Trudnoća u žena s prirođenom srčanom bolesti: individualizirana strategija

Pregnancy in Women with Congenital Heart Disease: Individualized Strategy

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SAŽETAK: Porastom broja odraslih bolesnica s prirođenom srčanom bolesti (PSBO) češće ćemo se susretati s problemom komplikacije trudnoće u ovoj populaciji. Pacijentice s intermedijarnom ili vrlo kompleksnom prirođenom srčanom bolesti, često s reduciranom funkcijom srca u situaciji povećanoga minutnog volumena, što je slučaj u trudnoći, bit će izložene problemima kao što su zatajivanje srca, aritmije, gubitak ploda, preuranjeni porođaj, djeca manje porođajne težine i sl. Trudnoća može značiti i neposrednu opasnost za morbiditet i mortalitet majke, ali i biti povezana s lošijim kasnijim ishodom. Prisutna je opasnost za dijete, kao što su restrikcija rasta ili teratogeni utjecaj lijekova. U većina bolesnica s PSBO-om trudnoća je moguća uz povećani rizik za majku i za dijete. Prikazujemo pet bolesnica s umjerenom ili kompleksnom srčanom greškom i trudnoćom. Pacijentice smo stratificirali prema riziku i prikazali potrebu praćenja takvih bolesnica u specijaliziranom centru za PSBO.

SUMMARY: The increase in the number of adult female patients with congenital heart disease (ACHD) will result in pregnancy complications in this populations becoming a more common problem faced by physicians. Patients with intermediate or very complex congenital heart disease, often accompanied by reduced heart function with increased cardiac minute volume, as is the case in pregnancy, will be susceptible to health issues such as heart failure, arrhythmia, loss of pregnancy, pre-term birth, low birthweight, etc. Pregnancy can also represent a direct danger to the morbidity and mortality of the mother, but can also be associated with poorer outcomes after the pregnancy. There are dangers for the child as well, such as restricted growth or the teratogenic effects of drugs. In most patients with ACHD, pregnancy is possible but with an increased risk for the mother and child. We present five patients with moderate or complex heart defects and pregnancy. We stratified patients according to risk and demonstrated the need for monitoring such patients in a specialized ACHD center.

KLJUČNE RIJEČI: prirođena srčana bolest odraslih, trudnoća, stratifikacija rizika.

KEYWORDS: adult congenital heart disease, pregnancy, risk stratification.

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Nedavno smo hrvatsku kardiološku javnost obavijestili o rastućemu problemu odraslih bolesnika s prirođenom srčanom bolešću (PSBO)[1,2]. Tematskim brojem časopisa *Cardiologia Croatica* nadali smo se povećati svijest o postojanju toga problema i pokazati napredak u liječenju ovakvih bolesnica. U ovome bismo članku osvijetlili jedan poseban aspekt, problem trudnoće u žena s PSBO-om, uključujući naša iskustva s takvim pacijenticama.

We recently informed the general cardiologic public in Croatia about the increasing problem of adult patients with congenital heart disease (ACHD)[1,2]. With this thematic issue of the *Cardiologia Croatica* journal, we hoped to increase the awareness of the problem and present some progress we have achieved over time. In this article, we will focus on one specific aspect of the issue: the problem of pregnancy in women with ACHD, including our experiences with these patients.

Zašto je trudnoća rizična u bolesnica s PSBO-om, nije teško razumjeti. Trudnoća je povezana s velikim hemodinamskim promjenama. Vrlo rano dolazi do hormonski uvjetovanog pada u sustavnoj vaskularnoj rezistenciji (SVR), što dovodi do kompenzatorne reakcije reninsko-angiotenzinskog sustava, na smanjenje "pre-loada" i "after-loada", a posljedica je porast volumena krvi i frekvencije srca. Sve to rezultira porastom udarnog/minutnog volumena (CO), koji se može gotovo udvostručiti na kraju trudnoće. I izvansrčana anatomija može negativno utjecati na hemodinamiku. U bolesnica s već reduciranom srčanom funkcijom, to može imati veliki utjecaj[3].

Kardiovaskularna smrtnost majke vezana za trudnoću vrlo je niska. Prema rezultatima statistike u Velikoj Britaniji, to je 2,3 na 100 000 trudnoća u 2011. godini[4]. Dobra je vijest da je udio bolesnica s PSBO-om u toj skupini iznimno mali, no drugi problemi mogu znatno utjecati na kasniji mortalitet i morbiditet[5].

Trudnoću u bolesnica s PSBO-om treba voditi prema točno određenom planu koji uključuje:

- evaluaciju stanja prije trudnoće
- izbjegavanje lijekova potencijalno rizičnih za dijete
- trudničku, kardiološku i opstetričku skrb
- brigu o fetalnom razvoju djeteta
- kardiološku i opstetričku skrb u vrijeme poroda
- skrb neposredno nakon poroda
- buduću kontracepciju
- eventualno genetičko savjetovanje
- eventualna antibiotsku profilaksu.

