Ultrafiltracija u bolesnika s akutnim zatajivanjem srca – prikaz bolesnika

Ultrafiltration in a Patient with Acute Heart Failure – Case Report

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SAŽETAK: Zatajivanje srca (HF) kao sindrom praćen brojnim simptomima i pojavnim oblicima s razlogom je tema mnogih radova, ali i smjernica svjetskih kardioloških društava. Prevalencija HF-a u osoba starijih od 70 godina iznosi više od 10 %. O ozbiljnosti same bolesti govori njezina smrtnost koja u jednogodišnjem razdoblju iznosi oko 20 %, a u petogodišnjem čak oko 53 %. Navedeni brojevi postavljaju pitanje otkrivaju li se pravodobno oboljeli te koji su dostupni modaliteti liječenja s obzirom na vrlo veliku smrtnost. Ovim je radom prikazano liječenje 67-godišnjeg bolesnika hospitaliziranog s kliničkom slikom anasarke. Zahvaljujući laboratorijskim nalazima i ehokardiografiji vrlo je brzo postavljena dijagnoza akutnog zatajivanja srca sa sniženom ejekcijskom frakcijom lijeve klijetke (LVEF). Kako su okolnosti dopuštale, u terapiju su postupno uvedeni lijekovi preporučeni smjernicama Europskoga kardiološkog društva (ESC). Usprkos višednevnoj primjeni vrlo visokih doza diuretske terapije, uspostavljena je dobra diureza, ali su, klinički, i dalje bili prisutni tjestasti edemi potkoljenica i natkoljenica te ascites. Zbog navedenoga, započeto je liječenje intermitentnom sporom ultrafiltracijom (SUF) koja se također nalazi u smjernicama ESC-a, no bez jasno definiranih preporuka o načinu primjene. Bolesnik je u devet navrata bio podvrgnut intermitentnom SUF-u s pomoću dijaliznog katetera. Navedenim je postupcima uspješno odstranjeno gotovo 25 litara tekućine, što je klinički dovelo do dekongestije. U nastavku prikaza opisuju se ponovne hospitalizacije i kontrolni pregledi kojima je prilagođivana farmakološka terapija te je ugrađen uređaj za srčanu resinkronizaciju. Sve navedeno dovelo je do poboljšanja kvalitete bolesnikova života, ali i do poboljšanja LVEF-a. Aktualna istraživanja bavila su se ultrafiltracijom kao nadomjesnim liječenjem u HF-u. Usprkos razlikama u istraživanim populacijama i modalitetima SUF-a, zajednički stav istraživanja jest da ultrafiltracija dovodi do dekongestije i hemodinamske stabilizacije, a većina autora navodi i smanjenu potrebu za rehospitalizacijom bolesnika. Budući da se smrtnost bolesnika nije smanjila, potrebno je i dalje istraživati primjenu ultrafiltracije i ostalih oblika liječenja u bolesnika s uznapredovalim HF-om.

SUMMARY: As a syndrome accompanied by numerous symptoms and with various manifestations, heart failure (HF) has been the topic of many scientific studies as well as guidelines of cardiological societies across the world. The prevalence of HF in people above 70 years of age is higher than 10%. The seriousness of the disease is clear from its mortality, which is approximately 20% in a one-year period and as high as 53% in a five-year period. These data raise the question whether patients are diagnosed in a timely manner and what treatment modalities are available given the very high mortality. Herein we describe the treatment of a 67-year-old patient hospitalized with a clinical picture of anasarca. Laboratory findings and echocardiography allowed rapid establishment of the diagnosis of acute heart failure with reduced left ventricular ejection fraction (LVEF). As circumstances allowed, medications were gradually introduced into the treatment based on the Guidelines from the European Society of Cardiology (ESC). Despite several days of application of very high doses of diuretic therapy, good diuresis was established, but pitting edema in the lower and upper legs were still clinically present, as was ascites. Due to the above, treatment was started using intermittent slow ultrafiltration (SUF), which is also mentioned in the ESC Guidelines, but with no clearly defined recommendations on how it is to be employed. The patient underwent intermittent SUF using a dialysis catheter on nine separate occasions. These procedures successfully eliminated almost 25 liters of fluid, clinically resulting in decongestion. We further describe the subsequent rehospitalizations and follow-up examinations which included adjustments to the patient's pharmacological therapy and the implantation of a cardiac resynchronization device. All of the above lead to improved patient quality of life, but also to improved LVEF. Recent studies have examined ultrafiltration as a supplemental treatment for HF. Despite the differences in the study populations and SUF modalities, the studies indicate that ultrafiltration leads to decongestion and hemodynamic stabilization, and most authors also report reduced need for rehospitalization. As patient mortality was not reduced, further studies are required on the application of ultrafiltration and other forms of treatment for patients with advanced HF.

KLJUČNE RIJEČI: akutno zatajivanje srca, ultrafiltracija, ejekcijska frakcija lijeve klijetke.

KEYWORDS: acute heart failure, ultrafiltration, left ventricular ejection fraction.

