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CLINICAL IMPORTANCE OF BIOCHEMICAL MARKERS OF CARDIAC DAMAGE IN HEMODIALYSIS PATIENTS

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KLINIČKI ZNAČAJ BIOHEMIJSKIH MARKERA SRČANOG OŠTEĆENJA KOD PACIJENATA NA HEMODIJALIZI

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ABSTRACT

Cardiovascular diseases are the most frequent cause of morbidity and mortality in patients on regular hemodialysis. Cardiovascular mortality in this patients subset is approximately 9% per year, and among cardiovascular complications, the left ventricle hypertrophy, ischemic heart disease and congestive heart failure are the most prevalent. Risk factors for atherosclerosis and cardiovascular complications in hemodialysis patients are: high blood pressure, lipid metabolism disorder, oxidative stress, microinflammation, hypoalbuminemia, anaemia, hyperhomocysteinemia, high concentration of asymetric dimethylarginine-ADMA and secondary hyperparathyroidism. Diagnostic strategy for early detection of patients with higher risk for cardiovascular complications should include the following: tests for cardiovascular risk factors detection (homocystein, ADMA), tests for estimation of microinflamation, coronary artery plaque instability and voulnerability risks (CRP), tests for detection of markers of ischemia and damage of cardiac tissue, (cTnT, cTnI), as well as myocardial function tests (ANP, BNP, Nt-proBNP). Precise detection of the most sensitive of high risk for cardiovascular complications enables right timing for adequate therapeutic strategy, which means high degree of survival of the patiens with end stage of renal disease.

Key words: renal dialysis, cardiovascular diseases, morbidity, mortality, diagnosis

SAŽETAK

Kardiovaskularne bolesti su najčešći uzrok morbiditeta i mortaliteta bolesnika koji se leče redovnim hemodijalizama. Stopa kardiovaskularnog mortaliteta kod ovih bolesnika iznosi približno 9% godišnje, a među kardiovaskularnim komplikacijama najveća je prevalencija hipertrofije leve komore, ishemijske bolesti srca i kongestivne srčane slabosti. U faktore rizika za razvoj ateroskleroze i kardiovaskularnih komplikacija kod bolesnika na hemodijalizi spadaju: povišen arterijski krvni pritisak, poremećaj metabolizma lipida, oksidativni stres, mikroinflamacija, hipoalbuminemija, anemija, hiperhomocisteinemija, povećana koncentracija asimetričnog dimetilarginina-ADMA i sekundarni hiperparatireoidizam. Dijagnostička strategija za rano otkrivanje bolesnika sa povećanim rizikom za razvoj kardiovaskularnih komplikacija treba da uključi: testove za određivanje faktora kardiovaskularnog rizika (homocistein, ADMA), testove za procenu mikroinflamacije, nestabilnosti plaka koronarnih arterija i rizika njegovog prskanja (CRP), testove za određivanje pokazatelja ishemije i oštećenja srčanog tkiva (cTnT, cTnI), kao i testove za određivanje pokazatelja funkcije miokarda (ANP, BNP, Nt-proBNP). Utvrđivanje najosetljivijih parametara visokogm rizika za razvoj kardiovaskularnih komplikacija omogućava pravovremenu primenu odgovarajuće terapijske strategije, koja obezbeđuje visok stepen preživljavanja bolesnika sa završnim stadijumom hronične slabosti bubrega.

Ključne reči: hemodijaliza, kardiovaskularne bolesti, morbiditet, mortalitet, dijagnoza

INTRODUCTION

Cardiovascular diseases are the most frequent cause of morbidity and mortality in patients on regular hemodialisys. Annual cardiovascular mortality in these patients is approximately 9% (1, 2), and among cardiovascular complications, the most prevalent are left ventricle hypertrophy, ischemic heart disease and congestive heart failure (1–6). Risk factors for cardiovascular complications in hemodialysis patients are: high blood pressure, lipid metabolism disorder, oxidative stress, microinflammation, hypoalbuminemia, anaemia, hyperhomocysteinemia, high concentration of asymetric dimethylarginine-ADMA, high blood flow through the vascular access for hemodialysis and secondary hyperparathyroidism (table 1) (6–17).

Table 1. Cardiovascular risk factors in hemodialysis patients.

