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Dijabetes i koronarna bolest srca: važnost regulacije glikemije

Diabetes and coronary artery disease: the importance of glycemic control

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SAŽETAK: Učestalost dijabetesa u snažnom porastu je diljem svijeta. Koronarna bolest srca (KBS) predstavlja najčešću makrovaskularnu komplikaciju dijabetesa. Striktna kontrola vrijednosti glukoze u krvi, neovisno o kliničkoj manifestaciji KBS, pridonosi boljitku pacijenta i smanjenju troškova liječenja.

KLJUČNE RIJEČI: dijabetes, ishemijska bolest srca, glukoza u krvi.

SUMMARY: The incidence of diabetes is highly rising worldwide. Coronary artery disease (CAD) is the most common macrovascular complication of diabetes. Strict control of blood glucose levels, regardless of clinical manifestation of CAD, contributes to the betterment of a patient and reduces medical costs.

KEYWORDS: diabetes, coronary artery disease, blood glucose.

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Dijabetes (DM) i njegove kronične komplikacije diljem svijeta predstavljaju veliki svjetski zdravstveni problem. Smatra se da trenutno u svijetu 366 milijuna ljudi boluje od DM, a do 2030. godine broj dijabetičara povećat će se na 552 milijuna. Broj oboljelih od DM povećava se u svim državama, a 80% posto svjetske populacije dijabetičara živi u zemljama u razvoju ili novoindustrijaliziranim zemljama.[1]

Prevalencija DM u Hrvatskoj u dobnoj skupini između 18 i 65 godina iznosi 6,1%. Ukupan broj dijabetičara u 2010. god. iznosio je približno 316.000, od čega nešto preko 190.000 bolesnika ima otkrivenu bolest, dok ih je gotovo 123.000 neotkriveno.[2]

Poznato je da osim genetskih čimbenika pri nastanku DM, posebice tipa 2, čimbenici okoliša i, nadasve životne navike, snažno utječu na učestalost DM. Fizička neaktivnost, alkohol te prehrambene navike (gojaznost), osim što su dobro poznati čimbenici rizika za nastajanje DM tipa 2, doprinose i lošijoj regulaciji već nastale bolesti. Životne i prehrambene navike dijabetičara te stoga i pridruženi čimbenici rizika zapravo su vrlo udaljeni od proklamiranih preporuka i smjernica diljem svijeta[3]. S druge strane, kontrola tjelesne težine i tjelesna aktivnost su kritični čimbenici za prevenciju i nastajanje DM i kod zdravih i u pojedinaca s već narušenom regulacijom glukoze u krvi[3,4].

Kardiovaskularne komplikacije su vodeći uzrok pobola i smrtnosti među pacijentima s DM. Rizik kardiovaskularne bolesti (KVB) je 2-4 puta veći među dijabetičarima nego u ostaloj populaciji[5]. Bolesnici s DM češće imaju nijemu ishemiju miokarda, a koronarna bolest srca (KBS) u dijabetičara

Diabetes (DM) and its chronic complications around the world represent a major world health problem. It is believed that currently 366 million people suffer from DM worldwide, and by the year 2030 the number of diabetics will increase to 552 million. The number of patients with DM rises in all countries, and 80% percent of the world's population suffering from diabetes live in developing countries or newly industrialized countries.[1]

The prevalence of DM in Croatia in the age group between 18 and 65 is 6.1%. The total number of diabetics in 2010 was approximately 316,000, of whom over 190,000 patients have the disease discovered, while nearly 123,000 have the disease undiscovered.[2]

It is known that besides genetic factors for occurrence of DM, particularly of type 2, the environmental factors and especially lifestyle factors greatly influence the incidence of DM. Physical inactivity, alcohol and eating habits (obesity), except for being well-known risk factors for the occurrence of DM type 2, they also contribute to poorer control of the already occurred disease. Living and nutritional habits of diabetics and therefore the associated risk factors are actually very far from the proclaimed recommendations and guidelines around the world[3]. On the other hand, weight control and physical activity are critical factors for the prevention and occurrence of DM both in healthy individuals and in individuals with the already impaired control of blood glucose[3,4].