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Uvod

Prema definiciji Europskoga kardiološkog društva (ESC), zatajivanje srca (HF) klinički je sindrom sastavljen od simptoma, kao što su nedostatak zraka, otjecanje gležnjeva i umor. Navedeni simptomi najčešće su praćeni znakovima poput povišenoga tlaka jugularnih vena, krepitacija nad plućima i perifernim edemima[1]. HF može biti uzrokovan svim bolestima koje dovode do strukturnih, mehaničkih ili električnih abnormalnosti srca[2]. Podjela tipova HF-a već se dugi niz godina određuje prema istisnoj frakciji lijeve klijetke (LVEF). Ako LVEF iznosi do 40 %, riječ je o HF-u s reduciranom istisnom frakcijom (HFrEF), a ono se odnosi na polovinu svih bolesnika s HF-om. HFrEF ujedno ima i najlošiju prognozu što se tiče preživljenja. Važnost navedene podjele ovisne o LVEF-u posebno dolazi do izražaja pri odabiru modaliteta liječenja. O važnosti dijagnosticiranja HF-a govori prevalencija koja se u odraslih kreće između 1 i 2 %, a, ako se promatra dobna skupina nakon 70. godine, prevalencija raste na više od 10 %. Etiološki, kao najznačajniji čimbenici u podlozi HF-a u zapadnim zemljama spominju se koronarna bolest srca (CAD) i arterijska hipertenzija. Vrlo je važno naglasiti da je akutna manifestacija zatajivanja srca (AHF) vodeći uzrok hospitalizacije bolesnika starijih od 65 godina. Prema pojedinim radovima, jednogodišnja smrtnost koju uzrokuju svi tipovi HF-a kreće se oko 20 %, dok petogodišnja iznosi oko 53 %[3]. Navedeno ga svrstava uz bok malignim bolestima s vrlo niskim preživljenjem. Zbog navedene učestalosti s razlogom se velika pažnja posvećuje načinima liječenja bolesnika, osobito onih s uznapredovanim HF-om. U Smjernicama ESC-a za liječenje uznapredovanog HF-a kao jedan od oblika liječenja spominje se i ultrafiltracija (UF).

Prikaz bolesnika

U svibnju 2021. godine na Klinici za bolesti srca i krvnih žila hospitaliziran je 67-godišnji bolesnik zbog otjecanja trbuha i nogu te otežanog disanja. Prema bolesnikovu navodu, tegobe su se pojavile otprilike mjesec dana prije dolaska u bolnicu, a u navedenom je razdoblju primijetio i da slabije mokri. Otprije je bolovao od psorijatičnog artritisa i hiperlipoproteinemije. Inicijalnom obradom u Objedinjenom hitnom bolničkom prijemu (OHBP) evidentira se znatno povišen NT-proBNP (8515 ng/L), uz hiponatremiju (Na 116 mmol/L) i jetrenu leziju (AST 675 U/L, ALT 1051 U/L). Također su zabilježene povišene vrijednosti upalnih parametara i bubrežne funkcije, a vrijednosti albumina bile su uredne (CRP 60,8 mg/L, ureja 13,7 mmol/L, kreatinin 105 µmol/L, albumini 46,9 g/L). Elektrokardiografski je utvrđena fibrilacija atrija nepoznatog vremena nastanka, frekvencije klijetki oko 96/min uz blok lijeve grane, a radiološki nad plućima obostrane zastojne promjene uz naglašeniji desnostrani pleuralni izljev. Iz kliničkoga se statusa izdvajala dispneja, auskultatorno nad plućima obostrano utišan disajni šum, fizikalni znakovi ascitesa i tjestasti edemi natkoljenica i potkoljenica.

Odmah nakon dolaska započeto je liječenje, s naglaskom na diuretsku terapiju, a uzorkovane su hemokultura i urinokultura. Ultrazvukom srca prikazane su uvećane sve srčane šupljine (LVIDd 65 mm, LA 71 x 65 mm, RV 32 mm, RA 65 x 48 mm) uz znatno reduciran LVEF od 20 do 25 % te globalnu hipokineziju. Opisana je i snižena sistolička funkcija desne klijetke, a doplerom umjerena mitralna i trikuspidalna regurgitacija

Introduction

According to the definition of the European Society of Cardiology (ESC), heart failure (HF) is a clinical syndrome comprising various symptoms, such as dyspnea, swollen ankles, and fatigue. These symptoms are usually accompanied by clinical signs such as elevated pressure in the jugular veins, lung crepitations, and peripheral edema[1]. HF can be caused by all diseases that lead to structural, mechanical, or electrical abnormalities in the heart[2]. For many years, HF types have been determined based on left ventricular ejection fraction (LVEF). If LVEF values are up to 40%, it is classified as HF with reduced ejection fraction (HFrEF), which comprises half of all patients with HF. HFrEF also has the poorest survival prognosis. The importance of the LVEF-based division is especially relevant for choosing the treatment modality. The importance of diagnosing HF is clear from its prevalence, which is between 1% and 2% in adults, and above 10% in the age group above 70 years of age. Etiologically, the most important factors underlying HF in Western countries are coronary artery disease (CAD) and arterial hypertension. It is important to emphasize that acute manifestation of heart failure (AHF) is the leading cause of hospitalization in patients older than 65. According to individual studies, one-year mortality for all types of HF is approximately 20%, whereas five-year mortality is approximately 53%[3]. This places HF on par with malignant diseases with very low survival rates. Given its high prevalence, it is clear why significant attention is focused on patient treatment modalities, especially in those with advanced HF. The ESC Guidelines for the treatment of advanced HF mention ultrafiltration (UF) as one mode of treatment.

