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RESULTS OF SYNTAX SCORE 2020 IN NONDIABETIC PATIENTS' PRIOR MYOCARDIAL INFARCTION WITH PRESERVED EJECTION FRACTION

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Abstract:The SYNTAX score is important to choose the optimal revascularization strategy: coronary artery bypass graft or percutaneous intervention in patients with prior myocardial infarction. The prognostic value of the score in predicting the rates of major adverse cardiac and cerebrovascular events (death, stroke, myocardial infarction, or revascularization) in the various SYNTAX scores substrata (≤22, 23-32, and ≥33) of patients treated by either percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) became only evident once the outcome of the SYNTAX trial was unraveled in 2009 (1 year follow up) and 2013 (5 years follow up). The SYNTAX Score (SS) 2020 and its derived variants intend to provide therapeutic advice or guidance as to appropriate treatment strategies for individual patients. The new scales created in recent years serve to improve the prediction of major cardiovascular events and allow the cardiac team to further optimize the choice of treatment techniques in individual patients.
Keywords: Myocardial infarction, Myocardial revascularization, Percutaneous intervention, SYNTAX score, Mortality, Major adverse cardiovascular events.

In recent years despite the widespread introduction of innovations in the medical industry, myocardial infarction (MI) remains a common social and medical problem among the adult population throughout the world as well as in Uzbekistan. In the US, every 60 seconds, one patient experiences MI [1,3]. More than 75% of the amount of total mortality in cardiovascular diseases occurs in low-and middle-income countries, and 85% of mortality is observed due to myocardial infarction and stroke [1,2,3]. 10 to 20% of patients died within a year after discharge. Moreover, more than 50 % of cases of death occur suddenly and in this group, in 4-5% of patients who died suddenly, repeated acute focal changes in the myocardium are detected during autopsy [1,4]. One of the most common complications after MI is the development of chronic heart failure to varying degrees and the occurrence of arrhythmias that are dangerous for life [3,6]. Revascularization of the coronary artery in patients undergoing MI improves the prognosis by reducing the occurrence of various complications [2,4,5,6]. Risk stratification is becoming an increasingly important part of the assessment of patients who are candidates for coronary revascularization. Predicting major adverse cardiovascular events (MACE) in patients before MI is essential. The SS is one such scale in patients for whom percutaneous intervention (PCI) is carried out, scores have been developed that allow to select of the optimal revascularization strategy and can predict outcomes which include the level of anatomical complexity of the coronary vessels, the conditions of comorbidity in the patient.

In recent years, the SS has been improved, that SS I gives conclusions based on the anatomical nature of the coronary vessels, while SS II has been recognized as a comorbidity condition affecting the course of the disease in the patient. On the SS III, however, the crown further optimizes the implementation of the procedure in the patient in the case when the difference in gradient pressures in the blood flow before and after stenosis, taking into account the functional state of the vessels [7,8,9,11]. Also in recent years, the logistic SS has been created, which makes it possible to predict the mortality rate due to 2 years of common diseases, taking into account the incidence of comorbidity in patients[17]. According to the type of practice carried out through the SS 2020, which was introduced into practice recently, 10-year mortality can be predicted and allows to choose the optimal method of revascularization (PCI or Coronary artery bypass grafting (CABG)) in patient [13,14]. The advantage of SS 2020 over previous SS with its prognostic prediction property has been proven in several trials [12,15,16]. The predictive model consisted of the prognostic index (includes age, creatinine clearance, left ventricular ejection fraction, smoking

status, medically treated diabetes, receipt of insulin, chronic pulmonary obstructive disease, and peripheral vascular disease), initial revascularization strategy (PCI vs. CABG), and two treatment interactions (three-vessel disease or left main coronary artery disease and anatomical SS). Considering that the occurrence of myocardial infarction due to modifiable risk factors can be changed in 90% of cases, through these scales is possible to achieve a reduction in the occurrence of various cardiovascular and cerebrovascular adverse conditions in patients.

The purpose of the study: to comparative assess the SS values in nondiabetic patients, preserved ejection fraction who had prior MI with coronary revascularization through the PCI.

Research methods: 161 patients recruited from 2019 to 2021, were assigned to undergo PCI with zotarolimus-eluting stents (Resolute Integrity, Medtronic, USA) of 39-75 years of age (mean age 60.1 ± 8.1 years)) of both sexes (82.5% of men) were taken to the study, who had different localization MI in their history, who had 40 days or more after the infarction, and with left ventricular ejection fraction (LVEF) above >40% (average LVEF=50.12±9.8%) were include study. Myocardial infarction is diagnosed according to the criteria of the fourth universal myocardial infarction determinant (ECS, 2018).

