Klinik SYNTAX Skoru İzole Koroner Arter Bypass Cerrahisi Sonrası Serebrovasküler Olayı Öngördürmektedir

Clinical SYNTAX Score Predicts Cerebrovascular Event After Isolated Coronary Artery Bypass Surgery

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ÖZ

GİRİŞ ve AMAÇ: *Serebrovasküler olay (SVO), koroner arter bypass cerrahisi (KABC) sonrası önemli bir mortalite ve morbidite nedenidir. İzole KABC sonrası SYNTAX skoru (SS) ile klinik SYNTAX skoru (KSS) ve SVO arasındaki korelasyonu araştıran herhangi bir veri literatürde mevcut değildir. Bu çalışmanın amacı SS ve KSS ile SVO riskinin öngördürücülüğünü araştırmaktır.*

YÖNTEM ve GEREÇLER: *Hastanemizde Ekim 2011 – Aralık 2013 tarihleri arasında izole KABC uygulanan 1850 hasta çalışmaya dahil edildi. Dışlama kriterlerine istinaden çalışmadan çıkarılan hastalardan sonra çalışmamıza 249 hasta dahil edildi. SVO, KABC sonrasında 30 gün içerisinde gelişen geçici iskemik olay ve inmeleri içermekteydi ve çalışma grubu operasyon sonrası SVO geçiren (PoSVO+) ve geçirmeyen (PoSVO-) şeklinde iki gruba ayrıldı. KSS hesaplaması amacıyla her hastanın KABC öncesi son anjiyografisi kullanılarak yapılan SS hesabına ek olarak diğer klinik parametreler (yaş, sol ventrikül ejeksiyon fraksiyonu, glomerüler filtrasyon hızı) kaydedildi.*

BULGULAR: *Uyku ve uyanıklık periyodları incelendiğinde; TASİ grubunda bulunan hastaların, POSİ ve LAİ gruplarındaki hastalara göre uyku dönemde başvuru oranlarının daha sık olduğu tespit edildi ve bu durum istatistiksel olarak anlamlı bulundu (p=0.045). Diğer grupların arasında herhangi bir istatistiksel anlamlı farklılık bulunmadı (p>0.05). Mevsimsel değişkenler incelendiğinde ise yine gruplar arasında istatistiksel olarak anlamlı bir fark tespit edilmedi (p>0.05). Ancak sonbahar ve kış döneminde yüzde olarak başvurularda bir artış olduğu saptandı.*

TARTIŞMA ve SONUÇ: *Bu çalışma, KSS'nin KABC yapılması planlanan hastalarda operasyon sonrasında gelişebilecek SVO öngörmede yararlı ve pratik bir skor olabileceğini göstermiştir. Bu nedenle bu hastalar için ameliyat öncesi buna uygun önlemler uygulanabilir.*

Anahtar Kelimeler: *SYNTAX, Klinik SYNTAX skoru, Koroner arter bypass cerrahisi, İnme*

ABSTRACT

INTRODUCTION: *Cerebrovascular event (CVE) is major cause of mortality and morbidity after coronary artery bypass surgery (CABG). There is no available data in literature investigating correlation between SYNTAX and clinical SYNTAX score (CSS) and CVE after isolated CABG. The aim of the study was to investigate predicting risk of CVE with SYNTAX and CSS.*

METHODS: *1850 patients underwent isolated CABG between October 2011 to December 2013 were included in the study in our hospital. 249 patients included in our study after eliminating patients having exclusion criteria. CVE included transient ischemic events and strokes in 30 days after CABG and two groups were determined as post-operative CVE (+) (PoCVE+) and post-operative CVE(-) (PoCVE-). SYNTAX score and additional clinical parameters (age, left ventricular ejection fraction (LVEF), glomerular filtration rate (GFR)) to calculate CSS were recorded for patients using last coronary angiography before isolated CABG.*

