Liječenje terminalnog zatajivanja srca u pacijenata s prirođenim srčanim bolestima

Treatment of Terminal Heart Failure in Grown Up Congenital Heart Disease

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SAŽETAK: Srčano zatajivanje vodeći je uzrok smrti u odraslih pacijenata s prirođenim srčanim bolestima, no taj se problem često može previdjeti zbog dobre tolerancije simptoma i niskih očekivanja o funkcionalnom kapacitetu kod većine. Premda neurohormonalna aktivacija prati isti obrazac kao i u zatajivanju srca kod stečene bolesti, temeljni pristupi u medicinskoj terapiji nisu uspjeli pružiti značajnu korist u smanjenju smrtnosti, najvjerojatnije zbog velikog raspona različitih uzroka srčanog popuštanja prisutnih u različitim morfologijama prirođenih srčanih bolesti, kao i onih povezanih s posebnim kirurškim zahvatima. Presađivanje srca moguće je izvesti u pacijenata s terminalnim zatajivanjem srca, no njihovo pravodobno otkrivanje i određivanje optimalnog trenutka za zahvat problematični su zbog niske osjetljivosti trenutačno postojećih metoda funkcijskog testiranja na otkrivanje promjene između stabilnog stanja niskoga funkcionalnog kapaciteta i pogoršanja. Moždani natriuretski peptid pokazao se kao dobar pokazatelj prognoze i detektor pogoršanja te bi u takvih pacijenata trebao biti redovito kontroliran tijekom praćenja.

SUMMARY: Heart failure (HF) is the leading mortality cause in adult congenital heart disease patients, but this problem is very often overlooked in these patients due to good tolerance of symptoms as well as low expectations for functional capacity in many of those patients. Although neurohormonal activation follows the same pattern as does HF in acquired disease, the cornerstones of medical therapy have failed to provide significant benefits in mortality reduction, most probably due to a very diverse range of causes for HF that are present in different morphologies of congenital heart disease, as well as connected to specific surgical treatments. Heart transplantation can be performed in patients with terminal HF, but detecting those and determining the optimal moment for enlisting is problematic due to the low sensitivity of currently applied functional testing methods to detect change between a steady state of low functional capacity and deterioration. B-type natriuretic peptide blood test is a good marker of prognosis and deterioration and should be monitored on a regular basis in these patients.

KLJUČNE RIJEČI: prirođena srčana bolest u odraslih, srčano zatajivanje, presađivanje srca.

KEYWORDS: grown-up congenital heart disease, heart failure, heart transplantation.

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Prema klasičnoj definiciji srčanog zatajivanja riječ je o kliničkom sindromu pri kojemu srce ne može ispuniti potrebe tijela. Novija definicija *American College of Cardiology* nešto je detaljnija te ga određuje kao složeni klinički sindrom koji može nastati kao posljedica svakoga strukturnog ili funkcionalnog srčanog poremećaja koji narušava sposobnost klijetke da se ispuni krvlju ili je istisne[1]. Pretpostavlja se, što je vjerojatno i točno, da gotovo svaki oblik srčane bolesti može dovesti do razvoja popuštanja srca[2]. No, postoji i populacija pacijenata koji, premda is-

The classical definition of heart failure (HF) states that it is a clinical syndrome in which the heart cannot meet the demands of the body. A more recent definition by the American College of Cardiology goes into more depth to define it as a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood[1]. It has been suggested, and it is probably correct, that virtually any form of heart disease can lead to the development of HF[2]. There is, how-

punjavaju kriterije za zatajivanje srca možda i više nego bilo koja druga skupina, tj. imaju prilično značajnu „srčanu nepravilnost", i dalje ostaju donekle zanemareni kad je riječ o popuštanju srca te o njegovu liječenju.

Što znači zatajivanje srca u odraslih pacijenata s prirođenom srčanom bolesti?

