

Šesnaest godina liječenja prirodnih srčanih bolesti odraslih: iskustvo iz Kliničkog bolničkog centra Ljubljana, Slovenija

Sixteen Years of Systematic Management of Adult Congenital Heart Disease – The experience of the University Medical Centre Ljubljana, Slovenia

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RECEIVED:
January 28, 2016

ACCEPTED:
February 11, 2016



SAŽETAK: Opisano je liječenje 1623 odrasla bolesnika s prirodnim srčanim bolestima tijekom 16-godišnjeg razdoblja u Kliničkom bolničkom centru Ljubljana. Prosječna dob bolesnika pri prvoj prezentaciji bila je 32 ± 14,8 godina. Predočujemo distribuciju dijagnoza prirodnih srčanih bolesti, način liječenja i smrtnost. Tijekom spomenutog razdoblja smrtnost je bila 3,82 %. Spekter dijagnoza i stopa mortaliteta u Sloveniji sukladna je podacima iz Europskog registra srčanih bolesti. Tim specijalista za prirodne srčane greške vodi brigu i o trudnicama sa srčanim bolestima.

SUMMARY: The management of 1623 adult patients with congenital heart disease in a 16-year follow-up period at the University Medical Centre Ljubljana is described herein. The mean patient age at the time of admission was 32±14.8 years (mean ± standard deviation; SD). The distribution of congenital heart disease, treatment, and mortality is presented. During the observation period, the mortality rate was 3.82%. The spectrum of congenital heart disease and the mortality rate in Slovenia correspond with data from the European Heart Survey. Care of pregnant women with heart disease is carried out by the same team of specialists as is care of patients with congenital heart disease.

KLJUČNE RIJEČI: prirodne srčane bolesti, odrasli.

KEYWORDS: congenital heart disease, adults.

CITATION: *Cardiol Croat.* 2016;11(1-2):38–42. | DOI: <http://dx.doi.org/10.15836/ccar2016.38>

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UVOD

Prirodna srčana bolest (PSB) najčešća je prirođena anomalija i pojavljuje se u oko 0,8 % novorođenčadi. Veliki napredak u pedijatrijskoj kardijalnoj kirurgiji i intervencijskoj kardiologiji, postignut u nekoliko posljednjih desetljeća rezultirao je povećanjem broja bolesnika s PSB-om koji prežive do odrasle dobi. Zbog toga smo suočeni s novom populacijom odraslih koji žive s PSB-om. Unatoč tomu, dosta je vremena i napora utrošeno dok prirodna srčana bolest odraslih (PSBO) nije prepoznata kao novo područje kardiologije.

Procijenjeno je da oko 2,3 milijuna odraslih u Europi živi s nekom od PSB. Ovo je mnogo više od pedijatrijske populacije s istim problemom kakve je oko 1,9 milijuna. Štoviše, ovaj će broj očekivano rasti. U ovom trenutku u Europi živi više odraslih nego djece s PSB-om¹.

Imajući u vidu ove brojeve, mora biti prepoznata potreba vezana za ovo, specijalno područje kardiologije. Liječnici koji specijaliziraju kardiologiju u odraslih bolesnika nedovoljno su educi-

INTRODUCTION

Congenital heart disease (CHD) is the most common inborn defect and occurs in approximately 0.8% of neonates. Major advances in pediatric heart surgery and pediatric interventional cardiology made in recent decades have resulted in a marked increase in the number of patients with congenital heart disease who survive into adulthood. We are therefore now faced with a new population of adults who live with congenital heart disease. Despite this, a significant period of time and effort passed before adult congenital heart disease (ACHD) was recognized as a new field of cardiology.

In Europe, it is currently estimated that a population of approximately 2.3 million adults live with CHD, which is significantly greater than the pediatric CHD population of about 1.9 million. What is more, these numbers are expected to rise. There are now more adults than children with CHD in Europe¹.

rani u području PSB-a. Glavni fokus njihove edukacije jesu koronarna bolest srca, zatajivanje srca i aritmije. U isto vrijeme pedijatrijski kardiolozi ne pokrivaju dostatno potrebe odraslih bolesnika s PSB-om.

