VELIKA VASKULARNA HIRURGIJA KOD GERIJATRIJSKE POPULACIJE: STRATIFIKACIJA SRČANOG RIZIKA

PREGLEDNI RAD

REVIEW ARTICLE

MAJOR VASCULAR SURGERY IN THE GERIATRIC POPULATION: CARDIAC RISK STRATIFICATION

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SAŽETAK

Oslanjanje na hirurgiju, poboljšanje hirurške tehnike i perioperativni menadžment doveli su do dramatičnog povećanja učestalosti hirurških zahvata kod starije populacije. Prema Evropskom kardiološkom društvu i Evropskom udruženju anesteziologa i intenzivista, velika vaskularna hirurgija je definisana kao visokorizična, s obzirom na učestalost infarkta miokarda i srčanog zastoja, koji je veći od 5%. Starost je nezavisni prediktor infarkta miokarda i srčanog zastoja. Promene srčane funkcije su primarne promene koje se javljaju sa starenjem. Stratifikacija rizika predstavlja skup procedura koje uključuju identifikaciju hroničnih sistemskih bolesti, utvrđivanje njihove težine i stabilnosti, kao i utvrđivanje potrebe za daljom evaluacijom i/ili optimizacijom terapije u cilju smanjenja perioperativnog i postoperativnog mortaliteta i morbiditeta. Pored primene skora rizika, tačna stratifikacija rizika zahteva kombinovanu primenu i preoperativnih i postoperativnih biomarkera. Ideja integracije biomarkera sa sistemima bodovanja jeste da se otkriju oni pacijenti sa klinički nemanifestovanom bolešću, koji nose rizik od smrtnosti, a sistemom bodovanja ostaju neotkriveni. Biomarkeri, kao što su *NT-proBNP* i visoko osetljivi C-reaktivni protein, imaju najveći prediktivni uticaj u gerijatrijskoj vaskularnoj hirurgiji.

Ključne reči: vaskularna hirurgija, biomarker, gerijatrija, procena rizika

ABSTRACT

Reliance on surgery, improvements in surgical techniques, and perioperative management have led to a dramatic increase in the frequency of surgical procedures in the elderly population. According to the European Society of Cardiology and the European Society of Anaesthesiology and Intensive Care, major vascular surgery is defined as high-risk, considering the frequency of myocardial infarction and cardiac arrest, which is higher than 5%. Age is an independent predictor of myocardial infarction and cardiac arrest. Heart function alterations are primary changes that occur with advancing age. Risk stratification represents a set of procedures that include identifying chronic systemic diseases, determining their severity, stability and the need for further evaluation and/or therapy optimization, with the aim of reducing perioperative and postoperative mortality and morbidity. In addition to the application of risk scores, accurate risk stratification requires the combined application of both preoperative and postoperative biomarkers. The main idea of integrating biomarkers with scoring systems is to reveal those patients with clinically unmanifested disease, who carry a mortality risk and remain undetected by scoring systems. Biomarkers, such as NT-proBNP and highly sensitive C-reactive protein, have the greatest predictive influence in geriatric vascular surgery.

Key words: vascular surgery, biomarker, elderly, risk score.

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UVOD

Procenjuje se da će u narednih osam godina biti 72 miliona Amerikanaca starijih od 65 godina [1]. Oslanjanje na hirurgiju, poboljšanje hirurške tehnike i perioperativni menadžment doveli su do dramatičnog povećanja učestalosti hirurških zahvata kod starije populacije [2]. Prema Evropskom kardiološkom društvu (engl. *European Society of Cardiology – ESC*) i Evropskom udruženju anesteziologa i intenzivista (engl. *European Society of Anaesthesiology and Intensive Care – ESAIC*), velika vaskularna hirurgija je definisana kao visokorizična, s obzirom na učestalost infarkta miokarda i srčanog zastoja, koji je veći od 5% [3]. Kako je ateroskleroza generalizovan proces, manje od jedne desetine pacijenata pripremljenih za veliku vaskularnu hirurgiju ima intaktne koronarne krvne sudove [4].

PATOFIZIOLOŠKI ASPEKT SRČANOG RIZIKA

Visoka učestalost koronarne arterijske bolesti (KAD), ali i hemodinamskih, metaboličkih, i neuroendokrinih poremećaja, kao i temperaturnih oscilacija, te rizik od ishemijskog oštećenja vitalnih organa, predstavljaju deo perioperativnog toka i razlog su većeg mortaliteta i morbiditeta u velikoj vaskularnoj hirurgiji, u odnosu na druge nekardiohirurške procedure.

