Original article **UDC: 616.127-005.8-053.9:616.13/.14-089**
doi:10.5633/amm.2022.0302

CORRELATION OF CLINICAL AND DEMOGRAPHIC FACTORS WITH THE OCCURRENCE OF MYOCARDIAL INFARCTION AND CARDIAC ARREST IN OLDER PATIENTS AFTER MAJOR ELECTIVE VASCULAR SURGERY

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The risk stratification as a part of preoperative preparation of patients involves a series of diagnostic and therapeutic procedures with the main objective of reducing peri/post-operative morbidity and mortality. The aim of the study was to identify a wide spectrum of preoperative clinical and demographic characteristics which were significantly associated with the occurrence of myocardial infarction and cardiac arrest (MICA) during six-month period after vascular surgical procedure, during 2017, 2018, 2019, the study included 144 patients (96 men-66.6 % and 48 women-33.3 %) over 65 years of age (average 70 years). MICA in the first six months after the intervention was associated with higher NYHA class ($p < 0.001$), previous coronary artery disease ($p < 0.001$), cardiomyopathy ($p < 0.05$) or previous myocardial infarction ($p < 0.05$), usage of calcium channel antagonists ($p < 0.05$) and antiplatelet drugs ($p < 0.001$), higher ASA score ($p < 0.01$), higher urea concentration ($p < 0.01$), lower ejection fraction ($p < 0.001$) and longer intensive care unit stay ($p < 0.001$). Using binary logistic regression method, multivariate analysis has identified previous coronary artery disease as a predictor of MICA occurrence ($p < 0.01$). In the multivariate Cox-regression model ($\chi^2 = 71.515$, $p < 0.001$), there were six independent predictors of survival without MICA. Previous coronary artery disease is most significant preoperative risk factor for MICA occurrence. Variables related to heart failure and high urea concentration are independent predictors for MICA.

Acta Medica Medianae 2022;61(3):14-19.

Key words: *myocardial infarction, cardiac arrest, vascular surgery*

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Introduction

The risk stratification as a part of preoperative preparation of patients involves a series of diagnostic and therapeutic procedures with the main objective of reducing peri/post-operative morbidity and mortality (1). Large elective vascular procedures are distinguished as procedures of the highest cardiac risk, because the frequency of 30-day myocardial infarction (MI) and cardiac arrest (CA) is more than 5% (2). In non-cardiac surgery patients, these two cardiovascular complications are associated with hospital mortality of nearly 60%. The same study Identified, the age over 65 years and vascular surgery procedures as the independent predictors of MICA (3). The importance of risk stratification is due to the aging of the population as well as the increasing frequency of vascular procedures in elderly patients (4). Albeit the most used, easy to implement and the only one given in European (2) and American (5) recommendations, Revised Cardiac Risk Index (RCRI) shows insufficient discriminatory power for cardiovascular complications after vascular surgery (6).

The aim of the study was to identify a wide spectrum of preoperative clinical and demographic charac-teristics which were significantly associated with the occurrence of MICA during six-month period after surgical procedure.

Materials and methods

During 2017, 2018, 2019, the study included 144 patients (96 men – 66.6 % and 48 women – 33.3 %) over 65 years of age (average 70 years). Patients were followed for six months after major elective vascular surgery (abdominal aortic aneurysm repair, carotid endarterectomy and lower limb revascularization). All participants underwent balanced endotracheal anesthesia. Preoperative examination of patients by anesthesiologists included a detailed evaluation of medical history, clinical examination, insight into biochemical, hematological and coagulation tests, electrocardiogram, chest X-ray and transthoracic ultrasonographic examination of the heart. All participants were preoperatively classified according to ASA (American Society of Anesthesiologist) (7) and NYHA (New York Heart Association) classification (8). Patients with decompensated heart failure and unstable coronary disease were not included in the study.

Myocardial infarction was defined as indicative electrocardiogram changes and new-onset cardiac troponin I elevation greater than three times as the upper reference limit. Absence of heart contraction as the consequence of ventricular fibrillation, pulseless ventricular tachycardia and pulseless electric activity were a hallmark for cardiac arrest. The research was accredited by Ethics Committee of the Faculty of Medicine, University of Niš and conducted at the Clinic for Cardiovascular Surgery, University Clinical Center Niš, in accordance with the principles of the Declaration of Helsinki. The obligation of the investigators was to collect the signed informed consents of the study participants before inclusion.

Statistical analysis

We used Statistical Package for Social Sciences (SPSS 21.0; Chicago, IL, USA) for data analysis. Qualitative variables were presented as frequencies in contrast to quantitative variables, which were presented as means with SDs or medians with interquartile ranges. Student's t-test and Mann-Whitney U-test were used for quantitative variables and Fisher's Exact Probability Test was performed for qualitative variables. Prediction of myocardial injury and cardiac arrest were determined by univariate and multivariate binary logistic and Cox-regression modeling. A p-value less than 0.05 was considered to be a measure of statistical significance. Data analyzing was performed using Statistical Package for Social Sciences (SPSS 21.0; Chicago, IL, USA) and a p-value less than 0.05 was recognized as measure of statistical significance.

