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ZNAČAJ DIJAGNOSTIKE POREMEĆAJA TIREOIDNE FUNKCIJE: UTICAJ SUPKLINIČKIH POREMEĆAJA NA BOLESTI SRCA

Sažetak: Supklinička oboljenja štitaste žlezde na više načina povezana su sa kardiovaskularnim bolestima. Najčešći srčani poremećaji kod bolesnika sa supkliničkom hipotireozom su dijastolna disfunkcija leve komore i smanjen funkcionalni kapacitet srca, te time oslabljen kardiopulmonalni odgovor pri naporu. Prema publikovanim podacima, supklinička hipotireoza u vezi je sa povećanim nivoom holesterola, povećanim rizicima od koronarne bolesti srca i bolesti aorte, te povećanim kardiovaskularnim mortalitetom.

Bolesnici sa supkliničkom hipertireozom imaju povećan rizik od nastanka atrijalne fibrilacije, što dalje može dovesti do tromboembolijskih događaja; disfunkcija može dovesti do srčane dekompenzacije i hronične srčane slabosti.

S obzirom na to da su supklinička oboljenja štitaste žlezde obično progresivna, jasan je veliki značaj pravovremene funkcionalne dijagnostike lečenju sprečavanja kardiovaskularnih komplikacija.

Ključne reči: tireoidna žlezda, srce, hipofunkcija, hiperfunkcija

Abstract: Subclinical thyroid disease in many ways are associated with cardiovascular disease. The most common cardiovascular disorders in patients with subclinical hypothyroidism are diastolic dysfunction and reduced functional capacity of the heart, and thus weakened cardiopulmonary response during exercise. According to published data subclinical hypothyroidism is associated with abnormal cholesterol levels, increased

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risk of coronary heart disease and diseases of the aorta, and increased cardiovascular mortality.

Patients with subclinical hyperthyroidism are at increased risk of atrial fibrillation, which may lead to thromboembolic events; increased left ventricular mass is related to the sudden cardiac death; significant diastolic dysfunction can lead to cardiac decompensation and chronic heart failure.

Given that subclinical thyroid disease is usually progressive, is a clear great importance of timely functional diagnostics in the treatment and prevention cardiovascular complications.

Key words: thyroid, subclinical, hypothyreoidism, hyperthyreoidism

Uvod: Eksperimentalni i klinički dokazi čvrsto podržavaju koncept da tireoidni hormoni imaju fundamentalnu ulogu u kardiovaskularnoj homeostazi, kako u fiziološkim, tako i u patološkim uslovima.

Postoje dokazi da pacijenti s akutnim i hroničnim srčanim bolestima, kao i oni koji podležu kardiohirurgiji, mogu imati izmenjen periferni metabolizam tireoidnih hormona, koji potom može biti u vezi sa promenom srčanih funkcija. Disfunkcija štitne žlezde prouzrokuje značajne promene u kardiovaskularnom sistemu. Opsežni dokazi indikuju da kardiovaskularni sistem odgovara na minimalne, ali perzistentne promene u nivou cirkulišućih hormona, što je tipično za osobe sa supkliničkom tireoidnom disfunkcijom.

Efekti supkliničke hipotireoze na kardiovaskularni sistem

Uopšteno, tokom mirovanja broj otkucaja srca i krvni pritisak kod pacijenata sa supkliničkom hipotireozom su normalni. Pojedina ispitivanja pokazala su i značajnije hipofunkcionalne abnormalnosti u parasimpatičkom nervnom sistemu, te povećanje prevalence arterijske hipertenzije kod ovih pacijenata. Najznačajnija srčana abnormalnost prisutna kod pacijenata sa supkliničkom hipotireozom jeste dijastolna disfunkcija leve komore, koja se karakteriše usporenom relaksacijom miokarda i oslabljenim ranim punjenjem komore. Promene su prisutne kako i miru, tako i tokom opterećenja. Često je ovo u vezi sa različitim stepenom slabosti sistolne funkcije leve komore, što postaje jače izraženo tokom opterećenja.

Studije su pokazale da pacijenti sa supkliničkom hipotireozom imaju na nekoliko načina oslabljen kardiopulmonalni odgovor pri fizičkom opterećenju. Studija, kojom je ispitivana prognostička uloga supkliničke hipotireoze kad 400 pacijenata sa hroničnom srčanom slabošću (Lacoviello et al, Univerzitetska klinika, Bari) obuhvatala je dijagnostičke procedure (EKG, ECHO srca, ERGO-test), kao i analize krvi kojim su

ispitivani: renalna funkcija, elektroliti, gram-hemoglobin, NT-proBNP, fT3, fT4, TSH nivo, pokazala je da je samo praćenje nivoa TSH signifikantno za pogoršanje hronične srčane slabosti, tj. da je TSH nezavisan prediktor pogoršanja hronične srčane slabosti.

Hipotireoza, naročito u supkliničkoj formi, česta je kod pacijenata sa hroničnom srčanom slabošću koji primaju Amiodaron. Najnovije preporuke u tretmanu takvih pacijenata jesu primena supstitucione terapije Levotiroxin-om, bez potrebe isključivanja Amiodarona iz terapije, uz redovno testiranje tireoidne funkcije.