Starost je nezavisni prediktor infarkta miokarda i srčanog zastoja [5]. Promene srčane funkcije su primarne promene koje se javljaju sa starenjem. To uključuje sledeće: smanjenu kontraktilnost i popuštanje miokarda, povećani pritisak punjenja srca, nisku β-adrenergičku osetljivost, povećanu aktivnost simpatičkog autonomnog nervnog sistema i posledično povećanje perifernog vaskularnog otpora. Vaskularno starenje je stimulisano prisustvom primarnih kardiovaskularnih bolesti i stanja, kao što su hipertenzija i ateroskleroza. Gubitak funkcionalne organske rezerve i povezanost starenja sa hroničnim sistemskim oboljenjima, tzv. multimorbiditet, dobro su poznati faktori koji su u vezi sa perioperativnim i postoperativnim srčanim rizikom kod starijih osoba. Uticaj multimorbiditeta na progresiju gubitka funkcionalnog kapaciteta je značajno veći od očekivanih sumiranih individualnih uticaja [6]. Zbog visokog rizika od povećanog postoperativnog mortaliteta, predlaže se da se određeni hirurški zahvati proglase visokorizičnim kod pacijenata starijih od 65 godina, iako se takvim ne smatraju u opštoj populaciji [7]. Kombinovanjem svih rizika koje nose i velika vaskularna hirurgija i starije životno doba, dobija se podgrupa pacijenata sa izuzetnim srčanim rizikom.

MODELI STRATIFIKACIJE RIZIKA

Stratifikacija rizika predstavlja skup procedura koje uključuju identifikaciju hroničnih sistemskih bolesti,

INTRODUCTION

It is estimated that, in the next eight years, there will be a total of 72 million Americans older than 65 years [1]. Reliance on surgery, improvements in surgical techniques, and perioperative management have led to a dramatic increase in the frequency of surgical procedures in the elderly population [2]. According to the European Society of Cardiology (ESC) and the European Society of Anaesthesiology and Intensive Care (ESAIC), major vascular surgery is defined as high-risk, since the incidence of myocardial infarction and cardiac arrest is higher than 5% [3]. Bearing in mind that atherosclerosis is a generalized process, less than a tenth of the patients prepared for major vascular surgery have intact coronary blood vessels [4].

PATHOPHYSIOLOGICAL ASPECT OF CARDIAC RISK

A high frequency of coronary artery disease (CAD), but also of hemodynamic, metabolic, and neuroendocrine disorders, and of oscillations in temperature, as well as the risk of ischemic damage to vital organs are all connected to perioperative recovery, causing higher mortality and morbidity in major vascular surgery, as compared to other non-cardiosurgical procedures.

Age is an independent predictor of myocardial infarction and cardiac arrest [5]. Changes in cardiac function are primary changes occurring with old age. These include the following: decreased contractility and weakening of the myocardium, increased cardiac filling pressure, low β-adrenergic sensitivity, increased activity of the sympathetic autonomous nervous system, and consequent increase in peripheral vascular resistance. Vascular ageing is stimulated by the presence of primary cardiovascular diseases and conditions, such as hypertension and atherosclerosis. Loss of functional organ reserve and the link between ageing and chronic systemic diseases, so called multimorbidity, are well known factors linked with perioperative and postoperative cardiac risk in elderly patients. The influence of multimorbidity on the progression of functional capacity loss is significantly higher than the expected sum of the individual effects [6]. Due to high risk of increased postoperative mortality, it is recommended to pronounce certain surgical procedures as high-risk in patients over 65 years, although they are not perceived as such for the general population [7]. A combination of all the risks that both major vascular surgery and advanced age carry creates a subgroup of patients with exceptional cardiac risk.

RISK STRATIFICATION MODELS

Risk stratification represents a set of procedures that include identifying chronic systemic diseases, deter-

utvrđivanje njihove težine, stabilnosti, te utvrđivanje potrebe za daljom evaluacijom i/ili optimizacijom terapije, u cilju smanjenja perioperativnog i postoperativnog mortaliteta i morbiditeta.

