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ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Changes in risk factors trends in coronary surgery over the past decade – a single-center validation

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SUMMARY

Introduction/Objective The risk factors in coronary patients indicated for surgery change during the years. The aim of this study was to analyze the trends of risk factors which enter into the composition of the European System for Cardiac Operative Risk Evaluation (EuroSCORE II).

Methods The research included 3996 patients who underwent coronary surgery from January 2012 to December 2020 at our clinic. For estimation of the risk factors and evaluation of the operative risk, the EuroSCORE II model was used. Kruskal–Wallis H test was used for testing differences of values of numerical variables between years. The calibration and the discriminative power of the EuroSCORE II were assessed by comparing the observed to the expected mortality ratio and by using area under the receiver operating characteristic curve (AUC).

Results Old age has shown a significant increasing trend ($p < 0.0005$), as well as diabetes mellitus on insulin therapy, before surgery ($p = 0.004$). The significant declining trend have shown: extracardiac arteriopathy ($p = 0.003$), critical preoperative condition ($p = 0.013$), preoperative NYHA Classes III or IV ($p < 0.0005$) and preoperative angina pectoris CCS Class IV ($p < 0.0005$). The mean value of the EuroSCORE II decreased from 1.73 to 1.53 ($p < 0.0005$). The observed mortality was 1.70% and the mean, predicted by the EuroSCORE II, was 1.75%. The O/E mortality ratio was 0.98; 95% confidence interval 0.95–1.03. The AUC was 0.825.

Conclusion Over the past decade the risk profile of patients for coronary surgery has changed. The mean value of the EuroSCORE II has a declining trend with a good predictive and discriminative power.

Keywords: cardiac surgery; risk factors; trends

INTRODUCTION

Risk stratification involves preoperative determination of operative risk based on number and severity of patients' risk factors. The essence of the model for outcome prediction and risk stratification in cardiac surgery is to single out risk factors that are important in relation to the outcome. A good calibration of the model exists if the difference between the expected outcome and the observed outcome is small, ideally zero. The discriminative power of the model is the ability to distinguish between low and high-risk groups in relation to the outcome.

European System for Cardiac Operative Risk Evaluation (EuroSCORE) was developed in the period 1995–1999 [1]. The model was initially additive [1].

In 2003, a logistics model was developed that proved to be better, especially in groups of patients with increased operative risk [2].

The application of EuroSCORE on other continents showed some differences in the risk profile of coronary patients indicated for surgical treatment. In Australia, the incidence of female sex, chronic obstructive pulmonary disease, extracardiac arteriopathy, reoperation, and emergency surgery was higher than in the European population [3]. In China, there were more patients with neurological deficits, while old age, chronic obstructive pulmonary disease, extracardiac arteriopathy, renal failure, unstable angina pectoris, recent myocardial infarction and left ventricular dysfunction were less common [4].

We analyzed the trends of all relevant risk factors of the additive EuroSCORE, from 2001 to the end of 2008. During the observed years, old age, extracardiac arteriopathy, recent myocardial infarction and emergency operation as risk factors significantly changed with an increasing trend, while chronic lung disease, neurological dysfunction and unstable pectoral angina had a decreasing trend [5]. The risk for isolated coronary artery bypass graft surgery (CABG) given by additive EuroSCORE increaseed over the years, but operative mortality decreased [6].

The EuroSCORE II, with new relevant risk factors, was defined and introduced into routine use in 2012. The initial results have shown better prediction than its original version. In our first study, from the beginning of 2012, the EuroSCORE II satisfactorily predicted hospital mortality and had solid discriminative power [7]. Recent results showed that the EuroSCORE II produces a valid risk prediction and outperforms the earlier models [8].

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The last two decades have seen a change in the risk profile of patient indicated for coronary surgery due to an increased number of percutaneous coronary interventions (PCI) with the implementation of various types of stents.

The aim of this study was to analyze the trends of risk factors in patients indicated for coronary surgery which make up the EuroSCORE II and to assess the predictive and discriminative power of the model.

