

# Almanah 2014.: prirodene srčane greške

## Almanac 2014: Congenital Heart Disease

Peter C Kahr\*,  
Gerhard-Paul Diller

Division of Adult Congenital and Valvular Heart Disease, Department of Cardiovascular Medicine, University Hospital Muenster, Muenster, Germany

**SAŽETAK:** Ovaj almanah sažima važne članke o prirođenim srčanim greškama objavljene od 2012. do 2014. godine u časopisu „Heart“ i ostalim većim kardiološkim časopisima. Navest ćemo članke koje smatramo veoma važnima u ovom području. Iako je svrha bila pružiti sveobuhvatan pregled područja, bilo je potrebno usredotočiti se na određene teme. Izbor je članaka dakle nužno subjektivan.

**SUMMARY:** This Almanac summarises important congenital heart disease articles published between 2012 and 2014 in Heart and other major cardiac journals. It highlights what the authors perceive to be highly relevant articles in the field. While the aim was to provide a comprehensive overview of the area, a focus on certain areas of interest was required. The selection is, therefore, by necessity a subjective one.

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**\*ADDRESS FOR CORRESPONDENCE:** Peter C Kahr, Division of Adult Congenital and Valvular Heart Disease, Department of Cardiovascular Medicine, University Hospital Münster, Albert-Schweitzer-Campus 1, Gebäude: A1, Münster 48149, Germany. / E-mail: [pckahr@gmail.com](mailto:pckahr@gmail.com)

**ORCID:** Gerhard-Paul Diller, <http://orcid.org/0000-0003-3050-5248>

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### EPIDEMIOLOGIJA I FETALNA KARDIOLOGIJA

Zastupljenost prirođenih srčanih grešaka (PSG) pri rođenju procjenjuje se na između 75 i 90 na 10 000 živorođenčadi i ukupnih trudnoća, pri čemu analize podskupina pokazuju stopu prekida trudnoće do 76% za fetuse sa složenom anatomijom bolesti ili univentrikularnim srcem (**tablica 1**).<sup>1</sup> Istraživanje u Ujedinjenom Kraljevstvu istaknulo je bitnu varijaciju u prednatalnoj stopi dijagnoze PSG-a na osnovi podataka Nacionalnog instituta za istraživanje kardiovaskularnih ishoda te je ponudilo smjernice za poboljšanje probira i analize podataka o majčinstvu.<sup>2,3</sup> Potrebna su daljnja istraživanja kako bi se odredile prognoze i komorbiditet, pogotovo za razmjerno rijetke prednatalne poremećaje kao što su izolirani desni aortni luk, sa svrhom poboljšanja savjetovanja roditelja.<sup>4</sup> Zastupljenost PSG-a u odraslih sada se procjenjuje od 3 na 1000 prema Quebec CHD bazi podataka do 6,1 na 1000 na temelju sustavnoga pregleda literature.<sup>5,6</sup> Ipak, ovo je dinamična populacija te se predviđa porast u broju odraslih

### EPIDEMIOLOGY AND FOETAL CARDIOLOGY

The prevalence of congenital heart disease (CHD) at birth is estimated to be between 75 and 90 per 10 000 for live births and total pregnancies with subgroup analyses showing rates of termination of pregnancy up to 76% for fetuses with complex anatomy or univentricular hearts (**Table 1**).<sup>1</sup> A UK study also highlighted the significant variation in prenatal detection rates of CHD based on National Institute for Cardiovascular Outcome Research data and provided recommendations for how to improve screening performance and audit maternity data.<sup>2,3</sup> Additional research is required to delineate prognosis and comorbidities, especially for relatively infrequent prenatal findings such as isolated right aortic arch, in order to improve parent counselling.<sup>4</sup> The prevalence of CHD in adults is now estimated to be between 3 and 6.1 per 1000 based on data from the Quebec CHD database and on a systematic review of the literature, respectively.<sup>5,6</sup> However, this is a dynamic popu-

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pacijenata s PSG-om od oko 60% tijekom sljedećeg desetljeća. Stoga će investicije u ljudski i fizički kapital vjerojatno biti nužne kako bi se pacijentima s PSG-om omogućilo da dosegnu puni životni potencijal.<sup>7,8</sup>

## Jedna klijetka

Trenutačno postoji nekoliko palijativnih pristupa za pacijente sa sindromom hipoplazije lijevoga srca i sličnim anomalijama desne klijetke. Kirurški postupci uključuju „hibridni pristup“ te Norwood i Sano procedure kojima je svima krajnji cilj u pacijenta postići potpunu Fontanovu anatomiju.<sup>9</sup> Iako, prema istraživanjima, vrsta palijativne njege ne utječe na smrtnost takvih pacijenata,<sup>10-13</sup> optimalni pristup i dalje nije jasan, s razlikama među pojedinim podskupinama. Primjerice, usporedba kratkoročnih i srednjoročnih rezultata „hibridnoga pristupa“ nije otkrila nikakve razlike u smrtnosti usprkos mnogo većim kirurškim rizicima (prema „Aristotle“ bodovnoj skali) u „hibridnoj skupini“ (**slika 1**).<sup>14</sup>

Napredni modaliteti slikovnoga prikaza možda će s vremenom dovesti do optimizacije kirurških strategija i poboljšanja dugoročnih ishoda u ovim izazovnim slučajevima. Kardiološka magnetna rezonancija omogućuje vizualizaciju dinamike toka u pacijenata s potpunim kavopulmonarnim spojem.<sup>15</sup> Gubitak snage u Fontanovu tunelu – za koji se pretpostavlja da je ključan čimbenik u smanjenu kapacitetu tijekom opterećenja u Fontanovu sindromu – bio je mnogo manji u bolesnika s interatrijalnim tunelom u usporedbi s pacijentima s ekstrakardijalnim tunelima. Iako gubitak snage eksponencijalno raste porastom srčanog indeksa tijekom dobutaminskog stres testa, nije pronađena korelacija između gubitka snage i kapaciteta u testovima kardiopulmonalnim testiranjem.

Iako se smrtnost nakon operacije po Fontanu znatno smanjila tijekom prošlih desetljeća,<sup>16,17</sup> postoperativne izljevi, enteropatija s gubitkom proteina (EGP) i disfunkcija jetre i dalje su ozbiljni izazovi. U retrospektivnom istraživanju na 42 pacijenta s EGP-om, smrtnost je trenutačno manja nego u povijesnim podacima.<sup>18</sup> Usprkos tomu, liječenje EGP-a i dalje je teško, a atrijalne se aritmije pojavljuju u 67% pacijenata. Ovaj članak može biti posebno bitan kliničarima jer iznosi detaljan plan liječenja bolesnika s EGP-om nakon operacije po Fontanu. Disfunkcija jetre i bubrega – česte kasne komplikacije bolesnika podvrgnutih operaciji po Fontanu – mogu pomoći u predviđanju loših kasnijih ishoda u pacijenata.<sup>19</sup> U skladu s očekivanjima, veći broj bodova prema MELD-XI modelu za kasnu jetrenu – alatu za procjenu rada bubrega i jetre – koreliraju s povećanim rizikom od srčane smrti ili transplantacije.<sup>20</sup> Uvođenje bodovanja MELD-XI u kliničku praksu moglo bi biti korisno pri predviđanju srednjoročnih i dugoročnih ishoda u ovoj, rastućoj populaciji pacijenata.

