

Zatajivanje srca u 2015. i 2016. godini

Heart Failure in 2015/2016

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Uvod

Zadnjih godina publicirane su brojne studije o zatajivanju srca (ZS). Većina nije rezultirala značajnijim otkrićima, bilo u dijagnostičkom bilo u terapijskom smislu. No, ipak su se dobili neki zanimljivi zaključci. Dodatno, na Europskom kongresu o zatajivanju srca, koji je održan u Firenci 21. svibnja 2016., objavljene su nove Smjernice Europskog kardiološkog društva (ESC) za dijagnostiku i liječenje akutnog i kroničnog zatajivanja srca.^{1,2}

Smjernice ESC-a za dijagnostiku i liječenje akutnog i kroničnog zatajivanja srca

Glavne promjene u Smjericama u usporedbi s prethodnim izdanjem iz 2012. godine:

1. Ustanovljen je novi termin za pacijente sa ZS-om i istisnom frakcijom lijeve klijetke (LVEF) od 40 do 49 %: "ZS sa srednjom (srednje očuvanom) EF (HFmrEF)". Vjeruje se da će identifikiranje ove posebne podskupine poticati istraživanja koja bi utvrdila obilježja, patofiziologiju i liječenje ovakvih pacijenata.
2. Izdane su jasne preporuke za postavljanje dijagnoze ZS-a sa sniženom EF (HFpEF), srednjom EF (HFmrEF) i očuvanom EF (HFpEF).
3. Preporučena je novi algoritam za dijagnozu ZS-a u neakutnim stanjima; temelji se na evaluaciji vjerojatnosti postojanja ZS-a.
4. Izdane su preporuke sa svrhom da se prevenira ili odgodi razvoj simptomatskog ZS-a ili prevenira smrtnost prije početka simptoma.

Introduction

A number of studies on heart failure (HF) have been published in recent years, most of these revealing no significant discoveries in terms of diagnosis or therapy. However, some interesting conclusions have been reached. In addition, new Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure of the European Society of Cardiology (ESC) were launched at the European Heart Failure Congress, held on May 21, 2016 in Florence, Italy^{1,2}.

ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure

The new Guidelines bring the following major changes relative to the previous 2012 version:

1. A new term has been introduced for patients with HF and left ventricular ejection fraction (LVEF) of 40%-49%: "HF with medium (mildly reduced) EF (HFmrEF)". Identification of this specific subgroup is believed to stimulate research focused on determining the characteristics, pathophysiology and management of these patients.
2. Distinct recommendations have been issued for diagnosing HF with reduced EF (HFpEF), mildly reduced EF (HFmrEF) and preserved EF (HFpEF).
3. A new algorithm for diagnosing HF in non-acute states has been recommended; it is based on evaluating the likelihood of HF.
4. There are recommendations with the aim to prevent or delay development of symptomatic HF, or to prevent mortality before the onset of symptoms.

5. Postavljene su indikacije za uzimanje novog kombiniranog lijeka, sakubitril/ valsartana, prvog u klasi angiotenzin receptor inhibitora neprilizina.
6. Promijenjene su indikacije za resinkronizacijsku terapiju.
7. Preporučen je koncept ranog započinjanja adekvatne terapije. Naime, dijagnostika i terapija akutnog ZS-a trebala bi ići paralelno – pristup "vrijeme do terapije" (već dugo prihvaćen u liječenju akutnoga koronarnog sindroma).
8. Izdan je novi algoritam za dijagnostiku i liječenje akutnog ZS-a, koji se temelji na prisutnosti ili odsutnosti kongestije ili hipoperfuzije.

KRITERIJI ZA PODTIPOVE ZATAJIVANJA SRCA

Kriteriji za podtipove zatajivanja srca jesu:

- **HF_rEF**: LVEF < 40 %, uz simptome i znakove ZS-a
- **HF_mEF**: LVEF 40 – 49 %, uz simptome i znakove ZS-a, povišene vrijednosti natriuretskih peptida te najmanje jedan od dodatnih kriterija: relevantna strukturna bolest srca ili dijastolička disfunkcija
- **HF_pEF**: LVEF ≥ 50 %, uz simptome i znakove ZS-a, povišene razine natriuretskih peptida te najmanje jedan od dodatnih kriterija: relevantna strukturna bolest srca ili dijastolička disfunkcija.