Case report

In May 2021, the Clinic for Cardiovascular Diseases hospitalized a 67-year-old patient due to swelling in the abdomen and legs and breathing difficulties. According to the patient, the issues had manifested approximately a month before admission, during which he had also noted reduced urination. The patient was also suffering from psoriatic arthritis and hyperlipoproteinemia. Initial examination at the Integrated Emergency Hospital Admission (IEHP) found significantly elevated NT-proBNP (8515 ng/L), with hyponatremia (Na 116 mmol/L) and a liver lesion (AST 675 U/L, ALT 1051 U/L). Additionally, increased values of inflammatory parameters and kidney function were observed, whereas albumin values were normal (CRP 60.8 mg/L, urea 13.7 mmol/L, creatinine 105 µmol/L, albumins 46.9 g/L). Electrocardiography determined atrial fibrillation with unknown time of onset and ventricular frequencies of approximately 96/min with left branch block, while radiological examination showed venous congestion and interstitial edema over both sides of the lungs with more pronounced right-sided pleural effusion. The clinical status was notable for dyspnea, diminished breath sounds on both sides of the lungs, physical signs of ascites, and pitting edema on the upper and lower legs.

Treatment was commenced immediately upon presentation, with an emphasis on diuretic therapy, and hemoculture and urine culture were sampled. Cardiac ultrasounds showed enlargement of all the heart cavities (LVIDd 65 mm, LA 71 x 65 mm, RV 32 mm, RA 65 x 48 mm), with significantly reduced LVEF of 20-25%, as well global hypokinesis. Reduced systolic

(PG max. 39 m/s, Vmax. 3,6 m/s, IVC 22 mm bez adekvatnoga inspiratornog kolapsa, sPAP 54 mmHg, TAPSE 16 mm). Zbog prije spomenute jetrene lezije učinjen je ultrazvuk abdomena, a potom i CT abdomena i zdjelice kojim se prikažu morfološke promjene jetre, vjerojatno u sklopu ciroze. Tumorski procesi nisu evidentirani. Usprkos postupnom povećavanju doze parenteralnog diuretika furosemida na 1 g, postignuta je dobra diureza, no bez poboljšanja kliničkoga stanja i regresije periferne kongestije. Stoga se 18. dana hospitalizacije započelo s intermitentnom sporom ultrafiltracijom (SUF) preko dijalitičkog katetera u desnoj unutarnjoj jugularnoj veni. Navedenim je liječenjem, nakon ukupno 9 provedenih postupaka trajanja tri do četiri sata, znatno poboljšano bolesnikovo stanje i reducirana periferna kongestija uz evakuaciju gotovo 25 litara tekućine. Tjelesna težina prije prvog SUF-a iznosila je 109 kg, a nakon posljednjeg 85 kg. Postavke UF-a bile su oko 500 mL/h, a protok krvi 200 do 250 mL/h. Tijekom boravka praćene su stacionarne vrijednosti troponina T oko 100 ng/L, dok su se vrijednosti ureje i kreatinina povećavale do 26,9 mmol/L i 213 µmol/L, a NT-proBNP-a do 17345 ng/L. Zbog porasta upalnih parametara i uroinfekcije bolesnik je uspješno liječen i antimikrobnom terapijom. Nakon gotovo mjesec dana hospitalizacije, optimiziran do granica mogućnosti, bolesnik se otpušta kući na nastavak kućnog liječenja uz kontrolu 5 dana nakon otpusta, a dogovoren je i termin koronarografije 2 mjeseca poslije otpusta. Nekoliko dana prije otpusta bilježeni su gotovo uredni parametri bubrežne funkcije i elektrolita. Kao glavna dijagnoza postavljena je CAD u sumnji uz prvu manifestaciju HF-a u kliničkoj slici anasarke, a kao ostale važnije dijagnoze novootkrivena fibrilacija atrija i blok lijeve grane te lezija jetre u sklopu ishemijskog hepatitisa. Bolesnik je otpušten uz sljedeću terapiju: pantoprazol 40 mg, bisoprolol 10 mg, eplerenon 25 mg, amiodaron 200 mg, rivaroksaban 20 mg, sakubitril/valsartan 2 x 49/51 mg, furosemid 500 mg, kalijev citrat / kalijev hidrogenkarbonat 2 eff. i 1 eff. naizmjenično dnevno, atorvastatin 20 mg i sulfasalazin 2 x 500 mg.