Prema ovom algoritmu, prvo je pravilo savjetovanje prije začeća. Naš je cilj ustanoviti stanje i optimizirati kardiološki status buduće majke, kao i razmotriti probleme: utjecaj trudnoće na neposredne i kasne posljedice na srce, ali i rizike za dijete. Pregled prije trudnoće treba uključiti povijest bolesti, klinički status, elektrokardiogram te ehokardiografiju kojom se može ustanoviti funkcija klijetki, funkcija valvula, stanje krvnih žila (provodnika) i tlakove u plućima. Ako treba, potrebno je učiniti alternativne slikovne ili druge pretrage (magnetna rezonancija), test opterećenja i, u slučaju sumnje na plućnu vaskularnu rezistenciju (PVR), kateterizaciju srca. U nekim je slučajevima razumno učiniti i genetsko savjetovanje. Nažalost, u mnogim slučajevima pacijentice se prvi put prezentiraju u našoj ambulanti, već trudne! Rizik od trudnoće potrebno je determinirati, najbolje prema **WHO stratifikaciji rizika u trudnoći** (*ESC preporuke za liječenje kardiovaskularnih bolesti tijekom trudnoće*)[6]. Sve bolesnice s PSBO-om mogu se stratificirati u četiri grupe (I. – IV.).

Grupa s niskim WHO rizikom

- U bolesnica s operiranim atrijskim septalnim defektom (ASD) i ventrikulskim septalnim defektom (VSD) bez komplikacija može se očekivati normalna trudnoća (I.).
- U pacijentica s neoperiranim ASD-om i malim VSD-om, s dobrom funkcijom lijeve klijetke i bez plućne hipertenzije (PH), očekuje se normalna trudnoća (II.) Lijevo-desni pretok može se i smanjiti zbog pada u SVR-u. Postoji mali rizik za razvoj atrijskih aritmija i teoretski rizik za paradoksnu embolizaciju u ASD-u.[7]

It is not hard to see why pregnancy is full of risk for patients with ACHD. Pregnancy in any women is associated with significant hemodynamic changes. Due to hormonal changes, there is a very early drop in systemic vascular resistance (SVR), leading to compensatory renin-angiotensin reaction on pre- and afterload drop, with a correspondent rise in blood volume and heart rate. This results in increased cardiac output (CO), which can be almost doubled at the end of the pregnancy. Extra-cardiac anatomy can also have a negative effect on hemodynamics. In patients with already decreased cardiac function, this can have a severe impact[3].

Maternal cardiac mortality during pregnancy is very low. Based on data from the British statistical office, it was 2.3 per 100 000 pregnancies in 2011[4]. The good news is that patients with ACHD only make up a small portion of this group, but other problems occur during pregnancy that can influence later mortality and morbidity[5].

Pregnancies in patients with ACHD should be managed according to a precise plan that includes:

- Evaluation before pregnancy
- Avoidance of drugs harmful to the baby
- Cardiac and obstetric care prior to delivery
- Fetal development care
- Cardiac and obstetric care during labor
- Post-delivery care
- Future contraception
- Genetic counseling (if needed)
- Antibiotic prophylaxis (if needed)

According to this algorithm, the first rule is pre-conception counseling. Our goal is to establish and optimize the future mother's heart condition, and discuss the following issues: immediate and late effects of pregnancy on the mother's cardiac condition and risk to the baby. The pre-pregnancy examination includes history and clinical status, ECG, echocardiography (ECHO) to establish ventricular function, valves, vessels (conduits), shunts, and pulmonary pressure. If necessary, alternative imaging or other methods such as nuclear magnetic resonance (MR), exercise capacity testing, and heart catheterization in suspected high pulmonary vascular resistance (PVR), should be performed. In some cases, genetic counseling is advised. Unfortunately, patients sometimes come to our outpatient clinic already pregnant! Pregnancy risk should be determined, which is best done according to **WHO risk stratification during pregnancy** (ESC Guidelines on the management of cardiovascular diseases during pregnancy)[6]. All patients with ACHD can be stratify into four groups (I-IV).

Low who risk stratification group

- In patients with surgically corrected atrial septal defect (ASD) and ventricular septal defect (VSD) without complication, a normal pregnancy can be expected (I).
- In un-operated ASD and small VSD with good left ventricular function and no pulmonary hypertension (PH), normal pregnancy is expected (II). The left-to-right shunt can decrease because of the fall in SVR. There is a small risk of atrial arrhythmias and a theoretical risk of paradoxical embolization in ASD.[7]

- Pulmonalna stenoza (PS) s gradijentom nižim od 60 mmHG (I.).

Grupa sa srednjim WHO rizikom

- Pri PS-u s gradijentom višim od 60 mmHg i tlakom u desnoj klijetki višim od 75 mmHg preporučuje se intervenirati prije trudnoće. Neliječena teška PS nosi visoki rizik od desnostranoga srčanog popuštanja (II. – III.)
- Operirana Fallotova tetralogija (TOF) (II.)
- Marfanov sindrom može uzrokovati disekciju aorte tijekom trudnoće, ali rizik nije jako visok ako je dimenzija ascendentne aorte manja od 4,0 do 4,5 cm (II. – III.).

Grupa s visokim WHO rizikom

- U bolesnica s transpozicijom velikih arterija (TGA) nakon operacije atrijskog „swicha" (po Senning-Mustardu), u trudnoći nastale promjene u funkciji desne klijetke, kao i kompetenciji sustavne valvule, mogu ostati trajno! (III.).
- Mehaničke valvule nose veliki rizik u trudnoći. Nema konsenzusa za najbolji režim antikoagulacije u trudnoći (prekid trudnoće, tromboza zalistka, teratogenost za dijete) (III.).
- Neoperirani TOF, danas rijedak, nosi visoki rizik od porasta cijanoze (III.).
- Problemi u trudnoći česti su u bolesnica s Fontanovom cirkulacijom (III.).