Velika raznolikost PSB-a rezultira različitim tipovima kliničkih problema, kako u djece, tako i u odraslih. Bolesti koje se pojavljuju u kasnijoj dobi, kao što su arterijska hipertenzija i koronarna bolest srca imaju važnu ulogu u prirodnom tijeku PSB-a i njezinu pogoršanje. Zbog svega navedenog, bolesnici s PSBO-om traže posebnu, integriranu brigu, uzimajući u obzir i posebna stanja, kao što su trudnoća, nekardiokirurški operacijski zahvati i sl. Spekter PSB-a, kao i kasne komplikacije također se mijenjaju zahvaljujući poboljšanju kirurških tehnika. Stoga je jasno da za učinkoviti liječenje bolesnika s PSBO-om trebamo kardiologe specijalno educirane za PSB koji se mogu nositi sa svim ovim posebnim zahtjevima. Potrebni su i posebni centri za liječenje PSBO-a.

Briga o bolesnicima s PSBO-om treba biti koordinirana iz regionalnog ili nacionalnog centra za PSBO. Jedan takav centar trebao bi voditi brigu o populaciji od oko 5 do 10 milijuna stanovnika². Najvažnije aktivnosti takvoga, specijaliziranog centra jesu: inicijalna procjena stanje bolesnika sa sumnjom na PSB ili već dokazanom bolešću, praćenje i trajna briga za bolesnike s umjerenim ili kompleksnim PSB-om, provođenje kirurških ili intervencijskih postupaka, procjenu rizika i potporu pri nekardiokirurškim operacijskim zahvatima, trudnoći te provoditi edukaciju i istraživanja u tom području.

ORGANIZACIJA SKRBI ZA BOLESNIKE S PRIROĐENIM SRČANIM BOLESTIMA ODRASLIH U SLOVENIJI

Od 1998. godine bolesnici s PSBO-om sustavno su liječeni u Kliničkom bolničkom centru Ljubljana, koji je jedini specijalizirani centar za liječenje PSBO-a u Sloveniji.

Slovenija ima 2 milijuna stanovnika. Procijenjena prevalencija PSBO-a u Europi je oko 1500 bolesnika na milijun stanovnika te je očekivani broj takvih bolesnika u Sloveniji oko 3000.

Stopa je nataliteta u Sloveniji 20 000 godišnje. Uzimajući u obzir činjenicu da je incidencija PSB-a 1 %, a preživljenje oko 90 %, godišnje je u Sloveniji oko 180 novih bolesnika s PSB-om.

U timu za PSBO pri KBC-u Ljubljana rade četiri kardiologa, dva pedijatra, jedan kardiovaskularni kirurg i jedan radiolog te se po potrebi priključuju ginekolog i medicinski genetičar. Kao rezultat takve organizacije i timskog rada, postignut je veliki napredak u rezultatima liječenja.

KBC Ljubljana jedini je specijalizirani centar za PSBO u Sloveniji koji je opremljen svim potrebnim sadržajima: odrasla i pedijatrijska kardiologija, neinvazivna i invazivna kardiologija, intervencijska kardiologija, elektrofiziologija, kao i poliklinika. Rutinski kirurški zahvati izvode se samostalno, no kod kompleksnijih zahvata ovisimo o gostujućem kirurgu iz inozemstva koji je specijaliziran za PSBO. Centar ima i organiziranu posebnu brigu za liječenje trudnica sa srčanim bolestima u suradnji s ginekologom i medicinskim genetičarom.

Kontinuitet skrbi za bolesnika na prijelazu iz pedijatrijske u odraslu dob provodi se u vrijeme najveće stabilnosti bolesti, u dobi od 18 godina. Trajne konzultacije s pedijatrijskim kardiologom koji je liječio bolesnika su moguće, pa i poželjne.

