; MS — mitral stenosis; MR — mitral regurgitation; PR — pulmonic regurgitation, TR — tricuspid regurgitation.

**Comorbidities in patients with valvular heart disease (%)**



**Figure 2.** Comorbidities (expressed in %) in hospitalized patients with valvular heart disease hospitalized in Clinical Hospital Sveti Duh, Department for Cardiovascular Diseases in 2011.

CHD — coronary heart disease; MI — myocardial infarction; PCI — percutaneous coronary intervention; CABG — coronary-artery bypass graft; PM — pacemaker.

## Aortni zalistak

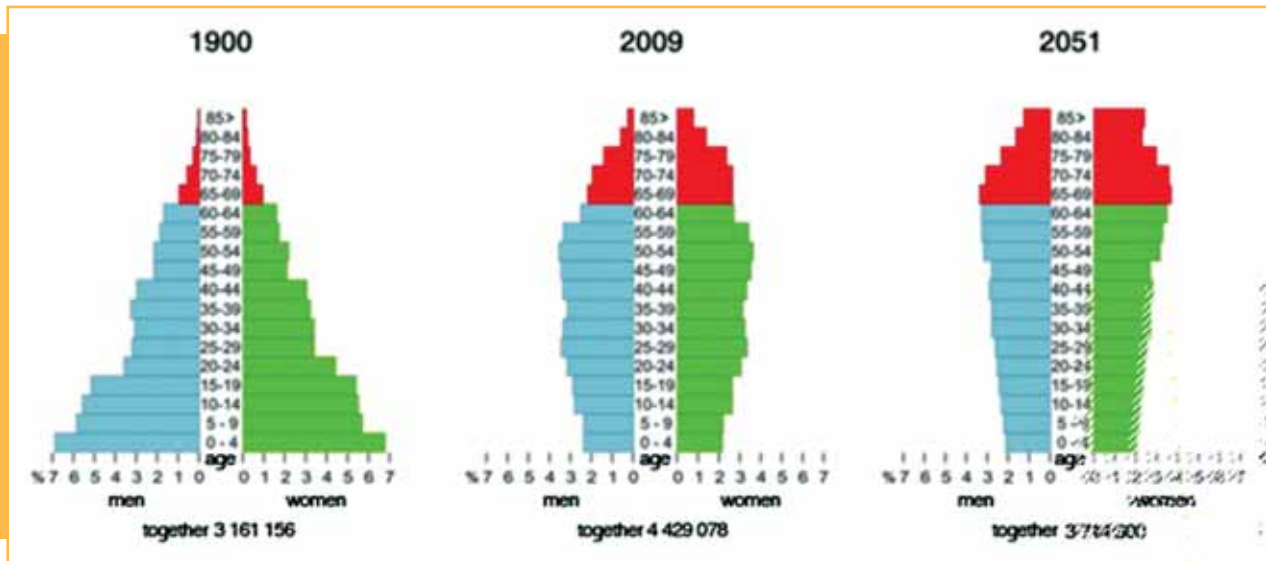
U svakodnevnoj kliničkoj praksi sve se češće susrećemo s patologijom aortne kalcificirajuće stenozе koja se ne može posve poistovjetiti s aterosklerotičnim procesom s kojim ima neke zajedničke crte i gotovo iste rizične čimbenike. Poseban je problem vezan uz procjenu stupnja aortne stenozе (AS) i uz prosudbu o potrebi kirurškog liječenja. Najviše pacijenata (90%) ima blagu do umjerenu AS, a tek 10 % teški oblik AS. Postavlja se pitanje o praćenju tih bolesnika i o njihovoj adekvatnoj informiranosti o bolesti pazeći da ih ne operetimo s obzirom na relevantnost patologije, tim više što se uglavnom radi o osobama bez ikakvih simptoma. Potrebno je voditi računa o čestom komorbiditetu AS i KBS koje imaju zajedničke čimbenike rizika.