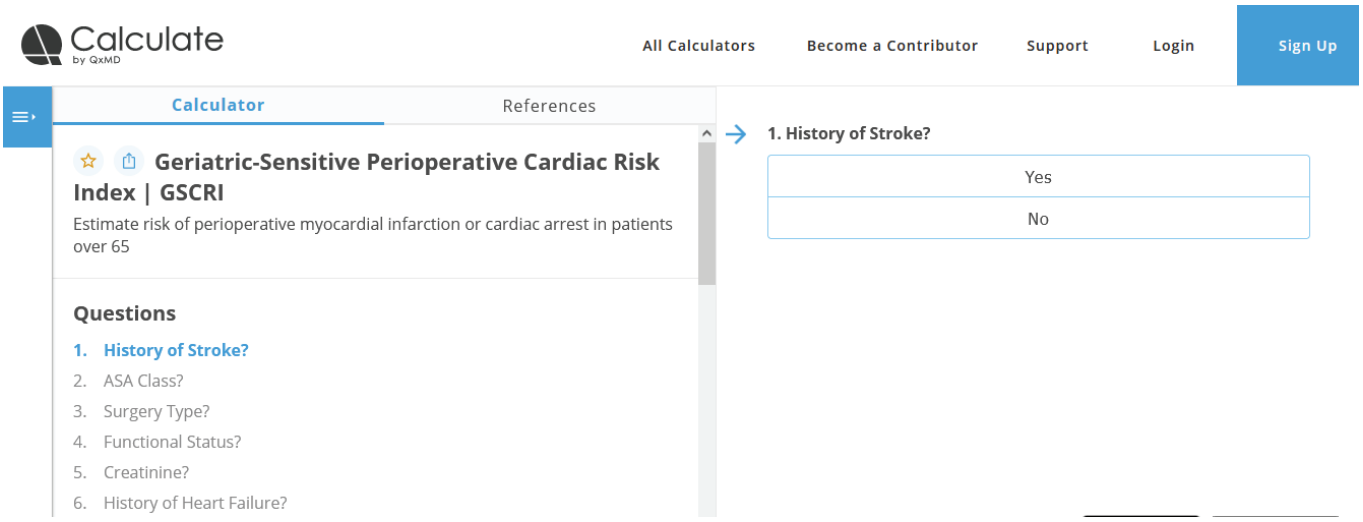
Nedostatak univerzalne definicije za velike neželjene srčane događaje (engl. *MACE - major adverse cardiac events*), razlike u testovima biomarkera visoke osetljivosti, promena načina na koji se određene kardiovaskularne komplikacije definišu u skorovima rizika, pojava velikog broja modela stratifikacije rizika koji nisu testirani u ovoj specifičnoj grupi, predstavljaju neke od glavnih prepreka u poređenju rezultata među studijama [8].

Modeli stratifikacije rizika mogu biti specifični za vrstu operacije (*Vascular Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity -V-POSSUM* ili *Geriatric Sensitive Cardiac Risk Index – GSCRI*), (Slika 1, Slika 2), ili nespecifični i široko korišće-

mining their severity, stability, as well as determining the need for further evaluation and/or therapy optimization, with the aim of reducing perioperative and postoperative mortality and morbidity.