NOVI ALGORITAM ZA DIJAGNOZU ZATAJIVANJA SRCA U NEAKUTNIM STANJIMA

U bolesnika u kojih se simptomi ili znakovi ZS-a očituju prvi put, u neakutnom obliku, u ambulantom obiteljskog liječnika ili u bolničkim poliklinikama, treba prije svega utvrditi je li riječ o ZS-u.

Dijagnoza se temelji na anamnezi (koronarna bolest srca, arterijska hipertenzija, kardiotoksični lijekovi, iradijacija, uporaba diuretika...), simptomima (vlažni hropci, ortopneja, paroksizmalna noćna dispneja, srčani šum), fizikalnom nalazu (bilateralni edemi, povećan jugularni venski tlak i dr.) i na 12-kanalnom elektrokardiogramu (eventualna prisutnost abnormalnosti).

Ako su svi navedeni elementi uredni, dijagnoza ZS-a nije vjerojatna te bi trebalo tražiti druge uzroke. Pronađe li se bar jedna abnormalnost, potrebno je napraviti analizu natriuretskih peptida. Kod povišenih vrijednosti natriuretskih peptida (ili ako se njihova analiza ne može realizirati), potrebno je obaviti ehokardiografski pregled. Pozitivne vrijednosti natriuretskih peptida jesu: BNP ≥ 35/pg/mL, NT-proBNP ≥ 125/pg/mL. Nakon postavljanja dijagnoze treba odrediti etiologiju i početi adekvatno liječenje.

PREPORUKE SA SVRHOM DA SE SPRIJEČI ILI ODGODI RAZVOJ SIMPTOMATSKOG ZATAJIVANJA I SPRIJEČI SMRTNOST PRIJE NASTUPA SIMPTOMA

Postoje podatci da se početak ZS-a može odgoditi ili spriječiti intervencijama kojima je svrha korekcija čimbenika rizika ili liječenjem asimptomatske sistoličke disfunkcije lijeve klijetke.

5. Indications have been established for administration of a novel combined drug, sacubitril/valsartan, the first one in the class of angiotensin receptor/neprilysin inhibitors (ARNIs).
6. Indications for cardiac resynchronization therapy (CRT) have been changed.
7. The concept of early initiation of appropriate therapy is recommended, i.e. the diagnosis and therapy of acute HF should be performed in parallel – the 'time to therapy' approach (adopted in the management of acute coronary syndrome for years now).
8. A new algorithm for the diagnosis and treatment of acute HF, based on the presence or absence of congestion or hypoperfusion, has been issued.

CRITERIA FOR HEART FAILURE SUBTYPES

The criteria for heart failure subtypes are as follows:

- **HF_rEF**: LVEF <40%, with symptoms and signs of HF;
- **HF_mEF**: LVEF 40%-49%, with symptoms and signs of HF, elevated natriuretic peptide levels, and at least one of the additional criteria: relevant structural heart disease or diastolic dysfunction; and
- **HF_pEF**: LVEF ≥50%, with symptoms and signs of HF, elevated natriuretic peptide levels, and at least one of the additional criteria: relevant structural heart disease or diastolic dysfunction.

THE NEW ALGORITHM FOR DIAGNOSING HEART FAILURE IN NON-ACUTE STATES

In patients presenting with symptoms or signs of HF for the first time and in non-acute form, it should first be established at the family physician office or hospital polyclinic whether it is a case of HF.

The diagnosis is based on patient history (coronary heart disease, arterial hypertension, cardiotoxic drugs, irradiation, use of diuretics, etc.), symptoms (moist rales, orthopnea, paroxysmal nocturnal dyspnea, heart murmur), physical finding (bilateral edema, elevated jugular venous pressure, etc.) and 12-lead electrocardiogram (the possible presence of abnormalities).

If all these elements prove normal, the diagnosis of HF is not likely and other causes should be looked for. Finding at least one abnormality requires natriuretic peptide analysis. In case of elevated natriuretic peptide levels (or if natriuretic peptide analysis is not available), echocardiography should be performed. Positive values of the brain natriuretic peptides (BNP) are as follows: BNP ≥35/pg/mL and NT-proBNP ≥125/pg/mL. Upon making the diagnosis, the etiology should be determined and appropriate treatment introduced.

RECOMMENDATIONS AIMING TO PREVENT OR DELAY DEVELOPMENT OF SYMPTOMATIC HEART FAILURE OR TO PREVENT MORTALITY BEFORE THE ONSET OF SYMPTOMS

There are data indicating that the onset of HF can be delayed or prevented by interventions for correction of risk factors or therapy for asymptomatic systolic left ventricular dysfunction. For example, in individuals older than 40 with known

Primjerice, u osoba starijih od 40 godina koje imaju poznate kardiovaskularne rizike može pomoći analiza natriuretskih peptida.