Given these numbers, it must be recognized that there is a need for a special field of cardiology for ACHD. Cardiologists who specialize in adult patients have in fact become increasingly unfamiliar with CHD. The main focus in cardiology today is on coronary artery disease, heart failure, and arrhythmias. At the same time, pediatric cardiology does not adequately cover the needs of adults who live with CHD.

The great diversity in CHD results in various types of clinical problems arising not only in children, but also in adults. Diseases that develop at an advanced age, such as arterial hypertension and coronary artery disease, have a significant impact on the natural history of CHD and its deterioration. Therefore, ACHD patients require special integrated care, while also taking into account other medical conditions such as pregnancy, non-cardiac surgery, etc. The spectrum of CHD and late complications are now also changing due to the development of improved surgical techniques. It is therefore clear that cardiologists who are specially trained in CHD and aware of all these special issues are needed for the effective management of ACHD patients. Furthermore, special centers for ACHD are also required.

The care of patients with ACHD should be coordinated by regional or national ACHD centers. Approximately one such center should be created to serve a population of 5 to 10 million people². The most important activities of specialized centers are: initial assessment of suspected or already detected CHD, the follow-up and continuing care of patients with moderate and severe complex lesions, further surgical and percutaneous interventions, risk assessment and support for noncardiac surgery, pregnancy, and training and research activities.

THE ORGANIZATION OF CARE FOR ADULT CONGENITAL HEART DISEASE IN SLOVENIA

Since 1998, patients with ACHD have been systematically managed at the University Medical Centre Ljubljana (UMC), which is the only specialized center for ACHD in Slovenia.

Slovenija has 2 million inhabitants. The estimated prevalence of ACHD in Europe is approximately 1500 patients/1 million inhabitants, so the expected number of patients with ACHD in Slovenia is 3000.

The birth rate in Slovenia is 20 000 newborns per year. If taking into consideration that there is a near 1% incidence in CHD and a survival rate of approximately 90%, then it follows that there are about 180 new CHD patients in Slovenia each year.

Our ACHD team works hand in hand with four cardiologists, two pediatricians, one cardiovascular surgeon, and one radiologist. If necessary, we also work with obstetricians and geneticists. As a result of this organization and cooperative work, we have seen great benefits in treatment results.

UMC Ljubljana is the only specialized center for ACHD in Slovenia that is equipped with all required facilities: adult and pediatric cardiology, non-invasive and invasive cardiology, intervention cardiology, electrophysiology, and an outpatient clinic. Routine surgical procedures are performed independently, but we depend on a visiting foreign surgeon who is specialized in CHD for more complex procedures. The center for ACHD has also organized special care for the treatment

Broj je bolesnika izgubljenih u praćenju u Sloveniji zanemariv zahvaljujući činjenici da su svi pedijatrijski bolesnici s PSB-om liječeni u pedijatrijskom odjelu iste ustanove i izravno se transferiraju na kardiološki odjel za odrasle.

REZULTATI

U razdoblju od 16 godina, između 1998. i 2014., liječena su 1623 odrasla bolesnika s PSBO-om. Među njima bila je 921 bolesnica (56,7 %). Prosječna dob pri prijmu bila je $32 \pm 14,8$ godina. Najmlađi je bolesnik bio u dobi od 16 godina, a dva najstarija imala su 80 godina – jedan muškarac s neoperiranim atrijskim septalnim defektom i jedna žena s restriktivnim ventrikulskim septalnim defektom.

Slika 1 prikazuje broj pregledanih bolesnika u poliklinici. Uključeni su samo prvi pregledi, a ne i kontrole. Broj se pacijanata postupno povećavao, a sada je prosječan broj novih pacijanata 95 godišnje. Od ta 1623 bolesnika, u 446 njih (27,4 %) PSB je prvi put dijagnosticiran u odrasloj dobi. Broj se kasno dijagnosticiranih bolesnika konstantan u promatranom razdoblju.