Cardiovascular complications are the leading cause of morbidity and mortality among the patients with DM. The risk of cardiovascular disease (CVD) is 2 to 4 times higher among diabetics than in the other population[5]. Patients with DM

je često višežilna[6]. U usporedbi sa zdravom populacijom ukupna smrtnost od infarkta miokarda četiri je puta veća među muškarcima i čak sedam puta veća među ženama. Srčana bolest (68%) i moždani udar (16%) predstavljaju najčešće uzroke smrti u pacijenata dijabetičara[5]. Također, potreba za transluminalnom koronarnom angioplastikom i koronarnim premosnicama, kada se jednom i razvije infarkt miokarda, dvostruko je veća među muškarcima oboljelim od DM[5].

I u Hrvatskoj KVB predstavljaju vodeći uzrok smrti s udjelom od 49,6% u ukupnom mortalitetu 2009. god. Od ukupnog broja umrlih od KVB te godine 43% je umrlo u bolnici, a 57% izvan bolnice. Analiza prema spolu pokazuje da su KVB u oba spola vodeći uzrok smrti. Za žene taj udio iznosi 56,4%, a za muškarce 42,6%. Sama KBS uzrok je smrti 21,4% žena i 18,8 % muškaraca[6].

Ovakav porast broja dijabetičara, a stoga očekivano i kardiovaskularnih komplikacija DM uzrokuje i porast troškova liječenja.

Troškovi liječenja dijabetesa

Prema ADA (engl. American Diabetes Association) trenutni izravni troškovi liječenja DM i komplikacija u Sjedinjenim Američkim Državama iznose 174 milijarde dolara. U to nisu uračunati troškovi invaliditeta, izostanka s posla ili prerane smrti[5]. I u Hrvatskoj DM predstavlja veliko financijsko opterećenje. Prema podacima Hrvatskog zavoda na zdravstveno osiguranje tijekom 2009. godine. samo za liječenje DM potrošeno je 2,5 milijarde kuna, odnosno 11,49% proračuna. Od tih troškova najveći udio (85,72%) troškovi su liječenja komplikacija dijabetesa, odnosno posljedica loše regulacije glikemije, dok je ostatak (14,28%) utrošen za lijekove i kontrolu dijabetičara[3]. Jednako tako ovdje nisu uračunati troškovi invaliditeta, radne nesposobnosti ili prerane smrti od komplikacija DM.

Patogeneza koronarne bolesti srca u dijabetičara

Disfunkcija endotela predstavlja osnovni mehanizam ubrzanih aterosklerotskih promjena krvnih žila u pacijenata s DM. Povećan rizik razvoja kroničnih komplikacija u dijabetičara posljedica je zajedničkog djelovanja čimbenika rizika, kao što su dislipidemija, arterijska hipertenzija, hiperglikemija, hiperinzulinemija. Povećan oksidativni stres sa stvaranjem završnih produkata glukozilacije, tromboza i fibrinoliza, dovode do progresije ateroskleroze i pojave neželjenih kardiovaskularnih događaja[7].

Dijabetes pospješuje nakupljanje pjenušavih stanica u subendotelnom prostoru, stvaranje plaka i oslobađanje molekula, posrednika upale.Ta upalna reakcija dovodi do prekomjerne ekspresije receptora za završne produkte glikoziliranja, što izravno kolerira s razinom glikoliziranog hemoglobina (HbA1c). Posljedična povišena aktivnost metaloproteinaze matrixa može destabilizirati plak.[5] I promjene u vaskularnoj funkciji, odnosno povišene razine endotelina-1, pospješuju vazokonstrikciju, povećavajući hipertrofiju glatkog mišićja krvne žile te aktivirajući sustav renin-angiotenzin. Istodobno snižene razine prostaciklina i dušičnog oksida potiču trombocite na agregaciju što još pogoršava funkciju endotela[8,9]. Osim pojačane aktivacije trombocita stvaranje prokoagulantnih faktora (poput tkivnog faktora) i sniženje antikoagulanata (npr. protein C i anti trombin III) stvaraju prokoagulantno stanje[10]. Povišene razine inhibitora tipa 1 za tkivni plazminogen aktivator smanjuje fibrinolizu i pospješuje

tend to have silent myocardial ischemia, while coronary artery disease (CAD) in diabetics is often multi-vessel[6]. Compared to the healthy population, the total mortality from myocardial infarction in diabetics is four times higher among men and even seven times higher among women. Heart disease (68%) and stroke (16%) are the most common causes of death in patients with diabetes[5]. The need for transluminal coronary angioplasty and coronary bypass grafts, once the myocardial infarction is developed, is twice as high among men suffering from DM[5].