Neovisno o tome o kakvoj je ozljedi srca riječ, bilo da se radi o infarktu, infekciji, toksinu, genetskoj nepravilnosti, arterijskoj hipertenziji ili bolesti zalistka, može doći do nastanka zajedničkog sindroma koji obilježavaju progresivno ograničenje tjelesne sposobnosti i neurohormonalna aktivacija. Stoga bi moglo biti korisnije gledati na popuštanje srca kao na kontinuitet od asimptomatske slabije funkcije klijetke s umjerenom neurohormonalnom aktivacijom do ozbiljne disfunkcije sa simptomima u mirovanju i izraženom neurohormonalnom aktivacijom[3].

Popuštanje srca kod prirođenih srčanih bolesti spoj je nasljednih čimbenika i stečenih stresora. Kod ovih pacijenata popuštanje srca vjerojatnije je posljedica višegodišnjih ustrajnih nepravilnosti u arterijskom tlaku i/ili volumenu, a ne posljedica gubitka miocita zbog infarkta miokarda ili naslijeđenih intrinzičnih abnormalnosti stanica miokarda[3]. Premda je dugo nedostajalo literature o ovoj temi, u tom je području u međuvremenu došlo do znatnog napretka te se pokazalo kako je neurohormonalna aktivacija prisutna u prirođenim srčanim bolestima odraslih (PSBO), kako u simptomatskim, tako i u asimptomatskim bolestima[4]. Dosta podataka pokazuje da pacijenti sa složenim prirođenim srčanim bolestima, čak i nakon kirurškog zahvata, često imaju povišene razine moždanoga natriuretskog peptida (BNP) koje koreliraju s klasifikacijom udruge *New York Heart Association* (NYHA) i smrtnošću[5-7]. Osim toga, neurohormonalna aktivacija u bolesnika s PSBO-om nosi obilježja kroničnog zatajivanja srca u kojih se događa porast vezan za težinu simptoma i izraženost slabije funkcije klijetke te nije nužno vezan uz anatomski supstrat[4].

Koji je utjecaj popuštanja srca na bolesnike s prirođenom srčanom boleš ću?

Prema postojećim procjenama, broj odraslih osoba s prirođenim srčanim bolestima iznosi 1,2 milijuna u Europi i oko milijun u SAD-u[8,9]. To je posljedica velikih napredaka u kardiotorakalnoj kirurgiji i pedijatrijskoj srčanoj njezi tijekom posljednjih pedeset godina. Nažalost, jednom kada ti pacijenti dosegnu zrelu dob, i dalje su suočeni s povećanim rizikom od smrti u usporedbi s općom populacijom[10]. Proučimo li registar CONCOR (državni registar pacijenata s prirođenim srčanim bolestima u Nizozemskoj), koji procjenjuje rizik i uzroke povećane smrtnosti u odraslih pacijenata s prirođenim srčanim bolestima, primijetit ćemo kako je zatajivanje srca vodeći uzrok smrti[11]. Vjerojatnost popuštanja srca povećava se s godinama i ovisi o izvornoj nepravilnosti te je najveća u bolesnika s jednom klijetkom, Fallotovom tetralogijom (TOF) i transpozicijom velikih arterija (TGA)[11,12].

Varljivo ponašanje simptoma u bolesnika s prirođenim srčanim bolestima

Simptomi su u ovakve populacije vrlo česti s oko 25 % pacijenata nakon Fontanove operacije simptomatično deset godina nakon zadnjeg zahvata[13], 75 % neoperiranih bolesnika s prirođeno

ever, a population of patients who, despite fulfilling the defining criterion for HF possibly better than any other group, i.e. that of having an important 'abnormality of the heart', have remained somewhat overlooked with regard to an appreciation of their HF and its treatment.

What constitutes heart failure in grown up congenital heart disease?