Očekivano, većina bolesnika koji dolaze u polikliniku mlađa je od 30 godina. Samo je trećina bila starija od 30 godina u trenutku prvog posjeta. Zanimljivo da je vrlo mali broj bolesnika u grupi do 30 godina starosti prvi puta dijagnosticiran u odrasloj dobi (9,5 %). U grupi bolesnika s više od 30 godina, međutim, situacija je posve različita – postotak bolesnika s PSB-om dijagnosticiranih prvi put u odrasloj dobi dramatično raste (63,7 %) (**slika 2**). Ovaj rezultat govori u prilog dobre pedijatrijske kardiološke skrbi u Sloveniji u proteklih 30 godina.

U skupini bolesnika bez cijanoze atrijski septalni defekt (ASD) bio je najčešća malformacija (31,8 %). ASD je i najčešća anomalija otkrivena u odrasloj dobi. Ovakav rezultat ne iznenađuje i sukladan je rezultatima Europskog registra za PSB.³

Očekivano, najčešća cijanotična srčana bolest jest Fallotova tetralogija. Razočaravajuća je činjenica da naša grupa obuhvaća čak 45 bolesnika s Eisenmengerovim sindromom. U samo nekoliko ovakvih bolesnika dijagnoza je postavljena u odrasloj dobi (**slika 3**).

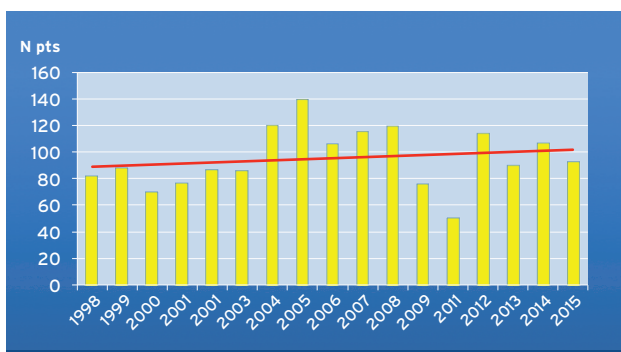


FIGURE 1. The number of patients who visited the outpatient clinic. Only first referrals are included. The trend line is in red.

of pregnant women with heart disease, in cooperation with obstetricians and geneticists.

Transfer to adult care is carried out during a period of medical stability at the age of 18. Continuous consultation with the referring pediatric cardiologist is possible and even desirable after the transfer. The number of patients lost to follow-up is very low in Slovenia because all pediatric patients with CHD are treated at the Department of Paediatrics, UMC Ljubljana, and are directly transferred to the Department of Cardiology in Ljubljana.

RESULTS

Over a period of 16 years between 1998 and 2014, 1623 adult patients with CHD were admitted. Of these, 921 patients were women (56.7%). The mean age at the time of admission was 32 ± 14.8 (mean \pm standard deviation; SD) years. The youngest patient was 16 years old, the oldest two patients were 80 years old – one man with an unoperated atrial septal defect and one woman with restrictive ventricular septal defect.

Figure 1 displays the number of patients who visited our outpatient clinic. Only first referrals are included, follow-up visits are not. The number of patients rose gradually, with there now being an average number of 95 new patients per year. Of these 1623 patients, 446 (27.4%) were diagnosed in adulthood. The percentage of patients diagnosed late in adulthood remained constant throughout the observation period.

As expected, the majority of patients came to the outpatient clinic before the age of 30. Only one third of the patients who came to the outpatient clinic were over the age of 30 at the time of their first visit. It is especially interesting that very few patients in the younger group were first diagnosed in adulthood (9.5%). However, in the group of patients over the age of 30, the situation is completely different – the percentage of patients who first had their CHD diagnosed in adulthood rose dramatically (63.7%) (**Figure 2**). These results indicate good quality pediatric cardiologic care in Slovenia over the last 30 years.

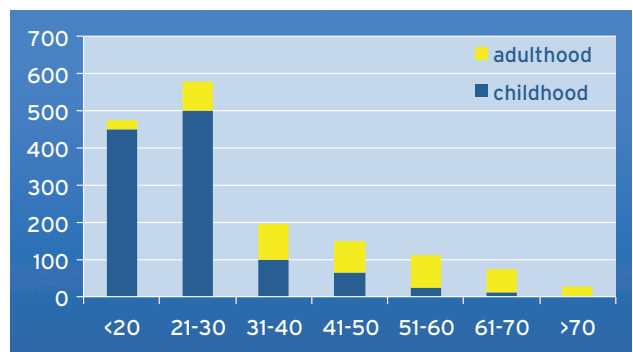


FIGURE 2. The age range of patients registered at our center; patients diagnosed in childhood (blue bars) and patients first diagnosed in adulthood (yellow bars).