Najčešća valvularna patologija u Hrvatskoj kao i u zemljama zapadnog svijeta postaje AS. S obzirom da u Hrvatskoj nemamo epidemioloških studija o prevalenciji AS napravili smo projekciju njene prevalencije na temelju poznatih podataka u Europi, pretpostavljajući da je ista u Hrvatskoj kao u europskom okruženju. U europskoj populaciji starijoj od 65 godina, njena je prevalencija 4%. Ako to projiciramo na hrvatsku populaciju stariju od 65 godina (**Slika 3**), dolazimo do zaključka da u Hrvatskoj ima 30.500 pacijenata s AS bilo kojeg stupnja. Prema istim procjenama samo njih 20% bili bi kandidati s indikacijom za kirurški zahvat. U apsolutnim brojkama to znači da bi godišnje trebalo biti oko 6.000 operacija AS. Ako se od toga odbije 30% pacijenata koji imaju neku od kontraindikacija za kirurški zahvat, taj bi se broj smanjio na 4.000 pacijenata (**Tablica 1**). Činjenice govore da se postotak operacija AS značajno povećao, ali je još uvijek ispod te procjene. Prema dobivenim podacima iz hrvatskih kardiokirurških centara najveći je broj operacija na aortnom zalisku, u odnosu na ostale valvularne operacije (**Slika 7**). U apsolutnim brojevima radi se o 500 operacija godišnje, što

## Aortic valve

In daily clinical practice we are more and more facing the calcific aortic stenosis pathology which can not be completely identified with the atherosclerotic process, although they have some common characteristics and almost the same risk factors. A particular problem is associated with the assessment of the aortic stenosis (AS) degree and the judgment of a need for surgical treatment. Most patients (90%) have mild to moderate AS, and only 10 % of patients have severe AS. The issue that is raised is associated with monitoring of these patients and their appropriate awareness about the disease thereby making sure that we should not burden them considering the relevance of pathology, especially since these are mostly the people who have no symptoms. It is necessary to pay attention to frequent comorbidity, AS and CAD that have common risk factors.

The AS is the most common valvular pathology in Croatia and Western countries around the world. Since there are no epidemiological studies on prevalence of AS in Croatia, we have made a projection of its prevalence on the basis of known data in Europe, assuming this is the same in Croatia as in the European environment. In the European population over 65 years of age, its prevalence is 4%. If we demonstrate it on the Croatian population over 65 years of age (**Figure 3**), we come to a conclusion that there are 30,500 of patients with AS of any degree. According to the same estimations, only 20% of them would be candidates showing an indication for surgical procedure. According to the same estimations, it means that there should be some 6,000 surgeries of AS on an annual basis. If we deduct 30% of patients who have contraindications to the surgical procedure, this number would be reduced to 4,000 patients (**Table 1**). The facts show that the rate of surgeries of AS has significantly increased, but is still below this estimation. According to the data obtained from the Croatian cardiac surgery centers, the largest number of surgeries has been performed on



**Figure 3.** Population of Croatia distributed by gender and age in 1900, 2009 and a projection of 2051. Incidence of aortic stenosis is greater in elderly population. Change in population age structure has an impact on aortic stenosis incidence trend in that three periods of time.

**Table 1.** Projection of prevalence of aortic stenosis in Croatia and EU.

	European Union	Croatia
Population older than 65	77 000 000	762 633 (17%)*
Prevalence %	4 %	?
Prevalence (n)	3 000 000	30505
Eligible for surgery	20 %	?
Number of surgery indications	600 000	6101
Operations per year	~ 60 000	~ 450

\* Population data of Croatia based on data from Croatian Institute for Statistics as of June 2007 (adapted from lit. 2.)

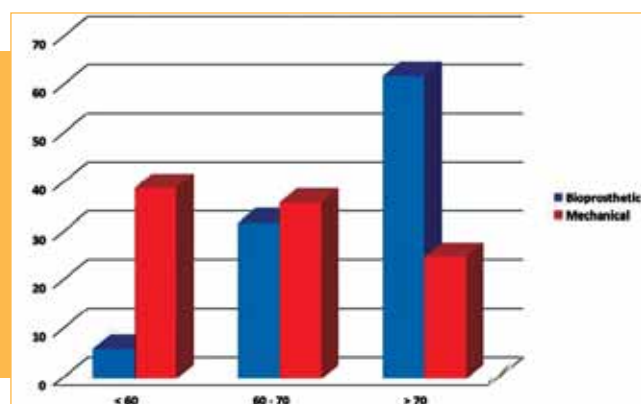
je još uvijek nedovoljno u odnosu na potrebe na temelju dobivenih projekcija. Možemo spekulirati je li to zbog velikog broja neprepoznatih slučajeva, konzervativnijeg stava naših kardiologa, razilaženja između smjernica i kliničke prakse ili zbog uskog grla kardijalne kirurgije. Po svemu sudeći, radi se o kombinaciji svih ovih elemenata.