Iduća je hospitalizacija uslijedila već za četiri dana, i to zbog ijatrogene hiperkalemije. Naime, bolesnik je zabunom uzimao 4 vrećice kalij citratnog praška za otopinu dnevno. Tijekom boravka, nakon korekcije elektrolitskog disbalansa, obavljena je ranije planirana koronarografija kojom se ustanovi blaga aterosklerotska bolest lijeve i desne koronarne arterije bez značajnih stenoza. Navedenim je isključen CAD kao etiologija HF-a, a postavljena je sumnja na tahikardiomiopatiju. S obzirom na i dalje prisutnu fibrilaciju atrija s tahiaritmijom klijetki uz široki blok lijeve grane, indicirana je ablacija AV-čvora te implantacija uređaja za srčanu resinkronizaciju. Nakon oporavka bubrežnih parametara bolesnik je otpušten kući kardijalno kompenziran uz smanjenje doze bisoprolola na 1,25 mg, furosemida na 250 mg uz kalijev citrat / kalijev hidrogenkarbonat 1 eff., sakubitril/valsartana na 2 x 24/26 mg, a od preostale terapije zadržan je rivaroksaban 20 mg, eplerenon 25 mg, atorvastatin 20 mg i sulfasalazin 2 x 500 mg.

U srpnju 2021. godine bolesnik dolazi na kontrolni pregled. Navodi kako se osjeća dobro, nije dobivao na tjelesnoj težini, bubrežni su parametri bili stacionarnih vrijednosti, a NT-proBNP 7223 ng/L. Nastavljena je dosadašnja terapija uz korekciju bisoprolola na 5 mg i ponovno uvođenje amiodarona od 100 mg.

Bolesnik je ponovno hospitaliziran u rujnu 2021. godine zbog akutizacije kroničnog HF-a, vjerojatno precipitiranoga

function of the right ventricle was also observed, and Doppler ultrasound found moderate mitral and tricuspid regurgitation (PG max 39 m/s, Vmax 3.6 m/s, IVC 22 mm without adequate inspiratory collapse, sPAP 54 mmHg, TAPSE 16 mm). Abdominal ultrasound was performed due to the previously mentioned liver lesion, followed by CT of the abdomen and pelvis, which showed morphological changes in the liver, most likely due to cirrhosis. Tumor processes were not observed. Despite gradually increasing the dose of the parenteral diuretic furosemide to 1 g, good diuresis was achieved, but with no improvement in the clinical state and no regression of peripheral congestion. Therefore, on the 18th day of hospitalization, intermittent slow ultrafiltration (SUF) was commenced using a dialysis catheter in the right internal jugular vein. This treatment, after a total of 9 procedures lasting three to four hours, significantly improved the clinical state of the patient and reduced peripheral congestion, with the evacuation of almost 25 liters of fluid. Body weight before the first SUF was 109 kg, and was 85 kg after the last SUF procedure. UF settings were 500 mL/h, and blood flow was 200 to 250 mL/h. During hospitalization, we also monitored stationary troponin T values, which were approximately 100 ng/L, while urea and creatinine values increased to 26.9 mmol/L and 213 µmol/L, respectively, whereas NT-proBNP increased to 17345 ng/L. Due to the increase in inflammatory parameters and urinary tract infection, the patient was also successfully treated with antimicrobial therapy. After almost a month of hospitalization, the clinical state of the patient was optimized as much as possible, and the patient was discharged to home care, with follow-up scheduled 5 days later and a coronarography scheduled 2 months after discharge. A few days before discharge, nearly normal kidney function and electrolyte parameters were observed. CAD was assumed as the main diagnosis, followed by the first manifestation of HF with a clinical picture of anasarca, and with other significant diagnoses including newly discovered atrial fibrillation and left branch block, as well as a liver lesion as a consequence of ischemic hepatitis. The patient was discharged with the following therapy: pantoprazole 40 mg, bisoprolol 10 mg, eplerenone 25 mg, amiodaron 200 mg, rivaroxaban 20 mg, sacubitril/valsartan 2 x 49/51 mg, furosemide 500 mg, potassium citrate / potassium bicarbonate 2 eff. and 1 eff. alternating daily, atorvastatin 20 mg, and sulfasalazine 2 x 500 mg.

The next hospitalization took place only four days later due to iatrogenic hyperkalemia. This was caused by the patient mistakenly using 4 doses of potassium citrate powder in the solution daily. During this hospital stay, after correcting the electrolyte disbalance, the previously planned coronarography was performed, which found mild atherosclerotic disease of the left and right coronary arteries without significant stenosis. This excluded CAD as the etiology of HF and raised suspicion of tachycardiomyopathy. Given the still present atrial fibrillation with tachyarrhythmia of the ventricles with a wide left branch block, ablation of the AV node and CRT device implantation was indicated. After recovery of kidney parameters, the patient was discharged, cardialy compensated with the reduction of the bisoprolol dose to 1.25 mg, furosemide to 250 mg with potassium citrate / potassium bicarbonate 1 eff., and reduction of sacubitril/valsartan to 2 x 24/26 mg, and retention of rivaroxaban 20 mg, eplerenone 25 mg, atorvastatin 20 mg, and sulfasalazine 2 x 500 mg.