Results

During the first six months after the intervention, MICA was noted in 16 (11.1%) patients. Ten of these patients (62.5%) had MICA in the first month. Eleven patients (68.8%) had only one event, in two patients two events were observed, and three events in three patients. Three patients (2.1%) died during the follow-up. Both myocardial infarction and cardiac arrest were of equal frequency, each in 8 patients (24.2%).

MICA in the first six months after the intervention was associated with higher NYHA class ($p < 0.001$), previous coronary artery disease ($p < 0.001$), cardiomyopathy ($p < 0.05$) or previous myocardial infarction ($p < 0.05$), usage of calcium channel antagonists ($p < 0.05$) and antiplatelet drugs ($p < 0.001$), higher ASA score ($p < 0.01$), higher urea concentration ($p < 0.01$), lower ejection fraction ($p < 0.001$) and longer intensive care unit stay ($p < 0.001$) (Table 1).

Using binary logistic regression method, multivariate analysis has identified previous coronary artery disease as a predictor of MICA occurrence within six months after the intervention ($p < 0.01$) (Table 2).

Similar predictors were identified for six months survival without MICA. In the multivariate Cox-regression model ($\chi^2 = 71.515$, $p < 0.001$), there were six independent predictors of survival without MICA. Previous coronary artery disease increased the risk 163 times ($p < 0.001$), while previous cardiomyopathy or previous myocardial infarction increased the risk 14 times ($p < 0.05$) and 29 times ($p < 0.01$), respectively. Use of nitrates was associated with 89 times greater risk ($p < 0.01$). Higher ASA score by 1 unit bared 500 times higher risk ($p < 0.05$). Increased uremia, with each unit increased the risk 1.7 times ($p < 0.05$) (Table 3).

Table 1. Correlation of clinical and demographic factors with occurrence of MICA six months after procedure

	With MICA	Without MICA	p-value
Age (years)	71.25 ± 5.46	69.48 ± 3.43	1.269 (0.222)*
Gender (male)	3 (18.8%)	47 (36.7%)	1.311 (0.177) †
Dyspnea (NYHA class)	2.75 ± 0.58	2.09 ± 0.63	4.022 (0.000)*
Atrial fibrillation	0 (0.0%)	7 (5.5%)	0.117 (1.000) †
Previous cerebrovascular insult	2 (12.5%)	40 (31.3%)	1.598 (0.152) †
Previous coronary artery disease	10 (62.5%)	21 (16.4%)	15.262 (0.000) †
Previous cardiomyopathy	5 (31.3%)	13 (10.2%)	4.018 (0.031) †
Prior percutaneous coronary intervention	1 (6.3%)	4 (3.1%)	0.000 (0.450) †
Previous myocardial infarction	6 (37.5%)	19 (14.8%)	3.632 (0.036) †
Prior coronary artery bypass graft	1 (6.3%)	1 (0.8%)	0.396 (0.211) †
Previous hypertension	13 (100.0%)	106 (82.8%)	2.054 (0.132) †
Previous diabetes mellitus	6 (37.5%)	47 (36.7%)	0.000 (1.000) †
Insulin-dependent diabetes mellitus	5 (31.3%)	28 (21.9%)	0.276 (0.527) †
Insulin-independent diabetes mellitus	1 (6.3%)	19 (14.8%)	0.307 (0.700) †
Previous hyperlipidemia	5 (31.3%)	28 (21.9%)	0.276 (0.527) †
Smoking	8 (50.0%)	49 (38.3%)	0.400 (0.421) †
Family history	10 (62.5%)	46 (35.9%)	3.179 (0.056) †
Beta-blocker	13 (81.3%)	91 (71.1%)	0.313 (0.557) †
ACE inhibitor	15 (93.8%)	91 (71.1%)	2.682 (0.070) †
Calcium channel antagonist	9 (56.3%)	30 (23.4%)	6.181 (0.013) †
Antiplatelet therapy	13 (93.8%)	67 (52.3%)	8.328 (0.001) †
Statins	10 (62.5%)	58 (45.3%)	1.067 (0.288) †
Diuretics	2 (12.5%)	22 (17.2%)	0.014 (1.000) †
Nitrates	3 (18.8%)	7 (5.5%)	2.099 (0.083) †
AAAR	6 (37.5%)	25 (19.5%)	4.685 (0.196) †
CE	7 (43.8%)	73 (57.0%)	
AFBP	1 (6.3%)	2 (1.6%)	
FPBP	2 (12.5%)	28 (21.9%)	
ASA score	3.0 (3.0-3.0)	2.0 (2.0-2.0)	2.997 (0.003) ‡
Hemoglobin	12.6 (12.0-14.1)	13.6 (12.4-14.4)	1.139 (0.255) ‡
Creatinine	100.5 (78.9-134.0)	88.2 (79.2-108.0)	1.446 (0.148) ‡
WBC count	7.4 (6.0-9.6)	7.2 (6.0-8.1)	0.579 (0.563) ‡
Platelet count	233.5 (179.2-242.0)	225.5 (183.8-273.8)	0.903 (0.367) ‡
Urea	7.6 (5.5-9.8)	5.6 (5.1-6.8)	2.616 (0.009) ‡
LDL	2.64 ± 0.77	2.82 ± 0.98	0.731 (0.466)*
HDL	1.2 (0.9-1.3)	1.2 (1.0-1.3)	0.118 (0.906) ‡
EF (%)	47.25 ± 4.52	55.35 ± 7.25	6.232 (0.000)*
BMI (kg/m2)	26.10 ± 2.02	25.63 ± 2.63	0.688 (0.492)*
ICU (days)	3.5 (3.0-4.0)	1.0 (1.0-2.0)	4.962 (0.000) ‡