Kirurški pristup kod AS bitno ovisi o dobi. Podaci hrvatskih kardiokirurških centara ukazuju da se u 2011. godini u Hrvatskoj u mlađih od 60 godina uglavnom ugrađivao mehanički aortni zalistak, kod onih između 60 i 70 godina omjer je bio blago u korist mehaničkih zalistaka, dok su se kod starijih od 70 godina bitno preferirali biološki zalisci (Slika 4).

the aortic valve, compared to the other valvular surgical procedures (Figure 7). In absolute numbers there are about 500 surgeries per year, which is still insufficient compared to needs on the basis of obtained projections. We can speculate whether this is due to a large number of unidentified cases, more conservative attitude of our cardiologists, discrepancy between the guidelines and clinical practice or due to a bottleneck in cardiac surgery. By all accounts, this is the combination of all these elements.

Surgical approach in AS greatly depends on the age. The data obtained from the Croatian cardiac surgery centers show that in 2011 a mainly mechanical aortic valve was implanted in persons under 60 years of age in Croatia, while there was a slightly higher number of implantation of

**Figure 4.** Proportion of implanted biological vs. mechanical aortic valves in Croatia in 2011 in three age groups. In younger patients there is a tendency of implanting mechanical valves while in older age groups biological valves are mostly chosen.



Postoji također tendencija rekonstrukcijskih zahvata na aortnom zalisku kod aortne regurgitacije.

## Postupci transkateterske implantacije aornih zalistaka

Tijekom 2011. godine započelo se po prvi puta u Hrvatskoj s transkateterskom implantacijom aornih zalistaka (TAVI) u Klinici Magdalena u Krapinskim Toplicama, gdje je učinjeno 14 zahvata transfemoralnim putem, a jedan putem lijeve subklavije (zbog premalog kalibra i promjena zdjeličnih arterija). Bolesnici su bili u dobi od  $82 \pm 4$  (74-89) godine, dok je logističkim Euroscorem predviđeni kirurški mortalitet iznosio  $20 \pm 11$  (4-47). Svi su zahvati bili primarno uspješni (100%). Intrahospitalni i 30-dnevni mortalitet iznosio je 0%; u daljnjem praćenju umro je jedan bolesnik (od nekardijalne, plućne bolesti), tako da 6-mjesečni mortalitet trenutno iznosi 6,7%. Intrahospitalne komplikacije (amiodaronsko zatajivanje jetre, tamponada, prolazno krvarenje na mjestu punkcije i Prostar šava, reanimacija tijekom zahvata, aspiracijska pneumonija i sepsa, sve kod po jednog bolesnika/bolesnice) bile su nefatalne i samo su u dva slučaja značajno produžile boravak u jedinici intenzivnog liječenja, odnosno bolnici. U Kliničkoj bolnici Dubrava učinjeno je ukupno 14 zahvata — 11 s Corevalve protezom i 3 s Edwards Sapien protezom. U 30-dnevnom praćenju jedan bolesnik je doživio cerebrovaskularni inzulit, a u 6-mjesečnom praćenju drugi je umro od nekardijalnog uzroka. Ovo svakako predstavlja dobar početak ove metode u Hrvatskoj.

## Mitralni zalistak

Postoji značajan pad stečenih valvularnih grešaka uzrokovanih streptokoknim infekcijama. S obzirom na to da je najčešća srčana greška, kao posljedica streptokokne infekcije mitralna stenoza, a u njezinoj sjeni i ostale valvularne greške, uočava se pad incidencije mitralnih stenoza u razvijenim zemljama s višim socioekonomskim standardom i širom upotrebom antibiotika u njezinu liječenju, pa tako i u Hrvatskoj (Slika 5). Taj pad s latencijom od 20 do 30 godina, od

mechanical valves in those who are between 60 and 70 years of age, while biological valves were significantly preferred in persons over 70 years of age (Figure 4). There is also a trend of reconstruction surgeries on aortic valve in case of aortic regurgitation.