In July 2021, the patient presented for follow-up. He reported he was feeling well and had not been gaining weight, while kid-

desnostranom pneumonijom. Primjenom diuretske terapije postignuta je obilna diureza uz regresiju fizikalnih znakova kongestije, a antibiotičkom terapijom gotovo potpuna regresija subjektivnih simptoma i inicijalno znatno povišenih vrijednosti upalnih parametara. Uz navedeno, laboratorijski se ovoga puta bilježi blaga hipotireoza, zbog čega je uvedena nadomjesna terapija. Ultrazvučno je utvrđen EF od 30 % uz tešku hipodiskineziju interventrikularnog septuma i inferiorne stijenke uz održanu kontraktilnost bazalnog segmenta inferolateralne stijenke. Doplerom je zabilježena blaga do umjerena mitralna i trikuspidna regurgitacija. Bolesnik je otpušten uz korekciju doze furosemida na 250 + 250 mg, eplerenona na 50 mg, amiodarona na 200 mg i sakubitril/valsartana 2 x 49/51 mg. Uz dosadašnju terapiju uveden je dapagliflozin 10 mg i levotiroksin 25 µg.

Kontrolni je pregled obavljen potkraj studenoga iste godine. Budući da je bio dobroga općeg stanja i kardiopulmonalno kompenziran, zbog prije navedene problematike odlučeno je da mu se ugradi CRT-D uređaj. Nastavljena je dosadašnja terapija uz korekciju eplerenona na 25 mg i 50 mg naizmjenično te amiodarona na 100 mg. Potkraj prosinca iste godine bolesnik je pozvan na ugradnju CRT-D uređaja u svrhu postizanja resinkronizacije. Nakon uspješne implantacije, učinjena je i radiofrekventna ablacija AV-čvora, a uređaj je reprogramiran na biventrikulski VVIR 70 – 110/min. Trećeg dana boravka bolesnik je otpušten kući, bez promjena u dosadašnjoj terapiji.

Iduća kontrola bila je u lipnju 2022. godine. Bolesnik tada navodi da se osjeća relativno dobro, a klinički nije bilo znakova kardijalne dekompenzacije. Testirana funkcija elektrostimulatora bila je uredna, uz porast praga stimulacije elektrode lijevog ventrikula te se zbog navedenog povećao prag i trajanje stimulusa. Elektrokardiografski je zabilježena fibrilacija atrija uz biventrikularni *pacing* 70/min. Krajem srpnja učinjena je ehokardiografija kojom su prikazane i dalje uvećane sve četiri srčane šupljine, no znatno manje u usporedbi s prijašnjim nalazima (LVIDd 53 mm, LVIDs 38 mm, LA 60 mm, RV 23 mm). Ovoga puta LVEF bilježi znatan porast na 45 %, uz i dalje prisutnu akineziju inferiorno bazalno i hipokineziju inferoseptalne stijenke. Doplerom su evidentirani blaga mitralna regurgitacija i trag trikuspidne regurgitacije (Vmax. 2,4 m/s, PGmax. 23 mmHg, sPAP 28 mmHg). Nakon izvedenog ultrazvuka bolesnik je još dvaput pregledan u kardiološkoj ambulanti, posljednji put u prosincu 2022. godine, pri čemu navodi da se osjeća sve bolje, uz dobro podnošenje umjerenog napora.

Rasprava

Smjernice ESC-a za liječenje HFrEF-a navode farmakoterapiju kao temelj za postizanje triju glavnih ciljeva, a to su: redukcija mortaliteta, prevencija ponovnih hospitalizacija i poboljšanje kliničkoga statusa[1]. Kao tri najvažnije skupine ističu se beta-blokatori, antagonisti mineralokortikoidnih receptora (MRA) i inhibitori angiotenzin konvertirajućeg enzima (ACE-I) ili inhibitori neprilizina i angiotenzinskih receptora (ARNI). Uz navedene, svakako treba izdvojiti inhibitore natrijeva glukoznog transportnog proteina (SGLT-2) i diuretike, osobito Henleove petlje. Upravo posljednje navedena skupina lijekova ima važnu ulogu u liječenju akutnog, ali i kroničnog HF-a i prateće retencije tekućine. Kada je riječ o AHF-u, diuretici Henleove petlje najčešće se primjenjuju intravenski, a doza se povećava sve do regresije kongestije. U pojedinih se

ney parameters had stationary values, and NT-proBNP was 7223 ng/L. The therapy was continued, with the correction of bisoprolol to 5 mg and reintroduction of amiodarone 100 mg.