SLUČAJ 1.

MD, 1981.god. – „šum na srcu" poznat od djetinjstva

- Posljednje dvije godine intolerancija napora, planirana trudnoća.
- Dijagnosticirana PS (gradijent 94 mmHg, širina anulusa 21 mm) (**slika 1**).
- Preporučena perkutana intervencija (PTA) prije trudnoće.
- Uspješna PTA dvama balonima 16 + 13 mm (**slika 2**).
- Pacijentica je trudna, ne očekuju se komplikacije i planira se normalni vaginalni porođaj.

Ovaj slučaj je dobar primjer evaluacije prije trudnoće, a preporučena intervencija znatno je optimizirala njezin ishod.

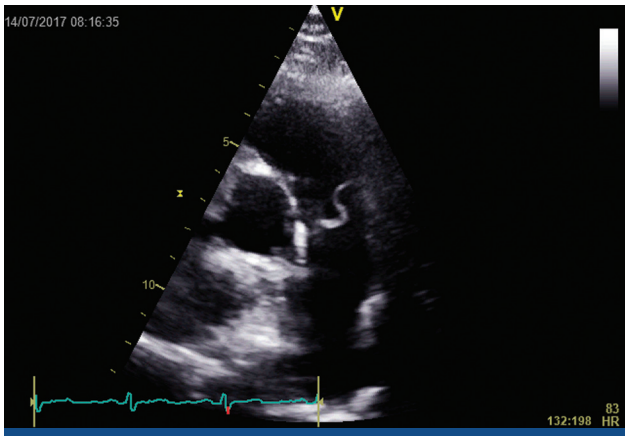

FIGURE 1. Echo finding of a congenital valvular pulmonary stenosis.

- Pulmonary stenosis (PS) with a gradient lower than 60 mmHg is also not a high risk for pregnancy (I).

Intermediate WHO risk stratification group

- It is recommended to treat severe PS before pregnancy (RVP>75 mmHg, P gradient >60 mmHg). Untreated PS caries high risk for right heart failure (II-III).
- Repaired Tetralogy of Fallot (TOF) is a moderate risk for pregnancy (II).
- Marfan syndrome can cause dissection during pregnancy, but the risk is not so high if the dimensions of the ascending aorta are less than 4.0-4.5 cm (II-III).

High WHO risk stratification group

- Transposition of the great arteries (TGA) after atrial switch (Senning-Mustard procedure); changes in RVEF and systemic valve competence can be permanent! (III).
- Mechanical valves carry a great pregnancy risk. There is no consensus on the best anticoagulation regime in pregnancy (risk for pregnancy termination, thrombosis risk, teratogenicity risk for the baby) (III).
- Un-operated TOF, rare today, carries a risk of cyanosis (III).
- Pregnancy problems are common in Fontan patients (III).

CASE 1

MD, 1981, "murmur" known from childhood

- Effort intolerance in the last two years, pregnancy planed.
- Valvular pulmonary stenosis (PS) diagnosed (gradient 94 mmHg, annulus 21 mm) (**Figure 1**).
- Pre-pregnancy intervention recommended.
- PTA successful with two balloons 16+13 mm (**Figure 2**)
- Pregnant, so far without complication, a normal vaginal delivery is expected.

This case is a good example of pre-pregnancy evaluation and optimized pregnancy outcome due to the advised intervention.

CASE 2

JS, 1989, healthy

- Mother died at 47 years of age (sudden death from aortic rupture, previous operation of cerebral aneurysm).
- 2015: sister successfully operated for ascending aortic aneurysm (9 cm).
- Accompanying her sister for postoperative ECHO control, somebody of echo staff she was pregnant (23 weeks) and offered her ECHO control as well.
- ECHO revealed 4.5 cm of sinus Valsalva, Cesarean section recommended (**Figure 3**).
- Birth was uneventful, and the patient is in regular follow-up; small progression of aortic dimension (4.7 cm) after 1.5 years.

The case is an example of the importance of screening. Marfan syndrome with aortic dilatation carries high risk for aortic dissection during pregnancy or delivery!