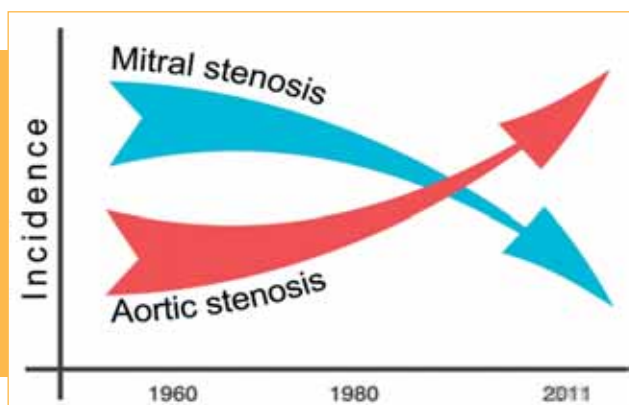
## Procedures of transcatheter aortic valve implantation

In 2011, transcatheter aortic valve implantation (TAVI) was initiated for the first time in Croatia at the Magdalena Clinic in Krapinske Toplice, where a total of 14 procedures were performed by applying transfemoral approach and one by applying the left subclavian approach (due to small caliber and changes to pelvic arteries). The patients were aged  $82 \pm 4$  (74-89), while the surgical mortality predicted by the logistic Euroscore was  $20 \pm 11$  (4-47). All the procedures were primarily successful (100%). Intra-hospital and 30-day mortality was 0%; in the further follow-up one patient died (of non-cardiac, pulmonary disease), so that the 6-month mortality is currently 6.7%. Intrahospital complications (amiodarone induced liver failure, tamponade, transient bleeding at the puncture place and Prostar stitch, resuscitation during the procedure, aspiration pneumonia and sepsis, all with one male/female patient) were nonfatal and in only two cases they significantly prolonged stay in intensive care unit or in hospital. A total of 14 procedures — 11 with Corevalve prosthesis and 3 with the Edwards Sapien prosthesis were performed at the University Hospital Dubrava. In the 30-day follow-up, one patient had a stroke, and in the 6-month follow-up the other died from a non-cardiac cause. This is certainly a good beginning for applying this method in Croatia.

## Mitral valve

There is a significant decrease in acquired valvular diseases caused by streptococcal infections. Since mitral stenosis, as the consequence of streptococcal infection, is the most common heart diseases, and all other valvular diseases in its background, we can observe a fall in the incidence of mitral stenosis in developed countries with a higher socio-economic standard and a wider use of antibiotics in its treatment, including Croatia as well (Figure 5). This decline in latency

*Figure 5. Trend of valvular pathology incidence in Croatia in last decades corresponds to changes in other countries of Europe. Lower incidence of mitral stenosis is linked to antibiotic treatment of rheumatic fever while higher rate of calcifying aortic stenosis is a result of longevity.*



kada su se antibiotici počeli agresivno koristiti u liječenju streptokoknih infekcija, tj. u vremenu potrebnom za razvoj manifestne reumatske valvularne bolesti, upravo se sada događa.

Danas je dominantna patologija mitralnog zaliska mitralna regurgitacija, iza AS druga po pojavnosti valvularna patologija. U našem ispitivanju našli smo da je ona najčešća valvu-

from 20 to 30 years, when antibiotics started to be used aggressively in the treatment of streptococcal infections, that is, during the time required for the development of manifest rheumatic valvular disease, is happening right now.