The patient was hospitalized once again in September 2021 due to acute phase of HF, most likely being precipitated by right-sided pneumonia. Application of diuretic therapy achieved ample diuresis with the regression of physical symptoms of congestion, and antibiotic therapy achieved almost complete regression of subjective symptoms and initially significantly increased inflammatory parameter values. In addition, this time laboratory tests found mild hypothyreosis, which led to the introduction of supplements. Ultrasound examination found EF of 30%, with severe hypokinesia of the interventricular septum and the inferior wall, with preserved contractility of the basal segment of the inferolateral wall. Doppler ultrasound found mild to moderate mitral and tricuspid regurgitation. The patient was discharged with a correction of furosemide dosing to 250 + 250 mg, eplerenone to 50 mg, amiodarone to 200 mg, and sacubitril/valsartan to 2 x 49/51 mg. In addition to continuing previous therapies, dapagliflozin 10 mg and levothyroxine 25 µg were introduced.

Another follow-up examination took place at the end of November 2021. The patient was in a good general state, with well-compensated heart and lungs, and implantation of a CRT-D device was decided upon due to the issues described above. Current therapy was continued, with a correction in eplerenone to alternating between 25 mg and 50 mg, and amiodarone to 100 mg. At the end of December of the same year, the patient was invited to CRT-D device implantation in order to achieve resynchronization. After successful implantation, radiofrequency ablation of the AV node was also performed, and the device was reprogrammed to VVIR 70-110/min. The patient was discharged after three days, with no changes in therapy.

The next follow-up examination was in June 2022. The patient reported feeling relatively well, and there were no clinical signs of cardiac decompensation. Functional testing of the pacemaker was normal, with an increase in the stimulation threshold for the left ventricular lead, which lead to increased threshold and stimulus duration. Electrocardiographic examination found atrial fibrillation with biventricular pacing 70/min. Near the end of July, another echocardiographic examination was performed, showing that all four heart cavities were still enlarged, but significantly less in comparison with earlier findings (LVIDd 53 mm, LVIDs 38 mm, LA 60 mm, RV 23 mm). This time, LVEF significantly increased to 45%, with still present inferior basal akinesis and hypokinesis of the inferoseptal wall. Doppler examination showed mild mitral regurgitation and traces of tricuspid regurgitation (Vmax 2.4 m/s, PGmax 23 mmHg, sPAP 28 mmHg). After the ultrasound, the patient was examined twice more in the cardiological clinic, the last time being in December 2022, when he stated he was felling increasingly well, with good tolerance for moderate exertion.

Discussion

The ESC Guidelines for the treatment of HFrEF list pharmacotherapy as the foundation for the achievement of three main goals, these being: mortality reduction, preventing rehospitalizations, and improving clinical status[1]. The three most important groups of medications are beta blockers, miner-

bolesnika pojavljuju rezistencija na diuretsku terapiju i nemogućnost adekvatnog smanjenja kongestije pa je tada, prema preporukama ESC-a jačine IIa i razine značajnosti dokaza C, indicirana nadomjesna bubrežna terapija.

Jedan od najčešćih oblika nadomjesne terapije jest ultrafiltracija, a samim time predmet je brojnih istraživanja. Do sada provedena randomizirana istraživanja često su dovodila do oprečnih rezultata. Tako je 2007. godine objavljeno prospektivno randomizirano istraživanje *UNLOAD* kojim su promatrane dvije skupine bolesnika s AHF-om (više od 70 % bolesnika s HFrEF-om)[4]. Jedna je skupina liječena isključivo UF-om do 500 mL/h, a druga intravenskim diureticima Henleove petlje. UF se provodio u trajanju do 8 sati, a u prosjeku se po postupku uklanjalo 2611 ± 1002 mL. Važno je naglasiti da je riječ o jednom od prvih istraživanja takvog tipa. U zaključku rada navodi se da rana UF dovodi do većeg gubitka tjelesne težine i tekućine od intravenskih diuretika Henleove petlje, ali isto tako smanjuje broj rehospitalizacija i nepredviđenih posjeta liječniku.

Godine 2012. objavljeno je istraživanje jednake tematike, ali se ovoga puta uz HF pratilo i pogoršanje bubrežne funkcije[5]. Rezultati istraživanja pokazali su da je za bolesnike s AHF-om praćenim perzistentnom kongestijom i slabijom bubrežnom funkcijom bolja progresivna primjena intravenskih diuretika u odnosu prema UF-u. UF se primjenjivao s postavkama filtracije od 200 mL/h, a medijan trajanja iznosio je oko 40 sati. Obje skupine bolesnika imale su gotovo jednak gubitak tjelesne težine i odstranjenja tekućine, ali je UF bio praćen većim brojem neželjenih događaja i znatnijim pogoršanjem bubrežne funkcije. Iste je godine skupina iz Cleveland klinike objavila rezultate istraživanja primjene spore kontinuirane ultrafiltracije (SCUF) u bolesnika s uznapredovanim HF-om[6]. U istraživanje su bile uključene 63 osobe refraktorne na standardnu terapiju, s progresivnom oligurijom i pogoršanjem bubrežne funkcije. Svi su bolesnici imali LVEF između 11 i 41 %, a prosječna je vrijednost bila 26 %. Diuretska je terapija nastavljena u bolesnika s održanom diurezom, a u svih je započet SCUF 100 – 400 mL/h (prosječno 200 mL/h), ovisno o kliničkom i hemodinamskom stanju bolesnika. U zaključku rada autori navode kako je liječenje SCUF-om dovelo do znatnoga hemodinamskog poboljšanja stanja bolesnika, iako je izostalo poboljšanje bubrežne funkcije. Usprkos navedenom, potreba za liječenje SCUF-om potvrđuje izrazito teško stanje bolesnika, kao i rezultati ovog istraživanja koji govore da je gotovo trećina bolesnika preminula u tom boravku, a jednogodišnja je smrtnost bila čak 70 %. Važno je naglasiti da nijedna smrt nije nastupila kao komplikacija SCUF-a, već je u podlozi gotovo svih bila daljnja progresija HF-a.