RESULTS: *In present study, age (p=0.002), total cholesterol (p=0.048), glucose (p=0.022), uric acid (p=0.032), creatinine (p=0.022), neutrophil count (p=0.06), circumflex-saphenous grafting (CX-SVG) (p=0.01), CSS (p=0.003) were found statistically higher in PoCVE(+) group. Additionally, LVEF (p=0.019) and GFR (p=0.013) were detected lower in PoCVE(+) group. logistic regression of significant parameters showed that, average age (p=0.017), increased glucose levels (p=0.08), existence of CX-SVG (p=0.011) and CSS (p=0,026) were found contributed factors. CSS >8 predicts CVE with sensitivity of 78.6, specificity of 68.9*

DISCUSSION AND CONCLUSION: *This study showed CSS might be a useful and practical score to predict CVE in patients who planned to undergo CABG therefore precautions might be taken before surgery for these patients.*

Keywords: *SYNTAX, Clinical SYNTAX Score, Coronary artery bypass surgery, Stroke*

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INTRODUCTION

Coronary artery bypass grafting (CABG) is the method of choice in patients with left main coronary artery (LMCA) or 3-vessel disease (1). One of the most important complications of CABG surgery is the cerebrovascular events (CVE). CVE, especially in post-operative state, is considered as a serious risk for patients undergoing CABG. The etiology of CVE after CABG is still controversial and multifactorial. Trials have showed that the increased severity of coronary artery disease (CAD) is related to postoperative CVE (2).

SYNTAX score (SS) is a guide to decide the method of revascularization in patients with CAD and uses coronary anatomy for calculation (3,4). In the past decade, SS has become one the major factor to decide the revascularization method and has been advocated in guidelines (5). Because the SS is closely related to the severity of CAD, there are trials those show the relationship between SS and severity of systemic atherosclerosis (6). Several of the studies disputed that the outcomes could not be based on angiographic variable only but the clinical factors of the patients would impact the outcomes. For this purpose, clinical factors additionally calculated with the SS and another score has been calculated as clinical SYNTAX score (CSS). The trials showed that the prediction of adverse clinical outcome of the surgery might be improved with CSS (7).

The objective of this trial was to predict risk of CVE after CABG surgery by using SS and CSS.

METHODS

The investigation conforms with the principles outlined in the Declaration of Helsinki. The study was approved by the local ethics committee. All participants gave written informed consent before inclusion.

Study population

This study was designed as a case-control, single center study. 1850 consecutive patients who were admitted to large volume tertiary training and research hospital with a diagnosis of LMCA or multi-vessel CAD and underwent CABG surgery, were enrolled between October 2011 and December 2013. These patients were followed up in the first 30 days after the surgery and post-operative data was recorded. The patients who had significant carotid artery occlusive, previously known or diagnosed atrial fibrillation were not included in our study group in the beginning. The exclusion criteria were history of CABG surgery in emergent conditions (182 patients), severe concomitant valve diseases (781 patients), congenital heart diseases (47 patients), CABG without cardiopulmonary bypass (189 patients), severe liver failure (118 patients), malignancy (78 patients). 206 patients whose preoperative SS and CSS could not be calculated because of insufficient data were excluded from the study. After the exclusion criteria had been applied, a total 249 patients were enrolled in the present study.

Data collection

The demographic data comorbidities and cardiovascular risk factors and physical examinations and clinical data on admission were obtained a systemic review of patient files and hospital records. Preoperative data included age, gender, diabetes, hypertension, hyperlipidemia, left ventricular ejection fraction (LVEF), smoking, previous myocardial infarction and previous percutaneous coronary intervention. All hematological and biochemical parameters were analyzed before the CABG surgery. Glomerular filtration rate (GFR) was calculated according to the creatinine levels measured before CABG surgery with Cockroft-Gault formula. Hypertension was defined as systolic and/or diastolic blood pressure ≥140/90 mmHg, previously diagnosed hypertension, or use of any antihypertensive medications. Diabetes mellitus was defined as fasting plasma glucose levels of more than 126 mg/dL in at least two consecutive measurements, previously diagnosed diabetes, or use of anti-diabetic medications such as oral anti-diabetic agents or insulin. Smoking status was defined as the history of tobacco use at admission or in the last six months prior to the visit.

