Hipertrofija lijeve klijetke u djece i adolescenata s arterijskom hipertenzijom

Left ventricular hypertrophy in children and adolescents with arterial hypertension

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SAŽETAK: Arterijska hipertenzija u djece i adolescenata postala je sve važniji javnozdravstveni problem jer je njezina prevalencija u porastu. Longitudinalne su studije pokazale da će djeca, a osobito adolescenti s arterijskom hipertenzijom vjerojatno postati hipertenzivni odrasli s rizicima od kardiovaskularnih bolesti. Iako su kardiovaskularne bolesti vrlo rijetke u djetinjstvu, povišen arterijski tlak može već u dječjoj i adolescentnoj dobi uzrokovati promjene na ciljnim organima. Hipertrofija lijeve klijetke najčešće je traženo oštećenje ciljnih organa uz pedijatrijsku hipertenziju. U više različitih studija nađena je pozitivna korelacija između visine arterijskoga tlaka i indeksa mase lijeve klijetke, a prevalencija hipertrofije lijeve klijetke u djece s hipertenzijom je 8–41 %. Uočena je povezanost arterijske hipertenzije u djece i adolescenata i krutosti arterija, debljine intime-medije, kao i drugih kardiovaskularnih rizika.

SUMMARY: The growing prevalence of arterial hypertension in children and adolescents is becoming an ever-greater public health problem. Longitudinal studies show that children and in particular adolescents with arterial hypertension are highly likely to become hypertensive adults, including the risk of cardiovascular disease. Although cardiovascular diseases are very rare in childhood, elevated arterial pressure can cause lesions of target organs already in childhood and adolescence. Left ventricular hypertrophy is a target organ lesion that is most frequently searched for in pediatric hypertension. Several studies have reported positive correlation between arterial pressure and left ventricular mass index, while the prevalence of left ventricular hypertrophy in children with hypertension was 8–41%. An association was found of arterial hypertension in children and adolescents with arterial stiffness, intima-media thickness, and other cardiovascular risks.

KLJUČNE RIJEČI: arterijska hipertenzija, djeca, adolescenti, hipertrofija lijeve klijetke.

KEYWORDS: arterial hypertension, children, adolescents, left ventricular hypertrophy.

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Uvod

Arterijska hipertenzija (AH) u djece i adolescenata postala je sve važniji javnozdravstveni problem jer je njezina prevalencija u porastu i u djece od 8 do 18 godina iznosi 2–3,6 %, a u adolescenata od 18 godina oko 10 %[1]. Primarna AH danas je jedna od najčešćih kroničnih bolesti u adolescenciji. Epidemija pretilosti koja se pojavila zadnjih godina znatno je pridonijela porastu prevalencije AH koja u prekomjerno teške i pretile djece iznosi čak 27–47 %[2]. Longitudinalne su studije pokazale da će djeca, a osobito adolescenti, s AH vjerojatno postati hipertenzivni odrasli s rizicima od kardiovaskularnih bolesti (KVB)[3].

Introduction

The growing prevalence of arterial hypertension (AH) in children and adolescents is becoming an ever-greater public health problem. The prevalence of AH in children aged 8–18 years has been estimated to 2–3.6 % and in adolescents aged 18 to 10 %[1]. Primary AH currently is one of the most common chronic diseases in adolescents. The epidemic of obesity witnessed in recent years has contributed considerably to the increase in the prevalence of AH, which is as high as 27–47 % in overweight and obese children, respectively[2]. Longitudinal studies have indicated that children and in particular adolescents with AH are likely to suffer from hypertension as adults, including the risk of cardiovascular disease (CVD)[3].

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Oštećenje ciljnih organa u djece s arterijskom hipertenzijom

Iako su KVB vrlo rijetke u djetinjstvu, povišena vrijednost arterijskoga tlaka (AT) može već u dječjoj i adolescentnoj dobi uzrokovati promjene na ciljnim organima: povećanje debljine intime medije karotidnih arterija (cIMT), smanjenu rastegljivost brahijalne arterije, povećanu brzinu širenja pulsnog vala (PWV) kroz arterijsku stijenku i augmentacijski indeks (AIx), što upućuje na povećanu krutost arterija, zatim hipertrofiju lijeve klijetke, oštećenje bubrega te promjene na očnoj pozadini[4-9]. Oštećenje ciljnih organa nastalo uz AH u adolescentnoj dobi označuje znatan rizik od kardiovaskularnih događaja u odrasloj dobi.