METHODS

The research included 3996 consecutive patients who underwent isolated coronary surgery at Institute of Cardiovascular Diseases of Vojvodina, from January 2012 to December 2020 and was approved by the Ethics Committee of Institute of Cardiovascular Diseases of Vojvodina (No.: 1515-1/3). For each patient the EuroSCORE II was calculated prospectively, using the formulas available at the EuroSCORE website (www.euroscore.org). The postoperative mortality was considered as death from any cause within 30 days of the operation. Data were collected prospectively and analyzed retrospectively. Statistical analysis was performed using the IBM SPSS Statistics, Version 19.0 (IBM Corp., Armonk, NY, USA). The Kruskal–Wallis H test was used for testing differences of values of numerical variables between years. Relation between qualitative data was tested using the χ^2 test. Spearman's test was used to determine the strength and direction of association between two numerical variables. The calibration of the EuroSCORE II was assessed by comparing observed (O) to expected (E) postoperative mortality ratio and by Hosmer–Lemeshow (H-L) test. The discriminative power of the EuroSCORE II was examined using area under the receiver operating characteristic curve (AUC), where cut-off, sensitivity, and specificity were determined. The differences were considered significant if $p < 0.05$.

RESULTS

Total number of coronary patients operated in the period from 2012 until 2020 was 3996. During that time, it has come to significant changes in the frequency of some risk factors (Figures 1–6). Table 1 shows all the changes in the frequency of risk factors related to the patients who were operated on.

The average age of coronary patients who were operated on was 64.4 ± 1.17 (35–88) years. Over time, the patients get older. The observed years and the age of the patients were positively correlated ($r = 0.860$, $p = 0.003$), with an increasing trend (Figure 1).

There were 24.4% female patients. The frequency of female sex through the observed period was similar. The frequency of risk factors related to impaired kidney function, expressed by creatinine clearance < 85 ml/min, was 32.7%. It was significantly different through the observed period ($p < 0.0005$), but no trend was observed.

The observed years and frequency of extracardiac arteriopathy were related ($p = 0.003$). The years and average percentages of extracardiac arteriopathy in those years

Table 1. Risk factors from European System for Cardiac Operative Risk Evaluation (EuroSCORE) II in relation to time, significance, and trends

Risk factors	Total	2012	2013	2014	2015	2016	2017	2018	2019	2020	p	Trend
Age (years)	64.4 (35–88)	62.83	62.39	64.99	64.22	64.21	64.67	64.78	65.72	65.82	< 0.0005	↑
Female sex (%)	24.4	25.2	26.3	31.6	22.1	25.3	21.7	23.7	25.2	22.9	0.177	-
CC < 85 ml/min (%)	32.7	15	20.4	27.6	49.9	60.2	36.7	25.6	29.1	19.4	< 0.0005	-
Extracardiac arteriopathy (%)	15.3	19	20.9	11.6	15.5	15.7	14.1	13.2	12.2	14.6	0.003	↓
Poor mobility (%)	4.2	4.9	3.4	4.4	4.3	3.5	3.8	5.2	3.3	4.4	0.796	-
Previous cardiac surgery (%)	1.8	1.5	1.4	2.7	1.4	2.2	2.0	1.7	6	3.5	0.170	-
Chronic lung disease (%)	7.1	8.5	6.7	5.8	8.0	5.1	7.2	7.7	7.1	6.7	0.597	-
Critical preoperative state (%)	1.7	2.3	2	3.1	1.2	2.5	2.8	1.2	0.4	0.3	0.013	↓
Diabetes on insulin (%)	13	10.2	13.7	11.1	11.2	11.4	13.5	15.3	12.4	19.7	0.004	↑
NYHA III, IV (%)	16.9	27.7	32.4	25.8	13.3	13.1	10.4	9.1	12.8	18.1	< 0.0005	↓
AP-CCS Class IV (%)	6.6	9.1	7.8	8.4	6.7	13.9	9.8	1.9	1	0.3	< 0.0005	↓
LVEF < 50% (%)	36.3	32.3	36.6	33.8	38	35.3	41.4	33.2	38.4	38.4	0.064	-
Recent myocardial infarction (%)	25.9	27.1	26.3	21.8	26.6	29.6	25.9	26.5	19.5	28.6	0.022	-
Pulmonary hypertension (%)	22.6	18.6	19.63	16.9	27.6	30.6	27.1	18.9	20.3	19.4	< 0.0005	-
Urgent operation (%)	4.7	6.1	5	9.3	2.7	3.5	5.6	3.4	5.3	3.8	0.003	-