Even in Croatia, CAD represent the leading cause of death, accounting for 49.6% of total mortality in 2009. Of the total number of persons who died of CAD that year, 43% died in hospital, and 57% outside the hospital. Analysis by gender shows that CVD in both sexes are the leading cause of death. In women it accounts for 56.4%, while in men it accounts for 42.6%. CAD itself is the cause of death in 21.4% and 18.8% in men[6].

This increase in a number of diabetics and consequently as expectedly in a number of cardiovascular complications of DM also causes an increase in medical costs.

Costs of diabetes treatment

According to American Diabetes Association the current direct costs of treatment of DM and its complications in the United States of America amounted to $ 174 billion. This does not include costs of disability, absenteeism and premature death[5]. In Croatia, DM is a great financial burden. According to the Croatian Institute for Health Insurance in 2009, HRK 2.5 billion or 11.49% of the budget was spent only on the treatment of DM. Of these costs, the largest percentage (85.72%) is attributed to the costs of treatment of complications of diabetes or consequences of poor glycemic control, while the remaining 14.28% is attributed to the costs of drugs and control of diabetes[3]. Similarly no costs of disability, work incapacity or premature death from complications of DM are included here.

The pathogenesis of coronary artery disease in diabetics

Endothelial dysfunction is the main mechanism of accelerated atherosclerotic changes in blood vessels in patients with DM. Increased risk of development of chronic complications in diabetic patients is a consequence of common effects of risk factors, such as dyslipidemia, hypertension, hyperglycemia, hyperinsulinemia. Increased oxidative stress followed by the formation of final products of glucosylation, thrombosis and fibrinolysis cause progression of atherosclerosis and occurrence of adverse cardiovascular events[7].

Diabetes accelerates the accumulation of foam cells in the subendothelial area, formation of plaque and release of molecules, the inflammation mediators. This inflammatory reaction leads to the excessive expression of receptors for glycosylation end-products, which directly correlates with the level of glycosylated hemoglobin (HbA1c). Consequential increased activity of metalloproteinase may destabilize the plaque.[5] The changes in vascular function or elevated levels of endothelin-1 stimulate vasoconstriction, increasing hypertrophy of smooth muscles and blood vessels and activating the renin-angiotensin system. At the same time, the decreased levels of prostacyclin and nitric oxide stimulate platelets to aggregation which further worsens the endothelial function[8,9]. In addition to increased platelet activation, formation

stvaranje ugruška, povećavajući vjerojatnost začepljivanja krvne žile[11].

Značaj dobre regulacije glikemije: zatajivanje srca

Tri su kriterija dobre regulacije DM: zadovoljavajuća glikemija natašte, zadovoljavajuća postprandijalna glikemija i zadovoljavajuća vrijednost HbA1c[7].

Rezultati DCCT (*The Diabetes Control and Complications Trial Research Group*) studije, koja prati dijabetičare tipa 1, upućuju da smanjenje frakcije HbA1c za svega 1% smanjuje ukupan rizik razvoja dijabetičkih komplikacija za 21%, rizik od mikrovaskularnih komplikacija za 37%, a rizik infarkta miokarda je manji za 14%[7,12]. Studija UKPDS (*The United Kingdom Prospective Diabetes Study*), koja prati dijabetičare tipa 2, također zahtjeva sve strože kriterije dobre reguliranosti DM. Tako su 2003. godine preporuke dobre regulacije bile glikemija natašte ispod 7,2 mmol/L, postprandijalna glikemija do 10 mmol/L, a HbA1c ispod 7 %[7,13]. Godine 2008. kriteriji dobre regulacije DM postaju još stroži te se danas smatra da je bolest dobro regulirana ako je glikemija natašte niža od 5,5 mmol/L, postprandijalna glikemija niža od 7,8 mmol/L te vrijednost HbA1c niža od 6,5%[7].

