

Valvularna bolest srca kod pacijenata na kroničnoj dijalizi

Valvular heart disease in patients undergoing chronic hemodialysis

Daniela Lončar^{1*}, Mithat Tabaković¹, Suada Mulić-Bačić¹, Đani Hadžović², Esad Brkić¹, Elnur Smajić¹, Lejla Jašarević¹, Amila Jašarević¹

¹ Javna zdravstvena ustanova Univerzitetski klinički centar Tuzla, Tuzla, Bosna i Hercegovina

² Javna zdravstvena ustanova Dom zdravlja Tuzla, Tuzla, Bosna i Hercegovina

¹ *The Public Health Institution University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina*

² *The Public Health Institution Health Center Tuzla, Tuzla, Bosnia and Herzegovina*

SAŽETAK: Valvularna bolest srca uobičajena je pojava kod pacijenta na kroničnoj dijalizi. Abnormalnosti uključuju valvularno i anularno zadebljanje te kalcifikaciju bilo koje od srčanih valvula, uzrokujući regurgitaciju i/ili stenozu. Valvularno zadebljanje ili skleroza kod pacijenata na kroničnom programu dijalize najčešće zahvaća aortnu i mitralnu valvulu. Kalcifikacija aortne valvule registrira se i do polovice hemodijaliziranih pacijenata, javljajući se od 10 do 20 godina ranije nego u općoj populaciji. Valvularna regurgitacija javlja se najčešće na mitralnoj, trikuspidnoj i nešto rjeđe aortnoj valvuli. Cilj rada bio je utvrditi učestalost bolesti srčanih zalistaka u asimptomatskih bolesnika na kroničnom programu dijalize.

U analizu je uključeno ukupno 50 pacijenata i to 35 (70%) liječenih hemodijalizom i 15 (30%) kontinuiranom ambulatornom peritonejskom dijalizom. Valvularno zadebljanje ili skleroza dijagnosticirani su kod 20 (40%) bolesnika. Kod 9 (18%) pacijenata dijagnosticirana je skleroza mitralnih, a kod 11 (22%) skleroza aortnih listića. Kalcifikacije srčanih zalistaka dijagnosticirane su kod 12 (31%) pacijenta. Blaga aortna stenozna bila je prisutna kod 3 (6%) pacijenta. Mitralna regurgitacija bila je dijagnosticirana kod 38 (76%) pacijenata, aortna regurgitacija kod 14 (28%), a trikuspidna regurgitacija kod 24 (48%) pacijenata.

Radi evaluacije stanja valvularanog aparata svim pacijentima na kroničnom programu dijalize potrebno je učiniti ehokardiografski pregled, obzirom na visoku učestalost valvularnih bolesti srca.

KLJUČNE RIJEČI: valvularna bolest srca, dijaliza, valvularna stenozna, valvularna regurgitacija.

SUMMARY: Valvular heart disease is a common phenomenon in patients undergoing chronic hemodialysis. Abnormalities include valvular and annular thickening and calcification of any of the heart valves, causing regurgitation and/or stenosis. Valvular thickening or sclerosis in patients undergoing chronic dialysis treatment usually affects the aortic and mitral valve. Aortic valve calcification is recorded in up to a half of hemodialyzed patients, occurring from 10 to 20 years earlier than in the general population. Valvular regurgitation occurs mostly in mitral, tricuspid and less commonly in aortic valve. The aim of the article was to determine the incidence of valvular heart disease in asymptomatic patients undergoing chronic dialysis.

The analysis involves a total of 50 patients, of whom 35 (70%) are treated by hemodialysis and 15 (30%) by continuous ambulatory peritoneal dialysis. Valvular thickening or sclerosis was diagnosed in 20 (40%) patients. Sclerosis of mitral cusps was diagnosed in 9 (18%) patients and sclerosis of aortic cusps was diagnosed in 11 (22%) patients. Heart valve calcifications were diagnosed in 12 (31%) patients. Mild aortic stenosis was present in 3 (6%) patients. Mitral regurgitation was diagnosed in 38 (76%) patients, aortic regurgitation in 14 (28%), and tricuspid regurgitation in 24 (48%) patients.