The patients suffering from diabetes mellitus, with a period of up to 40 days of MI, with a SS I ≥ 33 points were excluded from the study.

After admission to the hospital, all patients were evaluated on a comprehensive clinical and biochemical blood test, transthoracic echocardiography examination according to the LVEF Simpson method, as well as a selective coronary angiography (SC) examination. A local heart team considered all patients to be suitable for revascularization with PCI.

	General group	SYNTAX score ≤22		P
		1-2 vessel lesion	3 vessel lesion	
Age	61,2±8,4	59,5±8,32	62,72±8,97	0,178
Male	132 (81,9%)	95 (83,3%)	37 (78,7%)	0,187
BMI (kg/m2)	28,9±4,4	29,1±4,5	28,4±5,2	0,418
Cr clearance ml/min	81,0±15	80,9±16	81,2±15,3	0,711
LVEF (%)	51,4±8,1	50,7±9,6	52,3±9,1	0,312
PVD	1	0	1 (2,1)	
Hemoglobin (gr/l)	131±14,9	129±15,3	133±15,3	0,477
COPD	6 (3,7%)	5 (4,4%)	1 (4,3%)	
Leucocytes (10^9 /l)	7,22±2,3	7,2±2,4	7,27±2,6	0,788
Smoking	24 (14,9%)	17 (15%)	7 (14,9%)	
Hypertension	132 (81,9%)	92 (80,7%)	40 (85,1%)	0,711
Angina pectoris	65 (40,8%)	47 (41,2%)	18 (38,3%)	0,112
Unstable angina	96 (59,2%)	67 (58,8%)	29 (61,7%)	0,618
Revascularization range (%)	74,4%	78,4%	64,6%	
Beta blocker	182 (86,3%)	107 (93,9%)	43 (91,5%)	1,000
Statin	160(99,4 %)	114 (100 %)	46 (97,9 %)	0,788
ACEI/ARA	88 (54,7 %)	57 (50 %)	31 (66%)	0,414
MRB	86 (53,4%)	57 (50%)	29 (61,7%)	0,711
Trimetazidine	99 (61,5%)	75 (66%)	24 (51%)	0,312
Sacobutril/valsartan	38 (23,6%)	31 (27,2%)	7 (19,2%)	0,216
Nitrate	10 (6,2%)	7 (6,1%)	3 (6,4%)	
Antiarrhythmic	16 (10%)	12 (10,5%)	4 (8,5%)	

BMI- Body mass index, Cr –Creatinine, PVD- Peripheral vascular disease COPD- Chronic obstructive pulmonary disease, ACE/ARA - Angiotensin converting enzyme inhibitor/ARA- angiotensin receptor blocker, MRB- mineralocorticoid receptor blocker

The PCI was carried out through the standard wrist artery. All patients taking clopidogrel 300 mg and aspirin 75 mg before the procedure, with 5,000 ED of heparin administered intravenously at the time of intervention. Guideline-directed medical therapy was recommended for all patients. The study was conducted by ethical principles for medical research involving human subjects of the World Medical Association (Declaration of Helsinki). The ethics committee approved its protocol, and all patients signed informed consent. Patients were divided into 2 groups with 1-2 vessels lesion and 3 vessels of lesions according to the nature of coronary vessel injury based on the results of selective Coronaroangiography.

Calculating syntax score 2020

The SS I for each patient was calculated by scoring all coronary lesions with a diameter of stenosis ≥50% in vessels ≥1.5 mm as has been instructed on the SYNTAX score website https://syntaxscore2020.com/ calculated for all patients. SS II, logistic SS and SS 2020 were calculated based on SS I results and each participating patient, together with their history of heart diseases, and related risk factors (coronary anatomy (anatomical SS and the presence of unprotected LM disease) were collected with clinical characteristics (sex, age, creatinine clearance, left ventricular ejection fraction, chronic obstructive pulmonary disease and peripheral vascular disease) [10].

Statistical analysis

Primary analyses are presented as mean ± standard deviation or median and interquartile range and were compared with Mann- Whitney U test as appropriate. Comparisons for continuous variables with a normal distribution were performed by one-way analysis of variance (ANOVA) and the Chi-square test was used for all categorical variables. Statistical processing of materials Microsoft Office Excel 2013, Statistica 10. All statistical tests were *p* values of less than 0.05 and were considered statistically significant.

Results: When analyzing the prevalence, localization and severity of atherosclerotic lesions of the coronary arteries according to selective coronary angiography in the general group of patients was revealed that the most often hemodynamically significant stenosis was noted in the basins of the left anterior descending artery (LAD) – in 97.5% of cases, the right coronary artery RCA – in 50.9% of cases and the left circumflex artery (LCX) – in 29.8%.