*- t-test,
†- Chi-squared test,
‡-Z-test.

MICA - myocardial infarction and cardiac arrest;
NYHA - New York Heart Association;
ACE - angiotensin converting enzyme;
AAAR, repair of abdominal aortic aneurysm;
CE - carotid endarterectomy;
AFBP - aortobifemoral bypass;
FPBP - femoropopliteal bypass;
ASA - American Society of Anesthesiologist;
WBC - white blood cells;
LDL - low-density lipoprotein;
HDL - high-density lipoprotein;
EF - ejection fraction;
BMI - body mass index;
ICU - intensive care unit.

Table 2. Binary logistic regression model of MICA occurrence in the first 6 months after the intervention

	Univariate		Multivariate	
	OR (95% CI for OR)	p-value	OR (95% CI for OR)	p-value
Previous coronary artery disease	8.492 (2.785-25.897)	0.000	1905.829 (6.175-588189.405)	0.010
Previous cardiomyopathy	4.021 (1.208-13.386)	0.023	0.377 (0.026-5.549)	0.477
Previous myocardial infarction	3.442 (1.119-10.584)	0.031	0.017 (0.000-1.246)	0.063
Positive family history	2.971 (1.014-8.701)	0.047	0.469 (0.072-8.236)	0.828
Calcium channel antagonists	4.200 (1.442-12.233)	0.009	0.571 (0.058-5.581)	0.630
Antiplatelet drugs	13.657 (1.752-106.482)	0.013	11.819 (0.216-647.780)	0.227
Dyspnea (NYHA class)	7.683 (2.439-24.197)	0.000	3.020 (0.193-47.322)	0.431
ASA score	7.689 (1.679-35.212)	0.009	0.002 (0.000-1.024)	0.051
Urea	1.344 (1.096-1.648)	0.005	1.162 (0.820-1.648)	0.399
EF(%)	0.810 (0.727-0.904)	0.000	0.854 (0.723-1.008)	0.0622

MICA - myocardial infarction and cardiac arrest;
NYHA - New York Heart Association;
ASA - American Society of Anesthesiologist;
EF - ejection fraction.

Table 3. Cox regression model of survival without MICA in the first 6 months after the intervention

	Univariate		Multivariate	
	HR (95% CI for HR)	p-value	HR (95% CI for HR)	p-value
Previous coronary artery disease	6.801 (2.470-18.727)	0.000	163.054 (7.224-3680.348)	0.001
Previous cardiomyopathy	3.363 (1.168-9.685)	0.025	0.071 (0.008-0.618)	0.017
Previous myocardial infarction	2.944 (1.070-8.102)	0.037	0.034 (0.003-0.443)	0.010
Calcium channel antagonists	3.706 (1.379-9.958)	0.009	0.606 (0.121-3.025)	0.541
Antiplatelet drugs	12.152 (1.605-92.016)	0.016	5.230 (0.149-183.324)	0.362
Nitrates	3.576 (1.017-12.573)	0.047	89.035 (3.613-2194.056)	0.006
Dyspnea (NYHA class)	6.649 (2.257-19.586)	0.001	4.785 (0.439-52.131)	0.199
ASA score	6.910 (1.570-30.409)	0.011	0.002 (0.000-0.374)	0.020
Creatinine	1.013 (1.001-1.026)	0.039	0.990 (0.957-1.024)	0.558
Urea	1.294 (1.102-1.520)	0.002	1.674 (1.100-2.547)	0.016
EF(%)	0.843 (0.776-0.916)	0.000	0.907 (0.762-1.081)	0.276

MICA - myocardial infarction and cardiac arrest;
NYHA - New York Heart Association;
ASA - American Society of Anesthesiologist;
EF - ejection fraction.