Hipertrofija lijeve klijetke (LVH) najčešće je traženo oštećenje ciljnih organa uz pedijatrijsku AH zbog dostupnosti ehokardiografskoga pregleda kojim je otkrivamo. Prognostička važnost LVH-a u odraslih s AH-om kao neovisnim rizičnim čimbenikom za KVB nedvojbeno je potvrđena[10]. U preporukama *The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents* iz 2004. godine u rutinsku obradu djece s AH-om uključen je i probir za LVH-a kao čimbenika na temelju kojeg će se započeti ili intenzivirati antihipertenzivno liječenje[11].

Hipertrofija lijeve klijetke i procjena mase lijeve klijetke

Masa lijeve klijetke (LVM) u djece korelira prije svega s tjelesnom masom, ali količina masnoga tkiva, spol i AT također su čimbenici koji joj pridonose[12]. U studiji *Bogalusa* ponavljanim je mjerenjem LVM-a zaključeno da je tjelesni rast glavna odrednica rasta srca, ali da prekomjerna tjelesna masa pridonosi većoj masi miokarda nego se očekuje[13]. Određivanje LVM-a u djece je složeno s obzirom na povezanost mase srca s tjelesnom masom u djeteta koje raste. Brojne su studije upozorile na to da je najbolji način za izražavanje LVM-a indeks koji uključuje i visinu djeteta. Indeks mase lijeve klijetke (LVMI)[14] označuje odnos mase lijeve klijetke i visine djeteta na 2,7 potenciju (LVMI = LVM(g)/visina(m)^{2,7}). U literaturi se navode različite granične vrijednosti LVMI-ja za LVH u djece. U dokumentu *The Fourth Report on BP management in children and adolescents* navedena je granična vrijednosti za LVH kao i za odrasle – LVMI 51 (g)/ visina (m)^{2,7} pa se ta vrijednost često uporabljuje i u pedijatrijskih pacijenata[11]. Međutim, primjerenije je upotrebljavati centilne krivulje čija se uporaba preporučuje za djecu do devete godine, a iznad te dobi 95. percentila za djevojčice je 40 (g)/(m)^{2,7} i 45 (g)/(m)^{2,7} za dječake[15].

Hipertrofija lijeve klijetke i arterijska hipertenzija

Identifikacija djece s AH-om koja imaju rizike za loš kardiovaskularni ishod počiva prije svega na određivanju surogat-markera, ponajprije LVH koja je poznati čimbenik rizika u odraslih. U više različitih studija nađena je pozitivna korelacija između visine AT-a i LVMI-ja[16-18]. *Daniels i sur.* su u 8–41 % djece s AH našli LVMI viši od 95. percentile, a 10–15,5 % od njih je imalo LVMI > 51 g/m^{2,7}. U studiji *Stabouli i sur.* LVH je nađena u 20 % djece s AH-om[9]. Zanimljivo je da je isti postotak djece s prehipertenzijom kao i djece s AH-om imalo LVH. To upućuje na činjenicu da prehipertenzija isto tako znači rizik

Target organ lesions in children with arterial hypertension

Although CVDs are very rare in children, elevated arterial pressure can cause damage to target organs, such as increased carotid artery intima-media thickness (cIMT), decreased brachial artery elasticity, increased pulse wave velocity (PWV) through the arterial wall and augmentation index (AIx), pointing to increased arterial stiffness, left ventricular hypertrophy, kidney damage and ocular fundus changes already in childhood and adolescence[4-9]. Target organ lesions due to AH in adolescence imply a considerable risk of cardiovascular events in adulthood.

Wide availability of echocardiography to detect left ventricular hypertrophy (LVH) makes it a target organ damage most frequently searched for in pediatric AH. The prognostic value of LVH in adults with AH as an independent risk factor for CVD has been definitely verified[10]. Recommendations issued in The Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents from 2004 include screening for LVH as a factor to initiate or intensify antihypertensive treatment in the routine work-up for children with AH[11].

Left ventricular hypertrophy and left ventricular mass assessment

In children, left ventricular mass (LVM) correlates primarily with body mass, but the amount of adipose tissue, gender and arterial pressure also are contributing factors[12]. Repeated LVM measurements in the Bogalusa study suggested that somatic growth was the main determinant of heart growth, but that excessive body mass contributed to increased myocardial mass to greater extent than expected[13]. Determination of LVM in children is complicated due to the cardiac mass association with body mass of a growing child. Numerous studies have demonstrated that LVM index (LVMI), which also includes body height of the child, is the best method of expressing LVM in children. LVMI is the ratio of left ventricular mass and child's height raised to the 2.7 power (LVMI = LVM (g)/height (m)$^{2.7}$)[14]. A variety of LVMI borderline values for LVH in children are reported in the literature. The Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents states a borderline LVMI value for LVH of 51 (g)/height (m)$^{2.7}$, the same as in adults, and this value has been frequently used in pediatric patients as well[11]. However, using percentile curves is recommended in children aged ≤9 years, whereas 95th percentile of 40 (g)/height (m)$^{2.7}$ and 45 (g)/height (m)$^{2.7}$ should be employed in female and male children aged ≥9 years, respectively[15].