	General Group (n=161)	**1-2 vessels lesion (n=114)**	**3 vessels lesion (n=47)**	**χ^2**	**p**
LMCA	5 (3,1%)	0 (0,0%)	5 (10,6%)	**12,52**	**0,000**
LAD	157 (97,5%)	110 (96,5%)	47 (100,0%)	1,69	0,194
OMB	23 (14,3%)	13 (11,4%)	10 (21,3%)	2,65	0,104
DB	32 (19,9%)	13 (11,4%)	19 (40,4%)	**17,60**	**0,000**
RIM	12 (7,5%)	2 (1,8%)	10 (21,3%)	**18,39**	**0,000**
LCX	48 (29,8%)	20 (17,5%)	28 (59,6%)	**28,10**	**0,000**
RCA	82 (50,9%)	40 (35,1%)	42 (89,4%)	**39,23**	**0,000**

LMCA- left main coronary artery; DB - diagonal branch; LAD - left anterior descending coronary artery; OMB - obtuse marginal branch; RCA: right coronary artery; RIM - Ramus intermedia LCX: left circumflex artery

The comparison analysis showed that both groups did not differentiate coronary lesion levels. Also, the degree of hemodynamically significant stenosis in LAD and RCA was higher than in other vessels.

	General Group (n=161)		1-2 vessels lesion (n=114)		3 vessels lesion (n=47)		Mann-Whitney U Test		
	M±SD	Me [Q1; Q3]	M±SD	Me [Q1; Q3]	M±SD	Me [Q1; Q3]	U	Z	p
LMCA	64,0±19,8	55,0 [50,0; 80,0]	-	-	64,0±19,8	55,0 [50,0; 80,0]	0	0,000	1,000
LAD	88,0±13,3	90,0 [85,0; 99,0]	87,7±14,2	90,0 [85,0; 100,0]	88,7±11,0	90,0 [85,0; 95,0]	2515,5	0,269	0,788
OMB	76,7±19,1	75,0 [60,0; 90,0]	73,5±20,2	75,0 [60,0; 90,0]	80,9±17,5	87,5 [75,0; 90,0]	51,5	-0,817	0,414
DB	76,4±17,0	82,5 [67,5; 90,0]	77,7±17,2	85,0 [80,0; 90,0]	75,5±17,3	80,0 [65,0; 90,0]	113,5	0,370	0,711
RIM	77,1±15,3	80,0 [70,0; 90,0]	70,0±7,1	70,0 [65,0; 75,0]	78,5±16,3	87,5 [75,0; 90,0]	5	-1,010	0,312
LCX	78,4±18,8	85,0 [72,5; 90,0]	72,8±22,4	80,0 [45,0; 92,5]	82,5±14,9	85,0 [77,5; 90,0]	219,5	-1,265	0,2

According to the evaluation results in the general group of patients, the average score on the SS I was 14, which indicates a low risk of complications. With appropriate separation, the group of patients with 1-2 vessels SS I was 13.7 and the 3 vessels group was 14.8 does not differentiate the risk of complications comparable.

For a more reliable risk assessment, in terms of predicting long-term results after myocardial revascularization, an analysis was also performed on the SS-II scale, which, due to the presence of clinical indicators, is considered more predictive value than the SS-I and also allows to assess the risk of death over the next 4 years, depending on the type performed coronary intervention. According to the results of the assessment, considering the 1-2 vascular group nature of the coronary lesion, the risk of 4-year mortality after the supposed CABG was more than 24% lower, and 3 vascular lesion was less than 23% compared to the same risk after the assumed PCI. The clinical estimated 2-year total mortality significantly ($p = \mathbf{0,013}$) differentiated by the nature of the number of coronary lesions and the 2-year mortality of 1-2 vascular lesions group was below 23% compared with the 3 vascular lesions group. In addition, 3 vascular lesions group in the 5-year MACE with PCI are 22% higher and 10-year mortality is 17% higher than the estimated CABG.