Discussion

The main predictive factor in our study results is preoperative coronary artery disease. One in five men over the age of 75 suffers from it (9). When it comes to patients who are preparing for major vascular surgery, approximately 60% have advanced or severe coronary artery disease (10). Here we find an explanation for such a high association with the occurrence of MICA in a subgroup of elderly and vascular patients. We believe that CAD is responsible for the connection of many other factors, such as the preoperative use of nitrates and antiplatelet drugs, but also that it is in the etiopathogenesis of various forms of heart failure.

The ASA score has once again been confirmed as a reliable and simple system. Although the ASA scoring system is intended to assess general anesthesia risk, we believe that high ASA scores in vascular surgical patients are associated with the presence and/or sequelae of cardiovascular risk factors. In multicentric study, which included over 200 000 patients from the American College of Surgeons National Surgical Quality Improvement Program database, ASA score was also identified as independent predictor of MICA after non-cardiac surgery (6).

In our study, variables related with heart failure (low ejection fraction, echocardiographic verification of cardiomyopathy and high NYHA class) were associated with the occurrence of MICA. The group of patients with echocardiographically verified cardiomyopathy included asymptomatic patients with preserved EF but echosonography signs indicated diastolic insufficiency. Reasons for the high risk posed by diastolic dysfunction in vascular sur-

gery could be sudden changes in systemic vascular resistance, circulatory overload, impaired tissue perfusion, and ischemic-reperfusion damage (11). Therefore, we emphasize the need for routine and detailed preoperative echocardiographic examination even in asymptomatic patients. Increased urea is an independent predictor of MICA six months after vascular surgery. High urea concentration should not only be interpreted in the context of renal impairment but also increased sympathetic activity and activation of the renin-angiotensin-aldosterone system (12). Increased urea concentration may be a long-term marker of cardiovascular and all-cause mortality in elderly patients with decompensated heart failure (12, 13).

Conclusion

Previous coronary artery disease is most significant preoperative risk factor for MICA occurrence. Variables related to heart failure and high urea concentration are independent predictors for MICA six months after vascular procedure.

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Originalni rad **UDC: 616.127-005.8-053.9:616.13/.14-089**
doi:10.5633/amm.2022.0302

KORELACIJA KLINIČKIH I DEMOGRAFSKIH FAKTORA SA POJAVOM MIOKARDNOG INFARKTA I SRČANOG ZASTOJA KOD STARIJIH BOLESNIKA NAKON VELIKE ELEKTIVNE VASKULARNE HIRURGIJE

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Stratifikacija rizika je deo preoperativne pripreme bolesnika, koja uključuje niz dijagnostičkih i terapijskih postupaka sa glavnim ciljem smanjenja perioperativnih, odnosno postoperativnih morbiditeta i mortaliteta. Cilj studije je identifikacija širokog spektra preoperativnih kliničkih i demografskih parametara, koji su značajno povezani sa pojavom infarkta miokarda i srčanog zastoja (MICA), tokom šest meseci nakon vaskularne hirurgije. Tokom 2017., 2018. i 2019. godine studija je obuhvatila 144 bolesnika (96 muškaraca – 66,6% i 48 žena – 33,3%) starosti preko 65 godina (prosečno 70). MICA je u prvih šest meseci povezana sa višom NYHA klasom ($p < 0,001$), prethodnom bolešću koronarnih arterija ($p < 0,001$), kardiomiopatijom ($p < 0,05$), prethodnim infarktom miokarda ($p < 0,05$), upotrebom antagonista kalcijumovih kanala ($p < 0,05$), upotrebom antitrombocitnih lekova ($p < 0,001$), višom ASA klasom ($p < 0,01$), višom koncentracijom uree ($p < 0,01$), nižom frakcijom srčanog izbačaja ($p < 0,001$) i dužim boravkom u jedinici intenzivnog lečenja ($p < 0,001$). Multivarijantnom analizom binarne logističke regresije identifikovana je prethodna bolest koronarnih arterija, kao prediktor pojave MICA ($p < 0,01$). Multivarijantna analiza Koks regresije utvrdila je šest nezavisnih prediktora preživljavanja bez pojave MICA ($\chi^2 = 71,515$, $p < 0,001$). Prethodna bolest koronarnih arterija najznačajniji je faktor preoperativnog rizika za pojavu MICA. Varijable povezane sa srčanom insuficijencijom i visoka koncentracija uree nezavisni su prediktori pojave MICA.

Acta Medica Medianae 2022;61(3):14-19.

Ključne reči: *miokardni infarkt, srčani zastoj, vaskularna hirurgija*