

REVIEW ARTICLE

Evolution of the SYNTAX score (I, II, and II 2020): Development, application, and limitations in everyday clinical practice

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Summary

Surgical myocardial revascularization is the gold standard for myocardial revascularization in chronic coronary syndrome (CCS). The first randomized trials comparing bare metal stent (BMS) implantation and aorto-coronary bypass graft surgery (CABG) resulted in similar mortality and myocardial infarction rate, and a lower rate of repeat revascularization after CABG compared to BMS implantation, directing the development of drug-eluting stents (DES) with the lower rate of clinical restenosis. Over the years, there was a need for objective assessment and calculation of the risks and benefits of both surgical and percutaneous myocardial revascularization, and for determining whether one of these methods is preferable or equipoise for a specific patient. The SYNTAX score was used to quantify the complexity of coronary stenoses in a patient with CCS. However, two major flaws of the SYNTAX score I, (1) the absence of the assessment of functional significance of coronary stenosis, and (2) the absence of clinical variables that may influence perioperative mortality rate, were partially overcome with the development of SYNTAX score II. SYNTAX score II included clinical variables that showed the greatest association with mortality (age, creatinine clearance, left ventricular ejection fraction, unprotected left main coronary artery disease, female gender, peripheral vascular disease, and chronic obstructive pulmonary disease). SYNTAX score II 2020 represents SYNTAX score II with the addition of a 10-year clinical follow-up on mortality. The SYNTAX score II and II 2020 may change recommendations for myocardial revascularization based solely on SYNTAX score I. This review focuses on the development of these scores, their accuracy, predictive value, and limitations in practical applications in an individual patient with CCS, with a primary objective to disclose the development of SYNTAX scores I, II, and II 2020, their prognostic value, and limitations in routine clinical application in a process of making a recommendation for optimal myocardial revascularization in a patient with CCS.

Keywords: SYNTAX scores, myocardial revascularization, prognosis



INTRODUCTION

Surgical myocardial revascularization (CABG, coronary artery bypass graft) began in 1950 with the first implantation of the distal part of the left internal mammary artery (LIMA) in the superficial level of myocardium (1). The first real anastomosis of the distal part of LIMA on the coronary artery was performed in 1964 in the Soviet Union by Kolesov (on the obtuse marginal branch of left circumflex artery) and during the same year on the left anterior descending artery (LAD) in the United States of America by Spencer (2). However, the golden era of surgical myocardial revascularization began in 1967 when Rene Geronimo Favalaro at the Cleveland Clinic implanted the first saphenous vein graft (SVG) on the right coronary artery (RCA), a practice that lasted over two decades, during which LIMA was used only if SVG was unavailable or its implantation failed. The golden era of arterial myocardial revascularization began at the beginning of the '90s of the last century, reaching its peak with total arterial myocardial revascularization (2, 3). Thus, since the first SVG implantations, surgical myocardial revascularization has become the gold standard for myocardial revascularization in chronic coronary syndrome (CCS). The new, less invasive method of myocardial revascularization, percutaneous transluminal coronary angioplasty (PTCA), the first performed on September 16, 1977, challenged CABG in patients with multivessel coronary artery disease (CAD) (4-9). Soon afterward, percutaneous coronary interventions (PCI) with bare-metal stent (BMS) implantation were widely adopted, leading to a reduction in the rate of urgent repeat interventions. Based on these initially encouraging results, a series of randomized trials published since 2001 have compared the clinical outcomes of BMS implantation and CABG in patients with multivessel disease (10-21). The results of these studies, similar mortality and myocardial infarction (MI) rate, and a lower rate of repeat revascularization after CABG compared to BMS implantation, directed the development of drug-eluting stents (DES) towards the lower rate of clinical restenoses. The first-generation DES, consisting of a metal frame, carrier, and drug, either sirolimus or paclitaxel, liberated the field of interventional cardiology from diffuse in-stent restenosis (22), even in patients with multivessel disease (23). However, the risk of periprocedural stent thrombosis, particularly in long stented segments using sirolimus-eluting stents, was a serious warning for its broader application (24). Taxus stent, which eluted paclitaxel drug, was compared to CABG in the SYNTAX trial, a study of non-inferiority, testing the hypothesis that PCI, as a less invasive, cheaper, and potentially safer treatment, could be non-inferior compared to CABG in terms of efficacy, and therefore equally acceptable as CABG or even preferred method of myocardial revascularization in certain groups of patients (19).

The SYNTAX trial used the SYNTAX score (SYNTAX score I), specifically developed to address heterogeneity in coronary artery disease morphology. The subsequent SYNTAX score II was used in the SYNTAX II trial to predict all-cause mortality at 4 years, accounting not only for the morphological complexity of coronary disease but also for various clinical variables associated with a higher risk of death. The last, SYNTAX score II 2020, represents an improvement on the SYNTAX score II by predicting all-cause mortality at 10 years and the major adverse cardiac and cerebral events (MACCE) rate at 5 years, based on the SYNTAX score I and clinical variables associated with all-cause mortality in the SYNTAXES study.

This review focuses on the development of SYNTAX scores, their accuracy, and their limitations in practical applications for individual patients with CCS.