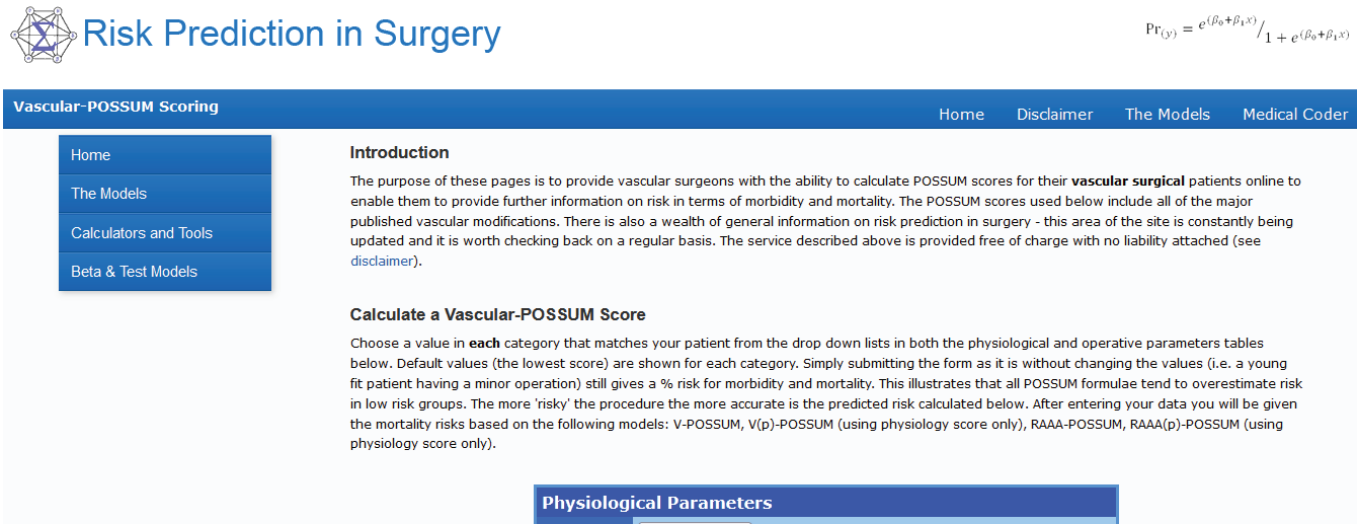
The lack of a universal definition for major adverse cardiovascular events (MACE), the differences among high sensitivity biomarker tests, the change in the way certain cardiovascular complications are defined in risk scores, the existence of a large number of stratification risk models, which have not been tested in this particular group, represent some of the major obstacles to comparing results among studies [8].

Risk stratification models may be specific to the type of surgery (Vascular Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity-V-POSSUM or Geriatric Sensitive Cardiac Risk Index – GSCRI), (Figure 1, Figure 2), or non-spe-



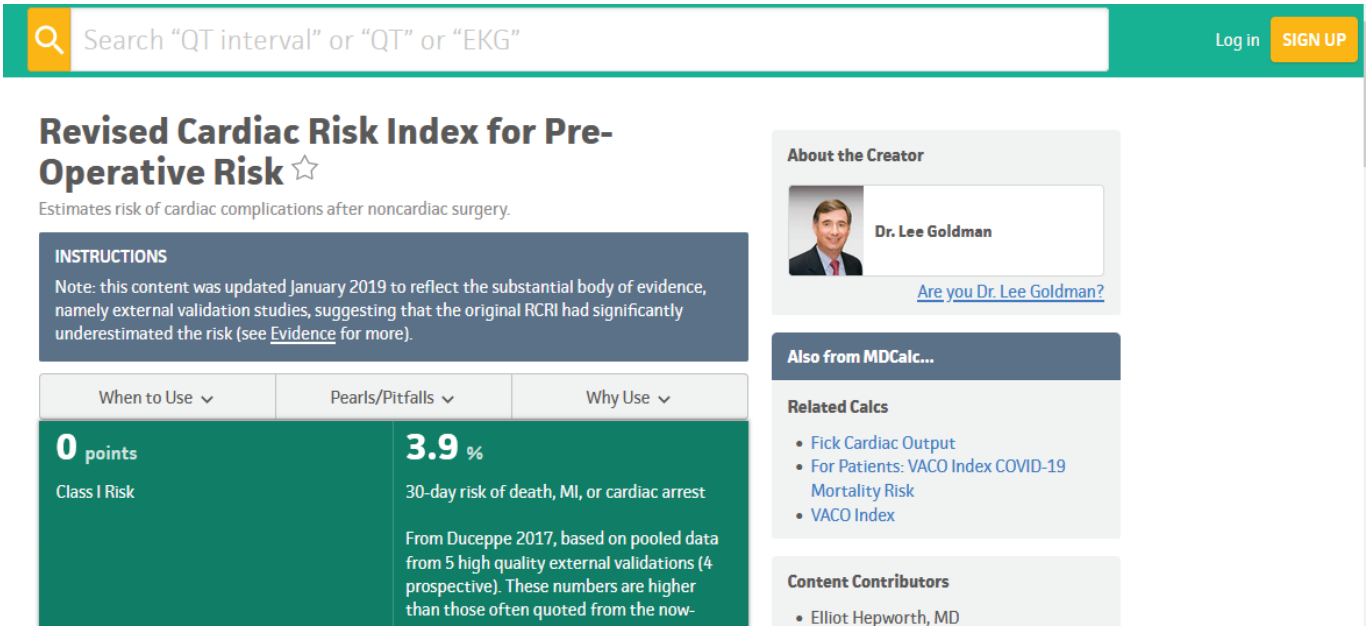
Slika 1. *Geriatric Sensitive Cardiac Risk Index (GSCRI)* [9]