Ukupno 600 bolesnika bilo je podvrgnuto kirurškoj korekciji u djetinjstvu, a 141 u odrasloj dobi. Sedamsto šezdeset devet bolesnika nije bilo operirano jer za to nije bilo potrebe ili su odbili operativni zahvat. Stotinu jedanaest bolesnika liječeno je intervencijski perkutanim tehnikama (ASD secundum, otvoreni ductus arteriosus, koarktacija aorte). U tri je pacijenta poduzeta transplantacija: jedna transplantacija srca i pluća (pacijent s pulmonalnom atrezijom) te dvije transplantacije srca (srčano popuštanje nakon operacije Fallotove tetralogije i pacijent s Ebsteinovom anomalijom).

Ukupno su 62 bolesnika (3,8 %) umrli tijekom 16-godišnjeg razdoblja (2,3 na 1000 godišnje). Prosječna dob u vrijeme smrti bila je $48,4 \pm 17,1$ godina (raspon dobi 20 do 83). Podatci su sukladni onima iz Europskog registra za PSBO, gdje je smrtnost bila 2,8% u petogodišnjem praćenju³. U osmogodišnjem praćenju u CONCOR nizozemskom registru za PSBO smrtnost je iznosila 2,8%, a prosječna dob u vrijeme smrti 48,8 godina (raspon dobi 20 do 91)⁴. Iznenađujuće, najčešća je dijagnoza bila ASD (10 bolesnika), slijedi Eisenmengerov sindrom (9 bolesnika) i kompleksne cijanotične greške (9 bolesnika) (slika 4). Prosječna dob u vrijeme smrti bolesnika s ASD-om bila je $68,4 \pm 3,5$ godina. U svih takvih bolesnika, osim u jednog, dijagnoza je postavljena u odrasloj dobi. Nijedan nije bio kirurški liječen, a većina je umrla od zatajivanja srca. Jedan je smrtni ishod bio povezan s trudnoćom u bolesnice s Eisenmengerovim sindromom.

BRIGA ZA TRUDNICE SA SRČANOM BOLESTI

Briga za trudnice uključena je u liječenje bolesnika s PSBO-om jer je većina trudnica sa srčanom bolesti upravo iz skupine s PSB-om. Tijekom sedam godina (između 2007. i 2014. godine) bilo je liječeno 187 trudnica sa srčanom bolešću. Većina je bolesnica bila iz ljubljanske regije, ali trudnice s kompleksnim greškama i iz drugih područja Slovenije također rađaju u Ljubljani. Integrirani tim kardiologa, ginekologa i anesteziologa vodi skrb o takvim bolesnicama.

Samo se u dviju bolesnica među njih 187 razvilo popuštanje srca u vrijeme trudnoće (u oba slučaja bolesnice s kardiomi-

In the acyanotic group, atrial septal defect (ASD) was the most common cardiac malformation (31.8%). Atrial septal defect was also the abnormality most often detected in adulthood. These results are not surprising and they correspond to the results of the European Heart Survey on CHD³.

As expected, the most common abnormality in the cyanotic group is tetralogy of Fallot. It was disappointing that there were still 45 patients with Eisenmenger syndrome in our group. Very few patients were diagnosed late in adulthood (Figure 3).

Overall, 600 patients underwent surgical corrections in childhood and 141 patients were operated in adulthood. 769 patients had never been operated, either because there was no need or because they refused the operation. 111 patients were treated percutaneously (atrial septal defect secundum, patent ductus arteriosus, coarctation of aorta). Three patients received transplantations: one heart and lung transplantation (a patient with pulmonary atresia) and two heart transplantations (heart failure after tetralogy of Fallot and Ebstein's anomaly).