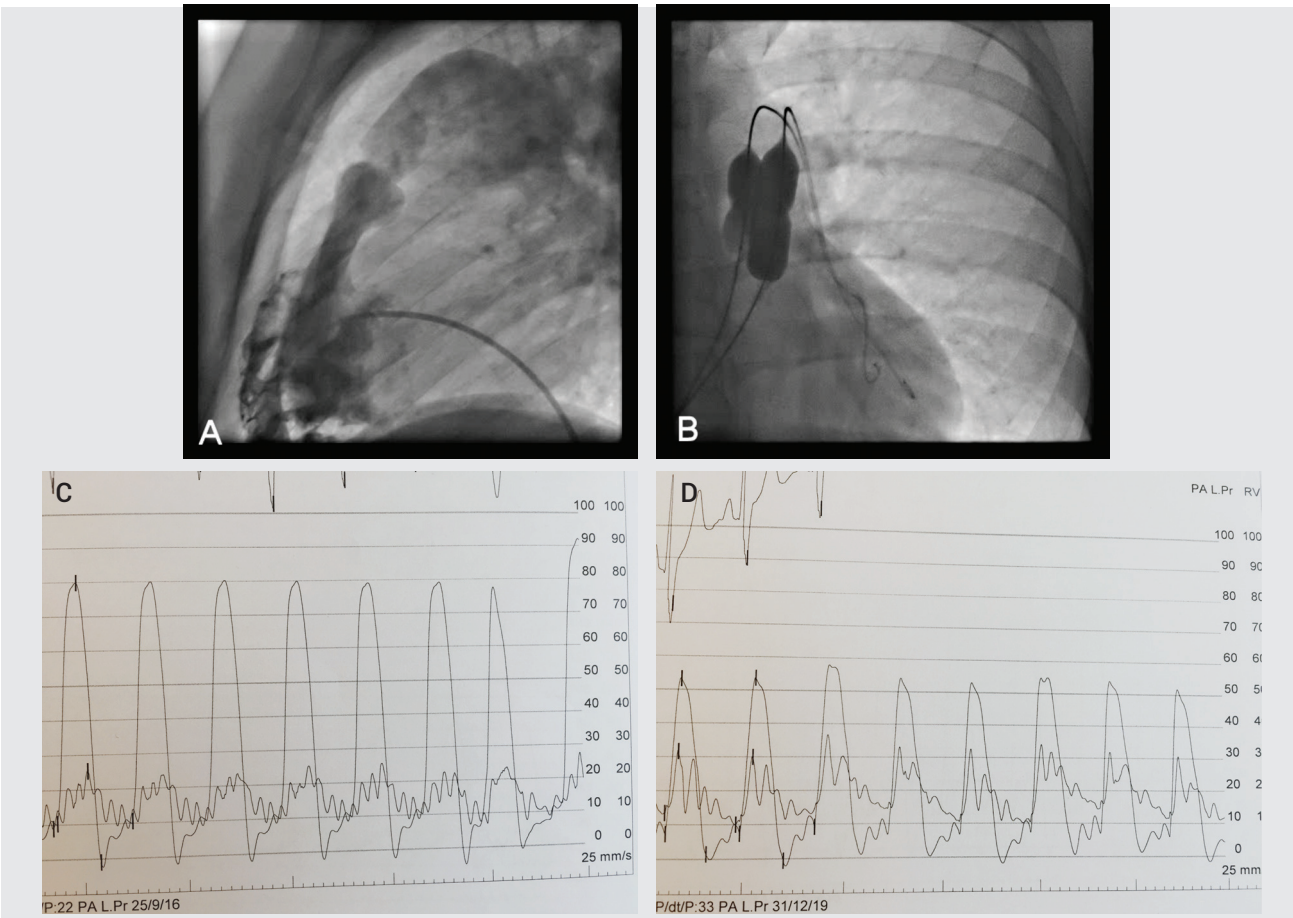

FIGURE 2. Percutaneous balloon dilatation of stenotic pulmonary valve: A) Pulmonary angiography before dilatation; B) Simultaneous inflation with two balloons; C) Pressure gradient before dilatation; D) After dilatation.

SLUČAJ 2.

JS, 1989. god., zdrava

- Majka joj je umrla s 47 godina (iznenadna smrt kao posljedica rupture aorte, prije toga operacija cerebralne aneurizme).
- Godine 2015. sestri je uspješno operirana aneurizma ascendentne aorte (9 cm).
- U pratnji sestre pri postoperacijskoj ehokardiografskoj kontroli, primjećeno je od strane osoblja da je pacijentica trudna (23 tjedna) te je i njoj ponuđen ultrazvučni pregled.
- Ustanovljena aneurizma Valsalvina sinusa širine 4,5 cm, preporučen je carski rez (**slika 3**).
- Porođaj je protekao bez komplikacija. Pacijentica je u redovitom praćenju, nakon 1,5 godina, praktično bez progresije dimenzije aorte (4,7 cm).

Slučaj je primjer potrebe za probirom rizičnih bolesnika. Marfanov sindrom s dilatacijom aorte veliki je rizik za disekciju aorte tijekom trudnoće i porođaja!

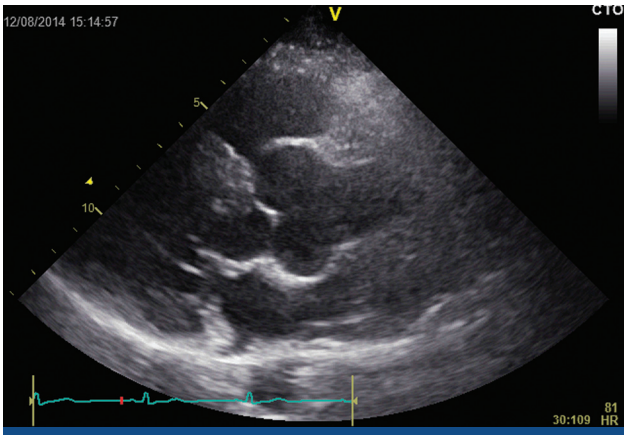

FIGURE 3. Dilatation of sinus Valsava in pregnant patient with suspected Marfan syndrome.

SLUČAJ 3.

PH, 1995. god., transpozicija velikih krvnih žila

- Operacija po Senning-Mustardu izvedena s 4 mjeseca, u redovitome pedijatrijskom praćenju. Zadnja kontrola u 12/2012. i tada je bila u **37. mjesecu trudnoće**. Opis ultrazvuka: normalna funkcija trikuspidne valvule (sustavne), dobra funkcija sustavne desne klijetke. U EKG nalazu opisana sinusna tahikardija 140/min.
- Tri tjedna poslije (1/2013.) normalni vaginalni porođaj; rodila zdravu djevojčicu.
- Ožujak 2013. hospitalizacija zbog teškoga srčanog popuštanja, pri čemu je referirana za premještaj u naš Centar (svibanj 2013.).
- Pri prvoj prezentaciji u EKG-u undulacija atrija, niska maksimalna potrošnja kisika na spiroergometriji (20 vol.% O_2), niska EF i značajna insuficijencija sustavne valvule na ultrazvuku srca (**slika 4**).
- Učinjena elektrokonverzija, od tada na terapiji s beta-blokatorom bez znatnih aritmija, u redovitim kontrolama u našem Centru. Kliničko i ehokardiografsko poboljšanje (**slika 5**).