CVE included postoperative stroke and transient ischemic attack (TIA). TIA was defined under guidance of Stroke Council of the American Heart Association / American Stroke Association as a transient episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischemia without acute infarction (8). Postoperative stroke defined as an episode of neurological dysfunction caused focal cerebral, spinal, or retinal infarction (9). CVE data was collected in the first 30 days after CABG surgery. CVE was confirmed by an independent neurologist with appropriate brain imaging.

Echocardiographic Evaluation

Baseline echocardiographic examinations were performed with standard commercial ultrasound system (Vivid 3, General Electric Vingmed, Horten, Norway) using 2.5-3.5 MHz multiphase-array probe before the surgery. Echocardiographic examination was performed by single investigator. LVEF was calculated by the modified Simpson's method from apical 4- and 2- chamber views. Any concomitant valvular diseases were noted before the surgery to evaluate if the patients were in exclusion criteria.

SS and CSS Calculation

Two cardiologists calculated the scores retrospectively. The SS was calculated for each patient with the guidance of described method in SYNTAX trial retrospectively from the recorded data (10). The described method is available in the website (www.syntaxscore.com) and the variables of the patients were entered to the calculator and the score was calculated via the website. The vessels with a diameter of ≥ 1.5 mm and the lesions with ≥ 50 % stenosis were scored. The last preoperative coronary angiogram was used for score calculation. The CSS was calculated according to the formula (CSS = SYNTAX score × modified ACEF score) in which is described elsewhere (11). Clinical parameters (age, LVEF, creatinine clearance) added to the anatomical parameters for calculating CSS. As for creatinine clearance, GFR was used in the formula.

Surgical Technique and Post-operative Follow-up

The CABG surgery was performed using standard surgical techniques with median sternotomy. Complete revascularization was performed when possible, using arterial conduits or a reverse saphenous venous graft (SVG). After surgery, all patients were transferred and followed up in intensive care unit (ICU). Operative detailed data about grafts were reviewed and recorded. The amount of the days in ICU and in-hospital stay were recorded after surgery.

The patients were divided to two groups who had CVE after the surgery during 30-day follow-up grouped as post-operative CVE (+) group (PoCVE +) and who had not as CVE (-) group. (PoCVE -)

Statistical Analyses

In the present study, statistical analyzes was performed by using NCSS (Number Cruncher Statistical System) 2007 statistical software (Utah, USA) pocket program. All data were analyzed descriptive methods (as mean ± SD) and comparison of parametric values between 2 groups was performed by means of an independent samples t test. For comparison of qualitative values, Chi 2 test was used. Logistic regression analysis was performed to investigate predicting parameters for PoCVE. Receiver Operating Characteristic (ROC) analysis were used to detect the area under curve (AUC) and the cut-off values of the SS and CSS in the prediction of PoCVE. All statistical tests were 2-sided and level of significance was set at $p < 0.05$.

RESULTS

The study included 249 patients who grouped as PoCVE - and PoCVE + and clinical, biochemical and hematologic characteristics of the patients are shown in Table 1. 14 patients (%5.6) had CVE during 30 days of follow-up. PoCVE + group had statistically higher age (P=0.002), lower LVEF (P=0.019), higher total cholesterol level (P=0.048), higher glucose level (P=0.022), higher creatinine (P=0.022), lower GFR (P=0.013) and higher neutrophil levels (P=0.006).