Posebno je važno liječiti arterijsku hipertenziju kao jedan od najpoznatijih čimbenika rizika za nastup ZS-a (SPRINT studija). Novi podatci govore da empagliflozin (inhibitor N-glukoza kotransportera 2) poboljšava prognozu pacijenata s dijabetesom tipa 2 (uključujući smanjenje smrtnosti i hospitalizacija zbog zatajivanja srca). Povoljne učinke može imati i prestanak pušenja. Osobe koje umjereno konzumiraju alkoholna pića imaju manji rizik od novonastalog razvoja ZS-a. Umjerena tjelesna aktivnost također može pomoći. Korisno je liječiti poremećaj glikemije, kao i prekomjernu tjelesnu težinu.

Statini smanjuju rizik od nekih kardiovaskularnih događaja i smrtnost te bi posredno mogli prevenirati ili odgoditi nastanak ZS-a. U bolesnika s koronarnom bolesti srca (KBS) uporaba ACE inhibitora može spriječiti ili odgoditi nastanak ZS i smanjiti kardiovaskularnu, kao i opću smrtnost.

Perkutana koronarna intervencija (PCI) kod akutnog infarkta miokarda s elevacijom ST segmenta može prevenirati ili odgoditi nastanak ZS-a smanjenjem infarktne zone. Primjena ACE inhibitora, beta-blokatora i antagonista mineralokortikoidnih receptora (MRA) odmah nakon infarkta miokarda, uz statine, može pomoći na isti način.

U asimptomatskih bolesnika s kronično reduciranom sistoličkom funkcijom lijeve klijetke (neovisno o etiologiji), primjena ACE inhibitora može smanjiti rizik od bolničkog liječenja povezanog sa ZS-om.

Primjena kardioverter defibrilatora (ICD) može se preporučiti u bolesnika s:

- asimptomatskom sistoličkom disfunkcijom lijeve klijetke (LVEF \leq 30 %) ishemijske etiologije, ako je prošlo najmanje 40 dana od akutnog infarkta miokarda
- asimptomatskom neishemijskom dilatativnom kardiomiopatijom (LVEF \leq 30 %) koji dobivaju optimalnu medikamentnu terapiju.

NOVI LIJEK ZA LIJEČENJE ZATAJIVANJA SRCA S DOBRIM REZULTATIMA

Neurohormonalni antagonisti (ACE inhibitori, MRA, beta-blokatori) dokazano mogu poboljšati preživljavanje u bolesnika s HFrEF te su preporučeni za liječenje svakog bolesnika s HFrEF, osim ako ne postoji kontraindikacija ili se ne podnose.

Novi, kombinirani lijek (LCZ696) sastoji se od blokatora angiotenzinskih receptora (valsartan) i inhibitora neprilizina (sakubitril). Rezultat nedavnog istraživanja pokazao je da je superioran u odnosu prema ACE inhibitoru (enalapril) u smanjenju rizika od smrti i hospitalizacija poradi ZS-a u studiji sa striktnim uključnim/isključnim kriterijima. Sakubitril/valsartan stoga je preporučan kao zamjena za ACE inhibitor u ambulantnih bolesnika s HFrEF koji su ostali simptomatski, unatoč optimalnoj terapiji, a koji odgovaraju kriterijima studije.

Lijekovi iz skupine blokatora angiotenzinskih receptora nisu dokazali znatno smanjenje smrtnosti u bolesnika s HFrEF, tako da njihova primjena treba biti ograničena na one

cardiovascular risks, analysis of natriuretic peptides can prove helpful.

It is of paramount importance to treat arterial hypertension as one of the best known risk factors for HF (SPRINT study). Recent data show that empagliflozin, a sodium-glucose cotransporter 2 inhibitor, improves prognosis of patients with diabetes mellitus type 2 (including reduced mortality and hospitalization for heart failure). Smoking cessation can also have favorable effects. The individuals using moderate amounts of alcoholic drinks are at a lower risk of *de novo* HF occurrence. Moderate physical activity is also useful. Glycemic impairment and overweight should also be treated properly.

Statins reduce the risk of some cardiovascular events and mortality, thus potentially preventing or delaying the occurrence of HF indirectly. In patients with coronary heart disease (CHD), the use of angiotensin-converting enzyme (ACE) inhibitors can prevent or delay the occurrence of HF, thus reducing cardiovascular as well as total mortality.