Regardless of the injury to the heart, be it by infarction, infection, toxin, genetic abnormality, hypertension or valve disease, a common syndrome can develop that is characterized by progressive exercise limitation and neurohormonal activation, and so it might be more helpful to view HF as a continuum from asymptomatic ventricular dysfunction with modest neurohormonal activation to severe ventricular dysfunction with symptoms at rest and marked neurohormonal activation[3].

HF in congenital heart disease is a combination of inherited factors and acquired stressors. Rather than due to the loss of myocites due to myocardial infarction or by inherited intrinsic abnormalities in myocardial cells, HF in these patients is most probably sculpted over many years by persistent abnormalities in cardiac pressure and/or volume[3]. Literature, quite silent on the topic for a long while, has now shown a significant progress in the field showing that neurohormonal activation is present in grown up congenital heart disease (GUCH), both in symptomatic and asymptomatic patients[4]. There is sufficient data showing that patients with complex congenital heart disease, even if surgically repaired, often have elevated B-type natriuretic peptide (BNP) levels that correlate both with NYHA Class and mortality[5-7]. Not only that, but neurohormonal activation in GUCH bears the hallmarks of chronic heart failure, increasing in relation to the symptom severity and ventricular dysfunction and not necessarily connected to the anatomic substrate[4].

What is the impact of heart failure in grown up congenital heart disease?

Current estimates place the ever expanding population of adults with congenital heart disease at 1.2 million in Europe and around 1 million in USA alone[8,9]. This is the result of major advances in cardiothoracic surgery and pediatric cardiac care over the last five decades. Unfortunately, when those patients reach adulthood, they still face and increased risk of death compared to the general population[10]. When we take the look at the CONCOR Registry which assessed the risks and causes of the increased mortality in GUCH patients, we find that HF is the leading cause of death[11]. The probability of HF appearing increases with age and is dependent on the original defect with single ventricles, Tetralogy of Fallot (TOF) and transposition of great arteries (TGA) having the greatest risk[11,12].

Disingenuous behavior of symptoms in patients with grown up congenital heart disease

Symptoms are quite frequent in this population with around 25% of Fontan patients symptomatic 10 years following procedure[13], 75% of unoperated congenitally corrected TGAs present-

ispravljenim TGA-om koji imaju simptome[14] te a 79 % pacijenata sa složenim prirođenim srčanim bolestima koji imaju ograničenja funkcijskog kapaciteta u klasi II ili više prema NYHA klasifikaciji[4]. S druge strane, odrasli pacijenti s prirođenim srčanim bolestima često su asimptomatični ili tvrde da nemaju simptome zato što cijelog života žive s njima, pa se ne obaziru na manje promjene u podnošenju tjelesnog napora[15].

Nekoliko istraživanja o funkcijskom kapacitetu provedenih na skupinama bolesnika sa složenijim oblicima PSBO-a pokazuju da pacijenti sa simptomima imaju znatno sniženu funkcijsku sposobnost u usporedbi s pacijentima bez simptoma, no obje skupine imaju znatno sniženo podnošenje tjelesnog napora te snižen kardiovaskularni kapacitet u usporedbi sa zdravom populacijom[16-18]. Na **slici 1.** vidimo da razliku između pretkliničkog i kliničkog zatajivanja u ovoj populaciji čini jedino prisutnost ili odsutnost simptoma, a drugih znakova gotovo da i nema.

Liječenje i kako mu pristupiti?

Uzmemo li u obzir činjenicu da u mnogim obilježjima popuštanje srca u bolesnika s PSBO-om oponaša kongestivno srčano zatajivanje zbog drugih uzroka, mogli bismo zaključiti kako bi liječenju trebalo pristupiti na jednak način. No, proučimo li temelje medicinskog liječenja prema postojećim smjernicama za popuštanje srca, tj. beta-blokatore, inhibitore angiotenzin konvertirajućeg enzima (ACE inhibitori), blokatore angiotenzinskih receptora te antagoniste mineralokortikoidnog receptora, primijetit ćemo da se njihova učinkovitost kod PSBO-a znatno razlikuje u usporedbi s općom populacijom koja boluje od popuštanja srca. Kao prvo, takvi su pacijenti jednoglasno isključeni iz svih većih randomiziranih i kontroliranih testiranja navedenih lijekova. Osim toga, sada postoji niz manjih, ali ipak randomiziranih i kontroliranih kliničkih ispitivanja koja nisu uspjela pokazati značajnu dobrobit tih terapija pri liječenju prirođenih srčanih bolesti[19-24].