Today, mitral regurgitation is the predominant pathology of mitral valve, in terms of incidence it is the second valvular pathology following the AS. In our trial we found that it is the

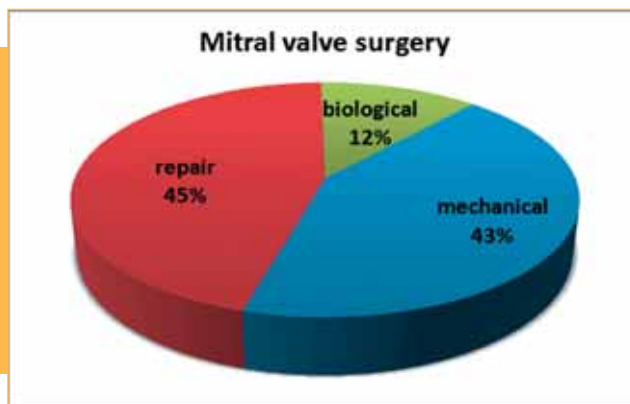
larna patologija hospitaliziranih bolesnika na kardiološkom odjelu (**Slika 1**). Treba istaći da to ne odražava stvaran odnos u prevalenciji mitralne regurgitacije i AS u općoj populaciji.

Kirurške procedure na mitralnom zalisku su ugradnja mehaničkog zaliska ili bioloških zalistaka. Posljednji imaju prednost jer ne zahtijevaju trajnu antikoagulacijsku terapiju, ali su s druge strane povezani s kraćim trajanjem implantiranog zaliska zbog strukturnih deterioracija, pa su sve češće reoperacije tih pacijenata. Zbog toga se biološke proteze češće

most common valvular pathology of patients hospitalized in the cardiology department (**Figure 1**). It should be noted that this does not reflect the real relationship between the prevalence of mitral regurgitation and AS in the general population.

Surgical procedures on the mitral valve are the implantation of a mechanical valve or biological valves. The benefit of the latter ones is that they do not require a permanent anticoagulant therapy, but on the other hand, they are associated with a shorter duration of the implanted valve due to struc-

**Figure 6.** Proportion of specific surgical procedures in treatment of mitral valve disease in Croatia in 2011.



koriste za starije pacijente dok se mlađima radije implantira mehanički tip proteza (**Slika 3**). Rekonstruktivni zahvati sve su češće tehnike, posebice na mitralnom zalisku jer nemaju ova dva nedostatka. Hrvatski prosjek u 2011. godini što se tiče omjera pojedinih tipova zahvata prikazan je na **slici 7** i pokazuje dobar trend u smislu povećanja omjera rekonstrukcijskih zahvata (**Slika 6**). Treba istaći da se radi o prosjeku i da varira od centra do centra.

Perkutane mitralne komisurotomije s obzirom na rijetkost mitralne stenoze, više se gotovo i ne provode i u izvještajima u protekloj godini ih nije bilo. Perkutani zahvati kod mitralne regurgitacije Mitraclip u Hrvatskoj se još uvijek ne rade, a njihovo mjesto još nije čvrsto etabliano u kliničkoj praksi.

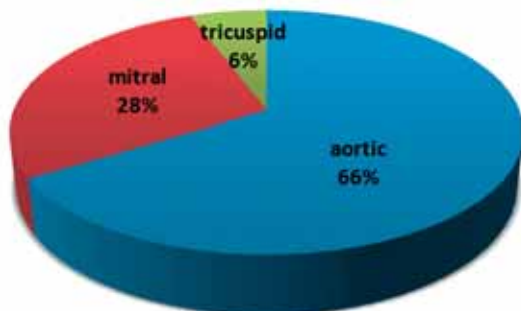
### Trikuspidalni zalistak

Trikuspidalni zalistak nazivamo i zaboravljenim zaliskom. Uočava se, međutim, sve više važnost i njegove korekcije.

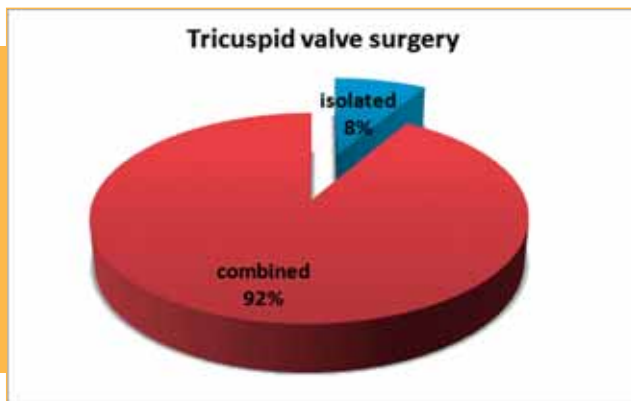
tural deteriorations, so the reoperations of these patients are becoming more and more common. Therefore, the biological prostheses are used more frequently in elderly patients, while a mechanical type of prosthesis is rather implanted in younger patients (**Figure 3**). Reconstructive surgical procedures are becoming more common techniques, especially in the mitral valve because they do not have these two disadvantages. The Croatian average in 2011 as regards the ratio of certain types of surgical procedures is shown in **Figure 7** and shows a good trend in terms of increasing the rate of reconstruction procedures (**Figure 6**). It should be noted that this is the Croatian average and it varies from one center to another.