CASE 3

PH, 1995, transposition of great arteries (TGA)

- Senning-Mustard operation was performed at 4 months, in regular pediatric FU. Last pediatric control was 12/2012; **37 months pregnant**. ECHO description: normal tricuspid valve (systemic) function, good systemic right ventricular function. In ECG, a sinus tachycardia 140/min was described.
- 3 weeks later, (1/2013) gave normal vaginal birth to a healthy girl.
- 3/2013: hospitalization for severe heart failure, referred to our center (5/2013).
- Atrial flutter at first presentation, low max oxygen consumption on spiroergometry (20 vol %O2), low EF, and significant systemic valve insufficiency on ECHO found (**Figure 4**).
- Electrocardioversion was done, on beta-blocker therapy without without significant arrhythmia, on regular follow-up. Improvement of clinical and ECHO findings (**Figure 5**).

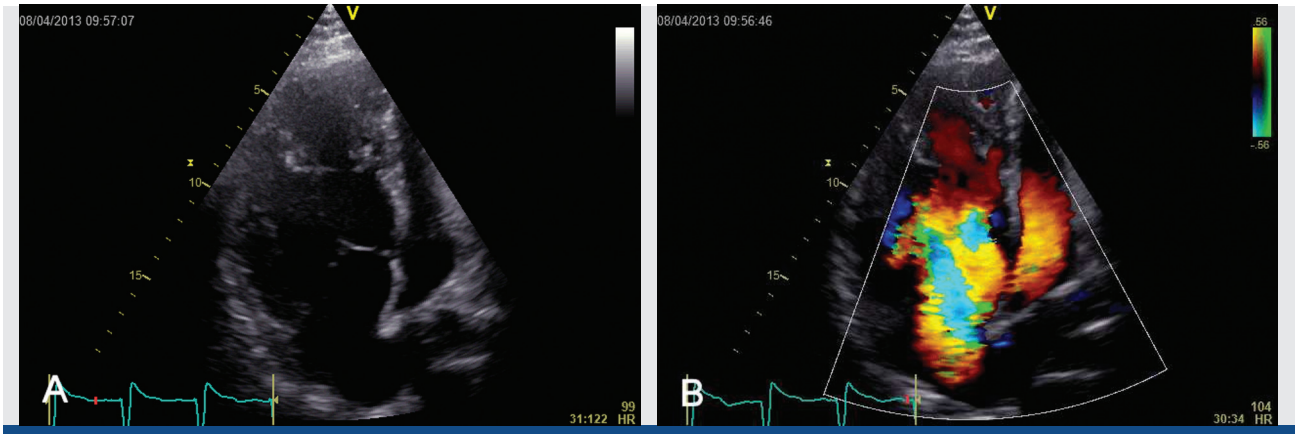

FIGURE 4. Echo finding of patient with systemic right ventricle (transposition of great vessels after Senning Mustard operation): A) Dilatation and systolic function reduction of systemic right ventricle; B) Significant systemic (tricuspid) valve regurgitation.

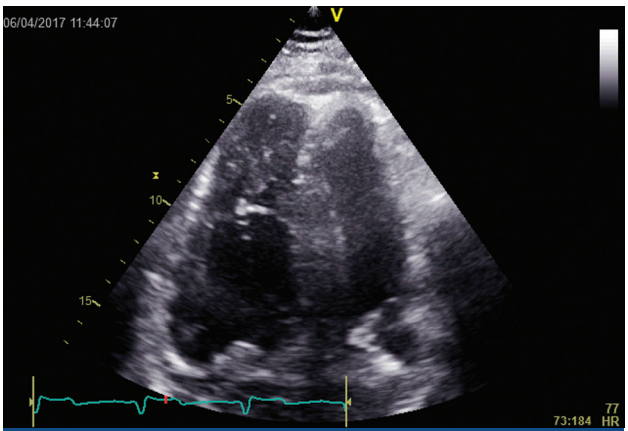

FIGURE 5. Improvement of systolic function of systemic right ventricle after pregnancy.

U ovom je slučaju pitanje je li pogoršanje sistoličke funkcije povezno s trudnoćom i je li neprepoznata aritmija bila prisutna i prije. Nakon trudnoće i konverzije u sinusni ritam, nasreću, poboljšala se sistolička funkcija sustavne klijetke i znatno smanjila insuficijencija sustavnog zalistka.

Prema literaturi,[8] u bolesnika s TGA-om nakon operacije po Senning-Mustardu, progresija dilatacije desne klijetke prisutna je u trećine bolesnika, a u 31 % oboljelih nije nastupio oporavak. Sistolička disfunkcija desne klijetke napredovala je u četvrtine bolesnika, a u većine nije nastupio oporavak. Trikuspidna regurgitacija napredovala je u 50 % bolesnica, od kojih se trećina nije oporavila! Majka mora biti upoznata s tim rizikom i, ako ga prihvati, potrebno je pažljivo praćenje tijekom trudnoće.