A total of 62 patients (3.8%) died during the 16-year study period (2.3 patients per 1000 per year). The mean age at the time of death was 48.4 ± 17.1 years (range: 20-83). The data are in agreement with the findings of the European Heart Survey on ACHD, where the mortality rate was 2.8% at 5-year follow-up³. At the 8-year follow-up of the CONCOR Dutch Registry for ACHD, the mortality rate was also 2.8% and the mean age at the time of death was 48.8 (range: 20.3-91.2)⁴. Surprisingly, the most common diagnosis in our group was ASD (10 patients), followed by Eisenmenger syndrome (9 patients) and complex cyanotic anomalies (9 patients) (Figure 4). The mean age at the time of death in the patients with ASD was 68.4 ± 3.5 years. All but one of these patients were diagnosed in adulthood. None had ever been surgically treated and the majority died of congestive heart failure. One death was related to pregnancy with Eisenmenger syndrome.

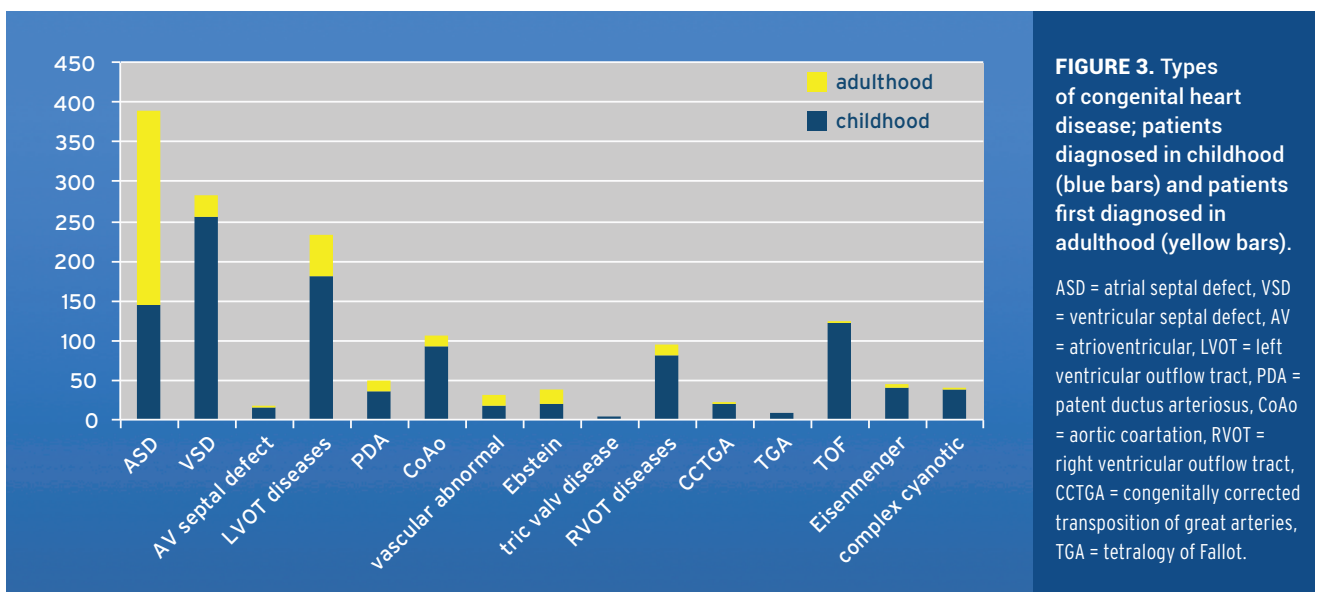
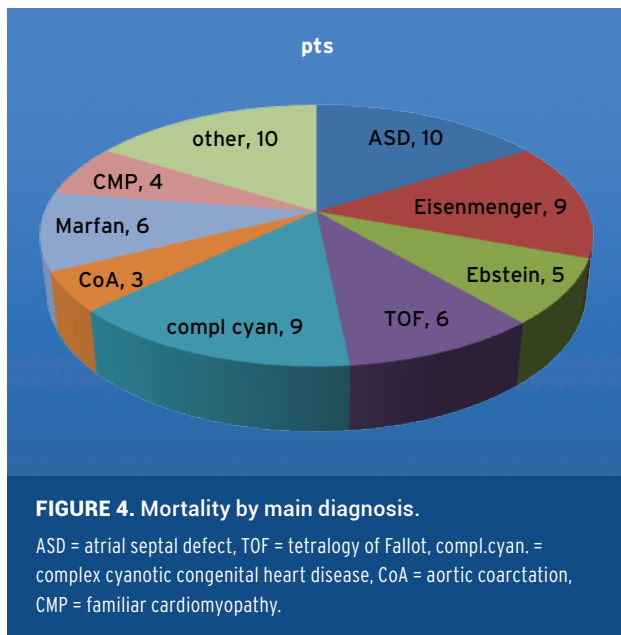