In acute myocardial infarction with ST-segment elevation (STEMI), primary coronary intervention (PCI) can prevent or delay the occurrence of HF by reducing the infarct zone. The administration of ACE inhibitors, beta-blockers and mineralocorticoid receptor antagonists (MRA) immediately after myocardial infarction, along with statins, can also prove useful.

In asymptomatic patients with chronic reduction of the left ventricular systolic function (irrespective of etiology), using ACE inhibitors can reduce the risk of hospital treatment for HF.

The use of implantable cardioverter defibrillators (ICD) is recommended in patients with:

- asymptomatic left ventricular systolic dysfunction (LVEF \leq 30%) of ischemic etiology, if at least 40 days have elapsed since acute myocardial infarction; and
- asymptomatic non-ischemic dilatative cardiomyopathy (LVEF \leq 30%) receiving optimal medicamentous therapy.

A NEW DRUG FOR HEART FAILURE TREATMENT WITH GOOD RESULTS

Neurohormonal antagonists (ACE inhibitors, MRA and beta-blockers) have been demonstrated to improve survival in patients with HFrEF and are recommended for treatment of all patients with HFrEF unless there is a contraindication for their use or patient intolerance.

A new combined drug (LCZ696) consists of the angiotensin receptor blocker (ARB) valsartan and the neprilysin (NEP) inhibitor sacubitril. Results of a recent study with strict inclusion/exclusion criteria showed it to be superior to ACE inhibitors (enalapril) in reducing the risk of death and hospitalization due to HF. Therefore, sacubitril/valsartan has been recommended as a substitute for ACE inhibitor in outpatients with HFrEF having remained symptomatic despite optimal therapy and meeting the study criteria.

Drugs from the group of angiotensin receptor blockers failed to demonstrate significant reduction of mortality in patients with HFrEF, therefore their use should be limited to patients not tolerating ACE inhibitors or those taking ACE inhibitors but not tolerating MRA.

bolesnike koji ne podnose ACE inhibitore ili na one koji uzimaju ACE inhibitore, ali ne toleriraju MRA.

Ivabradin snizuje povišenu frekvenciju srca, koja se često registrira u pacijenata s HFrEF, a pokazao je poboljšanje preživljavanja bolesnika sa ZS-om, tako da ga se preporučuje uključiti u skladu s kriterijima.

Navedeni se lijekovi daju pacijentima sa ZS-om najčešće zajedno s diureticima u bolesnika sa simptomima i/ili znakovima ZS-a.

PROMIJENJENE SU INDIKACIJE ZA SRČANU RESINKRONIZACIJSKU TERAPIJU

Srčana resinkronizacijska terapija (CRT) poboljšava srčane parametre u odabranih bolesnika s dijagnozom ZS-a, čime može smanjiti simptome, ukupni pobol i smrtnost, kao i poboljšati opći osjećaj bolesnika.

Preporuke za implantaciju CRT-a u bolesnika sa ZS-om jesu:

- CRT se preporučuje u simptomatskih bolesnika sa ZS-om, koji su u sinusnom ritmu, uz širinu QRS kompleksa ≥ 150 msec., a QRS ima morfologiju bloka lijeve grane te vrijednost LVEF-a $\leq 35\%$, unatoč optimalnoj primijeni lijekova, kako bi smanjili simptome, pobol i smrtnost (I A prema Smjernicama)
- o primjeni CRT-a trebalo bi se razmišljati u simptomatskih bolesnika, koji su u sinusnom ritmu, uz širinu QRS-a ≥ 150 msec., a QRS nema morfologiju bloka lijeve grane, uz vrijednosti LVEF-a $\leq 35\%$, unatoč optimalnoj terapiji, kako bi smanjili simptome, pobol i smrtnost (IIa B)
- CRT se preporučuje u simptomatskih bolesnika, koji su u sinusnom ritmu, uz QRS širinu 130 – 149 msec., a QRS ima morfologiju bloka lijeve grane, uz LVEF $\leq 35\%$, unatoč terapiji, kako bi se smanjili simptomi te morbiditet i mortalitet (I B)
- o primjeni CRT-a trebalo bi se razmišljati u simptomatskih bolesnika koji su u sinusnom ritmu, uz širinu QRS-a od 130 do 149 msec., a QRS nema morfologiju bloka lijeve grane, uz vrijednost LVEF-a $\leq 35\%$ unatoč optimalnoj medikamentnoj terapiji, kako bi smanjili simptome, pobol i smrtnost (IIb B)
- primjena CRT-a, prije nego stimulacija desne klijetke, preporučuje se u bolesnika s HFrEF (bez obzira na NYHA razred) koji imaju indicaciju za ventrikularnu stimulaciju i visoki stupanj AV bloka kako bi smanjili pobol. Navedeno uključuje i pacijente s fibrilacijom atrijske (I A)
- CRT bi se trebao razmatrati u pacijenata s vrijednosti LVEF $\leq 35\%$ u NYHA III. – IV. stupnju, uz optimalnu primjenu lijekova, kako bi smanjili simptome, pobol i smrtnost ako su pacijenti u fibrilaciji atrijske i imaju širinu QRS-a ≥ 130 msec. (IIa B)
- u pacijenta s dijagnozom HFrEF-a koji su dobili konvencionalni elektrostimulator ili ICD, a u kojih je nastupilo pogoršanje ZS-a, unatoč optimalnoj terapiji, uz visoku zastupljenost stimulacije desne klijetke, može se razmišljati o primjeni CRT-a. Navedeno se ne odnosi na bolesnike koji imaju stabilni stadij zatajivanja srca (IIb B)
- primjena je CRT-a kontraindicirana u bolesnika s trajanjem QRS < 130 msec. (III A)
- u bolesnika sa širinom QRS > 130 msec. trebalo bi se razmišljati o ugradnji defibrilatora s CRT-om (CRT-D).

Ivabradine decreases elevated heart rate, which is frequently recorded in HFrEF patients, and has been associated with improved survival in HF patients; it is therefore recommended to include it in patient therapy, in line with the respective criteria.

The above mentioned drugs are administered together with diuretics in patients with symptoms and/or signs of HF.

MODIFIED INDICATIONS FOR CARDIAC RESYNCHRONIZATION THERAPY

Cardiac resynchronization therapy (CRT) improves cardiac parameters in selected patients diagnosed with HF, thus reducing the symptoms, overall morbidity and mortality, while upgrading the patient general condition.

The following are recommendations for CRT in HF patients:

- CRT is recommended in symptomatic patients with HF in sinus rhythm, with QRS complex width ≥ 150 msec, QRS showing left bundle branch block (LBBB) morphology, and LVEF $\leq 35\%$ while on optimal therapy, in order to reduce the symptoms, morbidity and mortality (I A according to Guidelines);
- CRT should be considered in symptomatic patients in sinus rhythm, with QRS width ≥ 150 msec, QRS not showing LBBB morphology, and LVEF $\leq 35\%$ while on optimal therapy, in order to reduce the symptoms, morbidity and mortality (IIa B);
- CRT is recommended in symptomatic patients in sinus rhythm, with QRS width 130-149 msec, QRS showing LBBB morphology, and LVEF $\leq 35\%$ despite therapy, in order to reduce the symptoms, morbidity and mortality (I B);
- CRT should be considered in symptomatic patients in sinus rhythm, with QRS width 130-149 msec, QRS not showing LBBB morphology, and LVEF $\leq 35\%$ despite optimal medication therapy, in order to reduce the symptoms, morbidity and mortality (IIb B);
- CRT rather than right ventricular stimulation is recommended in patients with HFrEF (irrespective of NYHA class) that have an indication for ventricular stimulation and high grade AV block, in order to reduce morbidity. This also includes patients with atrial fibrillation (I A);
- CRT should be considered in patients with LVEF $\leq 35\%$ in NYHA class III-IV despite optimal medication therapy, in order to reduce the symptoms, morbidity and mortality, if there is atrial fibrillation and QRS width ≥ 130 msec (IIa B);
- CRT can be considered in patients diagnosed with HFrEF having already received conventional pacemaker or ICD but have experienced HF exacerbation despite optimal therapy, along with high right ventricular stimulation. This does not apply to patients in stable stage HF (IIb B);
- CRT is contraindicated in patients with QRS duration < 130 msec (III A); and
- implantation of defibrillator with CRT (CRT-D) should be considered in patients with QRS width < 130 msec.

THE CONCEPT OF EARLY INITIATION OF APPROPRIATE THERAPY IS RECOMMENDED

The diagnosis and therapy of acute HF should proceed in parallel, implying the 'time to therapy is crucial' principle. Such an approach to treatment has been successfully employed in

PREPORUČEN JE KONCEPT RANOG ZAPOČINJANJA ADEKVATNE TERAPIJE

Naime, dijagnostika i terapija akutnog ZS-a trebale bi ići usporedno, što znači pristup "bitno je vrijeme do terapije"; ovakav se način liječenja već duže uspješno primjenjuje u liječenju akutnoga koronarnog sindroma (ACS).