SLUČAJ 4.

KS, 1994. god., kongenitalna mitralna valvularna greška

- U djetinjstvu je dvaput učinjena plastika mitralnog zaliska.
- Godine 2009. implantacija mehaničke valvule zbog teške mitralne regurgitacije (odluka roditelja).
- Godine 2015. prva trudnoća, spontani pobačaj u 8. tjednu (smrt fetusa).
- Posljednju godinu dana česte supraventrikulske tahikardije (SVT), planirana elektrofiziološka procedura, no pacijentica je u međuvremenu ponovno zatrudnjela. U šestome tjednu trudnoće prekinuto liječenje varfarinom i započeta terapija frakcioniranim heparinom. Nastavljena primjena beta-blokatora.
- Zbog ranije potrebe za visokom dozom varfarina (10,5 mg), frakcionirani heparin predviđen tijekom cijele trudnoće uz 75 mg acetilsalicilatne kiseline (od 14. to 32. tjedna trudnoće), redovite kontrole anti-Xa faktora (0,35-0,7 IU/mL).
- Ponovna epizoda SVT-a 220/min uspješno je prekinuta verapamilom pa je on uveden u redovitu terapiju umjesto beta-blokatora (**slika 6**).
- Ablacija je planirana nakon poroađaja, no, kako je u međuvremenu došlo do progresije ritmičkih smetnji ista je uspješno učinjena u šestom mjesecu trudnoće uz maksimalnu zaštitu od zračenja. U redovitoj je kontroli, za sada bez komplikacija. Planira se carski rez.

Slučaj je dobar primjer potrebe konzultacije s pacijentom (roditeljima) o mogućim strategijama liječenja. Mehanički je zalistak visoki rizik za buduću trudnoću i potrebno je to objasniti pacijentu (roditeljima), prije operacije!

In this case, the question is whether EF deterioration was associated with pregnancy and was arrhythmia unrecognized. After pregnancy and conversion to sinus rhythm, fortunately, improvement of systolic function and reduction of systemic valve regurgitation was observed.

In the literature[8] on patients with TGA after Senning-Mustard operation, RV dilatation progressed in 1/3 of patients and with no recovery in 31%. RV systolic dysfunction progressed in 25% of patients, in the majority with no recovery. Tricuspid regurgitation progressed in 50%, and 1/3 of patients did not recover! The mother should be informed about the risk, and if she is willing to take it, careful follow-up is needed.

CASE 4

KS, 1994, congenital mitral valve disease

- ×2 mitral valve repair in childhood.
- 2009: mechanic valve implantation for severe mitral regurgitation was performed (parents' decision).
- 2015: first pregnancy, miscarriage in the 8th week (fetal death).
- Last year: frequent SVT, electrophysiology was scheduled, but in the meantime there was second pregnancy; the patient presented at our center after 6 weeks: warfarin stopped, fractionated heparin introduced, beta blocker continued.
- High warfarin dose needed (10.5 mg), so fractionated heparin continued, aspirin 75 mg introduced (from 14 to 32 weeks), regular anti-Xa level control (0.35-0.7 IU/mL).
- New onset of SVT 220/min, stopped with verapamil (introduced instead of beta blocker for regular therapy) (**Figure 6**).
- Ablation was planed after delivery, but for increase in arrhythmia frequency, the procedure was done in the 6-th month of pregnancy, with maximal radiation protection. In regular FU, so far with no complication, Cesarean section planed.

The case is a good example of the need to discuss the treatment strategy with patients (parents). Mechanical valves represent a high risk for future pregnancy, and this should be explained to patients (parents) before surgery!

In meta-analysis of studies[9] examining the best anticoagulation strategy in pregnant women with mechanical valves, different anticoagulation regimes had different impacts on maternal death, thromboembolism risk, valve failure, but also

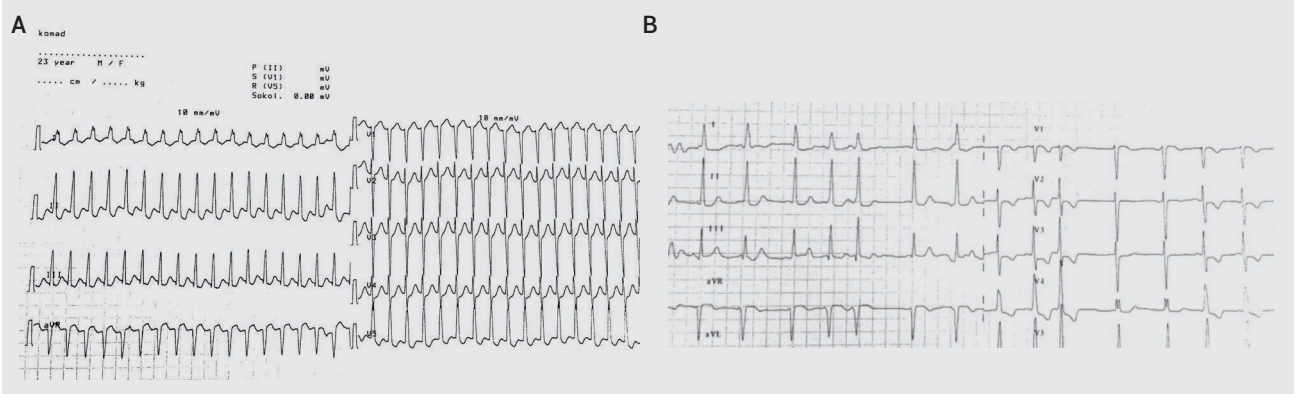

FIGURE 6. 12-lead ECG in pregnant patient with mechanical mitral valve; A) Supraventricular tachycardia 194/min; B) Sinus rhythm, after conversion with verapamil.