Nakon operacije po Fontanu pacijenti također imaju smanjenu skeletnu mišićnu masu, što je povezano s bitno manjim kapacitetom vršne vježbe.<sup>21</sup> Na osnovi podataka o znatno smanjenom resintezi fosfokreatina nakon vježbe, autori članka postavljaju hipotezu o postojanju „fontanske miopatije“, koju treba iscrpnije istražiti. Ti su podatci itekako važni jer je doprinos kompetentne mišićne pumpe ključan u pojačavanju udarnog volumena i srčanog indeksa tijekom vježbe u tim pacijenata.<sup>22</sup>

lation and an increase in the number of adult patients with CHD, with single ventricle physiology for example, by around 60% is predicted over the next decade. This is likely to require increased investment in human and physical capital so that patients with CHD reach their full life potential.<sup>7,8</sup>

## Single ventricle

Currently, there are several approaches for palliation of patients with hypoplastic left heart syndrome and related RV anomalies. Surgical procedures include the ‘Hybrid approach’, Norwood and the Sano procedure, all of which serve to ultimately transition the patient to a complete Fontan anatomy.<sup>9</sup> While it has been reported that the choice of palliation strategy may not affect mortality in this patient group,<sup>10-13</sup> the optimal approach remains elusive with differences seen in specific subgroups. As an example, comparison of early and mid-term results of the ‘hybrid approach’ demonstrated no mortality difference despite significantly higher surgical (Aristotle) risk scores in the ‘hybrid group’ (**Figure 1**).<sup>14</sup>

Advanced imaging modalities may eventually pave the way to optimising surgical strategies and improving long-term outcomes in these challenging patients. Cardiac MRI allows visualisation of the flow dynamics in patients with a total cavopulmonary connection.<sup>15</sup> Power loss in the Fontan tunnel – which has been suspected to be the major determinant of reduced exercise capacity in Fontan – was significantly lower in patients with an intra-atrial lateral tunnel compared with extracardiac tunnels. Although power loss increased exponentially with increasing cardiac index during dobutamine stress testing, no correlation between power loss and exercise capacity on cardiopulmonary exercise testing was demonstrated.

Although the overall mortality after the Fontan operation has decreased substantially over the last decades,<sup>16,17</sup> postoperative effusions, protein-losing enteropathy (PLE) and liver dysfunction remain significant challenges. In a retrospective study of 42 patients with PLE, current mortality was lower than in historic reports.<sup>18</sup> Nevertheless, PLE remains difficult to treat and atrial arrhythmias occur in 67% of patients. This article may be of particular relevance to the clinician as it provides a detailed treatment plan for patients with PLE after the Fontan operation. Liver and renal dysfunction – common late complications of Fontan patients – may help to predict adverse late outcomes in Fontan patients.<sup>19</sup> Consistent with expectations, increased Model for Endstage Live Disease - eXcluding INR (MELD-XI) scores – a tool to estimate renal and hepatic function – correlate with an increased risk of cardiac death or transplantation.<sup>20</sup> Implementation of the MELD-XI score into clinical practice may be useful in predicting mid-term and long-term outcomes in this growing patient population.

Patients after the Fontan operation also have reduced skeletal muscle mass, associated with markedly impaired peak exercise capacity.<sup>21</sup> Based on the finding of significantly decreased postexercise phosphocreatine resynthesis, the authors hypothesise the existence of a ‘Fontan myopathy’, which needs to be investigated in further detail. This finding is of particular relevance as the contribution of a competent muscle pump is essential to augment stroke volume and cardiac index during exercise in Fontan patients.<sup>22</sup>

**TABLE 1. Total and live birth prevalence of congenital heart defects: the EPICARD.**

ACC-CHD categories	N	LB Per cent	TOP Per cent	SB Per cent	Prevalence (per 10 000)			
					Total*	95% CI	Live birth <sup>†</sup>	95% CI
1. Heterotaxy, including isomerism and mirror imagery	37	21.6	75.7	2.7	1.2	0.8 to 1.6	0.2	0.1 to 0.5
2. Anomalies of the venous return	31	83.9	16.1	0.0	1.0	0.7 to 1.4	0.8	0.5 to 1.2
3. Anomalies of the atria and interatrial communications	182	95.6	4.4	0.0	5.7	4.9 to 6.6	5.5	4.7 to 6.4
4. Anomalies of the atrioventricular junctions and valves	213	51.2	42.7	6.1	6.7	5.8 to 7.7	3.5	2.8 to 4.2
5. Complex anomalies of atrioventricular connections	13	53.8	46.2	0.0	0.4	0.2 to 0.7	0.2	0.1 to 0.5
6. Functionally univentricular hearts	158	30.4	62.7	6.9	5.0	4.2 to 5.8	1.5	1.1 to 2.0
7. VSDs	1491	93.6	5.7	0.7	47.0	44.6 to 49.4	44.4	42.1 to 46.8
8. Anomalies of the ventricular outflow tracts	563	79.4	18.5	2.1	17.7	16.3 to 19.3	14.2	12.9 to 15.6
9. Anomalies of the extrapericardial arterial trunks	170	73.5	23.5	3.0	5.3	4.6 to 6.2	4.0	3.3 to 4.7
10. Congenital anomalies of the coronary arteries	9	100.0	0.0	0.0	0.3	0.1 to 0.5	0.3	0.1 to 0.5
All	2867	81.9	16.3	1.8	90.3	87.0 to 93.6	74.8	71.8 to 77.8
All, excluding cases associated with chromosomal anomalies	2471	89.2	9.8	1.0	77.8	74.8 to 80.9	68.4	67.3 to 73.2
All, excluding cases associated with chromosomal or other anomalies	2036	92.8	6.4	0.8	64.1	61.4 to 67.0	60.2	57.5 to 62.9
All, excluding cases associated with chromosomal or other anomalies and IVSD	930	84.2	14.0	1.8	29.3	27.4 to 31.2	24.9	23.2 to 26.7

\*Total number of births (denominator)=317 538.

<sup>†</sup>Total number of live births (denominator)=314 022.

CHD, congenital heart disease; IVSD, isolated ventricular septal defects; LB, live births; SB, stillbirths; TOP, termination of pregnancy; VSD, ventricular septal defect.

## Kirurški zahvati

Supravulvalna pulmonalna stenoza (SVPS) velik je problem nakon operacije zamjene arterija za transpoziciju velikih arterija (TVA) te se, prema povijesnim podatcima, pojavljuje u čak 55% slučajeva. Nedavni rezultati srednjoročnog istraživanja kod 120 pacijenata podvrgnutih izmijenjenoj verziji operacije zamjene arterija – s većim promjerom neopulmonalnog korijena i ekscizije koronarnih ušća u obliku ograničena dugmeta u obliku slova „O“ – pokazuju nižu stopu SVPS-a nakon 5 godina praćenja. U 97,1% slučajeva nakon 14,75 godina ponovna operacija za SVPS nije bila potrebna.<sup>23</sup> Autori takav ishod pripisuju vlastitoj tehnici u kojoj ostavljaju nedirnutim prerez ruba neopulmonalne arterije, no upozoravaju na to da su potrebna daljnja istraživanja kako bi se potvrdila njihova teza.

Dugoročno praćenje više od 1700 pacijenata u Nizozemskoj i Njemačkoj koji su bili podvrgnuti operaciji po Rossu pokazalo je dobru trajnost pulmonarnih vodova sa stopom 95% učesta-

## Surgery

Supravulvar pulmonary stenosis (SVPS) is a major problem after the arterial switch operation for transposition of the great arteries (TGAs), with a prevalence as high as 55% in historic studies. Recently, mid-term results from 120 patients undergoing a modified version of the arterial switch operation—with a higher transection of the neopulmonic root and excision of the coronary ostia as limited 'O'-shaped buttons—show a lower rate of SVPS beyond 5 years of follow-up. Freedom from reoperation for SVPS was 97.1% at 14.75 years.<sup>23</sup> The authors attribute these outcomes to their technique that leaves the transected edge of the neopulmonic artery intact, but caution that future research is required to validate these findings.