CC – creatinine clearance; NYHA – New York Heart Association; AP-CCS – Canadian Cardiovascular Society grading of angina pectoris; LVEF – left ventricular ejection fraction

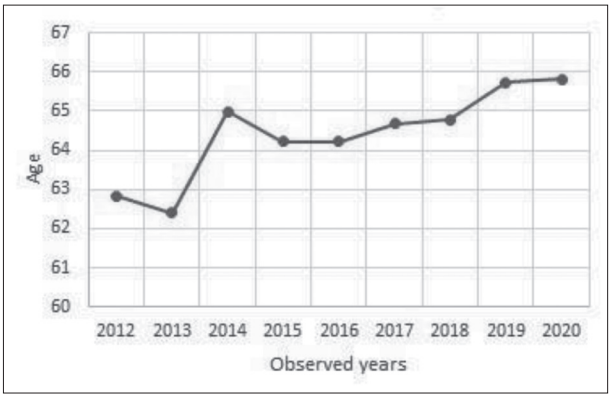


Figure 1. Trend of the mean age 2012–2020

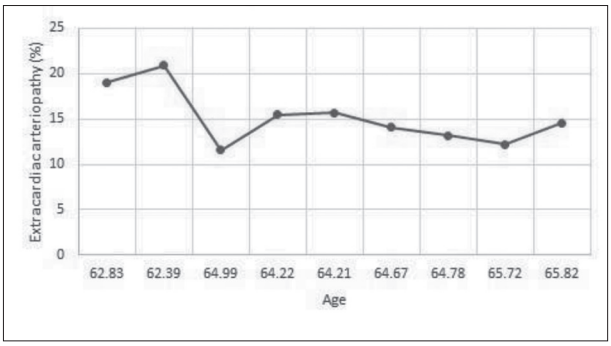


Figure 2. Frequency of extracardiac arteriopathy 2012–2020

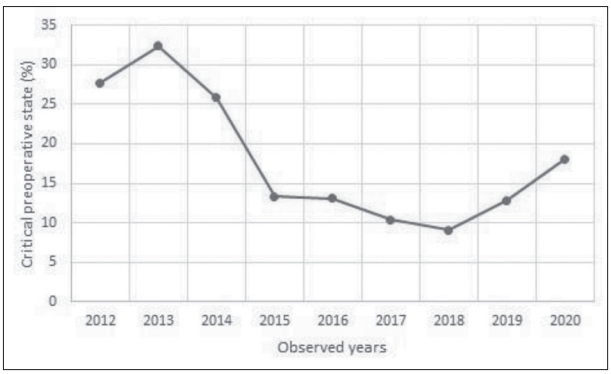


Figure 3. Average percentages of critical preoperative condition of patients 2012–2020

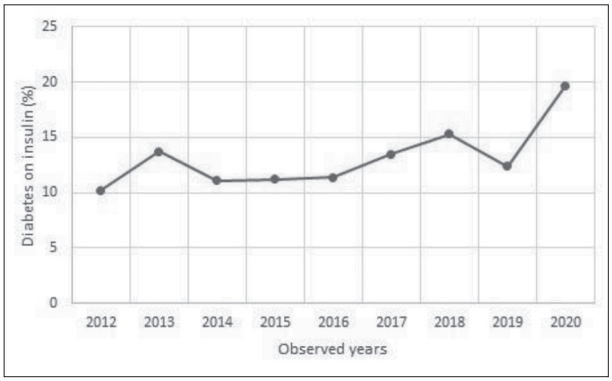


Figure 4. Percentage of patients with diabetes mellitus on insulin 2012–2020

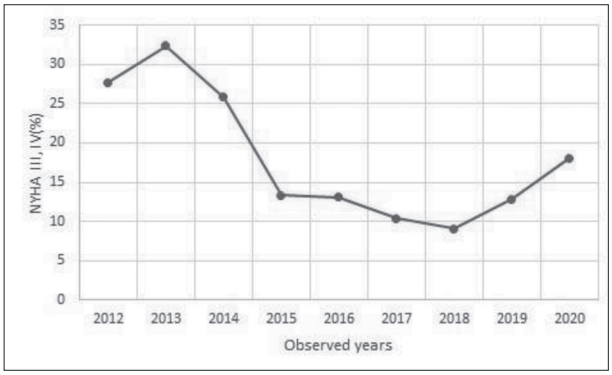


Figure 5. Frequency of patients in New York Heart Association (NYHA) Classes III or IV 2012–2020