Percutaneous mitral commissurotomies are almost no longer performed considering the rarity of mitral stenosis, they were not included in the last year reports. Percutaneous surgeries in case of mitral regurgitation Mitraclip in Croatia are not yet performed, and their status is not yet firmly established in the clinical practice.

**Percentage of valvular operations in 2011 in Croatia**



**Figure 7.** Heart valve surgery by specific valves showed in percentage. Aortic valve surgery dominates (66%) over mitral valve surgery (28%) and tricuspid valve surgery (6%).



*Figure 8. Tricuspid valve surgery — proportion of isolated and combined tricuspid valve surgery. Combined tricuspid valve surgery is much more present than isolated.*

S obzirom na dobivene podatke 6% kirurških valvularnih zahvata u 2011. godini čine zahvati trikuspidalnog zaliska, pa bi mogli reći da epitet zaboravljenog zaliska nije prikladan za kliničku praksu u 2011. godini u Hrvatskoj.

Kirurški zahvati na trikuspidalnom zalisku su u kombinaciji s drugim kardijalnim operacijama, a samo u 8% slučajeva izolirani (**Slika 7 i 8**).

Homografit tehnike zahtijevaju postojanje banaka materijala što ograničava njihovu široku primjenu. Tijekom 2011. godine postavljeni su njeni temelji u Hrvatskoj u Kliničkom bolničkom centru Zagreb. Minimalni kirurški zahvati izvođe se sve češće i postaju sve atraktivnija operativna tehnika u zahtjevima informiranih pacijenata.

## Zaključak

Patologija srčanih zalistaka doživjela je tijekom zadnjih dekada promjenu u pojavnosti patologije pojedinih zalistaka, što je rezultat vanjskih čimbenika: antibiotske terapije u liječenju streptokoknih infekcija i produljenja životnog vijeka populacije. Trendovi u Hrvatskoj slijede trendove u ostalim zemljama Europe. U samom pristupu liječenju postoji dinamizam s tendencijom sve manje invazivnih procedura, uvođenjem reparacija zalistaka te transkateterskih procedura. Postoji i u ovom segmentu potreba nacionalnog registra radi boljeg praćenja i donošenja kvalitetnijih odluka u strategiji pristupa ovim pacijentima.

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## Tricuspid valve

Tricuspid valve is also called the forgotten valve. However, greater importance is attached to its corrections as well. Considering the data obtained, 6% of valvular surgical procedures in 2011 were related to tricuspid valve surgeries, so we could say that the name of a forgotten valve is no longer appropriate for clinical practice in 2011 in Croatia.

Surgical procedures on the tricuspid valve are usually combined with other cardiac surgeries, and only 8% of all cases are isolated (**Figures 7 and 8**).

Homografit techniques require the presence of bank of materials which limits their wide application. During 2011, its foundations were set at the Clinical Hospital Center Zagreb in Croatia. Minimal surgical procedures are performed more and more common and they are becoming an increasingly attractive surgical technique regarding the requirements of informed patients.

## Conclusion

During the last decade, the pathology of heart valves has seen a change in the incidence of pathology of specific valves which is a result of external factors: antibiotic therapy in the treatment of streptococcal infections and prolongation of the life expectancy of the population. The trends in Croatia keep up with the trends in some other European countries. The approach to the treatment includes dynamism with a trend of a decreasing number of invasive procedures by introducing valve repairs and transcatheter procedures. There is a need in this segment for a national registry for the purpose of better monitoring and making better quality decisions in the strategy of the approach to these patients.