Long-term follow-up data on >1700 adults after Ross procedure in the Netherlands and Germany demonstrated good durability of the pulmonary conduits with a rate of freedom from regurgitation grade  $\geq 2+$  of 95% after 14 years, and freedom from reintervention of 80% at 15 years follow-up.<sup>24</sup>

losti izostanka stupnja regurgitacije od  $\geq 2+$  nakon 14 godina i bez potrebe za ponovnom intervencijom unutar 15 godina u 80% slučajeva.<sup>24</sup>

Novi podatci iz randomiziranog istraživanja Safe Paediatric Euglycemia After Cardiac Surgery pokazuju da pacijentima starijima od 60 godina pomaže stroga postoperativna glikemijska kontrola, dovodeći do niže stope infekcije. Mlađi pak bolesnici pokazuju povećanu stopu postoperativnih infekcija.<sup>25</sup> Potrebna su dodatna istraživanja kako bi se otkrili točni uvjeti pod kojima je preporučljivo uvesti strogu glikemijsku kontrolu.

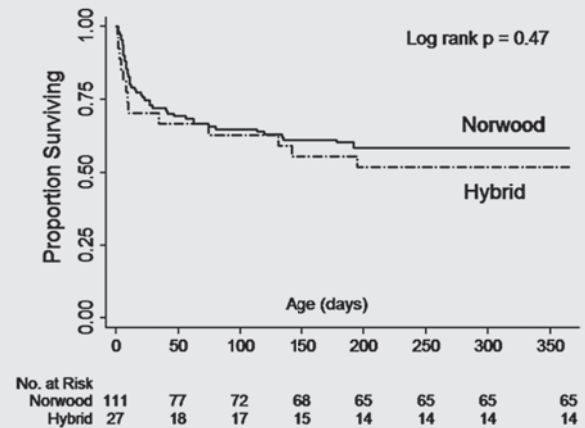
Kongenitalna stenoza aorte i ventrikularni septalni defekti dvije su teme rasprave među kirurzima i intervencionistima.<sup>26</sup> Nedavno rezultati srednjeročnog praćenja od  $10 \pm 7$  godina nakon primarnog liječenja aortne stenoze tijekom prve godine života pokazali povećanu stopu ponovne intervencije u pacijenata liječenih balonskom valvuloplastikom (HR 4,0;  $p = 0,001$ ).<sup>27</sup> U prospektivnom randomiziranom istraživanju 229 djece s perimembranskim ventrikularnim septalnim defektom liječeno je kirurškim ili intervencijskim zatvaranjem defekta. U tom su istraživanju intervencijski zahvati doveli do manje ozljeda miokarda (niže razine CK-MB i troponina I), kraćeg boravka u bolnici, smanjenih troškova liječenja i kraćega vremena oporavka.<sup>28</sup> Autori stoga zaključuju da su intervencijski postupci bolji izbor. Nakon dvije godine praćenja nije registrirana razlika u učestalosti zatvaranja, neželjenim ishodima i komplikacijama, a pitanje kasnog atrioventrikularnog bloka još uvijek nije riješeno.

Inovativni pristup postoperativne potpore obiteljima putem videokonferencija pokazao se izvedivim i uspješnim u smanjivanju učestalosti ponovnih hospitalizacija djece s PSG-om.<sup>29</sup> Računalne tehnike također mogu pomoći kirurzima u praćenju ishoda s prilagođenim rizikom u bolnici i međusobnoj usporedbi.<sup>30-32</sup>

## Tetralogija Fallot

Tijekom prošlih je desetljeća operativni postupak doživio izvanredan napredak, što je dovelo do vrlo niskih stopa rane smrtnosti i morbiditeta. Stoga se u bolesnika s tetralogijom Fallot (TOF) fokus usredotočuje na poboljšanje dugoročnih ishoda, od trećeg desetljeća života dalje. U istraživanju provedenu u Ujedinjenom Kraljevstvu dugoročno praćenje oboljelih s TOF-om definirano je kao praćenje do 45 godina nakon postupka.<sup>33</sup> Autori su dokazali da je godišnja stopa smrtnosti u tih pacijenata četiri puta veća nego u ostatku populacije tijekom prvih pet dekada života. U velikome multinacionalnom istraživanju (International Multicentre TOF Registry) kod 873 odrasla pacijenta s TOF-om proveden je probir za čimbenike rizika koji predviđaju smrt ili dugotrajnu ventrikularnu tahikardiju.<sup>34,35</sup> Na osnovi rezultata oslikavanje srčanom magnetnom rezonancijom, autori su izdvojili ejekcijsku frakciju lijeve klijetke, indeks desne klijetke, omjer mase i volumena desne klijetke i anamnestičke podatke o atrijalnim aritmijama kao nove čimbenike rizika za kasne neželjene ishode (slika 2). Čini se da su kapacitet opterećenja i funkcija lijeve klijetke postojani u odraslih pacijenata s TOF-om uz povećani volumni indeks na kraju dijastole ( $>150 \text{ mL/m}^2$ )<sup>36</sup> te nisu korisni za predviđanje stupnja disfunkcije desne klijetke. Pul-

FIGURE 1.



Interstage survival after the Norwood and Hybrid procedures. Retrospective analysis of survival data from the UK. Kaplan-Meier curve demonstrates no difference in survival despite significantly different Aristotle's scores between the two groups. Adapted from Lloyd et al.<sup>14</sup>

New data from the randomised Safe Paediatric Euglycemia After Cardiac Surgery trial demonstrated that patients  $>60$  days of age benefited from tight postoperative glycaemic control with lower rate of infections. In contrast, younger patients showed an increased incidence of postoperative infections.<sup>25</sup> Further trials are required to investigate the exact conditions under which tight glycaemic control may be advisable.

Two subjects of continuing discussion between surgeons and interventionalists are congenital aortic stenosis and ventricular septal defects.<sup>26</sup> Recently, mid-term follow-up at a mean duration of  $10 \pm 7$  years after primary aortic stenosis treatment during the 1st year of life showed increased rate of reintervention in patients with balloon valvuloplasty (HR 4.0,  $p=0.001$ ).<sup>27</sup> In a prospective randomised controlled trial, 229 children with perimembranous ventricular septal defect were assigned to surgical or interventional defect closure. In this study, interventional closure was associated with less myocardial injury (lower Creatine Kinase -MB (CK-MB) and cTnI levels), shorter hospital stays, reduced medical costs and faster recovery times.<sup>28</sup> The authors state that interventional closure appears to be the method of choice. However, at 2 years of follow-up there was no difference in closure rate, adverse events, and complications between groups and the issue of late atrioventricular block remains to be addressed.