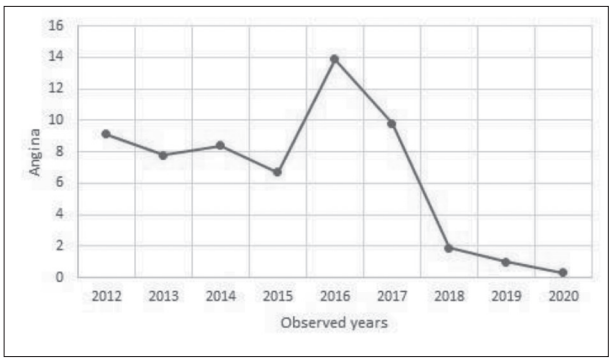


Figure 6. Average percentages of patients with angina pectoris Canadian Cardiovascular Society Class IV 2012–2020

were not correlated (r = -0.625, p = 0.072). This is close to statistical significance, which supports a negative correlation (Figure 2).

From 2012 until 2020 the percentage of patients with poor mobility or neurological deficit who were operated on was 4.2% and was similar during the observed period. It was the same with previous cardiac surgery and chronic lung disease, as risk factors.

The observed years and frequency of critical preoperative condition of patients were related (p = 0.013). The years and average percentages of critical preoperative condition were correlated (r = -0.669, p = 0.049), with a decreasing trend (Figure 3).

The percentage of patients who had diabetes mellitus on insulin therapy was 13%. The observed years and frequency of these patients were related (p = 0.040). The years and average percentages of patients who had diabetes on insulin therapy were correlated (r = 0.700, p = 0.036), with an increasing trend (Figure 4).

The observed years and frequency of patients in New York Heart Association (NYHA) Classes III or IV were related (p < 0.0005). The years and average percentages of patients in NYHA Classes III or IV were correlated (r = -0.720, p = 0.029), with a decreasing trend (Figure 5).

The observed years and the frequency of patients with angina pectoris Class IV, according to the Canadian Cardiovascular Society (CCS) were related (p < 0.0005). The total percentage of operated coronary patients with angina pectoris CCS Class IV was 6.6%. The years and average percentages of patients with angina pectoris CCS Class IV were close to statistical significance with

Table 2. Predictive power of the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II in coronary surgery

	Number of patients	EuroSCORE II-expected mortality (%)	Observed mortality %	O/E mortality ratio (95% CI)	H-L test p-value
Coronary surgery	3996	1.75	1.7	0.98 (0.95–1.03)	< 0.0005

O – observed; E – expected: CI – confidence interval; H-L – Hosmer–Lemeshow

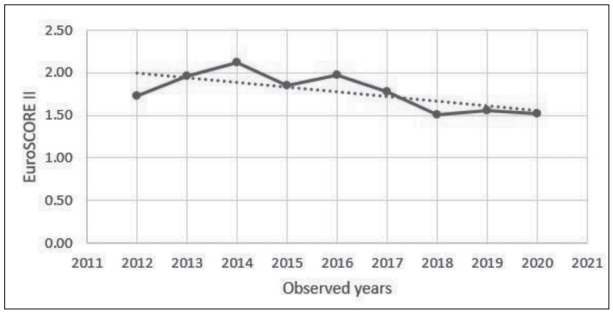


Figure 7. Trend of the mean value of the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II 2012–2020