U metaanalizi studija[9] koje su ispitivale najbolju antikoagulacijsku terapiju u trudnica s mehaničkim zalistkom, različiti antikoagulacijski terapijski režimi imali su različit utjecaj na smrtnost majke, tromboembolijski rizik, funkcionalnost valvule, ali i na spontani pobačaj fetusa, njegovu smrt i prirođene defekte. Varfarin je najbolji lijek za prevenciju tromboze zalistka (samo 5 %-tni rizik za majku), ali znači veliki teratogni rizik za dijete (do 45 %). Prisutan je i rizik od fetalnoga krvarenja (lijek prelazi placentarnu membranu). Niska doza varfarina (ako je dovoljna za dobru kontrolu koagulacije) nosi mnogo manji rizik, no u prvome tromjesečju treba je izbjegavati. Heparin ima oko 15 % rizika i za dijete, ali i za majku. Frakcionirani je heparin mnogo jednostavniji za uporabu. U nekih se bolesnika terapija može kombinirati: frakcionirani heparin u prva 3 i zadnja 2 mjeseca, a varfarin između toga, no nema idealnoga antikoagulacijskog režima u trudnoći!

SLUČAJ 5

MI, 1973. God., AV kanal (veliki VSD i „singl" atrij), teška PS

- Cijanoza od djetinjstva, ali zbog kompleksnosti greške operacija nije bila moguća.
- Godine 1998. u dobi od 25 godina učinjena Kawashima operacija (Fontanova cirkulacija).
- Godine 2000. normalna trudnoća, rodila vaginalnim putem normalnu djevojčicu, male porođajne težine
- Godine 2003. i 2006. zatvaranje pulmonalnih AV fistula
- Posljednje dvije godine pojava ascitesa, umjerena redukcija EF-a, bez znatne regurgitacije sustavne valvule, bez stenoza provodnika i bez PLE-a, kronična jetrena lezija, suspektna bolest jajnika (Meigsov sindrom?), adneksektomija u srpnju 2017., no ascites je i dalje prisutan, ali je klinički status stabilan.

Ovo je jedina pacijentica s Fontanovom cirkulacijom u našem PSBO registru s uspješnom trudnoćom. Nekomplicirana trudnoća možda je rezultat činjenice da je inicijalna operacija učinjena kasno (s 25 godina). Većina naših bolesnica s Fontanovom cirkulacijom opterećena je uobičajenim komplikacijama, koje se pojavljuju 20-ak godina nakon operacije, upravo kad dosegnu dob za trudnoću.

Trudnoća nakon operacije po Fontanu povezana je s visokim postotkom spontanog pobačaja. Rane[10] i kasne[11] studije donose iste zaključke: spontani pobačaj u trećine trudnica s Fontanovom cirkulacijom. Sedamdeset posto trudnoća završava preuranjenim porođajem, što znatno utječe na mortalitet i morbiditet djeteta. Kardiološke komplikacije u majke su rijetkost, a mortalitet nije zabilježen.

Bolesnice s PSBO-om kojima se trudnoća nikako ne preporučuje (WHO IV.)

1. Eisenmengerov sindrom (50 % mortalitet majke).
2. Marfanov sindrom s dilatiranim korijenom aorte >4,5 cm.
3. Teška aortna stenoza / koarktacija.
4. Ejekcijska frakcija <35 % sustavne klijetke.
5. Teška pulmonalna hipertenzija

Rizik za dijete u trudnica s PSBO-om uključuje:

- restrikciju rasta ploda (Fontanova cirkulacija, cijanoza, uporaba beta-blokatora)
- preuranjen porođaj (spontano ili katkad ijatrogeno)
- teratogenost (lijekovi)
- rekurencija PSBO-a je rijetka (3 – 5 %, uključujući i oca).

fetal spontaneous abortion, death, and congenital defects. Warfarin is the best drug for the prevention of valve thrombosis (only 5% risk for the mother) but has a high impact on congenital defect incidence in the fetus (up to 45%). There is also a risk of fetal hemorrhage (the drug is crossing placental membrane). Low-dose warfarin (if it is sufficient for good coagulation control) carries a much smaller risk. It should be avoided in the first trimester. Heparin carries approximately 15% risk for the child but also for the mother as well. Fractionated heparin is easier to use. The following combination can be recommended in some patients: fractionated heparin in the first 3 and last 2 months with warfarin in between; however, there is no a perfect anticoagulation regime for pregnancy!

CASE 5

MI, 1973, AV canal (large VSD and single atrium), severe PS

- Cyanotic from childhood, rejected for reconstruction due to complexity.
- 1998: Kawashima operation at 25 years of age (Fontan circulation).
- 2000: normal pregnancy, gave birth to a small but healthy girl by vaginal delivery.
- 2003 and 2006: pulmonary AV fistula closure.
- Last 2 years: ascites, moderate reduction of EF, no systemic valve regurgitation, no conduits stenosis, no evidence of PLE, chronic hepatic lesion, suspect ovarian disease (Meigs syndrome?); adnexectomy 7/2017, ascites still present, but clinical status is stable.