Innovatively, postoperative support of families with videoconferencing has been demonstrated to be feasible and to reduce rehospitalisations of infants with CHD.<sup>29</sup> Computerised techniques have also been shown to help surgeons monitor their risk-adjusted in-hospital outcomes and compare it to overregional benchmarks.<sup>30-32</sup>

monalna regurgitacija jedan je od glavnih uzroka smanjenja funkcije desne lijetke u pacijenata s TOF-om, iako ju neki pojedinci mogu podnositi desetljećima.<sup>37</sup> Nedavna metaanaliza ishoda nakon zamjene pulmonalnog zaliska (PVR) koristi se podatcima o više od 3100 pacijenata te pokazuje da je ukupna 30-dnevna smrtnost iznosila 0,87%, a petogodišnja smrtnost 2,2%.<sup>38</sup> Rizik od ponovne PVR procjenjuje se na 4,9% nakon pet godina. Iako otklon zbog pristranog objavljivanja ozbiljno ograničava spomenute rezultate, PVR se čini sigurnom metodom liječenja. S obzirom na nisku razinu rizika, sve veći broj asimptomatskih pacijenata danas se potvrđava zahvatu PVR, iako optimalni trenutak izvođenja postupka još uvijek nije jasan.<sup>39</sup>

Istraživanja se također usredotočuju na određivanje uloge lijeve klijetke na dugoročne ishode u pacijenata s TOF-om. Kod 413 pacijenata s TOF-om smanjena funkcija lijeve klijetke procijenjena transtorakalnom ehokardiografijom korelira s povećanim rizikom od iznenadne srčane smrti ili ventrikularnih aritmija opasnih za život.<sup>40</sup> Ti su podatci neovisni o produženju QRS kompleksa te se čini da ih se može smatrati dodatnim prediktorom rizika u tih pacijenata.

Veliko multicentrično istraživanje ehokardiografskim probom 474 odrasla pacijenta s korigiranim TOF-om<sup>41</sup> pokazalo je da 6,6% pacijenata ima povećani promjer aorte na osnovi opaženog i očekivanog omjera od > 1,5. Taj razmjerno mali

## Tetralogy of Fallot

In the last decades the operative treatment has dramatically improved with very low early mortality and morbidity. Therefore, the focus of attention is shifting to improving late outcomes of patients with Tetralogy of Fallot (ToF) from their third decade of life onwards. In a study from the UK, long-term outcome of patients with ToF was characterised with a duration of follow-up up to 45 years.<sup>33</sup> The authors demonstrate that the annual probability of death remains fourfold higher than that of the general population throughout the first five decades of life. In a large multinational study (International Multicentre TOF Registry; INdiCaTOR), 873 adults with ToF were screened for risk factors that are predictive of death or sustained ventricular tachycardia.<sup>34,35</sup> Based on cardiac MRI measurements, the authors identified RV and LVEF, RV mass index, RV mass-to-volume ratio and history of atrial arrhythmias as novel risk factors for late adverse outcome (**Figure 2**). Exercise capacity and LV function appear to be maintained in adult patients with ToF with increased RV end-diastolic volume index (>150 mL/m<sup>2</sup>)<sup>36</sup> and are not useful to predicting the degree of RV dysfunction. Pulmonic valve regurgitation is one of the main causes of decreased RV function in patients with ToF, although it may be tolerated for decades in some individuals.<sup>37</sup> A recent meta-analysis of outcomes after pulmonary valve replacement (PVR) including the data from more than 3100 patients, demonstrated that pooled 30-day mortality was 0.87% and 5-year mortality was 2.2%.<sup>38</sup> The risk for re-PVR was estimated to be 4.9% after 5 years. Although publication biases are a major limitation of these findings, PVR appears to be a safe treatment option. Given this low risk, increasing numbers of asymptomatic patients now undergo PVR, although optimal timing remains uncertain.<sup>39</sup>

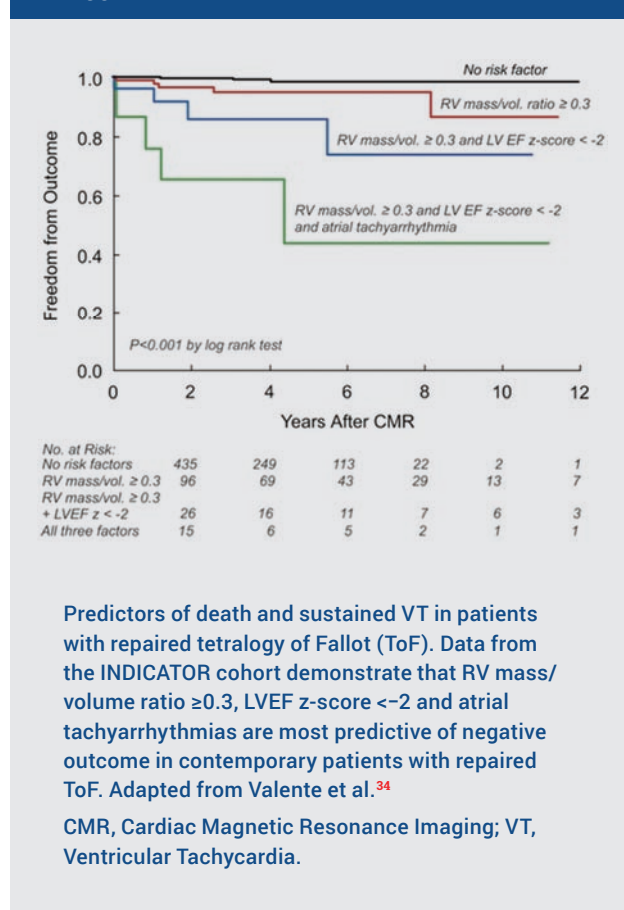
Research has also focused on delineating the role of the LV in determining long-term outcome in patients with ToF. In a sample of 413 adult patients with ToF, decreased LV function as assessed by transthoracic echocardiography correlated with a greater risk of sudden cardiac death or life-threatening ventricular arrhythmias.<sup>40</sup> This finding was independent of QRS prolongation and appears to be an additional risk predictor for this patient population.

In a large multicentre study, echocardiographic screening of 474 adults with repaired ToF<sup>41</sup> showed that only 6.6% of patients had an increased aortic diameter based on an observed-to-expected ratio >1.5. This relatively small proportion of patients is reassuring as previous estimates from smaller studies were much higher. Although it has previously been argued that immediate ToF repair in infancy may reduce the dilatation of the aortic root, no correlation between the duration of systemic-to-pulmonary shunt and the aortic diameter could be identified. Similarly, right aortic arch and aortic regurgitation were not predictive of increased aortic root diameter.

## Transposition of the great arteries

Long-term follow-up data on 400 patients operated with atrial switch operation for D-Transposition of the Great Arteries (D-TGA) between 1983 and 1999 (median follow-up time 18.7 years) was recently published from a single North American centre.<sup>42</sup> The investigators found that overall and arrhythmia-free sur-

FIGURE 2.



udio takvih pacijenata možemo smatrati ohrabrujućim jer su ranije procjene na temelju manjih istraživanja bile mnogo veće. Iako se prije tvrdilo da ispravljanje TOF-a nakon rođenja može smanjiti širenje korijena aorte, nije nađena nikakva povezanost između trajanja sistemsko-pulmonalnog shunta i promjera aorte. Također, desni aortni luk i aortna regurgitacija nisu mogli previdjeti povećan promjer njezina korijena.

## Transpozicija velikih arterija

Jedan sjevernoamerički centar nedavno je objavio istraživanje s dugoročnim praćenjem 400 pacijenata operiranih operacijom zamjene atrijske za D-transpoziciju velikih arterija (D-TGA) između 1983. i 1999. godine (srednje vrijeme praćenja od 18,7 godina).<sup>42</sup> Istraživači su otkrili da je preživljenje i razdoblje bez aritmije tijekom 25 godina iznosilo oko 97% u pacijenata koji su preživjeli rano postoperativno razdoblje. To su pozitivni rezultati u usporedbi s mnogo većim dotad registriranim aritmijama i učestalosti iznenadne smrti u bolesnika s operacijom zamjene atrijske (Mustard, Senning). Procjenjuje se da 92,9% pacijenata nije imalo neke neželjene događaje tijekom 25 godina. U najnovijem praćenju funkcija lijeve klijetke u većini je slučajeva bila odlična, a 97% pacijenata su bili u klasi NYHA I. Nekolicina smrti navedenih u tom istraživanju vjerojatno je bila povezana s infarktom miokarda ili imala podlogu u aritmijama.