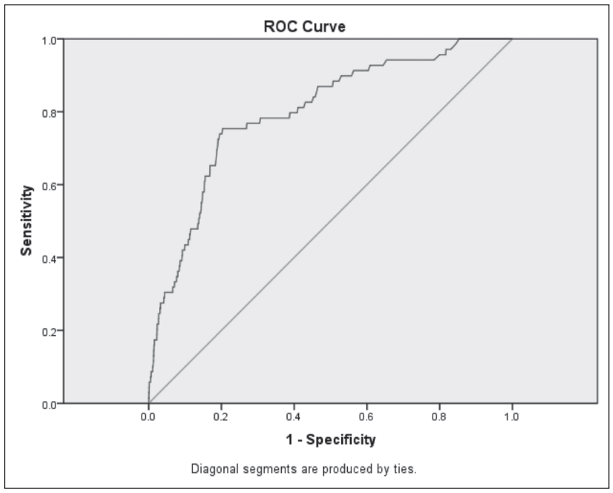


Figure 8. Discriminative power of the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II;
ROC – receiver operating characteristic

a decreasing trend (Figure 6), but were not correlated (r = -0.653, p = 0.056).

The percentage of patients with left ventricular ejection fraction < 50% did not change significantly during the observed period (p = 0.064). The highest percentage was registered in 2017 (41.4%), 2019 (38.4%), and 2020 (38.4%). The percentage of coronary patients who had a recent myocardial infarction, pulmonary hypertension, or undergone emergency surgery and were operated on changed significantly (p = 0.022; p = 0.0005; p = 0.003; respectively), but without trends during the observed years.

The mean value of the EuroSCORE II and years were in negative correlation (r = 0.695, p = 0.038). The mean value of the EuroSCORE II decreased from 1.73 in year 2012 to 1.53 in 2020 (p < 0.0005). Trend of the mean value of the EuroSCORE II from 2012 to 2020 is shown in Table 2 and Figure 7.

The mean value of the EuroSCORE II for all 3996 coronary patients was 1.75, while the observed mortality was 1.7%. The difference was not statistically significant (p = 0.132). The predictive power of the EuroSCORE II in coronary surgery is shown in Table 2.

The EuroSCORE II showed a very good discriminative power in the period of nine years (AUC curve = 0.799, p < 0.0005). The cut-off value was 2.05, sensitivity 0.754, and specificity 0.797 (Figure 8).

DISCUSSION

The aim of this retrospective single centre study was to analyze the trends of risk factors that are part of the EuroSCORE II in patients indicated for coronary surgery and to assess the predictive and discriminative power of the model.

Two risk factors, old age and diabetes mellitus on insulin therapy before surgery, in the observed group showed a significant trend of increase during the observed period.

Four risk factors – extracardiac arteriopathy, critical preoperative condition, preoperative NYHA Classes III or IV, and preoperative angina pectoris CCS Class IV – showed a significant declining trend. The frequency of other risk factors during the last decade was similar, with no trends.

Mean value of the EuroSCORE II decreased from 1.73 in year 2012 to 1.53 in 2020 and the trend was declining. The predictive power was good and the discriminative power was very good.

The epidemiology of ischemic heart disease and comorbidities may be geographically different due to population differences, but also differences in prevention, diagnosis and therapy [9, 10, 11]. One of the first analysis of more than 11,700 coronary patients who were operated on, from six European countries, showed that the mean age was the lowest in the UK and the highest in France. Chronic lung disease was most common in Germany and Spain and the rarest in Finland and Italy. Chronic renal insufficiency was registered in 12.2% of patients in the UK, in 10.6% of patients in Spain, and in 3.4% of patients in Finland. Emergency myocardial revascularization was indicated in 2% of patients in Spain, in 3.9% in the UK, in 4% in Finland, in 4.3% in France, in 4.5% in Germany, and in 4.6% in Italy [12]. Nawata et al. [13] have compared Asian patients undergoing isolated CABG surgery between 2013 and 2016 in Japan and the United States. The patients in Japan were older (69 *vs*. 65 years) with a smaller body surface area (1.65 m^2 *vs*. 1.81 m^2) and body mass index (24 kg/m^2 *vs*. 26 kg/m^2). The prevalence of chronic lung disease (82% *vs*. 86%), and diabetes mellitus (54% *vs*. 60%) were similar.

The risk factors, as well as the overall level of expected operational risk, are not constant, unchanging values. They can change over time, even in the same population. In our earlier study, in the period 2001–2008, old age, extracardiac arteriopathy, recent myocardial infarction and emergency operation, as risk factors, significantly changed

with an increasing trend, while chronic lung disease, neurological dysfunction, and unstable pectoral angina had declining trend [6].