Left ventricular hypertrophy and arterial hypertension

Identifying children with AH that are at risk of poor cardiovascular outcome relies primarily on determination of surrogate markers, firstly LVH as a well-known risk factor in adults. Several studies report on positive correlation between arterial pressure level and LVMI[16-18]. Daniels *et al.* found LVMI above 95th percentile in 8–41 % of children with AH, of which 10–15.5 % had LVMI >51 g/m$^{2.7}$. In the study by Stabouli *et al.*[9], LVH was recorded in 20 % of children with AH. Interestingly,

od posljedice na kardiovaskularnom sustavu i od oštećenja ciljnih organa kao i AH. Također su nađene više vrijednosti LVMI-ija u grupi djece s AH potvrđenom s 24-satnim kontinuiranim mjerenjem arterijskoga tlaka (KMAT). *Richey i sur.* našli su veće vrijednosti LVMI-ja u djece s AH registriranom u 24-satnom KMAT-u[19]. *McNiece i sur.* utvrdili su da je veći rizik od LVH u djece s AH-om I. i II. stupnja[7].

Hipertrofija lijeve klijetke nađena je i u djece s „hipertenzijom bijele kute" (WCH), što govori u prilog činjenici da to nije bezazleno stanje i da ima kliničku važnost[20].

Hipertrofija lijeve klijetke i vaskularni fenotip

Arterijska hipertenzija može biti uzrok, ali i posljedica oštećene vaskularne funkcije. Povećana krutost arterija neovisni je čimbenik rizika za nastanak KVB-a u odraslih. U mladih osoba zbog AH-a i pretilosti najprije nastaju reverzibilne, funkcionalne promjene vaskularnoga stabla koje poslije mogu postati fiksirane i ireverzibilne. U prvoj fazi promjene na krvnim žilama su reverzibilne te je stoga važno rano prepoznavanje i liječenje AH-a[21]. Najčešće upotrebljavani parametri za ocjenu vaskularne funkcije u odraslih jesu cIMT, PWV i AIX , no zbog nedostatka opreme, nedostatne standardizacije metoda, nedovoljno definirane važnosti u dijagnostici i nedostatka validacije u pedijatrijskih pacijenata još uvijek nisu uvedeni u pedijatrijsku praksu. Publicirano je nekoliko studija s normalnim vrijednostima za PWV i cIMT u djece i adolescenata[22-24]. Više studija upućuje na povezanost AH-a u djece i adolescenata, krutosti arterija i kardiovaskularnih rizika[25,26]. Također povećan cIMT, smanjena elastičnost arterija, kao i parametri krutosti arterija u nekim studijama koreliraju s LVH-om, neovisno o pretilosti[16,27].

Hipertrofija lijeve klijetke i pretilost

Pretilost i AH u djece i adolescenata progresivno se povećavaju zadnjih nekoliko desetljeća. Sve je više dokaza koji upozoravaju na ulogu ovih čimbenika rizika za KVB na razvoj oštećenja ciljnih organa kao što je LVH u djece. Iako su pretilost i AH često prisutne istodobno, u više je studija je dokazano da pretilost ima neovisnu ulogu u razvoju LVH-a, neovisno o hipertenziji[28]. Oko 30 % pretile djece ima hipertenziju[29]. Hipertrofija lijeve klijetke česta je u takve djece i udružena je sa sistoličkom hipertenzijom i inzulinskom rezistencijom. U djece s AH-om koja su ujedno prekomjerno teška ili pretila LVMI je veći nego što bi bilo da je riječ samo o hipertenziji. Pretilost u djetinjstvu neovisni je čimbenik za veću LVM u odrasloj dobi[30]. Brojni su hemodinamski i nehemodinamski čimbenici koji objašnjavaju ulogu pretilosti u razvoju LVH-a i remodeliranju srca.