The evaluation of the valve apparatus for all patients undergoing chronic dialysis program requires echocardiographic examination that is to be performed, considering the high prevalence of valvular heart diseases.

KEYWORDS: valvular heart disease, hemodialysis, valvular stenosis, valvular regurgitation.

CITATION: *Cardiol Croat.* 2013;8(1-2):67-70.

Uvod

Kardiovaskularne bolesti (KVB) vodeći su uzrok smrtnosti u pacijenata na kroničnoj dijalizi. Pacijenti s kroničnom bubrežnom insuficijencijom imaju 10-20 puta viši rizik razvoja

Introduction

Cardiovascular diseases (CVD) are the leading cause of mortality in patients undergoing chronic hemodialysis. Patients with chronic renal insufficiency are exposed to a 10 to

KVB u odnosu na opću populaciju. Kod pacijenata s kroničnim bubrežnim bolestima, osim uobičajenih, tradicionalnih čimbenika rizika za nastanak KVB (životna dob, dijabetes, pušenje cigareta, arterijska hipertenzija, pozitivna obiteljska anamneza), značaj imaju i dodatni čimbenici rizika karakteristični za uremijski sindrom (anemija, arteriovenska fistula, stalne promjene u volumenu krvi, stečena valvularna bolest, hiperparatireoidizam, porast umnoška kalcija s fosforom, preopterećenje aluminijem, manjak željeza, malnutricija, neadekvatna dijaliza i kronični upalni sindrom) koji aditivno ili sinergistički s jedne strane ubrzavaju klinički tijek bubrežne bolesti, a s druge strane značajno povećavaju rizik razvoja KVB.¹

Bolest srčanih zalistaka relativno je česta u dijaliziranih pacijenata.² Ehokardiografija predstavlja neprocjenjivo dijagnostičko sredstvo za detekciju valvularne bolesti srca i u bolesnika s prisutnim bubrežnim zatajenjem, kao i bez njega. Detektirane abnormalnosti uključuju valvularno i anularno zadebljanje te kalcifikaciju bilo koje od srčanih valvula što uzrokuje regurgitaciju i/ili stenozu.³ Valvularno zadebljanje ili skleroza najčešće zahvaća aortnu (55% do 69%) i mitralnu valvulu (40% do 60% dijaliziranih pacijenata).

Kalcifikacije mitralne i aortne valvule su čest nalaz u pacijenata na kroničnoj dijalizi s prevalencijom četiri do pet puta višom od opće populacije. Kalcifikacija mitralnog anulusa javlja se kod 10% do 50 % pacijenata u završnoj fazi bubrežne bolesti. Kalcifikacija aortne valvule se registrira kod 25% do 55 % hemodijaliziranih pacijenata, javljajući se 10 do 20 godina ranije nego u općoj populaciji. Prema istraživanju *Roberts* i *sur*⁴ kalcifikacija mitralnog prstena utvrđena je kod 42%, a kalcifikacija aortne valvule kod 35% dijaliziranih pacijenata. Kalcifikacija trikuspidne i pulmonalne valvule je rijetka.

Prisustvo srčane valvularne kalcifikacije predstavlja važan negativan prognostički faktor. Smrtnost kod pacijenata s valvularnom kalcifikacijom je viša nego u pacijenata bez kalcifikacije. Kalcifikacija valvula utvrđena ehokardiografski u dijaliziranih pacijenata povezana je sa 2,5 do 5,4x porastom rizika od kardiovaskularne smrti. Kalcifikacija valvula povezana je i s drugim biljezima ateroskleroze, kao što je npr. karotidna debljina intima-medija.⁵