Skupina poljskih znanstvenika, u članku objavljenom 2021. godine, analizirala je važnija dosad provedena istraživanja o UF-u u bolesnika s AHF-om[7]. Kao zaključak provedene analize navode kako je UF sigurna i efektivna metoda za postizanje dekongestije bolesnika. Osim uklanjanja tekućine, ta metoda znatno smanjuje broj neželjenih događaja, kao i hospitalizacija. U svrhu što bolje primjene metode UF-a, autori navode potrebu za izradom jasnih algoritama o njezinoj uporabi, kao i o praćenju određenih biomarkera s obzirom na potencijalnu ozljedu glomerula i tubula.

U sustavnom pregledu literature objavljenom u Cochrane bazi autori su analizirali randomizirana kontrolirana istraživanjima koja su uspoređivala ultrafiltraciju i diuretsku

alocorticoid receptor antagonists (MRA), and angiotensin-converting enzyme inhibitors or angiotensin receptor/neprilysin inhibitors (ARNI). In addition to the above, notable medications include sodium-glucose transport protein 2 (SGLT-2) inhibitors and diuretics, especially loop diuretics. This last group of medications has an important role in the treatment of both acute and chronic HF and the associated fluid retention. For AHF, loop diuretics are most commonly applied intravenously, and the dose is increased until congestion regresses. Resistance to diuretic treatment occurs in some patients, leading to a lack of adequate congestion reduction, in which cases renal replacement therapy is recommended according to the ESC Guidelines, at recommendation grade IIa and level of evidence C.

Ultrafiltration is one of the most common forms of replacement therapy, and has thus been the topic of numerous studies. Randomized trials conducted thus far have often reported contradictory results. The prospective randomized study *UNLOAD*, published in 2007, examined two groups of patients with AHF (more than 70% of patients with HFrEF)[4]. One group was treated only with UF up to 500 mL/h, while the other was treated with intravenous loop diuretics. UF was conducted over up to 8 hours, and an average of 2611 ± 1002 mL of fluid was removed per procedure. It is important to emphasize that this was one of the first studies of its type. In the conclusion, the authors stated that early UF led to higher fluid body weight loss than intravenous administration of loop diuretics, while also reducing the number of rehospitalizations and unscheduled visits to the physician.

A study on the same topic was published in 2012, additionally monitoring deterioration of renal function along with HF[5]. The study results showed that, for patients with AHF, progressive application of intravenous diuretics was superior in comparison to UF. UF was applied with filtration settings at 200 mL/h, and the median duration was about 40 hours. Both patient groups had almost the same body weight loss and fluid elimination, but UF was associated with a large number of adverse events and a more significant deterioration of renal function. In the same year, a group from the Cleveland Clinic published the results of a study on the application of slow continuous ultrafiltration (SCUF) in patients with advanced HF[6]. The study included 63 patients refractory to standard therapy, with progressive oliguria and deteriorated renal function. All patients had LVEF between 11% and 41%, with an average value of 26%. Diuretic therapy was continued in patients who maintained diuresis, and all patients underwent SCUF at 100-400 mL/h (average 200 mL/h), depending on the clinical and hemodynamic state of individual patients. In their conclusion, the authors stated that SCUF treatment led to significant hemodynamic improvement in their patients, although improvement in renal function was not present. Despite the above, the need to employ SCUF indicates the very severe state of the patient, and the results of this study show that almost a third of the patients died during observed hospitalization, and a one-year mortality was almost 70%. It is important to note that none of the deaths were the result of SCUF treatment complications, but were instead a consequence of further progression of HF as the underlying cause of death.

A group of Polish scientists published a metanalysis in 2021 that examined the more significant studies conducted thus far on UF in patients with AHF[7]. They concluded that UF is a safe and effective method for achieving decongestion in patients.

terapiju u bolesnika s AHF-om[8]. U pregled je uključeno 14 istraživanja s oko 1200 bolesnika. U dvama istraživanjima UF je služio kao dodatan modalitet liječenja uz diuretsku terapiju, a u preostalim istraživanjima bolesnici su bili liječeni diureticima ili UF-om. Rezultati istraživanja pokazali su da UF može imati mali ili nikakav učinak na smrtnost od svih uzroka u najduljemu dostupnom promatranom razdoblju. Usprkos navedenom, UF smanjuje broj rehospitalizacija zbog HF-a i ostalih uzroka, kako u 30-dnevnom razdoblju, tako i u duljem vremenu. Što se tiče potencijalnih komplikacija UF-a, u 30-dnevnom razdoblju ima mali ili nikakav učinak na povećanje serumskog kreatinina, ali, s druge strane, povećava vjerojatnost primjene ostalih naprednih oblika nadomjesne bubrežne terapije.