Hipertrofija lijeve klijetke u djece s kroničnom bubrežnom bolešću

Rizik od nastanka preuranjenih kardiovaskularnih promjena mnogo je veći u djece s kroničnom bubrežnom bolešću (KBB)[31]. Hipertrofiju lijeve klijetke nalazimo u pedijatrijskih pacijenata već u ranoj fazi KBB-a, a početkom dijalize prisutna je u 69–82 % bolesnika[32]. Često je prisutna u bolesnika i nakon transplantacije bubrega. Uočena je korelacija između pada glomerularne filtracije i povećanja LVM-a[33]. Poticaji su

LVH was detected in the same percentage of children with pre-hypertension and those with AH. This finding indicates that pre-hypertension also poses a risk of cardiovascular sequels and target organ damage as AH. Higher LVMI values were also recorded in the group of children with AH as confirmed by 24-hour continuous noninvasive arterial pressure monitoring (CNAP). Richey *et al.* found higher LVMI in children with AH as recorded by 24-hour CNAP[19]. McNiece *et al.* recorded a higher risk of LVH in children with AH grade I and II[7].

Left ventricular hypertrophy was also detected in children with white-coat hypertension, suggesting that it is by no means a harmless but a clinically relevant condition[20].

Left ventricular hypertrophy and vascular phenotype

Arterial hypertension can be the cause but also the sequel of impaired vascular function. Increased arterial stiffness is an independent risk factor for development of CVD in adults. In young individuals, AH and obesity lead to reversible functional changes of vascular tree, which may later become fixed and irreversible. In the initial stage, vascular lesions are reversible, therefore early recognition and treatment of AH is of utmost importance[21]. The most commonly used parameters for the assessment of vascular function in adults are cIMT, PWV and AIx; however, they have not yet been widely adopted in pediatric practice due to unavailable equipment, inadequate method standardization, inappropriately defined diagnostic role, and lack of validation in pediatric patients. There are several studies reporting normal PWV and cIMT values in children and adolescents[22-24]. Other studies point to the association of AH with arterial stiffness and cardiovascular risk in children and adolescents[25,26]. In some studies, increased cIMT, reduced arterial elasticity and arterial stiffness parameters were found to correlate with LVH independently of obesity[16,27].

Left ventricular hypertrophy and obesity

Obesity and AH have been on a progressive increase in the last few decades. There is a growing body of evidence pointing to the role of these risk factors for CVD in target organ damage such as LVH in children. Although obesity and AH frequently coexist, several studies have demonstrated that obesity has an independent role in LVH development, irrespective of hypertension[28]. Hypertension is present in about 30 % of obese children[29]. LVH is frequent in obese children and is associated with systolic hypertension and insulin resistance. In children with AH who are at the same time overweight or obese, LVMI is higher than it would be in the presence of hypertension alone. Obesity in childhood is an independent risk factor for higher LVM in adult age[30]. Numerous hemodynamic and non-hemodynamic factors explain the role of obesity in the development of LVH and cardiac remodeling.

Left ventricular hypertrophy in children with chronic kidney disease

The risk of premature cardiovascular lesion is significantly higher in children with chronic kidney disease (CKD)[31]. LVH is already found in the early stage of CKD in pediatric patients, and at the introduction of dialysis therapy it is present in 69–82 % of these patients[32]. LVH is frequently found in pa-

za razvoj LVH-a u djece s KBB-om višestruki. AH, povećana krutost arterija i dijastolička disfunkcija srca. S obzirom na to da LVH pokatkad nalazimo i u odraslih koji su u djetinjstvu imali bubrežnu bolest, preporučuje se ehokadiografsko praćenje pacijenata s KBB-om i onih na dijalizi svakih 6–12 mjeseci uz nastojanje da se umanje ostali rizici za nastanak KVB-a[34].

Zaključak

Hipertrofija lijeve klijetke mjera je oštećenja srca kao ciljnog organa u djece s AH-om i KBB-om. Ehokardiografsko mjerenje LVM-a dio je algoritma preporučena za obradu djece s AH-om, a primjenjuje se pri odluci o uvođenju medikamentnog liječenja te kao provjera odgovora na terapiju. Stoga se preporučuje da svako dijete s hipertenzijom i kroničnom bubrežnom bolešću ima početni ehokardiografski nalaz, kao i kontrolne provjere tijekom praćenja.

tients following kidney transplantation. A correlation was recorded between glomerular filtration decrease and LVM increase[33]. In children with CKD, there are multiple factors favoring LVH development, including AH, increased arterial stiffness and diastolic dysfunction of the heart. As LVH is occasionally found in adults with a history of kidney disease in childhood, echocardiographic monitoring at 6- to 12-month intervals is recommended in CKD patients and those on dialysis, along with reducing other CVD risk factors[34].

Conclusion

Left ventricular hypertrophy is a measure of heart damage as a target organ in children with AH and CKD. Echocardiographic determination of LVM is part of the algorithm recommended for the work-up of children with AH and is used when deciding on the introduction of medicamentous therapy, as well as in therapeutic response evaluation. Therefore, it is recommended that every child with hypertension and CKD undergoes initial and then follow up echocardiography.

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