Prema istraživanju *Raggi* i *sur*⁶ stanice odgovorne za kalcifikacije u srčanim valvulama mogle bi biti miofibroblasti. Najvažniji čimbenik u nastanku srčanih kalcifikata je sekundarni hiperparatireoidizam. Kalcifikati na srčanim zaliscima etiološki su vezani s hiperfosfatemijom, povećanim umnoškom kalcija i fosfora, hiperkalcemijom i kalcifikatima u krvnim žilama.⁷ Progresija valvularnih kalcifikacija može biti usporena liječenjem promijenjenog metabolizma kalcija, fosfora i paratiroidnog hormona u pacijenata podvrgnutih hemodijalizi te primjenom statina u općoj populaciji.⁸

Glavne valvularne abnormalnosti s kliničkim posljedicama koje su primjećene u dijaliziranih pacijenata su regurgitirajuće i stenotske lezije. Kod 15% do 20 % dijaliziranih pacijenata registrira se aortna stenozu, a hemodijaliza predstavlja važan čimbenik rizika za progresiju aortne stenozu.⁹ Visoka je učestalost mitralne (95%), trikuspidne (65%) i aortne (38%) regurgitacije.

Cilj rada bio je utvrditi učestalost bolesti srčanih zalistaka u asimptomatskih pacijenata na kroničnom programu dijalize.

Ispitanici i metode

U Klinici za interne bolesti Univerzitetskog kliničkog centra Tuzla u Tuzli provedeno je prospektivno istraživanje u koje

20 times higher risk of developing CVD compared to the general population. In patients with chronic kidney diseases, apart from the usual, traditional CVD risk factors (age, diabetes, smoking, arterial hypertension, positive family history), the importance is also attached to additional risk factors typical for uremic syndrome (anemia, arteriovenous fistula, permanent changes in blood volume, acquired valvular disease, hyperparathyroidism, increased product of calcium with phosphorus, aluminum overload, iron deficiency, malnutrition, inadequate dialysis, and chronic inflammatory syndrome), which on the one hand additively or synergistically accelerate the clinical course of the kidney disease, and on the other hand significantly increase the risk of developing CVD.¹

Valvular heart disease is relatively common in dialyzed patients.² Echocardiography is an invaluable diagnostic tool for detecting valvular heart disease even in patients with present renal failure and without it. The detected abnormalities include valvular and annular thickening and calcification of any of the heart valves, causing regurgitation and/or stenosis.³ Valvular thickening or sclerosis most commonly affects aortic (55% to 69%) and mitral valve (40% to 60% of dialyzed patients).

Calcification of the mitral and aortic valve is a common finding in patients undergoing chronic dialysis with the prevalence four to five times higher than in the general population. The calcification of the mitral annulus occurs in 10% to 50% of patients in the end-stage of kidney disease. Aortic valve calcification is recorded in 25 to 55% of hemodialyzed patients, occurring from 10% to 20 years earlier than in the general population. According to the study by *Roberts et al*⁴ the calcification of mitral annulus was found in 42% and aortic valve calcification was found in 35% of dialyzed patients. Calcification of tricuspid and pulmonary valve is rare.

The presence of heart valve calcification is an important negative prognostic factor. Mortality in patients with valvular calcification is higher than in patients without calcification. Valve calcification in dialyzed patients determined by echocardiography is associated with a 2.5 to 5.4 times higher risk of cardiovascular death. Valve calcification is associated with other markers of atherosclerosis, such as carotid intima-media thickness.⁵

According to the study by *Raggi et al*⁶ the cells accountable for the calcifications in the heart valves could be myofibroblasts. The most important factor in the development of cardiac calcification is the secondary hyperparathyroidism. Calcifications in the heart valves are etiologically associated with hyperphosphatemia, increased product of calcium and phosphorus, hypercalcemia, and calcifications in the blood vessels.⁷ Valvular calcification progression can be slowed down by the treatment of altered metabolism of calcium, phosphorus and parathyroid hormone in patients undergoing hemodialysis and the use of statins in the general population.⁸

Main valvular abnormalities with clinical consequences observed in dialyzed patients are regurgitant and stenotic lesions. Aortic stenosis is recorded in 15% to 20% of dialyzed patients, while hemodialysis is an important risk factor for the progression of aortic stenosis.⁹ A high incidence of mitral (95%), tricuspid (65%) and aortic (38%) regurgitation has been observed.