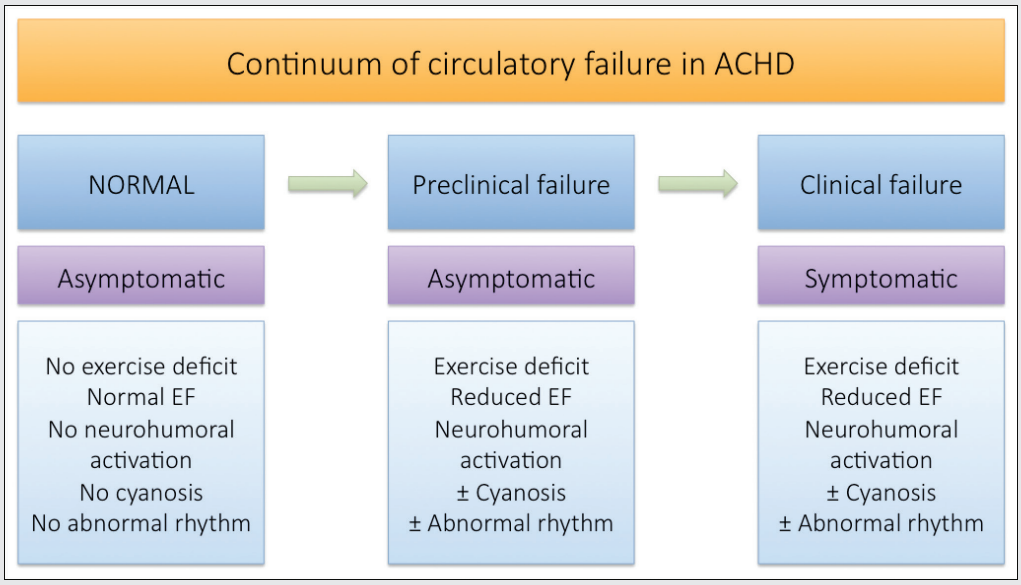
ing symptomatic[14], and 79% of patients with complex congenital heart disease having NYHA Class II or higher limitation in functional capacity[4]. On the other hand, GUCH patients are often asymptomatic or claim no symptoms due to the fact that living with symptoms has been a lifetime constant so little attention is attributed to minor variations in exercise tolerance[15].

Looking at several exercise studies performed in adult patient groups with more complex congenital disease, although patients with symptoms have significantly reduced exercise capacity compared to patients without symptoms, both groups have significantly lower exercise tolerance and cardiovascular capacity compared to the healthy population[16-18]. Looking at **Figure 1** we see that the difference between preclinical and clinical failure in this population is exclusively marked by the presence or absence of symptoms, but not much else.

Treatment and how do we approach it?

If we take into account that in many accounts HF in GUCH mimics congestive HF from other causes, we might draw the conclusion that we should approach the treatment in the same way. If we look at the cornerstones of medical therapy according to the current guidelines, the beta-blockers, ACE inhibitors, angiotensin receptors blockers and mineralocorticoid receptor antagonists, their results in GUCH patients significantly differ compared to the general HF population. First of all, these kind of patients where unanimously excluded from all the major randomized controlled trials of all of there drugs. Further on, there are now a host of, albeit small, randomized and controlled trials that have failed to show a significant clinical benefit of these therapies in congenital heart disease[19-24].