Uspriješivši pozitivnim učincima inhibicije renin-angotenzina u pacijenata s disfunkcijom lijeve klijetke, prethodna manja istraživanja pacijenata sa sistemskom desnom klijetkom nisu pronašla sličan učinak. Neučinkovitost inhibicije renin-angotenzina kod sistemske desne klijetke sada potkrepljuje i veće multicentrično, dvostruko slijepo, usporedno randomizirano kontrolirano istraživanje kod 88 odraslih pacijenata s transpozicijom TGA.<sup>43</sup> To istraživanje nije pronašlo nikakav učinak primjene 2x 160 mg valsartana ni na ejectionalnu frakciju desne klijetke ni na kapacitet opterećenja nakon tri godine praćenja.

U retrospektivnom istraživanju pronađena je povezanost volumnog indeksa na kraju diastole od  $>150 \text{ mL/m}^2$  te vršnoga diastoličkog tlaka  $<180 \text{ mmHg}$  tijekom vježbanja i neželjenih srčanih događaja prema zajedničkim ishodima koji uključuju smrt, ventrikularnu tahikardiju, tranzitornu ishemijsku ataku, infarkt miokarda, povećanje funkcionalnog stupnja prema NYHA ljestvici ili hospitalizaciju radi pogoršanja simptoma zatajivanja srca (ZS).<sup>44</sup> Bolesnici s takvim obilježjima imali su dvadeset puta veću godišnju stopu srčanih događaja. Klasične varijable EKG-a i transtorakalne ehokardiografije bili su manje prediktivni pa se stoga standardnom popratnom pregledu tih pacijenata preporučuju magnetna rezonancija i testiranje opterećenjem.

U studiji s uključenih 91 uzastopnih pacijenata podvrgnutom operaciji po Mustardu prije 1980. god. (prosječno vrijeme praćenja 35 godina) preživljenje je bilo 80% nakon 20 godina, 77% nakon 30 godina i 68% nakon 39 godina.<sup>45</sup> Iako je kapacitet opterećenja bio relativno stabilan tijekom zadnjih 10 godina praćenja u toj kohorti, funkcija desne klijetke ravnomjerno je smanjivala, a učestalost aritmija i ZS-a znatno rasla.

## Pulmonalna hipertenzija

U velikome kohortnom istraživanju bolesnika s Eisenmengerovim sindromom, ehokardiografski varijable povezane sa

vival at 25 years was around 97% in those patients that survived the immediate perioperative period. These results compare favourably with the much higher arrhythmia burden and incidence of sudden death previously reported in patients with atrial switch operation (Mustard, Senning). Freedom from any adverse events at 25 years was estimated to be 92.9%. At latest follow-up, LV function was excellent in most cases and 97% of patients presented in NYHA class I. The few deaths reported in this publication were presumably related to myocardial infarction or presumed arrhythmic aetiology.

Despite the beneficial effects of renin-angiotensin-inhibition for patients with LV dysfunction, previous small trials in patients with a systemic RV did not demonstrate a similar effect in this patient population. The lack of benefit of renin-angiotensin inhibition for a systemic RV is now corroborated by a larger multicentre, double-blind, parallel, randomised controlled trial involving 88 adults with transposition of TGA.<sup>43</sup> In this study, no effects of valsartan 160 mg twice daily on RV EF or exercise capacity could be demonstrated at 3 years of follow-up.

In a prospective study, RV end-diastolic volume index  $>150 \text{ mL/m}^2$  and peak systolic blood pressure below 180 mm Hg during exercise testing were associated with adverse cardiac events based on a combined end point including death, ventricular tachycardia, transient ischaemic attack, myocardial infarction, increase in NYHA functional class or hospitalisation for worsening symptoms of heart failure (HF).<sup>44</sup> Patients with these characteristics had a 20-fold higher annual event rate. Classical parameters from ECG and transthoracic echocardiography were found to be less predictive and, thus, MRI and exercise test were recommended to be implemented as additional components of standard follow-up in these patients.

In a study of 91 consecutive patients that underwent Mustard operation before 1980 (median follow-up 35 years), cumulative survival was 80% after 20 years, 77% after 30 years and 68% after 39 years.<sup>45</sup> Although exercise capacity remained relatively stable during the most recent 10 years of follow-up in this cohort, RV function decreases steadily while the prevalence of arrhythmias and HF increase significantly.

## Pulmonary hypertension

In a large cohort of contemporary patients with Eisenmenger syndrome, echocardiographic parameters associated with mortality included<sup>46</sup> indices of RV function (tricuspid annular plane systolic excursion, the ratio of RV effective systolic to diastolic duration) and right atrial area. Application of a novel score combining these predictors may help to risk stratify patients with Eisenmenger syndrome, particularly when assessment of functional class is otherwise difficult. In addition, brain-natriuretic peptide (BNP) levels have been shown to be related to outcome in this population.<sup>47</sup> Observational data from a large adult CHD centre in the UK demonstrated that 6 min walking distance and baseline oxygen-saturations were strong predictors of death in 210 adult patients with Eisenmenger syndrome,<sup>48</sup> while traditional markers of adverse outcome like functional class or peak exercise oxygen-saturations did not correlate with death. The authors state that patients who do not reach a 6 min walk distance  $\geq 350 \text{ m}$  or with baseline oxygen-saturations  $<85\%$  have a threefold increased

smrtnošću uključivale su 46 pokazatelje funkcije desne klijetke (sistolički pomak trikuspidnog prstena, omjer efektivnog trajanja sistole i diastole) i areja desne klijetke. Primjena novoga bodovnog sustava koji obuhvaća ove prediktore mogao bi pomoći pri stratifikaciji pacijenata s Eisenmengerovim sindromom, posebice pri inače složenoj procjeni funkcionalne klase. Pokazano je i da je razina moždanih natriuretskih peptida (BNP) također vezana za kliničke ishode u tih pacijenata.<sup>47</sup> Opservacijski podaci iz velikog PSG centra za odrasle u Ujedinjenom Kraljevstvu pokazuju da su udaljenost u šestominutnom testu hodanja i početna saturacija kisika snažni prediktori smrtnog ishoda kod 210 odraslih pacijenata s Eisenmengerovim sindromom,<sup>48</sup> dok uobičajeni markeri neželjenih ishoda poput funkcionalne klase ili saturacije kisika u vršnom opterećenju ne korreliraju sa smrtnosti. Autori tvrde da pacijenti koji ne prehodaju  $\geq 350$  m unutar šest minuta ili s početnom saturacijom kisika  $< 85\%$  imaju trostruko veći rizik od smrti.

Kod pedijatrijskih pacijenata s pulmonalne hipertenzijom (PAH), dodatna primjena sildenafilom čini se održivom opcijom nakon neuspjeha monoterapije bosentanom.<sup>49</sup> Preliminarni podaci o ishodima u pedijatrijskih pacijenata s PAH-om iz velikih multinacionalnih baza podataka pokazuju da je preživljenje značajno bolje u usporedbi s podacima iz starijih studija, no postoje razlike između podataka o preživljenju od plućne hipertenzije povezane s prirođenim srčanim greškama u odnosu na idiopatsku ili obiteljsku plućnu hipertenziju.<sup>50,51</sup> Kako bi se iscrpnije istražile razlike u preživljenju, prediktorima rizika i optimalnim metodama liječenja potrebna su daljnja istraživanja.