CATEGORY		RISK FACTORS
TRADITIONAL		Cigarete Smoking Hypertension Hyperlipidemia Diabetes mellitus Obesity
NON TRADITIONAL	HEMODYNAMIC	Anaemia Retention of Na+ and H2O AV fistula (QAV > 1000 mL/min)
	METABOLIC	Hypoalbuminemia Hyperhomocysteinemia Oxydative stress Microinflammation Secondary hyperparatireoidism

Modified according to reference (3).

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Laboratory tests in clinical cardiology

Four groups of laboratory tests are used in clinical cardiology: 1) tests for cardiovascular risk factors detection (homocystein, asymetric dimethylarginine-ADMA, C-reactive protein, lipids, oxidatively changed LDL lipoprotein-oxLDL, malondialdehid-MDA); 2) tests for estimation of microinflamation, (coronary artery plaque instability and voulnerability risks, choline, PAPP-A - protein A related with pregnancy); 3) tests for detection of markers of ischemia and damage of cardiac tissue, (IMA - Ischemia modulated albumin, Creatin kinase-CK, lactat dehydrogenase-LDH, SGOT-serum glutamat oxalat transaminase, cardiac troponin-cTn); 4) Myocardial function tests (ANP-atrial natriuretic peptid, BNP-brain natriuretic peptid, N terminal-pro BNP-Nt - proBNP) (figure 1) (18–21).

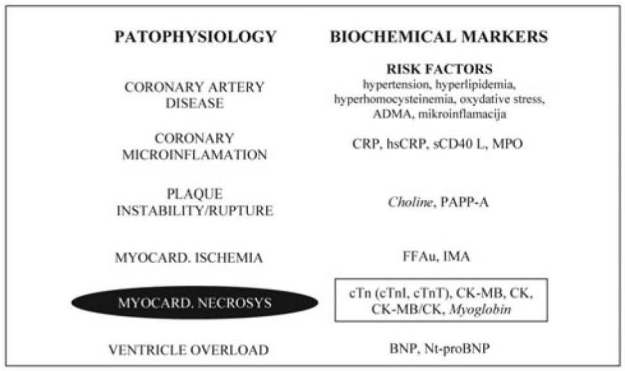

Figure 1. Biochemical markers for heart disease evaluation. Modified according to reference (18). CRP - C-reaktive protein, sCD40L - solubile CD40 ligand, MPO - myeloperoxydase, PAPP-A - protein A binded with pregnancy , FFA - free fatty acid, IMA - ischemia modulated albumin, CK - Creatine phosfokinase, CK-MB - Creatine kinase-isomer MB, cTnI - cardiac troponin I, cTnT - cardiac troponin T, BNP - brain natriuretic peptid, Nt-proBNP - N terminal fragment proBNP.

Test for risk factors determination and cardiovascular risk stratification

Homocystein is product of metabolism of essential aminoacid metionin (figure 2) (22). Metionin is demethylised into Sadenosylmetionin, which is important methyl group donor for different biological reactions. When S-adenosylmetionin lose methyl group it turns into homocystein, which can further be metabolised in two ways: by re-methylation process or by trans-sulfuration process (22–25). Re-methylation process has two ways. First way of re-methylation is included in the folate cicle. Metabolically active folate, 5-metyltetrahydrofolate (5-MTHF), in the presence of an enzyme from the folat cicle, reductase 5-MTHF, serves as a donor of the methyl groups, and the cofactor is vitamin B12. Other way of re-methylation uses betain as a methyl group donor, and doesn't depend on folate cicle, having rather small role in the re-methylation. By the process of trans-sulfuration, homocystein is transmitted into cystein, and for that reaction vitamin B6 is essential, as a cofactor, and enzyme β-cystation sintase (22–25). Average homocystein concentration in plasma of a healthy person is 6–12 μmol/L (22). In the patients who are treated with hemodialysis hyperhomocysteinemia is assumed if homocystein concentration in the plasma is ≥ 15 μmol/L (22). Mild hyperhomocysteinemia is assumed if homocystein concentration in the plasm is between 15–30 μmol/L, modest hyperhomocysteinemia is between 31–100 μmol/L, and true hyperhomocysteinemia is considered if plasma concentration of homocystein is above 100 μmol/L (23).