When looking at the failure of systemic morphologically left ventricle it may be reasonable to follow current HF guidelines[25], but in the case of a failing systemic right ventricle or a single ventricle morphology studies have not been as



EF = Ejection fraction, ACHD = Adult congenital heart disease

FIGURE 1. Progression of circulatory failure through phases.

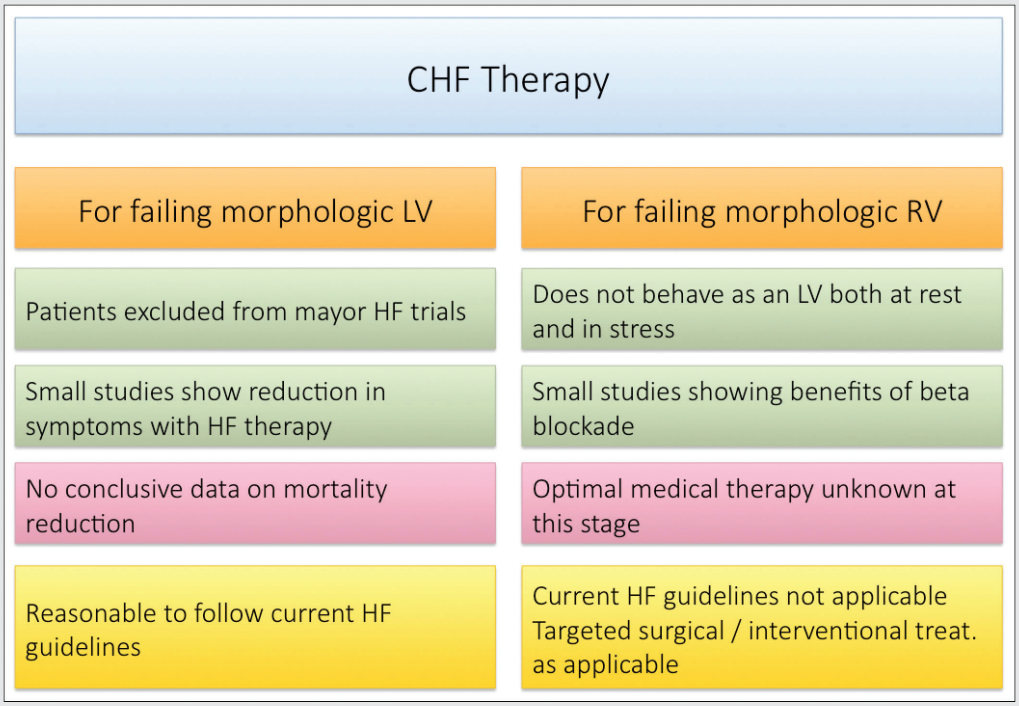


FIGURE 2. Overview of therapeutic modalities for heart failure in grown up congenital heart disease patients.

Pri proučavanju zatajivanja sistemske morfološki lijeve klijetke možda je razumno pratiti postojeće smjernice o zatajivanju srca[25], no, u slučaju zatajivanja sistemske desne klijetke ili kod morfologije jedne klijetke istraživanja ne podupiru u istoj mjeri sve navedene lijekove, osim beta-blokatora, za koje je pokazano pozitivno remodeliranje desne klijetke, smanjenje simptoma i povećanje tolerancije na tjelesni napor, no brojke u tim istraživanjima nisu bile dovoljne da bi mogle pokazati smanjenje smrtnosti[26-28]. Vjerojatno je temeljni problem to što samo usredotočenost na neurohormonalne putove nije dovoljna ako se suočavamo s brojnim čimbenicima koji utječu na djelotvornost dotične klijetke. Primjerice, u jednom zanimljivom istraživanju (*Derrick i sur.*) pokazalo se da je u pacijenata nakon operacije zamjene pretklijetki (Senning, Mustard) pad u srčanom volumenu tijekom tjelesnog napora ili infuzije dobutaminom posljedica smanjenoga atrio-ventrikularnog prijenosa krvi, a ne sistoličkog zatajivanja desne klijetke[29]. Nadalje, u pacijenata s prirođeno ispravljenom TGA, insuficijencija sistemskog (trikuspidalnog) zalistka bila je važan pretkazatelj disfunkcije desne klijetke i smrtnosti[30]. Oba ova nalaza podržavaju uvjerenje prema kojemu dodatno smanjenje tlačnog opterećenja medikamentnom terapijom u takvih pacijenata može biti pogrešan cilj za intervenciju, već treba uzeti u obzir moguće kirurške/intervencijske zahvate. Pregled terapijskih pristupa prikazan je na **slici 2.**