## Arterijske abnormalnosti u prirođenim srčanim greškama

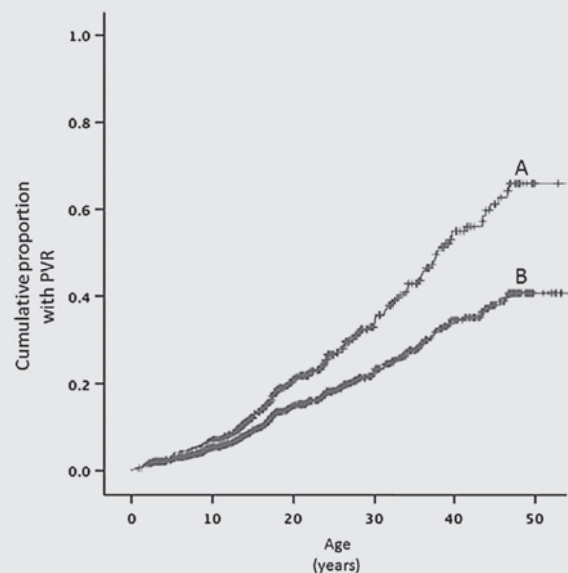
Istraživanja tijekom ovoga desetljeća pokazala su da pacijenti s korigiranom koarktacijom aorte imaju veći rizik od smrti nego opća populacija ili pacijenti s drugim vrstama koronarne bolesti srca (KBS),<sup>52</sup> što se pripisuje prije svega višoj prevalenciji KBS u toj skupini. U nedavnome velikom uzorku odraslih pacijenata s koarktacijom aorte iz Kanade ( $n = 756$ ) nije potvrđeno da je ta dijagnoza neovisni prediktivni čimbenik za razvoj KBS-a nakon korekcije za tradicionalne čimbenike rizika.<sup>52</sup> Te podatke potkrepljuju nedavni dokazi da nema klinički značajne razlike u endotelnoj funkciji između odraslih pacijenata s KBS-om i zdrave kontrolne skupine.<sup>53</sup>

## Zbrinjavanje prirodnih srčanih grešaka u odraslih

Zbog napredka u liječenju PSG-a tijekom prošlih desetljeća, rastućem se broju pacijenata s PSG-om pogrešno čini da su izliječeni. To dovodi do velikoga broja pacijenata koji ne dolaze na kontrolne preglede, što povećava rizik od lrazvoja neželjenih ishoda, uključujući povećanje učestalosti kasne smrtnosti, u usporedbi s pacijentima podvrgnutima praćenjima u specijaliziranim centrima za odrasle s PSG-om (slika 3).<sup>54,55</sup>

Otkrivanje prediktora rizika za kasne neželjene srčane događaje u rastućoj populaciji odraslih pacijenata s PSG-om danas je jedan od glavnih ciljeva u istraživanju. Nedavne studije pokazuju da je umjereno do teško smanjenje plućne funkcije neovisni prediktor smrtnosti, uz povećanje rizika od smrti za

FIGURE 3.



Prevalence of pulmonary valve replacement (PVR) stratified by quality of follow-up. Data from a UK cohort study demonstrates that the prevalence of PVRs in patients that are followed up under specialised care (A) is significantly higher than in patients without such care. Adapted from Wray et al.<sup>54</sup>

risk of mortality. In the paediatric pulmonary arterial hypertension (PAH) population, sildenafil add-on therapy appears to be a viable option when bosentan monotherapy fails.<sup>49</sup>

Preliminary data on outcomes in paediatric patients with PAH from large multinational registries show that overall survival has significantly improved in comparison to historic samples, but there are discrepancies between the reports in reported survival rates of PAH related to CHD versus idiopathic/familial PAH.<sup>50,51</sup> Further research will be necessary to investigate these differences with regard to survival, risk predictors and optimal treatment in further detail.

## Arterial abnormalities in congenital heart disease

Research in the last decade has demonstrated that patients with repaired Coarctation of the Aorta (CoA) have a higher risk of mortality than the general population or patients with other forms of coronary artery disease (CAD),<sup>52</sup> which has been attributed predominantly to an increased prevalence of CAD in this cohort. Now, in a large sample of adult patients with CoA from Canada ( $n=756$ ), the diagnosis of CoA was not found to be an independent predictor for CAD development after adjustment for traditional CAD risk factors<sup>52</sup> and this finding is supported by recent evidence of no clinically significant dif-

barem 1,6 puta u usporedbi s pacijentima s normalnom funkcijom pluća.<sup>56</sup> U istom se istraživanju pokazalo da su smanjeno vršno preuzimanje kisika i rezerva srčane frekvencije tijekom kardiopulmonalnog testa opterećenja dodatni prediktori smrtnosti.<sup>57</sup> Nedavno je objavljen prvi skup referentnih vrijednosti za odraslu populaciju s PSG-om, stratificiranu po podtipu PSG-a i spolu.<sup>58</sup> Pacijenti s odraslim PSG-om koji su tjelesno aktivniji također imaju bolje rezultate pri testiranju opterećenjem.<sup>59</sup> Dvadesetičetiri tjedna strukturiranoga aerobnog vježbanja u odraslih pacijenata s TGA-om znatno poboljšava varijable kardiopulmonalnoga testiranja opterećenjem i smanjuje simptome ZS-a bez negativnog učinka na sistemsku desnu klijetku.<sup>60</sup> Nedavno je pokazana i uspješnost primjene strukturiranog programa tjelesnih vježbi uz psihološki trening za poboljšanje ukupne razine aktivnosti u adolescenata s PSG-om.<sup>61</sup>

U istraživanju temeljenom na dvama velikim bazama podataka za odraslih pacijenata s PSG-om (koja uključuju gotovo 40 000 pacijenata u razdoblju između 1996. i 2005. godine) smrtnost nakon 30 dana hospitalizacije bila je niža u žena nego u muškaraca.<sup>62</sup> Muški je spol, uz implantaciju srčanog elektrostimulatora, također snažan prediktor smrtnosti unutar tri godine od hospitalizacije radi ZS, prema nizozemskom CONCOR registru.<sup>63</sup> Zanimljivo je da žene koje su bile trudne imaju najnižu stopu ukupne smrtnosti, što ne korelira s većom razinom korištenja zdravstvenim uslugama u toj populaciji.<sup>62</sup>

Podatci o preživljenju iz velikoga kohortnog istraživanja na starijim pacijentima s PSG-om (> 60 godina života, n = 375) tijekom petogodišnjeg praćenja u tercijarnom centru pokazali su mnogo veću smrtnost u usporedbi s mlađim pacijentima s PSG-om ili sa zdravom populacijom.<sup>64</sup> Najjači prognostički čimbenici bili su prisutnost KBS ili kongestivnog ZS-a, klasa prema NYHA i sistemiska disfunkcija klijetke. Zdravstveni bi se djelatnici trebali pripremiti za znatno povećanje broja starijih pacijenata s PSG-om tijekom idućih nekoliko desetljeća te biti spremni nositi se s posebnostima njihova stanja i pružiti im potrebnu njegu.