Posebno je važno navrijeme dijagnosticirati i liječiti pojedine komorbiditete: KBS, arterijsku hipertenziju, valvularnu bolest, aritmije (posebno fibrilaciju atrijske i ventrikularne poremećaje ritma), dijabetes, plućne bolesti (KOPB, astma), bolesti središnjega živčanog sustava (depresiju, moždani udar, autonomnu disfunkciju i dr.), poremećaje spavanja, anemiju, bubrežnu insuficijenciju, elektrolitski disbalans (posebno hipokalemiju i hiperkalemiju), dislipidemiju, kaheksiju/debljinu, uričnu dijatezu, artritis te erektilnu disfunkciju.

NOVI ALGORITAM ZA DIJAGNOSTIKU I LIJEČENJE AKUTNOG ZATAJIVANJA SRCA

Objavljen je novi algoritam za dijagnostiku i liječenje akutnog zatajivanja srca (AZS), koji se temelji na prisutnosti ili odsutnosti znakova kongestije ili hipoperfuzije.

Dijagnoza AZS-a podrazumijeva naglo pojavljivanje ili pogoršanje simptoma i/ili znakova ZS-a. To je za život opasno stanje koje zahtijeva žurnu dijagnostiku, liječenje i hospitalizaciju. Nastaje *de novo* ili kao pogoršanje kroničnog ZS-a; može biti uzrokovano primarnom srčanom disfunkcijom ili precipitirajućim čimbenicima. Najčešći su uzroci miokardna disfunkcija (ishemija, upala, toksični agensi), akutna insuficijencija zalistaka i tamponada perikarda. Pogoršanje kroničnog zatajivanja srca može nastati samo po sebi, no najčešće je povezano s precipitirajućim čimbenicima kao što su infekcija, nekontrolirana hipertenzija, poremećaj ritma, neadekvatno uzimanje lijekova ili hrane.

Klasifikacija AZS-a temelji se na kliničkom pregledu bolesnika. Važno je uočiti simptome i znakove kongestije ("vlažno" / "suho" stanje; da/ne) i hipoperfuzije ("hladno" / "toplo" stanje; da/ne). Kombinacijom, prepoznamo 4 skupine:

- topli i vlažni (dobra perfuzija i kongestija)
- hladni i vlažni (hipoperfuzija i kongestija)
- hladni i suhi (hipoperfuzija bez kongestije)
- topli i suhi (dobra perfuzija, bez kongestije).

Navedena klasifikacija pomaže u vođenju terapije u početnoj fazi, a može dati i prognostičke informacije.

U pacijenata s AZS-om posebno je bitna žurna dijagnostika uz rani početak liječenja.

Izbor iz nedavno objavljenih studija o zatajivanju srca

ADAPTIVNA SERVO-VENTILACIJA (ASV) U ZATAJIVANJU SRCA I CENTRALNA SLEEP-APNEJA

Sleep-apneja česta je prateća bolest u bolesnika sa zatajivanjem srca sa sniženom sistoličkom funkcijom lijeve klijetke. Opisana su 2 tipa poremećaja: opstruktivna *sleep-apneja* i centralna *sleep-apneja*. Prevalencija centralne *sleep-apneje*

the management of acute coronary syndrome (ACS) for quite a long time now.

It is of utmost importance to timely diagnose and treat particular comorbidities such as CHD, arterial hypertension, valvular disease, arrhythmias (atrial fibrillation and ventricular rhythm abnormalities in particular), diabetes, pulmonary diseases (COPD, asthma), central nervous system diseases (depression, stroke, autonomic dysfunction, etc.), sleep disorders, anemia, renal insufficiency, electrolyte imbalance (hypokalemia and hyperkalemia in particular), dyslipidemia, cachexia/obesity, uric diathesis, arthritis, and erectile dysfunction.

THE NEW ALGORITHM FOR DIAGNOSIS AND TREATMENT OF ACUTE HEART FAILURE

The new algorithm for diagnosis and treatment of acute heart failure (AHF), based on the presence or absence of the signs of congestion or hypoperfusion, has been issued.