Presađivanje srca u odraslih pacijenata s prirođenim srčanim bolestima

Glavne patologije pri kojima se poduzima presađivanje srca u bolesnika s PSBO-om jesu sistemska desna klijetka, jednokomorno srce s Fontanovom cirkulacijom ili bez nje te Fallotova

supportive in the case of all of those drugs except for beta-blockers that show some positive RV remodeling, symptom reduction and exercise tolerance increase, but the numbers in the studies were insufficient to show any mortality benefit[26-28]. The underlying problem is probably that just targeting the neurohormonal pathways is largely insufficient if we are dealing with a multitude of factors that influence the performance of said ventricle. For example, in this very interesting study by *Derrick et al* it has been shown that in patients after atrial redirection procedure a fall in stroke volume during exercise or dobutamine infusion was a consequence of of impaired atrioventricular transport rather than right ventricular systolic failure[29]. Furthermore, in patients with congenitally corrected TGA, those with significant systemic (tricuspid) valve insufficiency was a significant predictor of RV dysfunction and mortality[30]. Both of those findings support the notion that in these patients further afterload reduction with medical therapy could be a flawed target of intervention in the short term, and surgical/interventional procedures should be considered. A broad overview of therapeutic approach is presented in **Figure 2**.

Heart transplantation in grown up congenital heart disease

The main underlying pathologies for heart transplantation (HTx) in adult congenital heart disease are systemic right ventricles, univentricular heart with or without Fontan circulation, and tetralogy of Fallot[31]. They constitute a fairly small number of overall cardiac transplant patients with International Society for Heart and Lung Transplantation (ISHLT)

tetralogija[31]. Svi oni zajedno čine prilično malen udio ukupnoga broja pacijenata kojima treba presađivanje srca, a prema Registru međunarodnog društva za transplantaciju srca i pluća (ISHLT), otprilike 2 % svih presadbi srca otpada na ovu skupinu[32].

Pravodobno prepoznavanje mogućih kandidata za presađivanje srca od ključne je važnosti te u bolesnika sa stečenim bolestima srčanog mišića maksimalna potrošnja kisika u vremenu (V_{O2}) služi kao važan kriterij za pacijentovo uvrštavanje na listu čekanja za presadbu srca. Uobičajeno maksimum od < 12 do 14 mL/kg/min služi kao granična vrijednost. U bolesnika s PSBO-om pokazalo se da je sniženi V_{O2} povezan s povećanim rizikom od hospitalizacije i smrti[33,34], ali ostaje problem što subjektivan dojam samih bolesnika s PSBO-om o toleranciji fizičkog napora vrlo često ne odgovara objektivnim mjerenjima kapaciteta za tjelesni napor[35]. Problem leži u činjenici da mnogi pacijenti već započinju svoj klinički tijek sa sniženim V_{O2} u odnosu prema zdravoj populaciji te održavaju razine koje su vrlo blizu onima koje se očekuju kod kandidata za presađivanje srca, premda su simptomatski u redu[16], te tako postaju naviknuti na takvo stanje niže potrošnje, a njihovi subjektivni dojmovi o toleranciji tjelesnog napora ne odgovaraju objektivnim mjerenjima[35]. Drugi pokazatelj na koji bismo se mogli osloniti, BNP, potencijalno može biti iznimno vrijedan jer se pokazalo da predviđa iznenadnu srčanu smrt i ventrikularne poremećaje ritma čak i u onih bolesnika s PSBO-om koji nemaju zatajivanje srca. Osim toga, pokazalo se da je povećanje koncentracije BNP-a tijekom praćenja dobar pretkazatelj smrtnosti[36,37]. Stoga je preporučljivo u praćenju takvih bolesnika redovito i uzastopno testirati funkcijski kapacitet te pratiti BNP. Osim navedenog, i drugi čimbenici poput anemije, hiponatremije i bubrežne disfunkcije dokazani su znakovi povećanog rizika za smrtnost u ovakvih bolesnika, a mogu im se pridodati i plućna hipertenzija, ponovljena hospitalizacija zbog zatajivanja srca i srčana kaheksija[38-40].