Važnost dobre kontrole glikemije u kongestivnom zatajivanju srca naglašena je u članku *Irrabarren i sur.* koji su pratili 48.858 dijabetičara starijih od 19 godina i bez zatajivanja srca (ZS) tijekom razdoblja od 2,2 godine. Svaki porast HbA1c za 1% bio je povezan s većom učestalosti ZS za 8%, a vrijednost HbA1c od 10mmol/L u usporedbi s 7 mmol/L povećava rizik ZS za 1,56 puta.[14] Nadalje, Barzilay i sur. su prateći 5.201 pacijenta s DM kroz 5-8 godina dokazali da što je viša glikemija natašte, veća je i incidencija ZS (41% povećanje za svakih 3,4 mmol/L povišenja vrijednosti GUK natašte)[15]. Također, postoje podaci koji dokazuju da je dužina hospitalizacije pacijenata sa kongestivnim ZS povezana s kvalitetom regulacije DM, kako u trenutku prijma (glukoza u plazmi pri prijemu), tako i u kućnim uvjetima (HbA1c)[16]. Dungan i sur. su 2010. godine objavili studiju u kojoj su za mjerilo regulacije glikemije uzeli prosječnu razinu glukoze tijekom boravka, HbA1c i "indeks glikemijske labilnosti" (engl. *glycemic lability index*), odnosno varijabilnost (nestabilnost) glikemije. Analiza je uključila 748 pacijenata. Prosječna razina glukoze i HbA1c su neovisno povezani s ponovnim prijmom u bolnicu pacijenata s ZS u razdoblju od 30 do 90 dana od otpusta, ali ne i s ponovnim prijmom u razdoblju kraćem od 30 dana. Indeks glikemijske labilnosti nije bio povezan s većim rizikom od ponovne hospitalizacije[17]. Iz ovog je sasma jasno da dijabetičari koji istodobno boluju i od akutnog ZS imaju puno veću vjerojatnost smrtnog ishoda. Multicentrična (6 europskih zemalja, Meksiko i Australija) studija ALARM-HF, objavljena krajem 2011. god., kod 4.953 pacijenata hospitaliziranih radi ZS utvrdila je da su pacijenti s DM bili češće hospitalizirani radi edema pluća, akutnog koronarnog sindroma, a intrahospitalna smrtnost im je bila viša u odnosu na pacijente bez DM, usprkos istom intenzivnom liječenju[18].

Značaj dobre regulacije glikemije: akutni koronarni sindrom

U pacijenata s akutnim koronarnim sindromom, za koje se ranije nije znalo da imaju DM, vrlo su česte nenormalne razine glukoze. Čini se da se radi prvenstveno o lošoj funkciji beta-stanice, a manje je to posljedica stresa[19,20]. Studija

of procoagulant factors (such as tissue factor) and reduction of anticoagulants (e.g. protein C and anti-thrombin III) create procoagulant condition[10]. Elevated levels of type 1 inhibitor for tissue plasminogen activator reduces fibrinolysis and stimulates the creation of a clot, increasing the likelihood of clogging the blood vessels[11].

The importance of good glycemic control: heart failure

There are three criteria for good DM control: satisfactory value of fasting glycemia, postprandial glycemia and HbA1c[7].

The results of DCCT (The Diabetes Control and Complications Trial Research Group) study following the type 1 diabetics show that the reduction in HbA1c fraction by only 1% reduces the overall risk of development of diabetic complications by 21%, the risk of microvascular complications by 37% and the risk of myocardial infarction is lower by 14%[7,12]. The UKPDS (*The United Kingdom Prospective Diabetes Study*) study, which follows the type 2 diabetics also requires ever stricter criteria for good DM control. Thus, in 2003 the recommendations for good control were the fasting glycemia below 7.2 mmol/L, postprandial glycemia up to 10 mmol/L and HbA1c below 7 %[7,13]. In 2008, the criteria for good control of DM are becoming even stricter, and today, the disease is considered to be well controlled if fasting glycemia is below than 5.5 mmol/L, postprandial glycemia below than 7.8 mmol/L and HbA1c below than 6.5%.