Figure 1. Geriatric Sensitive Cardiac Risk Index (GSCRI) [9]



Slika 2. *Vascular Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (V-POSSUM)* [10]

Figure 2. Vascular Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (V-POSSUM) [10]



Slika 3. *Revised Cardiac Risk Index (RCRI)* [11]

Figure 3. Revised Cardiac Risk Index (RCRI) [11]

ni za nekardiohirurške procedure (*Revised Cardiac Risk Index – RCRI*), (Slika 3), [8,9,10,11,13].

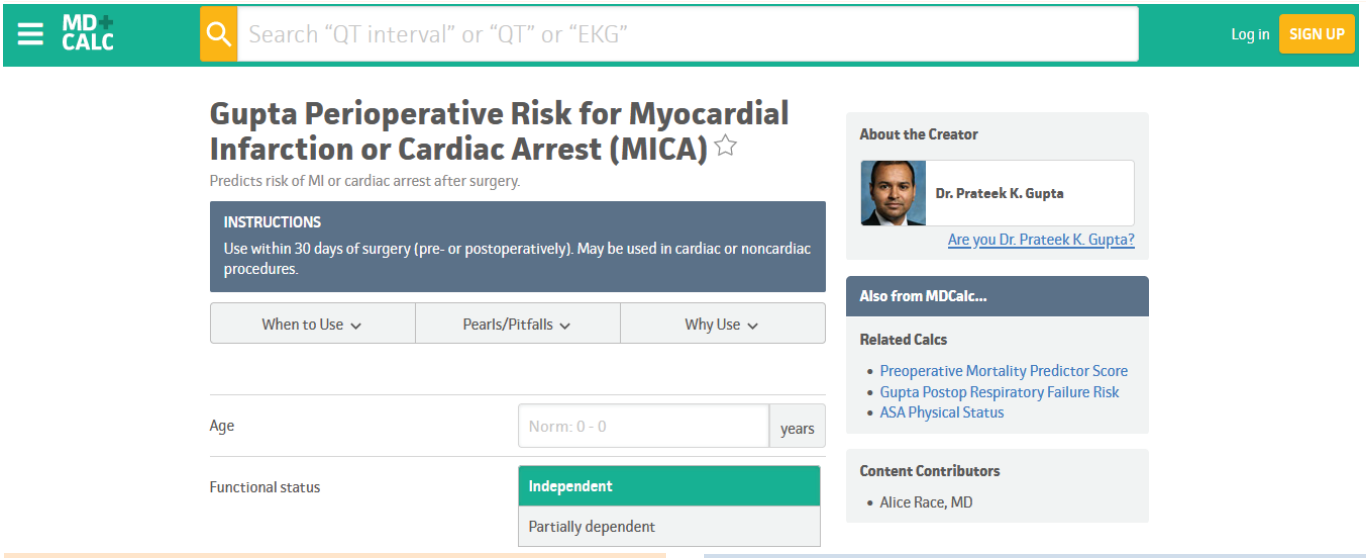
Neki modeli su dizajnirani da otkriju mali broj komplikacija, što ograničava njihovu primenu u svakodnevnoj kliničkoj praksi. Takav je *Gupta MICA – Myocardial Infarction or Cardiac Arrest* (Slika 4) skor, koji se široko koristi za nekardiohirurške procedure, ali je dizajniran da prati samo dve kardiovaskularne komplikacije – infarkt miokarda (engl. *myocardial infarction – MI*) i srčani zastoj (engl. *cardiac arrest – CA*), za koje se pokazalo da nisu prve dve najčešće komplikacije u gerijatrijskoj vaskularnoj hirurgiji, tokom šestomesečnog praćenja [8,12].

Skor Američkog društva anesteziologa (engl. *American Society of Anesthesiology* (*ASA*) *score*) i sistem klasifikacije Njujorškog udruženja kardiologa (engl. *New*

cific and widely used for non-cardiac surgery procedures (Revised Cardiac Risk Index – RCRI), (Figure 3), [8,9,10,11,13].