The diagnosis of AHF implies abrupt occurrence or exacerbation of the symptoms and/or signs of HF. It is a life-threatening state that requires urgent diagnosis, treatment and hospitalization. AHF occurs *de novo* or as chronic HF exacerbation, and can be caused by primary cardiac dysfunction or precipitating factors. The most common causes include myocardial dysfunction (ischemia, inflammation, toxic agents), acute valve insufficiency, and pericardial tamponade. Chronic HF exacerbation can occur independently, but it is most frequently associated with precipitating factors such as infection, uncontrolled hypertension, rhythm abnormalities, and inappropriate medication and food intake.

The classification of AHF relies on the patient clinical examination, which should reveal the symptoms and signs of congestion ('moist'/'dry' state; yes/no) and hypoperfusion ('cold'/'warm' state; yes/no). Using this combination, four groups are distinguished:

- warm and moist (good perfusion and congestion);
- cold and moist (hypoperfusion and congestion);
- cold and dry (hypoperfusion without congestion); and
- warm and dry (good perfusion, no congestion).

This classification helps determine therapy in the initial stage and may provide useful prognostic information.

Urgent diagnosis and early treatment initiation are of utmost importance in AHF patients.

Selected Reading from Recent Studies on Heart Failure

ADAPTIVE SERVO-VENTILATION (ASV) IN HEART FAILURE AND CENTRAL SLEEP APNEA

Sleep apnea is a frequent comorbidity in HF patients with decreased systolic left ventricular function. Two types of the disorder have been described, i.e. obstructive sleep apnea and central heart failure. The prevalence of central sleep apnea that usually manifests as Cheyne-Stokes respiration increases with the severity of sleep apnea. This form of the disease is associated with poorer prognosis.

je, koja se obično očituje kao Cheynes-Stokesova respiracija, povećava se s težinom zatajivanja srca. Ovaj je oblik bolesti vezan za lošiju prognozu.

Cilj studije SERVE-HF bio je utvrditi učinak adaptivne servo-ventilacije (ASV) koja isporučuje servo-kontroliranu inspiratornu tlačnu potporu na temelju ekspiratornoga pozitivnog dišnog tlaka, u pacijenata s umjerenim do težim oblikom zatajivanja srca i istisnom frakcijom lijeve klijetke $\leq 45\%$, koji predominantno imaju centralnu *sleep*-apneju. Ukupno 1325 pacijenata u NYHA III. stupnju ZS-a na adekvatnoj standardnoj terapiji bilo je uključeno i randomizirano na ASV ili na kontrolnu terapiju. Iznenađuje primjedba da je došlo do znatnog porasta ukupne i kardiovaskularne smrtnosti u skupini na ASV-u. Rezultati SERVE-HF u suprotnosti su s rezultatima prijašnjih manjih studija. Jedno od potencijalnih objašnjenja za ovaj porast kardiovaskularnog mortaliteta u centralnoj *sleep*-apneji, može biti kompenzatorni mehanizam; redukcija ovog adaptivnog respiratornog mehanizma uz ASV može biti štetna. Drugo je objašnjenje to da primjena pozitivnoga tlaka na dišni sustav može promijeniti srčanu funkciju, posebno u pacijenata sa sniženim pulmonalnim kapilarnim tlakom. Važna implikacija negativnog rezultata SERVE-HF studije jest da se ova procedura ne smije preporučivati u pacijenata sa ZS-om i sniženom sistoličkom funkcijom lijeve klijetke uz centralnu *sleep*-apneju te da se mora zaustaviti upotreba u pacijenata koji se upravo njome koriste. No, može se upotrebljavati kod opstruktivne *sleep*-apneje.

HIPOGLIKEMICI I ZATAJIVANJE SRCA

Studija EMPA-REG OUTCOME testirala je 2 doze inhibitora Na-glukoza kotransportera 2, empagliflozina, u usporedbi s placebom u 7020 bolesnika s dijabetesom tipa 2 i visokim kardiovaskularnim rizikom. Nakon opservacije tijekom 3,1 godine, primarni cilj (smrt od kardiovaskularnih događaja, nefatalni infarkt miokarda ili nefatalni moždani udar) bio je značajno snižen za 14 % u skupini na empagliflozinu. Zanimljivo, hospitalizacija poradi ZS-a, kao i zajednički ciljnih ishoda sastavljen od hospitalizacije poradi ZS-a ili smrti od kardiovaskularnih uzroka bili su također signifikantno sniženi. Možemo zaključiti da ovaj novi antidiabetički lijek, uz standardnu terapiju, nije samo siguran za uporabu u pacijenata sa ZS-om nego i povoljan za prevenciju hospitalizacija od ZS-a u bolesnika s dijabetesom tipa 2.