The importance of good glycemic control in congestive heart failure is highlighted in the article *Irrabarren et al.* who followed 48,858 diabetic patients over than 19 years and without heart failure (HF) older a period of 2.2 years. Any increase in HbA1c by 1% was associated with a higher incidence of HF by 8%, while the HbA1c value of 10mmol/L compared to 7 mmol/L increases the HF risk by 1.56 times.[14] In addition, Barzilay et al. have, by following 5201 patients suffering from DM throughout a period from 5 to 8 years proved that the higher fasting glycemia is, the greater incidence of HF it is (41% increase for each 3.4 mmol of increase in fasting blood glucose)[15]. Also, there is data showing that the length of hospitalization of patients with congestive HF is associated with DM control quality, not only at the time of admission (plasma glucose upon admission), but also in the home environment (HbA1c)[16]. In 2010, Dungan et al. published a study where they took the average glucose level during the stay, HbA1c and glycemic lability index, that is, the variability (instability) of glycema as the measure of glycemic control. The analysis included 748 patients. The average blood glucose and HbA1c are independently associated with hospital re-admission of patients with HF during a period from 30 to 90 days from discharge, but not with re-admission during a period shorter than 30 days. Glycemic lability index was not associated with higher re-hospitalization risk[17]. This shows that diabetics who suffer from acute HF are much more likely to face fatal outcome. Multicentric (6 European countries, Mexico and Australia) ALARM-HF study, published by the end of 2011, found in 4953 patients hospitalized for HF that the patients with DM were more frequently hospitalized for pulmonary edema, acute coronary syndrome, while the intra-hospital mortality was higher in them than in patients not suffering from DM, despite the same intensive treatment[18].

GAMI (Glucose tolerance in patients with Acute Myocardal Infarction) bila je dizajnirana da otkrije prevalenciju poremetnje metabolizma glukoze u pacijenata hospitaliziranih radi infarkta miokarda. OGTT test je bio učinjen 4-5 dana nakon infarkta, nakon otpusta iz bolnice i 3 mjeseca kasnije. Poremetnja metabolizma glukoze (intolerancija glukoze i novootkrivena šećerna bolest) je bila registrirana u dvije trećine ispitanika prilikom otpusta iz bolnice. Slična učestalost bila je registrirana i prilikom testiranja tri mjeseca kasnije, sugerirajući da povišena razina simpatičke aktivnosti nije osnovni uzrok ovom stanju[20,21].

Kod pacijenata s akutnim infarktom miokarda s elevacijom ST-segmenta (STEMI), koji nisu znali da imaju DM, usprkos učinjene revaskularizacije, registriran je viši mortalitet[21]. Vršna glikemija veća od 10 mmol/L bila je povezana s najvišim mortalitetom, dok su pacijenti s vršnom glikemijom između 7,7 i 10 mmol/L imali nižu stopu smrtnosti. Sukladno rezultatima ovog rada,čini se da bi tijekom liječenja u koronanoj intenzivnoj skrbi trebalo težiti glikemiji nižoj od 7,7 mmol/L, jer je vršna glikemija neovisan prediktor mortaliteta.[21]