FIGURE 3. Types of congenital heart disease; patients diagnosed in childhood (blue bars) and patients first diagnosed in adulthood (yellow bars).

ASD = atrial septal defect, VSD = ventricular septal defect, AV = atrioventricular, LVOT = left ventricular outflow tract, PDA = patent ductus arteriosus, CoAo = aortic coarctation, RVOT = right ventricular outflow tract, CCTGA = congenitally corrected transposition of great arteries, TGA = tetralogy of Fallot.



opatijom). Učestalost carskog reza bila je je 45,3 %. Nije bilo urgentnih operacija carskog reza zbog kardioloških razloga. To upućuje na to da su porođaji bili dobro pripremljeni. Nije registrirana smrtnost majke tijekom trudnoće i u poslijeporođajnom razdoblju. Učestalost pobačaja (3,9 %) i smrtnost čeda (0,8 %) u skladu su s rezultatima ROPAC registra za razvijene zemlje⁵.

ZAKLJUČAK

U Sloveniji je uspješno organizirana skrb za bolesnike s PSBO-om sukladno europskim preporukama. Razdoblje od 16 godina praćenja odraslih bolesnika s PSB-om upućuje na pojavnost takvih bolesti u Sloveniji. Spektar dijagnoza i liječenja PSBO-a sukladni su podacima iz europskog registra. Smrtnost bolesnika s PSBO-om unutar je predviđenih granica i ističe važnost specijalizirane brige za odrasle bolesnike s PSB-om. Uključena je i briga za trudnice sa srčanim bolestima, uz pažljivo praćenje koje provodi isti tima specijalista, uključujući i ginekologa.

CARE FOR PREGNANT WOMEN WITH HEART DISEASE

Care of pregnant women a part of the treatment of patients with ACHD because the majority of women with heart disease have congenital heart disease. Over a period of 7 years between 2007 and 2014, 187 pregnant women with heart disease were treated. These patients were mainly from the Ljubljana region, but patients with more complex lesions also came to our center from other parts of Slovenia and also give birth in Ljubljana. An integrated team of ACHD cardiologists, obstetricians, and anesthetists treated of these patients.

Only two patients out of 187 developed heart failure during pregnancy (both had cardiomyopathy). The percentage of caesarean sections was 45.3%. There were no emergency caesarean sections for cardiac-related reasons in our group. This indicates good preparation for delivery. There was no maternal mortality during pregnancy and in the follow-up period. The frequency of miscarriage (3.9%) and fetal mortality (0.8%) were in accordance with the results of the Registry on Pregnancy and Cardiac Disease (ROPAC) for developed countries⁵.

CONCLUSIONS

In Slovenia, we managed to organize care for patients with ACHD according to European recommendations. The 16-year follow-up of adult patients with CHD reflected the relative frequency of CHD in Slovenia. The spectrum of ACHD and the treatment was in agreement with European Heart Survey data. The mortality rate of patients with ACHD was within anticipated limits and emphasized the importance of specialized care for adults with CHD. Treatment of pregnant women with heart disease was included in the management of ACHD under the surveillance of the same team of specialists, also including obstetricians.

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