The surgical and post-operative parameters of the patients are shown in Table 2. The type of grafts used during surgery in both group were similar except there were significantly more circumflex (CX) – saphenous venous graft usage in PoCVE + group. (P=0.01) There were no significant difference in-hospital and ICU stays in between groups. Post-operatively, there were 64 patients (27.23%) who had post-operative AF in PoCVE- group and 6 patients (42.85%) who had post-operative AF in PoCVE- group. However, there was no significant difference between groups (p=0.075). Even though PoCVE + group had higher SS, there were not significant difference in SS between both groups. (PoCVE – group: 28.63 ± 5.92 vs. PoCVE + group: 31.54 ± 6.11, P=0.076) CSS was significantly higher in PoCVE + group. (PoCVE – group: 6.91 ± 4.22 vs. PoCVE + group: 10.36 ± 3.99, P=0.003)

Multivariate logistic regression analysis was performed to investigate predicting risk of PoCVE and for this purpose, age, LVEF, total cholesterol, glucose, GFR, Neutrophil to Lymphocyte Ratio (NLR), CX - Saphenous graft usage, SS and CSS

included in the analyses as independent parameters. Analyses showed that age (P=0.017), glucose levels (P=0.008), CX-Saphenous graft usage (P=0.011) and CSS (P=0.026) were determined as independent predictors for PoCVE after CABG. (Table 3)

ROC analysis was performed to detect the optimal cut-off value of SS and CSS in predicting PoCVE. AUC for SS was found as 0,648 (0,585-0,707) and for CSS was found as 0,725 (0,665-0,780). (Figure 1, Table 4) SS predicted PoCVE with a sensitivity of 85.71% and a specificity of 38.72% with Positive predictive value (PPV) of 17.7% and negative predictive value (NPV) of 97.8% and likelihood ratio (LR) + value was 1.40. CSS predicted PoCVE with a sensitivity of 78.57% and a specificity of 68.94% with PPV of 23.1% and NPV of 98.2% and LR + value was 2.53 (Table 5)

Table 1. Clinical characteristics, biochemical and hematologic parameters of the patients.

	PoCVE (-) n:235	PoCVE (+) n:14	P
Age, years	60.82 ± 6.81	66.71 ± 7.78	**0.002**
Female, n (%)	56 (23.83%)	2 (14.29%)	0.445
Male, n (%)	179 (76.17%)	12 (85.71%)	0.412
Diabetes mellitus, n (%)	99 (42.13%)	8 (57.14%)	0.270
Hypertension, n (%)	125 (53.19%)	10 (71.43%)	0.183
Smoking, n	96 (40.85%)	8 (57.14%)	0.230
LVEF, %	52.66 ± 9.38	46.57 ± 9.72	**0.019**
Total cholesterol, mg/dl	199.91 ± 52.24	227.21 ± 48.41	**0.048**
HDL, mg/dl	38.91 ± 11.83	40.21 ± 8.4	0.684
LDL, mg/dl	130.06 ± 42.62	145 ± 42.52	0.204
Triglycerides, mg/dl	198.24 ± 142.27	188.71 ± 79.81	0.804
Glucose, mg/dl	136.87 ± 56.94	174.02 ± 84.08	**0.022**
HbA1c, (%)	7.12 ± 3.67	7.82 ± 2.56	0.482
Creatinine, mg/dl	1.31 (0.47 – 4.6)	2.69 (0.52 – 7.89)	**0.022**
GFR, ml/min	92.27 ± 29.63	72.07 ± 25.82	**0.013**
Leucocyte, K/µl	8.92 ± 2.69	7.84 ± 2.14	0.144
Hemoglobine, g/dl	15.02 ± 2.17	14.22 ± 1.19	0.898
Platelets, $10^3/mm^3$	247.97 ± 69.09	244.57 ± 60.75	0.858
Neutrophil, K/µl	5.32 ± 1.37	6.36 ± 1.25	**0.006**
Lymphocyte, %	2.14 ± 0.63	2.03 ± 0.31	0.525
NLR, %	2.78 ± 1.37	3.15 ± 0.60	0.058
Previous MI, n (%)	105 (44.68%)	5 (35.71%)	0.512
Previous PCI, n(%)	87 (37.02%)	4 (28.57%)	0.524

EF: Ejection Fraction, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, GFR: Glomerular Filtration Rate, NLR: Neutrophil / Lymphocyte Ratio

Table 2. Surgical and post-operative characteristics of the patients.