METHODS

For providing adequate references for this review, we searched for the most relevant articles by using keywords as follows: "SYNTAX score", "myocardial revascularization", "chronic coronary disease" in PubMed database for the period between August 1, 2005, the date of publication of the SYNTAX score (15) and September 24, 2024, the date of publication of the latest guidelines of European society of cardiology on myocardial revascularization in CCS (25). This analysis included studies published only in English and conducted on humans. Several studies published outside this timeframe were also included due to their scientific significance for the development of the SYNTAX score. Priority was given to RCTs, original studies, and meta-analyses relevant to the development and validation of the SYNTAX score. References for the most-cited articles on this topic were also reviewed to identify additional relevant publications.

SYNTAX SCORE I

There is a clinical need for objective assessment and calculation of the risks and benefits of both surgical and percutaneous myocardial revascularization, and for determining the advantage or equipoise of one of these methods for an individual patient. Namely, in all randomized studies to date, the evaluated patients had coronary stenoses and varied clinical characteristics. Some patients may have anatomically complex and technically challenging coronary disease (26). It was obvious that PCI had a higher periprocedural risk in patients with left main coronary artery (LMCA) stenosis (27) and the RCA occlusion than in those with three focal stenoses on three coronary arteries. Besides that, some patients had diseased distal vasculature and poor run-off, while

some had severe comorbidities, having an increased risk of perioperative mortality. The first step in the objective assessment of an individual patient was the quantitative assessment of stenosis complexity using the SYNTAX score, as in the SYNTAX trial (28).

SYNTAX score is an angiographic tool for grading the complexity of coronary stenosis and predicting the risk of complications and adverse events (27). The SYNTAX score assesses the severity of coronary disease and its prognostic value based on the dominance of the coronary artery, the number of significant lesions (in total 12), their location, and complexity²⁷. SYNTAX score derived from the other classifications evaluating severity of CAD: 1. AHA classification of coronary artery segments, in which each segment is precisely defined, 2. Leaman score, based on the degree of coronary stenosis (diameter stenosis [DS]=50-99% and DS=100%, in first case multiplying factor [MF]=2.5, in the other MF=5), and the location of stenosis (MF=3.5 for proximal LAD, MF=1 for distal LAD) depending on the coronary artery dominance (MF=0 for RCA if Cx is dominant, and MF=1 if RCA is dominant artery) (29). Thus, the Leaman score assigned clinical importance to each stenosis based on the involved segment. The core of the Leaman score is a definition of significant coronary stenosis: stenosis with DS \geq 50% in the artery with a reference vessel diameter \geq 1.5 mm. For example, if the stenosis has DS=50% in the proximal segment of LAD, then the Leaman score is $2.5 \times 3.5 = 8.75$. The third classification used in the SYNTAX score was the AHA classification of stenosis complexity, which considered lesion length, eccentricity, calcium presence, and side branches. SYNTAX score increases by 1 point if one of these lesion characteristics is present. Fourth, the SYNTAX score is increased by 1 point in the presence of a bifurcation or trifurcation lesion. Also, total occlusions were precisely described, including lesion characteristics unfavorable for recanalization: length, blunted or absent stump, side branch presence, or ipsilateral collaterals via vasa vasorum ("bridging" collaterals). SYNTAX score is generated by responding to the following questions: the first three questions on the coronary artery dominance (drawback: there is no possibility of co-dominance), the number of lesions \geq 50% (not necessarily a hemodynamically significant lesion) and their locations, the remaining 11 questions refer to the description of unfavorable lesion characteristics, and the last 12th question is about run-off (28).

In the SYNTAX study evaluating patients with CCS and complex three-vessel disease with or without LMCA disease undergoing either PCI or CABG with intention to achieve complete revascularization (56.7% in the PCI and 63.2% in the CABG group), SYNTAX score differentiated patients according to the rate of major adverse cardiac events (MACE) dividing them into terciles: low (\leq 22), intermediate (23-32) and high SYNTAX score (\geq 33)^{27,28}. The SYNTAX score underwent internal validation (concordance index of 0.567) and external

validation (concordance index of 0.612²⁷). It was shown that patients with three-vessel disease and low or intermediate SYNTAX score (\leq 22 or 23-32) had similar 5-year all-cause mortality rates regardless of the revascularization method. In contrast, patients with a high SYNTAX score (\geq 33) had a higher mortality rate at 5 years after PCI than after CABG (17.8 vs 8.8%, $p=0.02$) (30,31). Patients with LMCA disease having low or intermediate SYNTAX score (0-32) had similar prognosis at 5 years after PCI as compared with CABG (major adverse cardiac and cerebral events, MACCE: 32.1 vs 31.3%, $p=0.7$) while those with high SYNTAX score (\geq 33) had better outcome after CABG (MACCE: 29.7 vs 46.5%, $p=0.003$, driven by lower rates of cardiac death and repeat revascularization, at the expense of a higher stroke rate) (32). The results of the SYNTAX trial were translated into guidelines on myocardial revascularization (33,34).