More than 80% of patients on hemodialysis has elevated plasma concentration of homocystein (16, 24). Hyperhomocysteinemia blocks activity of dimethylarginine dimethylhydrolase-DDAH enzyme, which has a specific role in the process of degradation of asymetric dimethylarginine and contributes in accumulation of ADMA in endothelial cells and triggering of atherosclerotic process (21–26). Hyperhomocysteinemia is the risk factor for atherosclerosis and cardiovascular complications in patients on hemodialysis (21–26).

Whole homocystein plasma concentration is independent predictor of cardiovascular mortality in patients on regular hemodialysis. Patients on hemodialysis with homocystein

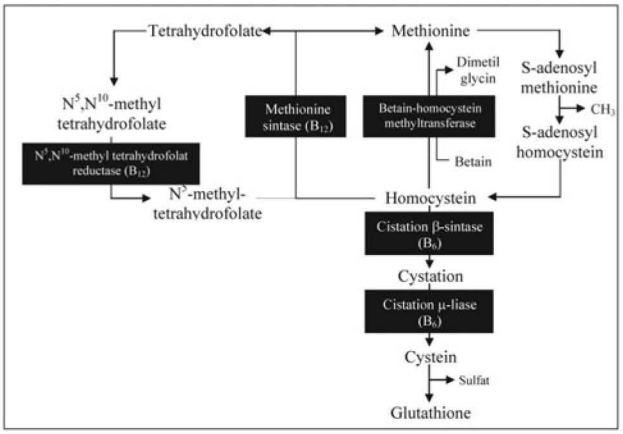

Figure 2. Biochemical paths of homocystein synthesis and degradation.

plasma concentration ≥ 37.8 μmol/L have 8.2 fold greater risk for cardiovascular mortality comparing to homocystein blood concentration bellow 22.9 μmol/L (27). Asymetric dimethylarginine is a result of degradation of methylated proteins (figure 3). Methylation of the arginine residuals inside different proteins and/or polypeptids is done by means of N-methyltransferase I and II (methylase I and II). S-adenosylmethyonine serves as a methyl groups donor for the process of methylation of arginine residuals of proteins. As a result of methylation of arginine residuals become S-adenosyl-L-homocystein (SAH) and methylised proteins (proteins that contain ADMA) (9–12). Enzyme protein arginine methyltransferase I (PRMT I) takes part in the processes of asymetric dimethylarginine-ADMA synthesis. By hydrolysis of methylated proteins ADMA is liberated. Asymetric dimethylarginine is the most important endogenous blocking substance of Nitrous oxyde-NO synthesis in endothelial cells (eNOS) (9–12). In healthy population, normal concentration of ADMA in plasma is ≤ 1,0 μmol/L, in patients on hemodialysis ≤ 2.2 μmol/L, and if in concentrations between 3–15μmol/L ADMA is blocking NO synthesis in endothelial cells and triggers the process of atherosclerosis. (12). Accumulation of ADMA in endothelial cells secondary leads to malfunction of the system of L-arginine/NO (9–12).

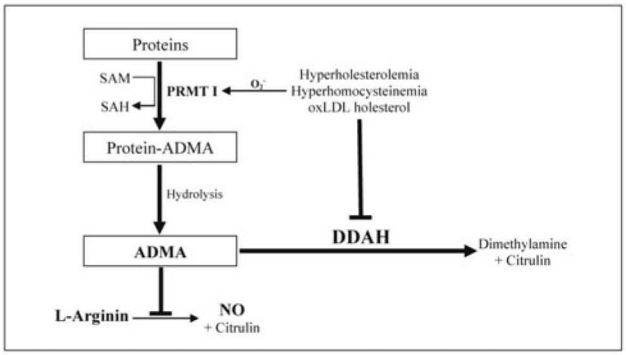

Figure 3. Biochemical paths of creation and degradation of asymmetric dimethylarginine-ADMA. SAH-S-adenosyl-L-homocystein, DDAH-dimethylarginine dimethylhydrolase, PRMT I-protein arginine methyltransferase I, NO-nitrous oxyde.

Main path of degradation of ADMA is processed by means of enzyme dimethylarginine dimethylhydrolase-DDAH. Upon the action of this enzyme ADMA is degrading till dimethylamine and L-citrulin (28). In hemodialysis patients elevated ADMA concentration is due to diminished activity of DDAH enzyme. Oxydative stress, microinflamation and hyperhomocysteinemia considerably diminish activity of this enzyme and elevate concentration of ADMA (28). Upon the enzyme aminotransferase dimethylarginine piruvate-DPT, one part of ADMA is metabolised into α-keto acids (28).