The aim of the article was to determine the incidence of valvular heart disease in asymptomatic patients undergoing chronic dialysis.

je uključeno 50 pacijenata koji su bili liječeni metodama kronične dijalize (hemodijalizom i kontinuiranom ambulatornom peritonejskom dijalizom). Svim ispitanicima bila je učinjena je transtorakalna ehokardiografija na aparatu Schiller AT-2 plus prema standardnom ehokardiografskom protokolu.

Rezultati

U istraživanje je bilo uključeno 50 pacijenata i to 22 muškarca (44%) te 28 žena (56%). Od ukupnog broja uključenih njih 35 (70%) bili su liječeni hemodijalizom, a 15 (30%) metodom kontinuirane ambulatorne peritonejske dijalize (CAPD). Prosječna životna dob ispitanika iznosila je $47,3 \pm 12,7$ godina. Prosječna dužina trajanja kroničnog dijaliznog liječenja iznosila je $42,6 \pm 17,2$ mjeseci. Od čimbenika rizika arterijska hipertenzija registrirana je kod 62% pacijenata, hiperlipidemija kod 60% te dijabetes kod 25% ispitanika.

Ehokardiografijom je u 20 pacijenata (40%) bilo registrirano valvularno zadebljanje ili skleroza i to kod 9 skleroza mitralnog, a kod 11 aortnog kuspisa.

Kalcifikacije srčanih zalistaka dijagnosticirane su kod 12 (31%) pacijenata, koji su bili prosječne životne dobi $53,4 \pm 8,6$ godina. Kod 8 pacijenata dijagnosticirane su kalcifikacije mitralnog, a kod 4 kalcifikacije aortnih kuspisa. Kod svih pacijenata s kalcificiranim srčanim zaliscima registrirana je hipertrofija lijeve klijetke, a kod 5 od 8 pacijenata bila je registrirana dilatacija lijevostranih srčanih šupljina.

Blaga aortna stenoza bila je dijagnosticirana kod 3, a blaga mitralna stenoza kod jednog ispitanika. Mitralna regurgitacija bila je utvrđena kod 38 (76%) pacijenata i to blaga u 13 (26%), umjerena u 19 (38%), srednje teška u 4 (8%) i teška u 2 (4%) ispitanika. Aortna regurgitacija bila je dijagnosticirana kod 14 (28%) pacijenata i to blaga kod 9 (18%), a umjerena kod 5 (10%) ispitanika. Trikuspidna regurgitacija bila je registrirana kod 24 (48%) pacijenata i to blaga kod 20 (40%), a umjerena kod 4 (8%) pacijenata.

U ovom istraživanju kongestivna srčana insuficijencija bila je prisutna u 17% ispitanika.

Diskusija

U ovom istraživanju utvrđena je visoka učestalost morfoloških i funkcionalnih abnormalnosti srčanih valvula u pacijenata na kroničnom programu dijalize. Degenerativne bolesti srčanih zalistaka povezane su s dužinom trajanja hemodijalize i promjenama u metabolizmu kalcija i fosfora.

Kalcifikacije srčanih zalistaka bile su dijagnosticirane kod 31% pacijenata. *Roberts i sur⁴* utvrdili su kalcifikacije mitralnog prstena kod 42%, a kalcifikacije aortne valvule kod 35% pacijenata na kroničnoj dijalizi.

U usporedbi s istraživanjima drugih autora registrirana je veća učestalost mitralne regurgitacije (76%) i aortne regurgitacije (28%). *Straumann i sur¹⁰* utvrdili su kod dijaliznih pacijenata učestalost mitralne regurgitacije od 11%, a učestalost aortne regurgitacije od 12%.