	PoCVE (-) n=235	PoCVE (+) n=14	P
LAD - Lima, n	230 (97.87%)	13 (92.86%)	0.235
LAD - Saphenous, n	15 (6.38%)	1 (7.14%)	0.910
Diagonal - Saphenous, n	115 (48.94%)	6 (42.86%)	0.658
IM - Saphenous, n	23 (9.79%)	3 (21.43%)	0.166
CX - Saphenous, n	48 (20.43%)	7 (50.00%)	**0.01**
CXOM - Saphenous, n	146 (62.13%)	8 (57.14%)	0.709
RCA - Saphenous, n	121 (51.49%)	8 (57.14)	0.681
RCA – PDA - saphenous, n	53 (22.55%)	3 (21.43%)	0.922
RCA-PL - saphenous, n	7 (2.98%)	1 (7.14%)	0.391
Graft per patient, n	3.22 ± 0.81	3.57 ± 0.51	0.108
Post-operative AF	64 (27.23%)	6 (42.85%)	0.075
SYNTAX Score	28.63 ± 5.92	31.54 ± 6.11	0.076
Clinical SYNTAX Score	6.91 ± 4.22	10.36 ± 3.99	**0.003**
Follow-up in ICU (days)	1.12 ± 0.65	1.5 ± 1.16	0.245
Follow-up in hospital (days)	8.69 ± 4.21	12.5 ± 7.59	0.085

LAD: Left Anterior Descending Artery, IM: Intermediar Artery, CX: Circumflex Artery, CXOM: Circumflex obtus marginalis artery, RCA: Right Coronary Artery, AF: Atrial fibrillation, ICU: Intensive Care Unit

Table 3. Multivariate Logistic Regression Analysis for the Investigation of Independent parameters for prediction of PoCVE

	B	S.E.	P	OR	OR % 95 GA	
					Low	High
Age	0.12	0.05	**0.017**	1.13	1.02	1.25
LVEF	-0.00	0.05	0.960	1.00	0.90	1.10
Total cholesterol	0.01	0.01	0.065	1.01	1.00	1.02
Glucose	0.01	0.00	**0.008**	1.01	1.00	1.02
GFR	-0.00	0.01	0.966	1.00	0.97	1.03
NLR	-0.14	0.35	0.682	0.87	0.44	1.71
CX Saphenous	1.60	0.63	**0.011**	1.14	1.08	1.20
Syntax score	0.04	0.05	0.443	1.04	0.94	1.16
Clinical Syntax Score	0.17	0.08	**0.026**	1.19	1.02	1.39

Table 4. The receiver operating characteristic (ROC) curve findings and with cut-off value for CSS

Clinical Syntax Score	**AUC**		**SE**		**95% CI**	
	0,725		0,079		0,665 - 0,780	
Clinical Syntax Score	**Criterion**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**+LR**
	>8	78,57	68,94	23,1	98,2	2,53

Table 5. Cut-off Values for SS and CSS

	Criterion	Sensitivity	Specificity	PPV	NPV	+LR
Syntax Score	**>25,5**	85,71	38,72	17,7	97,8	1,40
Clinical Syntax Score	**>8**	78,57	68,94	23,1	98,2	2,53