Zaključak

Kao što je navedeno u uvodnom dijelu rada, HF je zbog svoje učestalosti među starijom populacijom česta tema znanstvenih radova. U Smjernicama ESC-a vrlo su dobro opisani koraci u liječenju, kao i adekvatna terapija, ovisno o kliničkome stadiju i prezentaciji bolesnika. Bolesnik prikazan u navedenom slučaju liječen je terapijom propisanom Smjernicama, no zbog neadekvatnoga kliničkog odgovora primjenjivan je jedan od oblika nadomjesnoga bubrežnog liječenja, odnosno ultrafiltracija. Navedena se metoda također nalazi u smjernicama, no kao preporuka razine C. Opisanom je bolesniku s pomoću intermitentnog SUF-a uspješno odstranjeno otprilike 25 litara tekućine, što je dovelo do bržeg oporavka i ranijeg otpusta iz bolnice. Potom je nastavljena terapija lijekovima prema Smjernicama, a ugrađen je i CRT-D uređaj u svrhu resinkronizacije. Zahvaljujući svemu navedenom bolesnik je nakon 13 mjeseci od prve hospitalizacije oporavio LVEF s 20 – 25 % na čak 45 %, čime je zadovoljio kriterij za izmjenu početne dijagnoze HFrEF-a u HF s poboljšanom istisnom frakcijom (HFimpEF). S obzirom na rezistenciju na diuretike petlje, UF je, zasigurno, bio jedan od važnijih koraka u liječenju. Trenutačno dostupna literatura u vezi liječenja UF-om u bolesnika s AHF-om nema jednoznačne zaključke. Zajednički je stav da UF uspješno dovodi do dekongestije, odstranjenja tekućine i hemodinamske stabilizacije. Također većina istraživanja navodi kako UF smanjuje broj rehospitalizacija, ali i posjeta liječniku. Usprkos pojedinim pozitivnim učincima navedene metode, smrtnost bolesnika nije se promijenila te u pojedinim istraživanjima iznosi čak 70 % u prvoj godini. Stoga je potrebno nastaviti istraživanja primjene UF-a radi stvaranja smjernica za liječenje koje će, osim kvaliteti života, pridonijeti i njegovu produljenju.

In addition to fluid elimination, this method significantly reduces the number of adverse events and hospitalizations. With the goal of optimal employment of the UF method, the authors highlight the need for the development of clear algorithms for its use, as well for the monitoring of certain biomarkers, given potential glomerular and tubular damage.

In a systemic literature review published in the Cochrane database, the authors analyzed randomized controlled trials that compared ultrafiltration and diuretic therapy in patients with AHF[8]. The metanalysis included 14 studies with approximately 1200 patients. In 2 studies, UF was used as an additional treatment modality along with diuretic therapy, whereas the other studies treated patients with either diuretics or UF. Study results showed that UF can have little or no effect on all-cause mortality in the longest study period available. Despite the above, UF reduced the number of rehospitalization for HF and other causes, both in a 30-day period and in the longer term. As for potential complications of UF, it had little or no effect in a 30-day period on increasing serum creatinine, but it increased the likelihood of employing other advanced forms of renal replacement therapy.

Conclusion

As stated in the Introduction, HF is a common topic of scientific studies due to its high prevalence in the older population. ESC Guidelines clearly describe the various steps in the treatment, as well as adequate therapy, depending on clinical staging and patient presentation. The patient described herein received treatment based on the Guidelines, but, due to inadequate clinical response, we employed one of the forms of renal replacement treatment, namely ultrafiltration. This method is also present in the Guidelines, but with a recommendation grade C. In the present case, intermittent SUF successfully eliminated approximately 25 liters of fluid, leading to faster recovery and earlier discharge from the hospital. Medication therapy was continued based on the Guidelines, and a CRT-D device was implanted in order to achieve resynchronization. Due to the above, the patient experienced significant recovery 13 months after the first hospitalization, with LVEF improving from 20-25% to as high as 45%, fulfilling the criteria for changing the initial diagnosis of HFrEF to HF with improved ejection fraction (HFimpEF). Given the patient's resistance to loop diuretics, UF was certainly one of the more important steps in the treatment process. Currently available literature on the treatment of UF in patients with AHF does not allow for non-ambiguous conclusions. Studies indicate that UF successfully leads to decongestion, fluid elimination, and hemodynamic stabilization. Additionally, most studies report that UF reduces the number of rehospitalizations and visits to the physician. Despite some positive effects of this method, patient mortality was unchanged and reached as high as 70% in the first year in individual studies. It is therefore necessary to continue research on the application of UF with the goal of creating treatment guidelines that will, in addition to improving quality of life, contribute to improved survival.

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