Ovo istraživanje potvrdilo je činjenicu da je hipertrofija lijeve klijetke učestala u bolesnika na kroničnoj dijalizi. Glavni čimbenici rizika za njen razvoj su povišene vrijednosti arterijskog tlaka, arterioskleroza, aortna stenoza, anemija, povećan volumen ekstracelularne tekućine (retencija natrija i vode) i povećan protok krvi kroz vaskularni pristup za hemodijalizu.¹¹

Patients and methods

At the Department of Internal Medicine at the University Clinical Center in Tuzla a prospective trial was conducted involving 50 patients who were treated by applying the methods of chronic dialysis (hemodialysis and continuous ambulatory peritoneal dialysis). Conventional two-dimensional echocardiography was performed according to guidelines using a commercial ultrasound system (Schiller AT-2 plus).

Results

The study included 50 patients, 22 men (44%) and 28 women (56%). Of the total number of involved patients, 35 (70%) of them were treated by hemodialysis, and 15 (30%) by the method of continuous ambulatory peritoneal dialysis (CAPD). The average age of patients was 47.3 ± 12.7 years. The average length of chronic dialysis treatment was 42.6 ± 17.2 months. From the risk factors, hypertension was recorded in 62%, hyperlipidemia in 60% and diabetes in 25% of patients.

Echocardiography detected valvular thickening or sclerosis in 20 patients (40%), whereas sclerosis of mitral in 9 and sclerosis of aortic cusps in 11 patients.

The calcification of heart valve was diagnosed in 12 (31%) patients, whose average age were 53.4 ± 8.6 years. Mitral calcification was diagnosed in 8 patients, while calcification of aortic cusps was diagnosed in 4 patients. Left ventricular hypertrophy was recorded in all patients with calcified heart valves, while the dilation of the left-sided heart chambers was recorded in 5 out of 8 patients.

Mild aortic stenosis was diagnosed in 3, while mild mitral stenosis in one patient. Mitral regurgitation was detected in 38 (76%) patients, mild regurgitation was detected in 13 (26%), moderate in 19 (38%), medium severe in 4 (8%), and severe in 2 (4%) patients. Aortic regurgitation was diagnosed in 14 (28%) patients, whereas mild regurgitation was diagnosed in 9 (18%) and moderate in 5 (10%) of subjects. Tricuspid regurgitation was recorded in 24 (48%) patients, mild in 20 (40%), and moderate in 4 (8%) patients.

In this study, congestive heart failure was present in 17% of subjects.

Discussion

This study determined a high prevalence of morphological and functional abnormalities of heart valves in patients undergoing chronic dialysis program. Degenerative valvular heart diseases are associated with the length of hemodialysis and changes in the metabolism of calcium and phosphorus.

Heart valve calcifications were diagnosed in 31% patients. *Roberts et al⁴* determined calcification of mitral annulus in 42%, while the calcification of the aortic valve was determined in 35% of patients undergoing chronic dialysis.

In comparison with the trials conducted by other authors, a higher prevalence of mitral regurgitation (76%) and aortic regurgitation (28%) was recorded. *Straumann et al¹⁰* found the incidence of mitral regurgitation of 11%, and the incidence of aortic regurgitation of 12% in the dialyzed patients.

This study has confirmed the fact that the left ventricular hypertrophy is common in patients undergoing chronic hemodialysis. The main risk factors for its development are elevated values of blood pressure, arteriosclerosis, aortic steno-

Učestalost kongestivne srčane insuficijencije u ovoj skupini ispitanika bila je niža nego u bolesnika na hemodijalizi u SAD (46%) i u Europi (25%), a viša od onih u Japanu (6%).¹²

Zaključak

Učestalost valvularne srčane bolesti u pacijenata na kroničnom programu dijalize je visoka. Kalcifikacije srčanih zalistaka dijagnosticirane su kod gotovo trećine ispitanika, a mitralnu regurgitaciju imaju 3 od 4 bolesnika na kroničnom programu dijalize.

Ehokardiografski pregled predstavlja zlatni standard za procjenu morfologije i funkcije srčanih valvula. Ovu neinvazivnu i troškovno učinkovitu metodu potrebno je učiniti kod svih pacijenata liječenih kroničnom dijalizom.