	General Group (n=161)		1-2 vessels lesion (n=114)		3 vessels lesion (n=47)		Mann-Whitney U Test		
	M±SD	Me [Q1; Q3]	M±SD	Me [Q1; Q3]	M± SD	Me [Q1; Q3]	U	Z	p
SYNTAX Score	14,0± 6,2	14,0 [9,0; 18,0]	13,7± 6,7	13,3 [8,0; 18,0]	14,8 ±4,7	15,0 [10,0; 18,0]	2242	- 1,625	0,104
SYNTAX 2 PCI	28,6± 11,1	27,2 [22,0; 32,4]	28,3± 12,4	26,3 [21,6; 32,1]	29,5 ±7,3	28,7 [23,7; 34,9]	2221 ,5	- 1,699	0,089
Mortality PCI 4 year %	8,0±1 1,6	5,4 [3,5; 8,3]	8,2±1 3,5	5,1 [3,4; 8,0]	7,7± 4,9	6,1 [4,1; 10,1]	2216 ,5	- 1,718	0,086
SYNTAX 2 CABG	23,9± 11,8	22,3 [18,6; 27,6]	23,5± 12,9	21,3 [18,1; 26,5]	24,9 ±8,9	23,8 [19,8; 30,0]	2221	- 1,701	0,089
Mortality CABG 4 year %	6,1±1 1,5	3,6 [2,7; 6,1]	6,2±1 3,3	3,4 [2,6; 5,1]	5,9± 5,0	4,1 [2,9; 7,5]	2208	- 1,750	0,080
LogClin SYNTAX Score	4,4±1 2,0	2,0 [1,2; 3,5]	4,8±1 4,2	1,7 [1,1; 3,0]	3,3± 2,3	2,3 [1,6; 4,5]	**1638**	**- 2,474**	**0,0**

LogClin SYNTAX Score 2-year PCI mortality, %	4,4±12,0	2,0 [1,2; 3,5]	4,8±14,2	1,7 [1,1; 3,0]	3,3±2,3	2,3 [1,6; 4,5]	**1638**	**-2,474**	**0,013**
SYNTAX Score 2020 Mortality PCI 10 year, %	19,8±12,2	17,8 [9,8; 25,8]	-	-	19,8±12,2	17,8 [9,8; 25,8]	-	-	-
SYNTAX Score 2020 Mortality CABG 10 year, %	16,4±10,7	14,2 [8,1; 20,8]	-	-	16,4±10,7	14,2 [8,1; 20,8]	-	-	-
SYNTAX Score 2020 PCI 5-year MACE, %	14,9±7,3	13,5 [9,2; 19,8]	-	-	14,9±7,3	13,5 [9,2; 19,8]	-	-	-
SYNTAX Score 2020 CABG 5-year MACE, %	11,6±5,7	10,7 [7,0; 14,4]	-	-	11,6±5,7	10,7 [7,0; 14,4]	-	-	-
ARD 5- year MACE					3,3±2,3	3,5[2,1; 5,7]			
PCI – Percutaneous intervention, CABG – Coronary artery bypass grafting, MACE - major adverse cardiac event, ARD – Absolute risk difference									

Discussion The main goal of our study is to comparative assess SS 2020 in nondiabetic patients with prior MI and preserved lso evaluate incompatibly or not current revascularization guidelines results are manifested in modern currently scales such as SS 2020, although it is concordant with the procedure of PCI on the results of SS I and revascularization guidelines approved in 2018 by European Society of Cardiology, in patients without diabetes mellitus and preserved LVEF. The SS I is significant until today when choosing the optimal revascularization. It has been proven through several studies that SS II can predict a higher prognostic value to perform optimal revascularization and can predict morality better than SS I [8,9, 11]. In patients, no differences were found in the degree of anatomical coronary artery lesions in groups with 1-2 and 3 vessel lesions. For this reason, although the difference in results in anatomical SS I is less pronounced, however, it can be found in the study that the difference between the results of estimating SS II based on the individual clinical condition of the patient is significant. Especially when predicting logistic SS 2 years of total mortality, it can be noted that this difference is significant and reliable. Recent investigations showed that SS II-2020 for 5-year mortality well predicted the prognosis after PCI and CABG, and predicted Absolute risk difference of <4.5% and ≥4.5% can offer sensible treatment recommendations of either equipoise of PCI and CABG or CABG better [18]. In our study, the absolute risk difference is equal to 3.3%, and therefore SS II and SS 2020 results show 4 and 10 years of total mortality, while 5 years of MACE results show an advantage in CABG, but the Heart team allows the implementation PCI in patients with 3 vessels lesion group.

Limitation: a limitation of this study is the fact that randomized research has not been carried out due to the research design, also belonging to a single institute. We accept that the current population is based on strict inclusion criteria such as non-diabetic patients with preserved ejection fraction, not accepted prior revascularized patients. Also, these results are relevant only to the group recommended by the PCI by the heart team on revascularization guidelines (ESC 2018), the CABG recommended group does not include. Moreover, having a control group of patients with underground coronary artery bypass grafts would have enabled us to compare the previous value of the SYNTAX score for selecting the proper revascularization strategy. Therefore, the next step in our research would be to study to assess the predictive value of the clinical SYNTAX score on the MACE of patients undergoing PCI with clinical outcomes.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

Conclusion: In patients with nondiabetic and preserved ejection fraction SS I can play a major role to select a revascularization strategy, SS II may predict long-term outcomes following PCI in patients with 1-2 and 3-vessel disease. SS 2020 with 3 vessel lesion patients can increase the predictive value of the SYNTAX score.

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