This case represents the only Fontan patients with a successful pregnancy in our ACHD registry. The uncomplicated pregnancy may be result of late initial operation (at 25 years of age). The majority of our Fontan patients, are burdened with the usual complications occurring 20 years after the operation, when they reach the age for pregnancy.

Pregnancy after Fontan operation is associated with a high miscarriage rate. Older[10] and more recent[11] studies all reached the same conclusions: miscarriage occurs in 1/3 pregnancies in Fontan patients, and 70% pregnancies end with premature delivery, which has an impact on infant mortality and morbidity. Cardiac events are rare, and maternal mortality was not recorded.

Group of patients with ACDH strongly discouraged from pregnancy (WHO IV)

1. Eisenmenger syndrome (50% maternal mortality).
2. Marfan's syndrome with dilated aortic root (>4.5cm).
3. Severe aortic stenosis/coarctation.
4. Systemic ventricular ejection fraction <35%.
5. Severe pulmonary hypertension.

The risks for the baby in pregnant women with ACHD includes:

- Fetal growth restriction (Fontan circulation, cyanosis, beta-blockers users).
- Preterm delivery (spontaneous, sometimes iatrogenic).
- Teratogenicity (drugs).
- Recurrence of congenital heart disease is rare (3-5%, including paternal disease).

Lijekovi tijekom trudnoće veliki su problem. Postoje tzv. **sigurni lijekovi** (digoksin, blokatori kalcijskih kanala, beta-blokatori, tiazidi i furosemid, heparin, sildenafil, acetilsalicilatna kiselina u niskoj dozi). Neke od tih lijekova treba davati s oprezom u prvome tromjesečju trudnoće, neki usporuju rast ploda, a za neke se preporučuje pratiti koncentraciju. Neki lijekovi u trudnoći **nisu sigurni** ili njihovo djelovanje nije poznato (ACE i ARB inhibitori, varfarin u prva tri mjeseca, spirinolakton, bosentan, amiodaron itd.).

Tijekom porođaja naglasak je na njegovu planiranju i određivanju termina (ako je potrebno, pažljivo ga inducirati). U intermedijarnih i visokorizičnih bolesnica s PSBO-om porođaj treba biti u tercijarnom centru, a vrstu porođaja treba razmotriti s opstetričarom. U većine se bolesnica preporučuje vaginalni porođaj. Treba razmišljati o poziciji u vrijeme porođaja (sjedeća), analgeziji i trajanju porođaja. Antibiotska se profilaksa ne preporučuje pri vaginalnom porođaju. Carski rez treba izabrati u opstetričkim indikacijama, ali i pri nekim kardiološkim indikacijama: Marfanov sindrom, srčano popuštanje, mehaničke valvule.

Komplikacije se mogu očekivati u postporođajnom razdoblju, kao što su hemodinamske promjene (srčano popuštanje i plućni edem, hipertenzija, promjene u smjeru pretoka i cijanoza), krvarenja (pažljivo praćenje antikoagulacijske terapije), tromboembolijski incidenti (plućni ili sustavni u bolesnica s pretokom) i infekcije, koje su učestalije nakon carskog reza.

Zaključak

- Broj se bolesnica s PSBO-om povećava te se očekuje više trudnoća.
- Trudnoća je moguća u većine žena s PSBO-om, ali je prisutan povećani rizik i za majku i za plod.
- Strategiju, potencijalne rizike i moguće terapijske mogućnosti potrebno je prodiskutirati s bolesnicom.
- Rizik može biti smanjen dobrom kardiološkom skrbi u specijaliziranom centru za PSBO uz dostupan multidisciplinarni tim.
- Prema našem iskustvu, najosjetljivije razdoblje jest vrijeme tranzicije s pedijatrijske u odraslu kardiološku skrb.

Medication during pregnancy is of great concern. There are **safe drugs** (digoxin, Ca-channel blockers, beta-blockers, thiazide and furosemide, heparin, sildenafil, low dose aspirin). Some of these drugs should be given with caution in the first trimester, some can reduce fetal growth, and for some, drug concentration monitoring is recommended. Some drugs are **not safe drugs** or at least not proven to be safe (ACE and ARB inhibitors, warfarin in the first trimester, spironolactone, bosentan, amiodarone, etc.).

In peripartal care, the emphasis is on delivery planning and timing (and careful induction if necessary). In intermediate and high-risk patients, delivery should take place in a tertiary center, and the mode of delivery should be discussed with the obstetrician. In general, vaginal delivery is recommended. The birth position, analgesia, and time control must be considered. Antibiotic prophylaxis is not recommended in vaginal delivery. Cesarean section should be chosen for obstetric indications and selective cardiac states: Marfan syndrome, heart failure, mechanical valves.

Complications in post-partal care can be expected, such as hemodynamic changes (heart failure and pulmonary edema, hypertension, shunting changes, and cyanosis), hemorrhagic complication (careful anticoagulation therapy monitoring); thromboembolic incidents are possible (pulmonary, systemic in patients with shunts), and incidence of infection is higher after section.

Conclusion

- The number of patients with ACHD is growing; more pregnancies in these patients are expected.
- Pregnancy is possible in most women with ACHD, but there is an increased risk for the mother and fetus.
- Strategy, potential risks, and therapy choices if necessary, should be discussed with the patient.
- The risk can be diminished with proper care in a specialized ACHD center, with a multidisciplinary team available.
- In our experience, the most vulnerable period is the transition from pediatric to adult care.

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