Some models are designed to discover a small number of complications, which limits their application in everyday clinical practice. Such is the Gupta MICA – Myocardial Infarction or Cardiac Arrest (Figure 4) score, which is widely used for noncardiac surgery procedures, but is designed to monitor only two cardiovascular complications – myocardial infarction (MI) and cardiac arrest (CA), which have proven not to be the first two most common complications in geriatric vascular surgery, during a follow-up period of six months [8,12].

The American Society of Anesthesiology (ASA) score and the New York Heart Association (NYHA) Clas-



Slika 4. Gupta MICA (*Myocardial Infarction or Cardiac Arrest*) skor [12]

Figure 4. Gupta MICA (Myocardial Infarction or Cardiac Arrest) score [12]

York Heart Association – NYHA) predstavljaju neke od pouzdanih kliničkih alata u proceni anesteziološkog rizika i težine srčane insuficijencije, i nezavisni su prediktori za *MICA*-e, tokom prvih šest meseci nakon gerijatrijske vaskularne hirurgije [14]. Ova prediktivna vrednost *ASA* skora se manifestuje i u nekardiohirurškim procedurama i jedan je od razloga njene primene u definisanju nekog od modela rizika (*Gupta MICA*, *GSCRI*). U gerijatrijskoj vaskularnoj hirurgiji, daleko najčešća kardiološka komplikacija je dekompenzacija srčane insuficijencije, koja čini dve trećine svih velikih neželjenih kardiovaskularnih događaja. Po našem mišljenju, glavni faktor bolje prediktivne vrednosti *GSCRI* i *RCRI* skora, u odnosu na *Gupta MICA* skor, jeste to da ova dva skora uključuju podatke o istoriji srčane insuficijencije. Shodno tome, niska ejekciona frakcija i *NYHA* klasa su povezani sa svim *MACE* događajima tokom prvih šest meseci nakon vaskularne hirurgije, kod starijih pacijenata [8].

BIOMARKERI

Pored primene skora rizika, tačna stratifikacija rizika zahteva kombinovanu primenu i preoperativnih i postoperativnih biomarkera. Razlozi za to leže u nemogućnosti bilo kog jedinstvenog skora rizika da pređe vrednost od 0,8 površine ispod krive (engl. *AUC – area under the curve*) u c-statistici i sposobnosti biomarkera da otkriju većinu patofizioloških mehanizama koji su u osnovi kardiovaskularnih komplikacija, kao što su *stretch* i *stress* miokarda, inflamacija, aktivacija trombocita, ishemija, nestabilnost ili ruptura plaka, te neurohormonska aktivacija [15].

Nepredvidljivost, koja je generalno povezana sa velikom vaskularnom hirurgijom, u smislu obimnosti hirurške procedure, njenog trajanja, stepena krvarenja i perioperativne hemodinamske nestabilnosti, može se izbeći primenom postoperativne detekcije biomarkera [16].

Suština integracije biomarkera sa sistemima bodovanja jeste da se otkriju oni pacijenti sa klinički nemanifestovanom bolešću, koji nose rizik od smrtnosti, a sistemom bodovanja ostaju neotkriveni. Primeri za to su N-terminalni fragment pro-moždanog natriuretičkog peptida (engl. *N-terminal pro b-type natriuretic peptide – NT-proBNP*) i visoko osetljivi troponin test, koji povećavaju broj pacijenata koji će biti reklasifikovani kao visokorizični, u nesrčanoj hirurgiji [3,17]. Međutim, *NT-proBNP* i visoko osetljivi C-reaktivni protein (*high-sensitivity C-reactive protein – hs-CRP*) imaju najveći prediktivni uticaj u gerijatrijskoj vaskularnoj hirurgiji [8]. Biomarker *NT-proBNP*, ne samo da otkriva ishemiju miokarda, već i čitav niz morfoloških i funkcionalnih poremećaja leve pretkomore (dilatacija,

sification are some of the reliable clinical tools for assessing anesthesiological risk and the severity of cardiac insufficiency, i.e., heart failure, and are independent predictors of MICA, during the first six months after geriatric vascular surgery [14]. This predictive value of the ASA score is also applicable in noncardiac procedures and represents one of the reasons that it is used in defining some of the risk models (Gupta MICA, GSCRI). In geriatric vascular surgery, the most common cardiological complication, by far, is decompensation of cardiac insufficiency, which makes up for two thirds of all major adverse cardiovascular events. In our opinion, the main factors of the better predictive value of the GSCRI and RCRI scores, as compared to the Gupta MICA score, is that these two scores include data on the history of cardiac insufficiency. Consequently, a low ejection fraction and the NYHA class are connected with all MACE events during the first six months after vascular surgery, in older patients [8].