Received: 18th Dec 2012; Updated: 23rd Dec 2012

*Address for correspondence: Javna zdravstvena ustanova Univerzitetski klinički centar Tuzla, Trnovac bb, 75000 Tuzla, Bosnia and Herzegovina.

Phone: +387-35-303300

E-mail: danielamati@yahoo.com

sis, anemia, increased extracellular fluid volume (retention of sodium and water), and increased blood flow through the vascular access for hemodialysis.¹¹

The incidence of congestive heart failure in this group of subjects was lower than in patients undergoing dialysis in the USA (46%) and Europe (25%) and higher than those in Japan (6%).¹²

Conclusion

The incidence of valvular heart disease in patients undergoing chronic dialysis program is high. The calcifications of heart valves were diagnosed in almost one third of subjects, while 3 of the 4 patients undergoing chronic dialysis mitral regurgitation suffer from mitral regurgitation.

Echocardiographic examination is the golden standard for the assessment of morphology and function of heart valves. This non-invasive and cost-effective method needs to be applied in all patients treated by chronic dialysis.

Literature

1. Foley RN, Parfrey PS, Harnett JD, Kent G, Barre PE. Uremia related prognostic factors in dialysis patients: a cohort study from the start of dialysis therapy. *J Am Soc Nephrol.* 1993;4:356.
2. Kes P. Hemodijaliza: prošlost i sadašnjost. *Medicus.* 2001; 10(2): 269-282.
3. Raggi P, Boulay A, Chasan-Taber S, Amin N, Dillon M, Burke SK, et al. Cardiac calcification in adult hemodialysis patients: a link between end-stage renal disease and cardiovascular disease? *J Am Coll Cardiol.* 2002;39:695-701.
4. Roberts WC, Taylor MA, Shirani J. Cardiac findings at necropsy in patients with chronic kidney disease maintained on chronic hemodialysis. *Medicine (Baltimore).* 2012;91(3):165-78.
5. Wang AY, Ho SS, Wang M, Liu EK, Ho S, Li PK, et al. Cardiac valvular calcification as a marker of atherosclerosis and arterial calcification in end-stage renal disease. *Arch Intern Med.* 2005;165:327-32.
6. Raggi P, Chertow GM, Torres PU, Csiky B, Naso A, Nossuli K, et al. The ADVANCE study: a randomized study to evaluate the effects of cinacalcet plus low-dose vitamin D on vascular calcification in patients on hemodialysis. *Nephrol Dial Transplant.* 2011;26(4):1327-39.
7. Nestico PF, Depace NL, Kotler MN, Rose LI, Brezin JH, Swartz C, et al. Calcium phosphorus metabolism in patients with and without mitral anular calcium. Analysis of 30 patients. *Am J Cardiol.* 1983;51:497-500.
8. Pohle K, Maffert R, Ropers D, Moshage W, Stilianakis N, Daniel WG, et al. Progression of aortic valve calcification: association with coronary atherosclerosis and cardiovascular risk factors. *Circulation.* 2001;104:1927-32.
9. Hoshina M, Wada H, Sakakura K, Kubo N, Ikeda N, Sugawara Y, et al. Determinants of progression of aortic valve stenosis and outcome of adverse events in hemodialysis patients. *J Cardiol.* 2012; 59(1):78-83.
10. Straumann E, Meyer B, Misteli M, Blumberg A, Jenzer HR. Aortic and mitral valve disease in patients with end stage renal failure on long-term haemodialysis. *Br Heart J.* 1992;67(3):236-9.
11. Petrović D, Stojimirović B. [Left ventricle hypertrophy in patients treated with regular hemodialysis]. *Med Pregl.* 2008; 61(7-8):369-74.
12. Goodkin DA, Young EW, Kurokawa K, Prtz KG, Levin NW. Mortality among hemodialysis patients in Europe, Japan, and the United States: case-mix effects. *Am J Kidney Dis.* 2004 Nov;44(5 Suppl 2):16-21.