## Trudnoća i prirodene srčane greške

Tijekom prošle dvije godine objavljeni su ishodi velikih istraživanja i baza podataka vezanih za trudnoću u bolesnika s PSG-om.<sup>65</sup> Podatci iz Registry On Pregnancy And Cardiac disease pokazali su da je ZS česta komplikacija u trudnica sa srčanim bolestima (13% u više od 1300 sudionika).<sup>66</sup> Iako je najveća stopa ZS-a zamijećena na kraju drugoga tromjesečja ili pri porođaju, stopa ZS-a usko je povezana s preeklampsijom, preuranjenim porođajem i smrtnošću majke i djeteta. Ipak, pacijenti s PSG-om imaju razmjerno manji rizik od ZS-a u usporedbi s pacijentima s valvularnom bolesti srca, KBS-om ili kardiomiopatijom. Usprkos tomu, rizik od kardiovaskularnih događaja tijekom trudnoće, posebice aritmije i smrti, mnogo je veći u pacijenata s PSG-om (slika 4),<sup>66,67</sup> stopa carskog reza veća je (13% prema 8%), a novorođenčad češće ima nisku porođajnu težinu.<sup>67</sup> Važno je primijetiti da pacijenti sa složenim PSG-om imaju veći rizik od neželjenih kardiovaskularnih ishoda negoli pacijenti s jednostavnim PSG-om.

Prospektivno multicentrično kohortno istraživanje s uključenih više od 200 trudnica s PSG-om (ZAHARA II) otkrilo je

ference in endothelial function between adult patients with CoA and healthy controls.<sup>53</sup>

## Adult congenital heart disease management

Along with the improvements in the care of CHD during the last decades, an increasing number of patients with CHD have the erroneous impression of being cured. This leads to a large number of patients lost to follow-up, which have an increased risk of developing adverse outcomes, including increased late mortality, compared with patients under specialised adult CHD (ACHD) follow-up (Figure 3).<sup>54,55</sup>

Identification of risk predictors for late adverse events in the growing population of patients with ACHD is one of the major goals in current CHD research. Recent studies show that moderate to severe impairment of lung function is an independent predictor of mortality, with an at least 1.6-fold increased risk of death compared with patients with normal lung function.<sup>56</sup> In the same study, reduced peak oxygen uptake and heart rate reserve on cardiopulmonary exercise testing were additional predictors of mortality.<sup>57</sup> A first set of reference values for the adult CHD population, stratified by CHD-subtype and gender, has recently been published.<sup>58</sup> Also, patients with ACHD who are physically more active, tend to perform better on exercise testing.<sup>59</sup> Twenty-four weeks of structured aerobic exercise training of adult patients with TGA significantly improves cardiopulmonary exercise testing parameters and reduces HF symptoms without a negative impact on the systemic RV.<sup>60</sup> The benefits of a structured exercise programme combined with psychological training for improving overall activity in adolescents with CHD has also recently been demonstrated.<sup>61</sup>

In a study based on two large ACHD registries (including almost 40 000 patients between 1996 and 2005), 30-day in-hospital mortality was lower in female than in male patients.<sup>62</sup> Male gender, along with pacemaker implantation, was also highly predictive of 3-year mortality after admission for HF in the Dutch CONgenital CORvitia (CONCOR) registry.<sup>63</sup> Intriguingly, women with a pregnancy history had the lowest overall mortality, which did not correlate with a higher utilisation of health services in this population.<sup>62</sup>

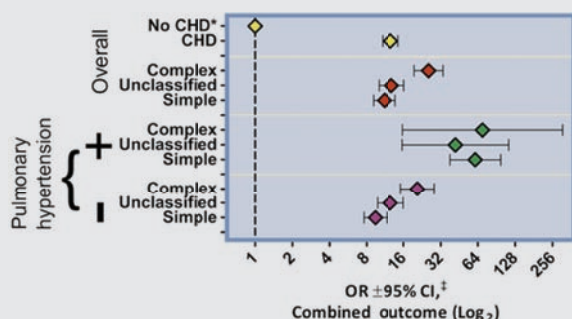
Survival data from a large cohort of elderly patients with ACHD (>60 years of age, n=375) during 5 years of follow-up at a tertiary ACHD centre demonstrated a significantly higher mortality compared with younger patients with ACHD or the normal population.<sup>64</sup> Strongest prognostic predictors were the presence of CAD or congestive HF, NYHA class and systemic ventricular dysfunction. Healthcare providers should anticipate a substantial increase in the number of elderly patients with ACHD over the next few decades and be prepared to meet their special problems and needs.

## Pregnancy and congenital heart disease

During the last 2 years, pregnancy-related outcomes in patients with CHD have been published from large trials or registries.<sup>65</sup> Data from the Registry On Pregnancy And Cardiac disease demonstrated that HF is a common complication in pregnant patients with cardiac disease (13%, of more than 1300 participants).<sup>66</sup> While the highest incidence of HF was found



FIGURE 4.



**Adverse cardiovascular outcome during pregnancy, stratified by congenital heart disease (CHD) complexity and presence of pulmonary hypertension.** Data from the largest US hospital discharge database demonstrates increased odds for adverse cardiovascular events (arrhythmias, cerebrovascular accidents, embolism, heart failure, death or a combined outcome) in patients with CHD compared with women who do not have CHD. OR±95% CI OR±95% CI on multivariate analysis; Adapted from Opotowsky et al.<sup>68</sup>

suboptimalne protoka krvi uteroplacentalnim Dopplerom u usporedbi s kontrolnom skupinom.<sup>69</sup> Multivarijatna analiza pokazuje da su prekonceptijske vrijednosti TAPSE (mjerilo sistoličke funkcije), visoka razina prekursora NT-proBNP-a, kao i mitralna regurgitacija i trikuspidna regurgitacija prediktori smanjenog indeksa otpora umbilikalne arterije, za kojeg je poznata povezanost s neželjenim porođajnim ili novorođenačkim zbivanjima. U tih je žena zamijećena veća vjerojatnost preeklampsije i rođenja djece manje gestacijske dobi (četverostruki porast za oba čimbenika). Na temelju tih istraživanja, prekonceptijska vrijednost TAPSE i NT-pro-BNP-a mogu postati korisni dodatni čimbenici u procjeni rizika u žena s PSG-om. Negativna prediktivna vrijednost NT-pro-BNP-a od <128 pg/mL u 20. tjednu gestacije procjenjuje se na 96,9%.<sup>70</sup>

Detalji principa liječenja trudnica s PSG-om s posebnim odjeljcima za pojedine podtipove bolesti može se pronaći u odličnom preglednom članku.<sup>71</sup>

## Svjetski teret kardiovaskularnih bolesti

Poduzeti su veliki naponi kako bi se poboljšali ishodi pacijenata s PSG-om ili reumatskim srčanim bolestima u zemljama u razvoju, a prema saznanjima iz odličnih afričkih preglednih članaka primjećuje se napredak u nekoliko područja.<sup>72-74</sup> U svojoj recenziji Zühlke i sur.<sup>72</sup> napominju da najviši prioritet treba pridati uvođenju sveobuhvatnih preventivskih programa i programa probira za supkliničke reumatske srčane bolesti, jer je ta skupina i dalje vodeći uzrok srčanih bolesti djece zemalja u razvoju. U skladu s tim, 2012. godine je Svjetska kardiološka federacija objavila nove smjernice utemeljene na dokazima sa

to be at the end of the second trimester or during childbirth, prevalence of HF was strongly associated with pre-eclampsia, premature birth and maternal and foetal mortality. However, patients with CHD had a relatively lower risk of developing HF compared with patients with valvular heart disease, ischaemic heart disease or cardiomyopathy. Nevertheless, the risk of cardiovascular events during pregnancy, particularly arrhythmias and death, is significantly elevated in patients with CHD (Figure 4),<sup>67,68</sup> the rate of caesarean section is higher than background (13% vs 8%) and offspring are more likely to have low birth weight.<sup>67</sup> Importantly, patients with complex CHD were found to have a higher risk of adverse cardiovascular outcomes than patients with simple CHD.