In the last decade only old age and the frequency of patients with diabetes on insulin therapy before surgery had an increasing trend. According to our findings, the mean age increased from 62.8 years in 2012 to 65.8 years in 2020, with a significant increasing trend. The number of PCI in our institution has rapidly increased, from 1946 in 2010 to 2777 in 2019. It is completely understandable that, with good prevention, improvements in medical therapy, and widespread use of PCI, coronary patients are coming to surgery older. Kindo et al. [14] have analyzed risk factors in two groups of patients, based on the years in which the operation was performed: Group A (2000–2003; 898 patients) and Group B (2009–2012; 1249 patients). They registered a significant increase in the prevalence of patients over 80 years of age (Group A = 4.3%; Group B = 6.8%; $p = 0.016$) and a significant increase of diabetes mellitus ($p < 0.0001$) over the years.

The prevalence of patients who were on insulin therapy before surgery in our study was 13%, for the whole observed period. The frequency has increased during the last nine years, from 10.2 % in 2012 to 19.7% in 2020. This is consistent with the data from the literature and may be explained by the fact that the onset of diabetes occurs in old age and may require several years to become clinically evident [9, 15].

In a recent study by Sharma et al. [16] the mean age of patients was found to be 58.87 years. The major comorbidities were hypertension in 88%, dyslipidemia in 69%, and type 2 diabetes mellitus in 51% of the patients [16].

Ziv-Baran et al. [17] compared changes in coronary patients' characteristics and outcomes during the first 15 years of the millennium. The period was divided into two sub-periods (2000–2008 and 2009–2014). Diabetes was more common in the later period ($p < 001$), while peripheral vascular disease and left main disease were more common in the earlier period [17].

The authors from Iran compared the risk factors of patients undergoing CABG surgery in 2010 and 2016. The frequency of diabetes mellitus increased in the second period (51.8% *vs*. 43.6%, $p = 0.025$), but the average age of patients significantly decreased (from 62.49 ± 8.05 to 58.09 ± 9.2) over time [18].

In a retrospective study Wang et al. [19] concluded that the diabetic patients had higher incidence of major adverse cerebral and cardiovascular events and mortality, after coronary surgery, compared with non-diabetic patients.

According to our results, the prevalence of coronary patients, who has extracardiac arteriopathy, for the whole observed period, was 15,3% and has a declining trend. The same trend was observed in the frequency of critical preoperative condition (the prevalence 1.7%), preoperative NYHA Classes III or IV (the prevalence 16.9%) and preoperative angina pectoris CCS Class IV (the prevalence 6.6%). Siregar et al. [20] presented the prevalence of the risk factors in 16 cardiothoracic centers in 46,883 consecutive cardiac surgery interventions in the Netherlands 2007–2009. The prevalences of the risk factors were as follows: extracardiac arteriopathy 12.2% (varied 9–16.5%), critical preoperative condition 4.7% (varied 2.2–8.7%), unstable angina pectoris 6.2% (varied 2.2–13.8%). Our declining trend of frequency of preoperative angina pectoris CCS Class IV could be explained by the fact that the majority of patients with this risk factor were referred to PCIs.

In a paper by Dinh et al. [21] from Australia, based on the research of 9372 patients in the 2001–2006 period, a considerable decline in the percentage of re-operations was registered (from 4.4% to 2.65%). It was explained by the improvement of the medical therapy and the increase of the number of PCIs.

According to Saeed et al. [22], South Asian and Middle-Eastern populations living in the West had significantly higher risk of diabetes and cardiovascular disease compared with native white Europeans. Effective and timely lifestyle intervention, education, physical activity, and diet can reduce the risk of diabetes.