BIOMARKERS

In addition to applying the risk score, precise risk stratification requires a combined application of both preoperative and postoperative biomarkers. The reasons for this lie in the inability of any of the risk scores, by themselves, to exceed 0.8 of the area under the curve (AUC) in c-statistics and the ability of the biomarkers to discover most of the pathophysiological mechanisms which are at the foundation of cardiovascular complications, such as myocardial stretch and myocardial stress, inflammation, platelet activation, ischemia, plaque instability or rupture, and neurohormonal activation [15].

Unpredictability, which is generally linked to major vascular surgery, in the sense of the scope of the surgical procedure, its duration, the degree of blood loss and perioperative hemodynamic instability, may be avoided with postoperative biomarker detection [16].

The main idea of integrating biomarkers with scoring systems is to reveal those patients with clinically unmanifested disease, who carry a mortality risk and remain undetected by scoring systems. Examples of this are the N-terminal pro b-type natriuretic peptide (NT-proBNP) and the high-sensitive troponin test, which increase the number of patients who are reclassified as high-risk in noncardiac surgery [3,17]. However, NT-proBNP and high-sensitivity C-reactive protein (hs-CRP) have the greatest predictive effect in geriatric vascular surgery [8]. The NT-proBNP biomarker reveals not only myocardial ischemia, but also a number of morphological and functional disorders of the left atrium (dilatation, fibrillation) and the left ventricle (increased myocardial mass, systolic/diastolic dysfunc-

fibrilacija) i leve komore (uvećanje mase miokarda, sistolna/dijastolna disfunkcija). Glavni razlog za superiornost ova dva biomarkera je bolja korelacija sa stepenom inflamacije, uzimajući u obzir sledeće činjenice:

Inflamacija igra ključnu ulogu u progresiji srčane insuficijencije, posebno kod srčane insuficijencije sa očuvanom ejekcionom frakcijom (engl. *heart failure with preserved ejection fraction – HFpEF*), koju gotovo isključivo nalazimo kod starijih osoba, posebno starijih žena, kod kojih je 90% novih slučajeva srčane insuficijencije upravo *HFpEF* [18,19];

Zapaljenje endotela je ključni faktor u nastanku rupture aterosklerotskog plaka, a stepen stenoze nije povezan sa lokacijom perioperativnog infarkta;

NT-proBNP i *hs-CRP* su povezani sa drugim inflamatornim biomarkerima, kao što su

IL-6 i pojava srčane insuficijencije kod starijih muškaraca [20,21].

ZAKLJUČAK

Velika vaskularna hirurgija nosi izuzetan rizik od velikih neželjenih kardiovaskularnih događaja, u prvom redu od pogoršanja postojeće srčane slabosti. Predikcija pojave svih kardiovaskularnih komplikacija, kao i kardiovaskularnog mortaliteta, predstavlja proces koji nosi brojne izazove. Najveću šansu za uspeh nekog prediktivnog sistema imaju kombinacije modela već stratifikovanih prema riziku i biomarkera, čiji je prediktivni potencijal proveren kod vaskularnih i/ili gerijatrijskih pacijenata.

Sukob interesa: Nije prijavljen.

tion). The main reason for the superiority of these two biomarkers is better correlation with the degree of inflammation, bearing in mind the following facts:

Inflammation plays a key role in the progression of cardiac heart failure, especially in heart failure with preserved ejection fraction (HFpEF), which we almost exclusively find in elderly patients, especially in elderly women, in whom 90% of all new cases of heart failure are HFpEF [18,19];

Inflammation of the endothelium is a key factor in the occurrence of atherosclerotic plaque rupture, while the degree of stenosis is not linked to the location of the perioperative infarction;

NT-proBNP and hs-CRP are linked to other inflammatory biomarkers, such as

IL-6 and heart failure in older men [20,21].

CONCLUSION

Major vascular surgery carries a very high risk of major adverse cardiovascular events, primarily the exacerbation of already existing heart failure. Predicting the occurrence of all cardiovascular complications as well as cardiovascular mortality is a challenging process. A predicative system has the highest probability of success if it is a combination of models that are already risk stratified and biomarkers, whose predictive potential has already been tested in vascular and/or geriatric patients.

Conflict of interest: None declared.

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