Osim toga, ako takvi bolesnici i budu podvrgnuti transplantaciji srca, rizik od komplikacija mnogo je veći nego kod uobičajene transplantacije, a bolesnici s prethodnim Fontanom, klasičnim Glennom ili bilo kojom drugom vrstom jednokomorne cirkulacije na kojoj je prije toga izveden kardiokirurški zahvat imaju još i viši rizik od postoperativnih komplikacija i smrtnosti[41]. U bolesnika s neispravljivom plućnom hipertenzijom (nepromjenjiv indeks plućne vaskularne rezistencije / PVR/ >5 WU/m^2 ili transplućni gradijent >15 mmHg koji ne reagira na vazodilatatornu terapiju) u obzir dolazi kombinirano srčano-plućno presađivanje[42]. O kojemu god obliku liječenja bila riječ, rano uključivanje kardiokirurga specijaliziranog za PSBO od presudne je važnosti u procjeni rizika, a samu operaciju također bi trebao obaviti kirurg s iskustvom u operacijama prirođenih srčanih bolesti. Premda je smrtnost u ranome postoperativnom periodu veća, dugoročno je rizik od smrti sličan kao i u ostalih kandidata za presađivanje srca te je u principu samo rani period onaj uistinu rizičan za takve bolesnike[43].

Rasprava

Liječenje bolesnika s PSBO-om i kliničkim aspektima popuštanja srca i dalje ostaje izazov. Optimalna medikamentna terapija ostaje nedovoljno dokazana, a premda je glavne smjernice za liječenje srčanog zatajivanja moguće primijeniti na bolesnike s popuštanjem morfološki lijeve klijetke, bolesnici

Registry reporting around 2% of heart transplant cases falling inside this cathegory[32].

Timely identification of possible candidates for HTx is essential, and in patients with acquired heart disease, maximal oxygen consumption per unit time (V_{O2}) has been used as an important criterion for listing for transplantation. Traditionally maximum of <12–14 mL/kg/min has been used as a cutoff value. It has also been shown in GUCH patients that reduced V_{O2} is associated with increased risk of hospital admission and death[33,34] and self-reported exercise tolerance poorly correlated with objective measures of exercise capacity[35]. Huge problem in this method is that many patients start their clinical journey with a reduced V_{O2} compared to the normal population and maintain levels which are quite close to what would be expected in HTx candidates while symptomatically fine[16], and self-reported excercise tolerance poorly correlates with objective measurements of exercise capacity[35]. Another marker that we might fall upon, BNP, has the potential to be very valuable since it has been shown to predict sudden cardiac death and ventricular arrhythmias even in GUCH patients not presenting with HF and temporal increases in BNP concentration have been found to predict mortality[36,37]. Therefore, it would be prudent to perform serial standardized exercise testing and BNP measurements in long-term follow-up of GUCH patients. Some other factors, such as anemia, hyponatremia and renal dysfunction have been identified as risk markers for mortality in GUCH patients, as are pulmonary hypertension, recurrent hospital admissions for heart failure and cardiac cahexia[38-40].