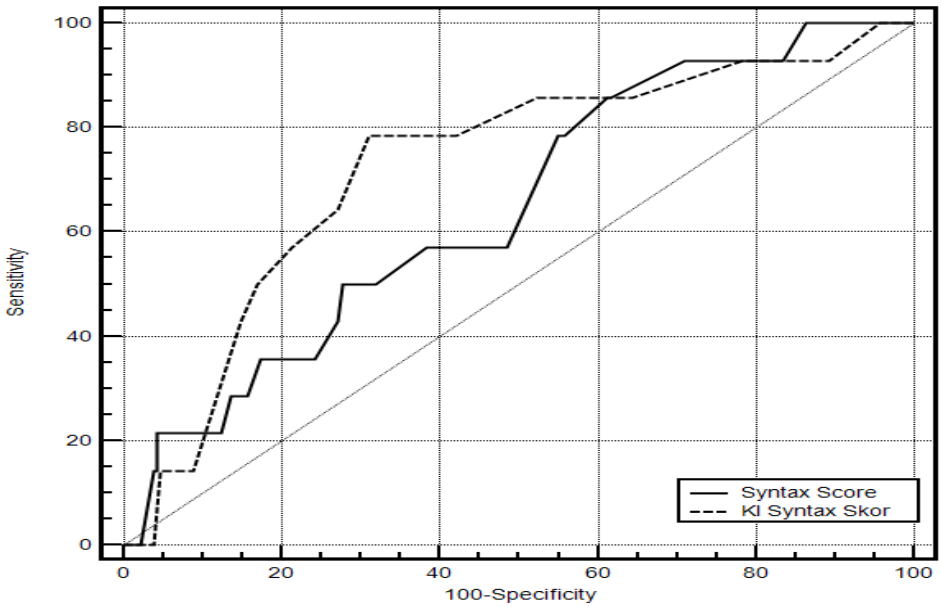

Fıgure 1. The receiver operating characteristic (ROC) curves in predicting differential diagnostic effect of SYNTAX score and CSS for PoS.

DISCUSSION

Just like cardiovascular events, stroke events show diurnal variation over 24 hours. It has been reported in many studies that ischemic stroke patients have an increased peak once in the morning and a second in the evening (1). In another study, the incidence of stroke was found to be highest between the times of 06:00-12:00 (10). Similarly, in our study, when all of the stroke patients were examined, it was seen that 88.5% of the admissions were between 07:00-23:59 hours.

The stroke types are divided into three main groups as ischemic, hemorrhagic, and subarachnoid hemorrhage (11). However, it is known that this classification has very serious diurnal differences (12). Therefore, the analysis of the subgroups in the OCSP classification of ischemic stroke showed more homogeneous results (8). Ripamonti et al. compared the asleep and awake periods with Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification in their study and determined a higher frequency of all subtypes in the asleep period (13). According to our OCSP classification subgroup analysis; stroke development was more frequent in the TACI group during the asleep period than in the POCI and LACI groups.

Decreased cerebral perfusion, which plays a role in the development of vasovagal syncope, increases significantly in the early morning hours and this circadian pattern also plays a significant role in the development of ischemic stroke (5, 14, 15). When our subgroups were examined; the fact that most of the cases occurred during the awake period, including this period of early morning times, can be considered as a result of this mechanism.

Stroke development is affected by external factors such as physical activity, immobilization, feeding habits, and stress (16-18). In addition to these external factors, changes in the week cycle or climate are reported as factors. It is reported that the risk of stroke development increases both in the first and the last days of the week and in the months when the temperature decreases (19, 20). In our study, monthly and seasonal analyzes were performed and it was found that the admissions were significantly higher in the autumn and the winter months when the weather was cold.

However, HT, DM, HL, smoking, a history of stroke, antiplatelet, or anticoagulant drug use were identified as independent risk factors for stroke (21). In our study, a high rate of co-morbidities was found in the stroke subtypes, including some of these risk factors simultaneously. This has been shown once again that these independent risk factors increase stroke frequency and tendency.

There are some limitations to our study. The most important limitation is that our study was performed in a single-center and it was designed retrospectively. Another limitation is the fact that

the onset of symptoms and the obtained data were dependent on the anamnesis and the file records. Similar prospective studies are needed such as this one in this regard.

CONCLUSION

To our knowledge, this is one of the few studies that analyzed stroke subgroups according to the OCSP classification of diurnal variation. It was determined that stroke development was more frequent during the asleep period in the patients in the TACI group, which usually had more serious involvement and more serious morbidity, than the patients in the POCI and LACI groups.

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