Patients on hemodialysis with left ventricle hypertrophy have highly significant statistically elevated plasma ADMA concentration comparing to the patients with normal left ventricle mass (10). By multivariant analysis it is proved that ADMA is independent risk factor for left ventricle hypertrophy (10). In hemodialysis patients ADMA is strong predictor of cardiovascular complications development and overall mortality (11). Every one μmol/l rise of ADMA in plasma is followed by overall risk mortality rise of 26% (11).

Microinflammation is independant risk factor for cardiovascular complications in patients on hemodialysis (29). Local and systemic inflammation have important role in pathogenesis of acute coronary syndrom. Inflammatory process has important role in prediction of plaque perspective, eg. plaque stability. C-reactive protein, reactant of acute phase of inflammation, has imortant role in the atherosclerosis process, progression and rupture of atherosclerotic plaque (29). Normal concentration of CRP in plasma is ≤ 5 mg/L, and concentration of CRP > 10 mg/L expresses elevated risk of development of cardiovascular complications in patients on hemodialysis (29).

Highly-sensitive CRP (hsCRP), serum amyloid A-SAA and other reactants of acute phase of inflammation and/or cytokines are used as a markers of inflammation and predictors of development of cardiovascular complications in hemodialysis patients (29, 30). Between hsCRP concentration and risks for coronary artery disease, there is statisticaly significant relation (29–31).

Tests for estimation of plaque instability and risk of its rupture

Elevated concentration of solubile CD-40 ligand indicates aggravated prothrombotic activity and possibility of development of coronary thrombosis. After thrombocyte activation there is significant rise and liberation of solubile fragments-CD40 ligands which express prothrombotic activity (sCD40L). Elevated concentration of sCD40L enables recruitment of certain subset of patients with elevated risk of acute coronary syndrom (18–21, 32).

(Myeloperoxidase)-MPO is an enzyme secreted by different inlammatory cells, including activated neutrophils and monocytes/macrophages, present in aterosclerotic plaques. Elevated myeloperoxydase concentration in serum is a predictor of development of acute coronary syndrome (18–21, 32).

Elevated activity of phospholipase D and choline liberation in plasma, is connected with aterosclerotic plaque rupture and onset of acute coronary syndrome Elevated concentration of choline in plasma, in patients with normal concentration of cardiac troponins, enables recruitment of certain subset of patients with elevated risk of unstable angina pectoris (18–21, 32).

Plasma Protein A binded with pregnancy - PAPP-A is a glycoprotein of high molecular weight (200 kD), which is synthetised in syncytio-trophoblasts. Presence of this protein is proved in unstable aterosclerotic plaque of coronary arteries, and elevated concentration in plasma is a warning sign of possible development of acute coronary syndrome (18–21, 32).

Tests for markers of ischemia and cardiac tissue damage

Free fatty acids-FFAs in blood of patients with acute myocardial ischemia show early signs of myocardial damage. Albumin modified by ischemia-IMA (ishaemia-modified albumin) is another marker of early myocardial damage (18–21, 32).

Traditional enzymes, like CK and LDH, due to their high molecular weight (84 kD and 144 kD) do not penetrate membrane untill the myocites aren't ireversibly destructed. (monophasic excretion) (19, 20, 32). Creatine kinase-CK is dimer composed of M and/or B subunits (CK-MM, CK-MB, CK-BB isoenzymes). Isoenzyme CK-MM is mostly in striated sceletal musculature (97% of whole CK) (32, 33). Isoenzyme CK-MB is mostly found in heart muscle, and accounts for 15–40% of total activity of Creatin kinase (32, 33). An insignificant amount of CK-MB is present in striated muscles as well (2–3% of total creatine kinase activity). Isoenzyme CK-BB is mostly present in brain, colon, ileum, stomach and urinary bladder (32, 33). Activity of whole creatine kinase-CK in plasma and concentration of isoenzyme CK-MB rise after 4–6 hours of myocardial damage, reaching the peak concentration after 12–24 hours, and after 48–72 hours it is getting back to normal values (32, 33). Isoenzyme MB creatine kinase (CK-MB) is more sensitive marker of myocardial damage than whole CK, but this isoenzyme concentration can be elevated after striated muscles damage as well (32, 33). Ratio CK-MB/total CK above 5% suggests myocardial infarction Š(CK-MB/CK) x100 (%)Ć. Concentration of total creatine kinase-CK > 232 U/L and CK-MB > 16 U/L, as well as ratio CK-MB/CK > 5% suggests acute myocardial infarction (33). There are two CK-MB isoenzymes of creatine kinase: CK-MB1 and CK-MB2. In normal blood CK-MB isoenzymes are equally distributed, in ratio 1:1. Substantial CK-MB2:CK-MB1 ratio changes 2–4h after myocardial damage. CK-MB2:CK-MB1 ≥ 1.5 ratio is used as a diagnostic criterion of myocardial damage (34, 61). Ratio of