Furthermore, if these patients undergo HTx, the risk of complications is significantly higher than in normal HTx and patients with previous Fontan, classic Glenn or any kind of univentricular heart that has previously undergone cardiac surgery are at an even more increased risk of perioperative morbidity and mortality[41]. Patients with an irreversible pulmonary hypertension (fixed PVR index of >5 WU/m^2 or a transpulmonary gradient >15 mmHg not responsive to vasodilator therapy) may be candidates for combined heart-lung transplantation[42]. Whatever the plan, early involvement of congenital heart cardiac surgeons is crucial in assessing the risk and the transplantation should be performed by a surgeon experienced in congenital heart surgery. Although mortality in early postoperative period is higher, long-term mortality falls in line with other types of heart transplant candidates[43].

Discussion

Treatment of GUCH patients with clinical aspects of HF remains challenging. Medical therapy remains unproven, and while general HF guidelines can be extrapolated on patients with the failure of the morphologic left ventricle, patients with a failure of morphologic right ventricle or single ventricle morphology behave differently. Beta-blocker therapy remains as the only one with any proven benefit in those patients. HTx, although viable alternative, is fraught with perioperative and early postoperative mortality, while determining the right timing for enlisting patients on the heart transplant list remains a challenge.

s popuštanjem morfološki desne klijetke ili s morfologijom samo jedne klijetke ponašaju se drukčije. Terapija beta-blokatorima i dalje je jedina s dokazanim dobrobitima za takve pacijente, dok sve druge skupine ne pokazuju poboljšanje. Premda je presađivanje srca valjana alternativa, problematična je zbog brojnih slučajeva rane postoperativne smrtnosti, a određivanje pravoga trenutka za uvrštavanje pacijenata na popis za presadbu srca i dalje je izazov.

U budućnosti je potrebno definirati optimalnu medikamentnu terapiju, što je moguće samo putem kontroliranih i randomiziranih ispitivanja nad odabranim podskupinama bolesnika s PSBO-om bez gomilanja različitih kongenitalnih morfologija s najvjerojatnije različitim uzročnicima popuštanja srca u isto praćenje kako bi se dostigle dostatne brojke. Osim navedenog, nadu za bolju budućnost pruža i mogućnost liječenja različitim medicinskim uređajima. Resinkronizacijska terapija mogla bi biti korisna pri sistoličkom popuštanju sistemske klijetke uz prisutno izrazito produljenje QRS kompleksa, što često nalazimo u bolesnika s prirođeno ispravljenom TGA ili nakon operacije zamjene pretklijetki, no, dok se spomenuta terapija ne pokaže djelotvornom u kliničkom istraživanju, ne možemo reći da će biti korisnija od mnogih drugih terapija koje pokazuju korist u stečenim oblicima popuštanja srca, dok su se u ovakvih bolesnika pokazale neučinkovitima. Uređaji za mehaničku cirkulatornu potporu sve se više rabe u djece kao privremeno rješenje prije presađivanja srca, no potrebno je više iskustva s odraslima, a potrebne su i određene kirurške vještine koje ne pronalazimo u većini kirurških centara, jer su sami uređaji većinom osmišljeni kao potpor morfološki lijevoj klijetki te se teže prilagođuju kompleksnoj morfologiji u PSBO-u.

The future needs to address the question of optimal medical therapy with controlled randomized studies in selected subgroups of patients with GUCH without hoarding different congenital morphologies with most likely different causes of HF to reach adequate numbers. Device therapy also holds promise in these patients. Cardiac resynchronization therapy might be helpful in failing ventricles with long QRS complexes like those often found in patients with ccTGA or atrial switch TGA, but until any kind of study is performed, it's use remains unproven. Ventricular assist devices are now used more and more in children as a bridge-to-transplant solution but need more experience in adults, as well as specific subset of surgical skills not found in most surgical centres, and are mostly designed for the support of a morphologic left ventricle.

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