S druge strane, postoje smjernice koje se zadovoljavaju ciljnim vrijednostima glukoze od 7,7-10 mmol/L u kritično bolesnih pacijenata kojima se preporuča se uporaba kontinuirane inzulinske infuzije[22]. Uobičajena shema primjene inzulina kritično bolesnim pacijentima je intravenoznom infuziju uz pomoć perfuzora tako da se u injekcijsku špricu od 50 ml navuče 50 jedinica brzodjelujućeg humanog inzulina (*Actrapid*, Novonordisk) te dopuni do 50 ml s 0,9% otopinom NaCl. Primjenjuje se brzinom 2-3 ml/h, a svakih se sat vremena kontrolira glikemija aparatima za brzo očitanje vrijednosti glukoze te po potrebi ubrza ili uspori brzina infuzije. Ova shema liječenja omogućuje vrlo preciznu (i polaganu) regulaciju glikemije, koju je moguće zadržati u točno željenom rasponu, uz manju vjerojatnost ozbiljnih hipoglikemija koje jednako tako mogu pridonijeti povećanom mortalitetu.[23] Dnevne varijacije glikemije su također povezane s pojavnošću i ozbiljnošću KBS u pacijenata s DM tipa 2. Nedavno objavljeni rad Su i sur. upućuje da fluktuacije razine glukoze mogu imati ozbiljnu ulogu u razvoju ateroskleroze u dijabetičara te da se napor u kontroli bolesti, osim na kontrolu razine HbA1c, glikemije na tašte i postprandijalne glikemije mora usmjeriti i na sprečavanje fluktuacije glikemije.[23] U ovu svrhu umjesto humanog inzulina mogu se upotrijebiti i moderniji analozi humanog inzulina, aspart (*Novorapid*, Novonordisk) i lispro (*Humalog*, Lilly) na isti način. Za pacijente koji nisu kritično bolesni, preporučene vrijednosti glikemije u plazmi natašte su niže od 7,7 mmol/L i niže od 10 mmol /L u slučajnom mjerenju[22].Njih je moguće liječiti intenziviranom terapijom po shemi bazal-bolus[22]. U tu svrhu mogu se upotrijebiti stariji NPH humani inzulin (*Humulin N*, Lilly) te noviji dugodjelujući analozi humanog inzulina detemir (*Levemir*, Novonordisk) i glargin (*Lantus*, Aventis) kao bazalni inzulini, a prije navedeni brzodjelujući analozi humanog inzulina kao prandijalna bolus terapija (neposredno prije obroka).

Postupci revaskularizacije miokarda (perkutana koronarna intervencija i koronarne premosnice) u dijabetičara su također povezani s većom stopom neuspjeha. Restenoza nakon revaskularizacijskih postupaka je češća u pacijenata s DM i to ima negativne posljedice na dugotrajno preživljenje[24]. Zanimljivo je da je hiperglikemija naglašeniji čimbenik rizika za povećanu smrtnost u mlađim dobnim skupinama pacijenata s preboljelim akutnim infarktom miokarda[25]. Usprkos većem mortalitetu pacijenata s DM i akutnim koronarnim sindromom, kao i višoj stopi reokluzije koronarnih krvnih žila u dija-

The importance of good glycemic control: acute coronary syndrome

In patients with acute coronary syndrome, who were not previously known to be suffering from DM, abnormal glucose levels are very frequent. It seems that it is primarily the poor beta cell function in question, rather than that it is the consequence of stress[19,20]. The GAMI study (Glucose tolerance in patients with Acute Myocardial Infarction) was designed to detect the prevalence of glucose metabolism disturbance in patients hospitalized for myocardial infarction. OGTT test was done 4 to 5 days following the infarction, after discharge from hospital and 3 months later. Glucose metabolism disturbance (glucose intolerance and newly discovered diabetes) was recorded in two-thirds of respondents at the time of discharge from hospital. A similar occurrence was recorded at the time of testing 3 months later, suggesting that elevated levels of sympathetic activity is not the main cause of this condition[20,21].

A higher mortality was recorded in patients with acute myocardial infarction with ST-segment elevation (STEMI) who were unaware of suffering from DM, despite revascularization performed[21]. Peak glycemia over 10 mmol/L was associated with the highest mortality, while the patients with a peak glycemia between 7.7 and 10 mmol/L had a lower mortality rate. According to the findings of this article, it seems that during the treatment in the coronary intensive care unit we should strive to lower blood glucose to 7.7 mmol/L, because the peak glycaemia is an independent mortality predictor.[21]