Kindo et al. [14] found that the prevalence of extracardiac arteriopathy has significantly decreased regarding the two observed periods (group A = 19%; group B = 22.8%; $p = 0.035$), as well as prevalence of preoperative angina pectoris CCS Class IV (group A = 25.9%; group B = 9.7%; $p < 0.0001$). Contrary to our results, they showed a significant increase in the prevalence of preoperative NYHA Classes III or IV (group A = 8.6%; group B = 15.2%; $p < 0.0001$). The prevalence of recent myocardial infarction has significantly decreased (from 11.4% to 8.3%; $p = 0.019$), as well as the prevalence of reoperations (from 4.2% to 2.3%; $p = 0.012$) and ejection fraction under 50% (from 32.4% to 27.4%; $p = 0.005$). The four risk factors that have not changed significantly over time are female patients, chronic obstructive pulmonary disease, severe kidney failure, and urgent surgery.

In our earlier report the additive EuroSCORE has increased over the years and has overestimated mortality [6]. In this study, the declining trend of the EuroSCORE II was found, but the model proved to be a good predictor of mortality. Recent studies showed that the EuroSCORE II produces a valid risk prediction and outperforms the earlier additive and logistic models. Koszta et al. [23] concluded that the EuroSCORE II predicted better, compared to the initial models (O/E ratio: 0.75; the H-L test, $p = 0.5789$). Paparella et al. [24] presented an external validation of the EuroSCORE II, based on the results of 6293 coronary patients who were operated on. The discriminative power of EuroSCORE II was excellent (AUC 0.830) and the model proved to be a good predictor of hospital mortality.

In 2019, Nežić et al. [25] confirmed a good calibration of the EuroSCORE II in coronary surgery and an excellent discriminative power (AUC = 0.84). Recent studies, from different countries, are also in accordance with our results [26, 27, 28].

The limitation of our study is a relatively small sample size for precise analysis of the results. Furthermore, as it reflects a single-center experience, the results may not represent national and international practice and outcome. Further multicenter examinations with a larger number

of patients are necessary for more precise evaluation of the results.

CONCLUSION

Over the past decade, the risk profile of patients undergoing coronary surgery has changed. Old age and diabetes mellitus on insulin therapy before surgery have shown a significant increasing trend, while extracardiac arteriopathy, critical preoperative condition, preoperative NYHA Classes III or IV, and preoperative angina pectoris CCS Class IV have shown a significant declining trend. The mean value of the EuroSCORE II has a declining trend with a good predictive and discriminative power.

Conflict of interest: None declared.

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Промене у трендовима фактора ризика у коронарној хирургији у последњој деценији – потврда једног центра

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САЖЕТАК

Увод/Циљ Фактори ризика коронарних болесника индикованих за хируршко лечење временом се мењају.
Циљ ове студије био је да се анализирају трендови фактора ризика који улазе у састав Европског система за процену срчаног оперативног ризика (*EuroSCORE* II) и да се процене његова калибрација и дискриминативна моћ.

Методе Истраживањем је обухваћено 3996 оперисаних коронарних болесника у периоду од јануара 2012. године до децембра 2020. године на нашој клиници. За процену фактора ризика и евалуацију оперативног ризика коришћен је модел *EuroSCORE* II. Краскал–Волисов *H* тест коришћен је за тестирање разлике вредности нумеричких варијабли кроз године. Калибрација модела процењена је поређењем стварног и очекиваног морталитета, а дискриминативна моћ испитана је уз помоћ површине испод *AUC* криве.

Резултати Старост болесника имала је растући тренд ($p < 0,0005$), као и дијабетес мелитус на инсулинској терапији ($p = 0,004$). Значајан тренд опадања имали су: екстракардијална артериопатија ($p = 0,003$), критично преоперативно стање ($p = 0,013$), преоперативна *NYHA* класа III или IV ($p < 0,0005$) и преоперативна ангина пекторис *CCS* класе IV ($p < 0,0005$). Просечна вредност *EuroSCORE* II опала је са 1,73 на 1,53 ($p < 0,0005$). Стварни морталитет био је 1,70%, а очекивани 1,75%. Однос стварног и очекиваног морталитета био је 0,98; 95% интервал поверења 0,95–1,03. Површина испод *AUC* криве била је 0,825.

Закључак Профил ризика болесника за коронарну кардиохируршку интервенцију променио се у последњој деценији. Просечна вредност *EuroSCORE* II има тренд опадања, уз добру предиктивну и дискриминативну моћ.

Кључне речи: кардиохирургија; фактори ризика; трендови