CK-MB isoenzymes normalizes after 18–30h. Normal ratio of isoenzymes CK-MB2:CK-MB1 = 1, which stays still after 6h of the onset of chest pain, excludes the diagnosys of myocardial infarction (32, 33). But, in hemodialysis patients activity of CK-MB after myocardial damage is not fully reliable. Activity of CK-MB can be elevated in 5–50% in hemodialysis patients even in the absence of cardiac symptoms or any data on cardiac damage (34). Isoenzymes LDH, as α-HBDH (α -hydroxybutyrate dehydrogenase) and LDH isoenzyme 1, are more specific in diagnostic of myocardial damage compared to whole LDH (32, 33).

Myoglobin is protein of 17 kD of molecular weight, being in cytoplasm of heart and striated myocites, and is easily liberated after cellular damage (33). Its concentration in blood elevates after 2–3 hours after myocardial damage. According to ESC/ACC (European Society of Cardiology/American College of Cardiology) myoglobin concentration and CK-MB in blood are used as early markers of myocardial damage (32, 33). Distribution of carbonic anhydrase III is limited to skeletal muscles, and its use in combination with myoglobin rises sensitivity of myoglobin in diagnostics of myocardial damage. Elevated ratio myoglobin/carbonic anhydrase III stresses myocardial damage (32, 33). Myoglobin concentration in blood is not used in routine clinical work (32, 33).

Cardiac troponins (cTnT and cTnI) mark myocardial cell destruction (20, 21). Complex of troponins consists of troponin C-cTnC, troponin T-cTnT and troponin I-cTnI, and its main function is regulation of contractility of heart muscle (33). Cardiac troponin I-cTnI (molecule weight of 26 kD) blocks activity of actinomyosine ATP-ase. Troponin C-cTnC (molecular weight 18 kD) is binding for cTnI, oposing the inhibiting effect of cTnI, and serves as a place for calcium binding, inevitable for the process of contraction. Troponin T-cTnT (molecular mass of 39 kD) stabilises complex cTnC/cTnI and bindes for actyn-myosyn filament (34, 61). A great deal of cardiac troponins (cTnI I cTnT) intracellulary are attached to myofibriles, and small amount is free (6–8% cTnT and 3–4% cTnI). Cardiac troponins are excreted in phase of reversible (citosolyc form) and irreversible (citosolyc and structure form) myocardial ischemia and enables early detection of minimal myocardial damage. According to guidelines of ESC/ACC (European Society of Cardiology/American College of Cardiology) cardiac troponins are used as markers for evaluation of acute coronary syndrom, due to higher sensitivity and specificity compared to other markers (table 2) (32, 33).

Table 2. Characteristics of markers of cardiac damage.

Proteins	Molekul weight	Early detection*	Duration	Sensitivity	Specificity
Protein-FA	12 kD	1.5 - 2.0 h	8 - 12 h	+++	++
Myoglobin	16 kD	1.5 - 2.0 h	8 - 12 h	+++	+
CK-MB	83 kD	2.0 - 3.0 h	1 - 2 days	+++	+++
Troponin I	33 kD	3.0 - 4.0 h	7 - 14 days	++++	++++
Troponin T	38 kD	3.0 - 4.0 h	7 - 14 days	++++	++++
CK	96 kD	4.0 - 6.0 h	2 - 3 days	++	++
sGOT	~103 kD	6.0 - 10.0 h	3 - 5 days	++	+
LDH	135 kD	6.0 - 10.0 h	5 - 7 days	++	+

* hours after the symptom onset, CK-creatine kinase, LDH-lactate dehydrogenase, sGOT-glutamate oxaloacetate transaminase

Elevated concentration of cardiac troponins is found in as much as 40% of patients on hemodialysis, without symptoms of acute coronary syndrome (34–38). In hemodialysis patients troponin T elevation can be due to left ventricle hypertrophy, systolic disfunction of left ventricle, voluminous left ventricle and myocardial stretching, coronary microcirculation disturbance, endothelial disfunction, oxydative stress and microinflammation, episodes of hypotension during hemodialysis, myocarial damage due to calcium and oxalate precipitation, and/or disturbance in troponin fragmentation, as a result of chronic kidney weakness or inadequate hemodialysis (34–38).