ZAHARA II, a prospective multicentre cohort study of more than 200 pregnant women with CHD demonstrated suboptimal uteroplacental Doppler blood flow patterns in comparison with controls.<sup>69</sup> On multivariate analysis, preconception tricuspid annular plane systolic excursion (a measure of RV systolic function), high precursor of B-type natriuretic peptide cTnI -cardiac Troponin I (NT-pro-BNP), as well as mitral and tricuspid regurgitation were predictors of a decreased umbilical artery resistance index, which is known to be associated with adverse obstetric and offspring events. Affected women were more likely to develop pre-eclampsia and deliver small for gestational age babies (both fourfold increase). Based on these findings, preconception tricuspid annular plane systolic excursion as well as NT-pro-BNP may become helpful adjuncts in the risk assessment for women with CHD. The negative predictive value of a NT-pro-BNP <128 pg/mL at 20-week gestation was estimated to be 96.9%.<sup>70</sup>

Further details of current principles of care for pregnant patients with CHD with special sections on many CHD subtypes have recently been summarised in an excellent review article.<sup>71</sup>

## Global burden of cardiovascular disease

Large efforts have been made to improve the outcome of patients with CHD or rheumatic heart disease (RHD) in the developing world and progress can be identified in several aspects as excellently reviewed for the African continent.<sup>72-74</sup> In their review, Zühlke et al.<sup>72</sup> point out that establishing comprehensive prevention programmes as well as efficient screening for subclinical RHD has highest priority, as RHD remains to be the leading cause of cardiac disease in children of low-income countries. Along these lines, a new evidence-based guideline was published by the World Heart Federation in 2012 with the intention to standardise RHD criteria on the basis of 2D and Doppler echocardiography.<sup>75</sup> These new guidelines have been found to be highly sensitive and specific in a prospective study of a high-risk population (Australian Indigenous population).<sup>76</sup> The increasing availability of small and portable echocardiography scanners may further help to transfer these guidelines into clinical practice even in the most resource-constrained settings, as successfully demonstrated by a group from Uganda.<sup>77</sup> Strategies like this should help to reduce the incidence of RHD related complications, including significant mitral stenosis and tricuspid regurgitation. A group from Korea demonstrated longterm follow-up data on patients after successful percutaneous mitral valvuloplasty

svrhom standardizacije ehokardiografskih pregleda kod reumatskih srčanih bolesti.<sup>75</sup> Nove smjernice pokazale su se jako osjetljivima i specifične u prospektivnoj studiji visoko rizične populacije (populacije australskih domorodaca).<sup>76</sup> Rastuća raspoloživost malih i prenosivih ehokardiografskih uređaja mogla bi dodatno pomoći širenju tih smjernica na kliničku praksu i u područjima s najograničenijim resursima, kao što je uspješno pokazala skupina iz Ugande.<sup>77</sup> Takve bi strategije trebale pomoći u smanjenju učestalosti komplikacija reumatskih srčanih bolesti, uključujući značajnu mitralnu stenozu i trikuspidnu regurgitaciju. Skupina iz Koreje iznijela je dugoročne podatke praćenja pacijenata nakon uspješne perkutane mitralne valvuloplastike radi reumatske mitralne stenozе (299 pacijenata tijekom praćenja do 19 godina) i pokazala da učestalost pojave trikuspidne regurgitacije raste čak i godinama nakon uspješne perkutane mitralne komisurotomije.<sup>78</sup> Ako se mitralna stenozа liječi zamjenom mitralnog zaliska, a pacijent ima prisutnu blagu do umjerenu trikuspidnu regurgitaciju ostvaruju se bolji ishodi ako se u kirurški postupak istodobno uključi i zamjena trikuspidnog zaliska.<sup>79</sup>

U zemljama u razvoju dijagnoza PSG-a često se otkrije kasno, što je povezano s mnogo većim teretom bolesti. Stoga je ranije otkrivanje PSG-a na razini populacije najvažniji kriterij za smanjenje cjeloživotnog tereta PSG-a u zemljama u razvoju. U vrlo velikom prospektivnom istraživanju na više od 120 000 novorođenčadi u Kini pokazan je primjer uspješnog uvođenja pulsne oksimetrije u zemljama u razvoju,<sup>80</sup> što pomaže pri otkrivanju oboljelih s ozbiljnim prirođenim srčanim greškama koji nisu dijagnosticirane kliničkim pregledom. Prednosti toga postupka također su brzina rada, kratko vrijeme probira i jednostavnost postupka u usporedbi sa širokom primjenom ehokardiografije. Prema tom istraživanju, učestalost lažnih negativnih nalaza za pulsnu oksimetriju bila je 0,3%, dok bez pulsne oksimetrije trostruko više novorođenčadi s kritičnim PSG-om i dvostruko više novorođenčadi s ozbiljnim PSG-om odlazi iz bolnice nedijagnosticirano.

## Slikovni prikazi i prikazi slučajeva prirođenih srčanih grešaka

Prikazi slučaja i slikovni prikazi čine velik dio publikacija o PSG. Omogućuju dodatan izvor edukacije i posebno su važne kao prikaz inovativnih tehnika u interventnoj pedijatrijskoj kardiologiji,<sup>37,81-85</sup> a podižu i svijest o vrlo rijetkim kongenitalnim patologijama.<sup>86-88</sup> Uz edukacijske članke o pojedinim temama iz područja PSG-a,<sup>89-90</sup> izvrstan su dopunski materijal koji sve nas u pedijatrijskoj kardiologiji održava adekvatno educiranima.

for rheumatic mitral stenosis (299 patients for up to 12 years) and found that the incidence for developing tricuspid regurgitation increases even years after successful percutaneous mitral commissurotomy.<sup>78</sup> If mitral valve replacement is performed for mitral stenosis, patients also benefit from concomitant tricuspid valve replacement if they have mild-moderate tricuspid regurgitation at the time of surgery.<sup>79</sup>

On the other hand, the diagnosis of CHD is also often delayed in low-income countries, which is associated with significant additional burden. Thus, earlier detection of CHD on a population-wide level is the most important criterion to reduce the lifelong burden of CHD in low-income countries. In a very large prospective trial involving more than 120 000 newborns in China, an example of successful implementation of pulse oximetry in low-income countries has been established,<sup>80</sup> which helps to identify patients with major CHD that are not diagnosed on clinical investigation alone. Further advantages of this technique, as opposed to widespread implementation of echocardiography, are the low workload, the short screening time and the simplicity of its performance. In their study, the false negative rate for pulse oximetry was 0.3%, while without pulse oximetry, three times more babies with critical CHDs and two times more babies with other major CHDs would have left the hospital undiagnosed.

## Images and case reports of congenital heart disease

Case reports and images constitute a significant proportion of publications on congenital heart defects. For the clinician, they provide an additional educational source and are especially important to illustrate innovative techniques in interventional paediatric cardiology<sup>37,81-85</sup> and to raise the awareness for very rare congenital pathologies.<sup>86-88</sup> In concert with educational articles on specific topics in CHD,<sup>89-90</sup> they provide an excellent adjunct to keep all of us in paediatric cardiology curious and up-to-date.

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