Studije su pokazale da je SY. LOW T3 jedan nezavisan prediktor i ranog i kasnog preživljavanja pacijenata sa akutnim srčanim udarom, kao i da je snižen fT3 nivo prediktor za jednosudovnu i za višesudovnu koronarnu bolest.

Postoji jaka veza između supkliničke hipotireoze i aterosklerotske kardiovaskularne bolesti, nezavisno od tradicionalnih faktora rizika: hiperholesterolemije, hipertenzije, pušenja, šećerne bolesti – ROTTERDAM STUDY.

Supklinička hipotireoza u vezi je sa aterogenim lipidnim profilom: povećanjem nivoa ukupnog holesterola, LDL-a, kao i oksidisanih lipoproteina male gustine u cirkulaciji. Takođe, deluje na profil hemostaze, tj. hiperkoagulabilni status. Kod pacijenata sa supkliničkom hipotireozom registrovano je i smanjenje endotelijum zavisnih medijatora vazodilatacije, koji su rani marker ateroskleroze.

Značajno je da se većina kardiovaskularnih i metaboličkih abnormalnosti poboljšava ili čak normalizuje kada se pacijenti sa supklinickom hipotireozom tretiraju sa L-T4. Da li pacijente sa supkliničkom hipotireozom treba tretirati na ovaj način ostaje predmet usaglašavanja.

Efekti supkliničke hipertireoze na kardiovaskularni sistem

Kada su u pitanju efekti supkliničke hipertireoze na kardiovaskularni sistem treba uzeti u obzir da se najčešće radi o *egzogenoj* supkliničkoj hipertireozi.

Najznačajnije abnormalnosti nađene kod pacijenata sa supkliničkom hipertireozom su: povećanje frekvence, povećanje prevalence supraventrikularnih aritmija, uvećanje mase leve komore, lako povećanje sistolne funkcije leve komore, kao i oslabljena dijastolna funkcija kao posledica usporene relaksacije miokarda.

Povećanje mase leve komore posledica je zadebljanja zidova leve komore, bez povećanja dimenzija šupljine, tzv. koncentrični remodeling.

Hipertrofija leve komore više korespondira sa dužinom trajanja supkliničke hipertireoze nego sa nivoom cirkulišućih tireoidnih hormona. Mehanizam odgovoran za hipertrofiju leve komore još nije u potpunosti rasvetljen, verovatno nastaje kao odgovor na hronično hemodinamsko opterećenje usled blagog hiperkinetskog kardiovaskularnog statusa (usporena relaksacija miokarda i oslabljeno punjenje leve komore).

Postoje sugestije da ova dijastolna disfunkcija jeste rezultat izmenjenog intracelularnog vezivanja kalcijuma usled redukovane ekspresije kalcijum ATP-aze na sar-

koplazmatskom retikulumu ili povećane ekspresije phospholambana-a, sa odloženim preuzimanjem kalcijuma od strane sarkoplazmatskog retikuluma. Postavlja se hipoteza da bi, u dužem periodu efekti metabolizma kalcijuma na hronično opterećenje srca trebalo da nadjača one prouzrokovane tireoidnim hormonima.

Abnormalnosti morfologije i funkcije leve komore značajno se smanjuju prevođenjem pacijenata u eurioisni status, kao i primenom lekova iz grupe beta-blokatora. Ovo potvrđuje hipotezu da je uključivanje srca u supkliničku hipertireozu reverzibilno i uglavnom determinisano funkcionalnim mehanizmima.

Postoje dokazi da je supklinička hipertireoza u vezi sa povećanjem kardiovaskularnog mortaliteta. Nekoliko faktora korelira sa ovim fenomenom: pacijenti sa supkliničkom hipertireozom, posebno stariji, imaju povećan rizik od nastanka atrijalne fibrilacije, što može uticati na povećanje incidence tromboembolijskih događaja; pokazano je da je povećanje mase LV *per se*, kao i srčane frekvence u vezi sa povećanim rizikom od nagle srčane smrti; poznato je da dijastolna disfunkcija može vremenom dovesti do razvoja ozbiljne dijastolne disfunkcije koja, posebno kod starijih, moze prouzrokovati srčanu dekompenzaciju i hroničnu srčanu slabost.

Terapeutske indikacije bile bi da kod kardiovaskularnih pacijenata, koji imaju benignu tireoidnu bolest, treba izbeći ili korigovati supkliničku hipertireozu, a kod bolesnika kod kojih je supklinički hipertireoidizam terapeutska indikacija (npr. diferencirani tireoidni kancer) L-T4 se primenjuje u manjim dozama od dovoljnih za postizanje stabilne TSH supresije, eventualno u kombinaciji sa beta-blokatorima.

Supklinička hipertireoza može biti očekivana:

– kod svih pacijenata sa istorijom atrijalne fibrilacije, naročito kod starijih
– pacijenata sa pogoršanjem angioznih tegoba
– pacijenata sa srčanom dekompenzacijom.

Zaključak

Imajući u vidu da simptomi i znaci od strane kardiovaskularnog sistema mogu biti jedina manifestacija tireoidne disfunkcije, kao i da perzistentna supklinička tireoidna disfunkcija može značajno povećati kardiovaskularni rizik, tireoidni status trebalo bi biti sistematski ispitivan kod: svih pacijenata sa novodijagnostikovanom kardiovaskularnom bolešću, kao i kod pacijenata sa pogoršanjem kardiovaskularne bolesti, posebno starije životne dobi.

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