In patients on regular hemodialysis, cardiac troponin T (cTnT), compared to troponin I (cTnI), is more sensitive marker of subclinical damage of myocardial cells („minimal myocardial damage"-MMD) and proved as a better predictor of overall cardiovascular mortality (39). Patients on hemodialysis with troponin T concentration >0.10 ng/mL express statistically lower survival rate compared to patients with troponin T concentration <0.03 ng/mL (40). Correlation of cardiac troponin T with left ventricle mass indicates importance of this parameter in depiction of patients with left ventricle hypertrophy and systolic function disturbance (41). Patients with cardiac troponin T concentration > 55 ng/L in serum, have 3,47 fold higher risk of left ventricle hypertrophy, while patients with concentration of cTnT > 150 ng/L have 3.30 fold higher risk of left ventricle systolic function disturbance, compared to patients with concentration of troponin T < 150 ng/L (41). Concentration of cardiac troponin T in serum can serve as a reliable screening parameter for estimation of morphology and function of left ventricle in clinically stable hemodialysis patients (41). Between concentration of cardiac troponin T in serum, interventricular septum thickness, thickness of the posterior left ventricle wall and left ventricle mass, there is highly statistically significant positive correlation (42, 43). Patients with elevated concentration of cTnT (cTnT > 0.10 ng/mL) in serum have significantly higher left ventricle mass index compared to patients with normal concentration of cTnT (44).

Two year mortality in patients with concentration of cTnT < 0.01 ng/mL is 8.4%, 26% in patients with mild elevation of cTnT (cTnT ≥ 0.01 and cTnT < 0.04 ng/mL), 39% in patients with serum cTnT (≥ 0.04 and < 0.10 ng/mL), and 47% in patients with extreme elevation of serum cTnT (cTnT ≥ 0.10 ng/mL) (42). Patients with serum cTnT concentration ≤ 0.040 ng/mL have greatest survival rate, and significantly different compared to patients with concentration of serum cTnT (cTnT ≥ 0.10 ng/mL)(42, 45).

Cardiac troponin I has greatest importance in diagnostics of acute coronary syndrome. According to AHA (American Heart Associatonion) Committee guidelines cardiac troponin I is used in diagnostics of myocardial damage in patients with unstable angina pectoris, without ST elevation. This enables diagnosis of myocardial damage before ECG registration of myocardial infarction (46, 47). After myocardial infarction cardiac troponin I can be detected in serum after 3–4 hours, and concentration remains elevated during 7–10 days (46, 47).

Troponin I is more sensitive marker of development of acute coronary syndrom compared to cTnT, and is used as a parameter for diagnostics and stratification of clinical difficulty of patients on hemodilaysis developing acute coronary syndrom (48). Patients with concentration of troponin I - cTnI in serum ≥ 0.15 ng/mL are marked as a pos-

itive ones, while concentration of cTnI < 0.15 ng/mL is considered normal (34). Concentration of troponin I in serum > 0.8 ng/mL stresses marked damage caused by, and according to guidelines of ESC/ACC (European Society of Cardiology/American College of Cardiology) diagnosys of acute aktnog myocardial infarction includes concentration of cTnI ≥ 2.0 ng/mL, table 3 (48). Incidence of development of cardiovascular complications in patients on hemodialysis with concentration of cTnI > 0.15 ng/mL statistically highly significant compared to the group of patients with cTnI < 0.15 ng/mL (44). Patients with concentration of cTnI ≥ 0.3 μg/L have higher risk of ACS compared to the patietns with a concentration of troponin I < 0.3 μg/L (49).

Table 3. Enzymes, isoenzymes, cardiac troponin I and their clinical importance in diagnosys of acute coronary syndrome.