There are guidelines that are met by the target glucose levels from 7.7 to 10 mmol/L in critically ill patients who received the recommendation that they should continuously use insulin infusion[22]. The usual scheme includes administering insulin to critically ill patients by intravenous infusion by using perfusor, so that 50 units of fast acting human insulin (*Actrapid*, Novonordisk) are put into the 50 ml injection syringe and filled with 0.9% NaCl solution up to 50 ml. It is applied at speed from 2 to 3 ml/h, and every hour, glycemia is controlled by portable blood glucose meters and if necessary, the rate of infusion is increasing or decreasing. This scheme allows a very precise treatment (and slow) control of glycemia, which can be maintained in exactly desired range, with a lower probability of severe hypoglycemia, which may also contribute to increased mortality.[23] Daily variations of glycemia are also associated with the occurrence and severity of CAD in patients with type 2 DM. The article recently published by Su et al. suggests that fluctuations in glucose levels can have a serious role in development of atherosclerosis in diabetic patients and that the effort to control the disease, except for the control of the HbA1c level, fasting and postprandial glycemia must be focused on prevention of glycemia fluctuation.[23] For this purpose, instead of humane insulin we can also use modern human insulin analogues, aspart (*NovoRapid*, Novonordisk) and lispro (*Humalog*, Lilly) in the same way. For patients who are critically ill, the recommended values of fasting plasma glycemia are below 7.7 mmol/L and below 10 mmol/L in a random measurement[22]. They can be treated with intensive therapy according to the basal-bolus scheme[22]. For this purpose, we can use some older NPH human insulin (*Humulin N*, Lilly) and the more recent long-acting human insulin analogues, detemir (*Levemir*, Novonordisk) and glargine (*Lantus*, Aventis) as basal insulin and the above mentioned fast-acting human insulin analogues can be used as prandial bolus therapy (shortly before a meal).

betičara, noviji podaci pokazuju da ovi pacijenti imaju i veću korist od agresivne revaskularizacije[24,26].

Nakon što prebole akutni infarkt miokarda, dijabetičari imaju veću šansu da u kratko vrijeme dožive novi infarkt, jer je DM nezavisni čimbenik rizika za ponovni nefatalni infarkt miokarda tijekom kraćeg razdoblja.[27]

Usprkos modernim, agresivnim, intenzivnim metodama liječenja STEMI u pacijenata s DM, mortalitet ostaje viši nego u pacijenata bez te bolesti[28]. Mnogobrojnije prateće bolesti, kasnija i manje zadovoljavajuća revaskularizacija i reperfuzija doprinose nepovoljnijem ishodu liječenja dijabetičara u odnosu na pacijente koji nemaju DM.[28]

Zaključak

Dijabetes i koronarna bolest srca predstavljaju sve češću problematiku u svakodnevnom radu. Potrebna je bolja kontrola DM, kako u svrhu sprečavanja nastajanja KBS, tako i tijekom liječenja ove kronične komplikacije i u ambulantnim i u bolničkim uvjetima. Dijabetolozi i kardiolozi moraju biti svjesni činjenice da postoji sve veća potreba za zajedničkom suradnjom u rješavanju ove problematike. To je jedini način da se postave i ostvare realni i dugoročno održivi ciljevi liječenja zajedničkih pacijenata.

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Myocardial revascularization procedures (percutaneous coronary intervention and coronary bypass) in diabetics are also associated with higher failure rate. Restenosis following the revascularization procedures is more common in patients with DM and it has a negative effect on long-term survival[24]. It is interesting that the hyperglycemia is more pronounced risk factor for increased mortality in younger age groups of patients with a history of acute myocardial infarction[25]. Despite the higher mortality of patients with DM and acute coronary syndrome, as well as a higher rate of reocclusion of coronary blood vessels in diabetic patients, the more recent data indicates that these patients have a greater benefit from aggressive revascularization[24,26].

After they recover from an acute myocardial infarction, diabetics have a greater chance to experience another heart attach in a short time, because DM is an independent risk factor for recurrent non-fatal myocardial infarction over a shorter time period.[27]

Despite the modern, aggressive, intensive methods of treatment of STEMI in patients suffering from DM, mortality remains higher than in patients not suffering from this disease[28]. Many accompanying diseases, later and less satisfactory revascularization and reperfusion contribute to unfavorable outcome of treatment in diabetic patients compared to patients not suffering from DM.[28]

Conclusion

Diabetes and coronary heart disease are more frequent problems in daily work. Better control of DM is required not only in order to prevent the occurrence of CAD, but also during the treatment of this chronic complication in outpatient and in-hospital environment. Diabetologists and cardiologists must be aware of the fact that there is ever greater need for mutual cooperation in resolving this issue. This is the only way to set and achieve realistic and sustainable long-term goals of treatment of common patients.

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