ALKOHOL I RIZIK OD ZATAJIVANJA SRCA

Konзумiranje alkohola u većoj mjeri dovodi do srčane disfunkcije, a katkad i do alkoholne kardiomiopatije. No, povezanost umjerenog konzumiranja alkoholnih pića i rizika od razvoja ZS-a kontroverzna je.

ARIC studija analizirala je 14 629 osoba (bez dijagnoze ZS-a u početku studije) koje su bilježile svoje konzumiranje alkoholnih pića. Tijekom prosječnog perioda praćenja od 24 godine, ZS se pojavio u 1271 muškarca i 1237 žena. Muškarci koji su konzumirali do 7 pića tjedno (1 piće = 14 g alkohola) imali su sniženi rizik od razvoja ZS-a u usporedbi s apstinencijom (HR = 0,80; 95 % CI, 0,68 – 0,94; P = 0,006). Ovakav "protektivni" učinak bio je manje izražen u žena (HR = 0,84; 95 % CI, 0,71 – 1,00; P = 0,05). U osoba koje su konzumirale alkohol u značajnoj

The aim of the SERVE-HF study was to assess the effect of adaptive servo-ventilation (ASV), which provides the servo-controlled inspiratory pressure support based on expiratory positive airway pressure in patients with moderate to severe form of HF and LVEF $\leq 45\%$ that predominantly suffer from central sleep apnea. The study included 1325 patients in NYHA class III HF on appropriate standard therapy, randomized to ASV or control therapy. Surprisingly, a significant increase in total and cardiovascular mortality was recorded in the ASV group. Results of the SERVE-HF study were opposite to the results of some earlier small studies. One of the potential explanations of this increase in cardiovascular mortality in central sleep apnea may imply the compensatory mechanism, as reduction of this adaptive respiratory mechanism may be detrimental in combination with ASV. Another explanation is that the use of positive pressure upon the respiratory system may modify cardiac function, in particular in patients with decreased pulmonary capillary pressure. An important implication of the negative result of the SERVE-HF study is that this procedure should not be advised in patients with HF, reduced systolic left ventricular function and central sleep apnea, and that it should be discontinued in such patients currently using it. However, the procedure can be used in patients with obstructive sleep apnea.

HYPOGLYCEMIC AGENTS AND HEART FAILURE

The EMPA-REG OUTCOME study tested two doses of empagliflozin, a sodium-glucose cotransporter 2 inhibitor, in comparison with placebo in 7020 patients with diabetes mellitus type 2 and high cardiovascular risk. Following 3.1-year observation, the primary endpoint (death from cardiovascular events, nonfatal myocardial infarction or nonfatal stroke) was significantly reduced by 14% in the empagliflozin group. Interestingly, hospitalization for HF and composite outcome consisting of hospitalization for HF or death from cardiovascular events were also significantly reduced. It is concluded that this novel antidiabetic agent administered along with standard therapy is not only safe for use in HF patients but is also beneficial for prevention of hospitalization for HF in patients with diabetes mellitus type 2.

ALCOHOL AND RISK OF HEART FAILURE

Excessive alcohol consumption leads to cardiac dysfunction and occasionally to alcoholic cardiomyopathy. However, the association of moderate alcohol consumption and the risk of HF is a controversial issue.

The ARIC study analyzed data obtained in 14,629 subjects (without HF diagnosis at study entry) having made records of their use of alcoholic drinks. During a mean 24-year follow up, HF developed in 1271 male and 1237 female subjects. The men that reported taking up to 7 drinks per week (1 drink = 14 g alcohol) had a lower risk of HF development as compared with alcohol abstainers (HR=0.80; 95% CI 0.68-0.94; p=0.006). This 'protective' effect was less pronounced in women (HR=0.84; 95% CI 0.71-1.00; p=0.05). In subjects taking alcoholic drinks in excess, the risk of HF did not differ from that recorded in abstainers, irrespective of sex.

mjeri rizik od ZS-a nije se razlikovao u usporedbi s apstinencijom, bilo da je riječ o ženama ili muškarcima.

Rezultati upućuju na to da umjereno konzumiranje alkoholnih pića može biti povezano s nižim rizikom od razvoja ZS-a.

These results suggest that moderate intake of alcoholic drinks may be associated with a lower risk of HF development.

LITERATURE

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