LABORATORY PARAMETER	TIME of DETECTION	CLINICAL IMPORTANCE
Whole creatin kinase - CK	4.0 - 6.0 h	CK > 232 U/L
Isoenzym MB Creatin kinase - CK-MB	2.0 - 3.0 h	CK-MB > 16 U/L
CK and isoenzymes CK-MB ratio	2.0 - 4.0 h	CK-MB/CK > 5%
Isoenzymes Creatinin kinase MB ratio	2.0 - 4.0 h	CK-MB 2/CK-MB 1 ≥ 1.5
Cardiac troponin I	2.0 - 4.0 h	cTnI ≥ 2.0 ng/mL

Tests for detection of myocardial function markers

In population of patients without kidney disease, cardiac natriuretic peptids are the most imortant markers of left ventricle damage. These are used as a screening test for early detection of patients with asymptomatic left ventricle disturbance. Early detection of these patients enables timely tretament with angiotensin convertase I blockers and beta blockers, which both prevent congestive heart failure. In this population of patients natriuretic peptids are not used for prognosis and stratification of patients with congestive heart failure, but for the estimation of eficacy of applied therapy for congestive heart failure (50–52).

In patients with ESKD (End Stage Kidney Disease) on hemodialysis, natriuretic peptids (ANP, BNP, Nt-proBNP) have small sensitivity in early detection of patients with heart failure. High prevalence of disturbance of morphology of left ventricle (hypertrophy of left ventricle present in 75% of patients) and volume overload in interdialysis time, diminsh diagnostic potential of BNP, as a screening test in diagnostics of heart failure in these patients (52). In these patients BNP is independent predictor of death and left ventricle hypertrophy (53, 54). Patients on hemodialysis with concentration of BNP > 36.1 pmol/L (concentration of ANP > 34.8 pmol/L) have significantly lower death rate (overall and cardiovascular mortality) compared to the patients with concentration of BNP < 14.3 pmol/L, or concentration of ANP < 17.9 pmol/L (52, 53). Between concentration of BNP and Left Ventricle Mass index - LVMi there is statistically significant positive corelation (52–54). Serum BNP concentration is used for estimation of „dry" body mass in patients on hemodialysis (52).

Diagnostic strategy

End stage kidney disease is a situation with high risk of cardiovacular complications (55), and heart disease of these patients are leading cause of death in this population. Markers of early detection of myocardial damage (troponin I, troponin T) enable depiction of patients with high risk of acute coronary syndrom-ACS, which enables adequate therapy (platelet IIb/IIIa glycoproteins antagonists) (56, 57).

Pointing out the most sensitive parameters for detection of patients with high risk of cardiovascular complications enable proper timing for adequate therapeutical strategy, therefore making high survival rate in patients with end stage kidney disease (55–58). Biochemical markers play key role in diagnostics and therapy of the patients with ACS. Early depiction of myocardial ischemia in the abscence of ireversible myocardial damage has a key role in prevention of ACS development. Exceptional importance belongs to the markers of early detection of myocardial ischemia/damage and to the markers of inflammation, coronary plaque instability and its rupture (18–21).

According to ESC/ACC (European Society of Cardiology/American College of Cardiology) Expert Committee guidelines, cardiac troponins (cTnT or cTnI) are used as a GOLD STANDARD in diagnostics of myocardial damage because of high specificity for heart tissue (34). Measuring concentration of cardiac troponins, cTn, in serum enables depiction of the subset of patients with elevated risk of main cardiovascular complicatons (34).

In patients with ESKD the use of multiple biomarker monitoring is inevitable for prediction of the outcome. C-reactive protein, homocystein, BNP and ADMA are high risk markers of cardiovascular complications in patients with ESKD (58–62). Simultaneous measurement of CRP and cTnI enables depiction of hemodialysis patients with elevated cardiovascular risk, in whom additional diagnostic monitoring and agressive cardiovascular risk factor correction are neccessary (58–62).

Primary strategy for lowering of cardiovascular mortality rate in hemodialysis patients should include antiaggregation therapy (Aspirin tabl. 100 mg/d), statins and beta-blockers, while secondary strategy includes coronary revascularization and percutaneous cardioverter defibrilator implantation (PCDs) (56).

Early detection of ESKD patients with high risk of cardiovascular complications enable adequate and timely therapy, thus lowering cardiovascular mortality rate and improving quality of life in these patients (62, 63).

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