The limitations of the SYNTAX score include its definition of angiographic stenosis significance (i.e., DS = 50%), which assigns equal weight to critical and borderline stenoses without assessing their functional significance. Diffuse disease was not included in the SYNTAX score, and the prognostic significance of each stenosis was rather approximate (i.e., dominant Cx=2.5, or proximal LAD=3.5). Also, co-dominance was excluded. However, two major flaws of the SYNTAX score were the lack of assessment of the functional significance of coronary stenosis and the absence of clinical variables or comorbidities that may have influenced the perioperative mortality rate.

Despite its limitations, the SYNTAX score I is a valuable tool for assessing the complexity of coronary lesions and predicting the inferiority or non-inferiority of PCI compared to CABG based on the risk of 4-year all-cause mortality after myocardial revascularization in patients with CCS.

SYNTAX SCORE II

This second drawback was overcome with the development of the Clinical SYNTAX score and, subsequently, SYNTAX score II. The Clinical SYNTAX score considered clinical variables that showed the greatest association with mortality in studies performed so far: age, serum creatinine level, and left ventricular ejection fraction (LVEF) (35). The clinical SYNTAX score improved with the application of a Cox proportional hazards model to the results of the SYNTAX study, disclosing basic clinical variables strongly associated with 4-year mortality in PCI or CABG groups, or in both groups (36). Those clinical variables were as follows: age, creatinine clearance rather than serum creatinine level, LVEF, and 4 new variables: unprotected LMCA disease, female gender, peripheral vascular disease, and chronic obstructive pulmonary disease (36). Such clinical variables were added to the

anatomical SYNTAX score, resulting in SYNTAX score II (36). SYNTAX score II underwent internal validation using a bootstrap resampling method in the SYNTAX study population, with a concordance index of 0.725 (37). External validation was performed in both the DELTA and CREDO-KYOTO registries, yielding concordance indices of 0.716 and 0.70, respectively (38, 39).

The SYNTAX score II was applied in the SYNTAX II study to improve objective decision-making between CABG and PCI based on anatomical and clinical variables. In that study, contemporary PCI in patients with three-vessel disease was compared with a historical surgical cohort from the SYNTAX study (35, 40). Contemporary “state of the art” PCI was defined as PCI based on SYNTAX score II results, lesion assessment by coronary physiology, implantation of second-generation DES with thin struts, optimization of DES implantation using intravascular ultrasound (IVUS), and a contemporary approach to CTO lesion revascularization (40). Thus, the SYNTAX II study was a multicenter, prospective, open-label study of a single cohort of patients with de novo three-vessel disease without LMCA disease. SYNTAX score II was applied to such patients, and those with balanced (“equipoise”) SYNTAX score II, because of overlapping confidence intervals for the 4-year mortality rate after either PCI or CABG, underwent further assessment by the “heart team”. If the “heart team” assessed that those patients were amenable to PCI, they were included in the study and were treated by contemporary PCI (“state of the art” PCI or SYNTAX II strategy). Therefore, even in the SYNTAX II study, some distrust was shown in the final decision on the mode of treatment, which was finally made by the “heart team” by evaluating all three groups of patients: those with an equipoise 4-year mortality rate, those with a recommendation for PCI, and those directed to CABG. However, a high concordance was observed between the SYNTAX score II and the “heart team” assessment. Interestingly, 2 of 17 patients in the PCI-recommended group required CABG, while 7 of 134 patients preferred PCI over the recommended CABG (40). “Heart team” confirmed recommendation for CABG in 123 of 134 (92%) patients (40).

Instantaneous free-ratio (iFR) was measured for all lesions for which the stent implantation was planned. If iFR was <0.86 , the lesion was treated with the Synergy stent implantation and the patient was taking optimal medical therapy; if iFR was >0.93 , the patient was put on optimal medical therapy only, while in the case of iFR 0.86-0.93, measurement of FFR was required for definite lesion assessment (35,40). iFR was performed in 1150 patients (73.8%), solely FFR in 27 patients (1.7%), and functional lesion assessment was not performed in 382 patients (24.4%). Of these 382 patients, the wire could not cross the lesion site in 127 (8.1%). In comparison, in 229 patients, wire crossing was not attempted because a CTO lesion was present or the operator decided not to perform

functional lesion evaluation. Importantly, in 31% of lesions in which iFR/FFR measurements were performed, PCI was deferred, and only optimal medical therapy was recommended. Of note, an algorithm for the treatment of serial lesions was created and used: iFR/FFR was measured for all lesions in a row, and if $iFR < 0.86$, then the stent was implanted in the angiographically most severe stenosis. After that, iFR/FFR was measured again for the series of remaining lesions. Mainly due to functional lesion assessment, the total number of lesions per patient treated was reduced from 3.5 in the SYNTAX study to 2.6 in the SYNTAX II study, including the reduction in the rate of 3-vessel PCI from 83% in the SYNTAX study to 37% in the SYNTAX II study (40). Success in CTO recanalization increased from 53% in the SYNTAX study to 87% in the SYNTAX II study. Use of IVUS was also increased from 5% in the SYNTAX study to 84% in the SYNTAX II study (40). Thus, the SYNTAX II strategy led to a decreased rate of any repeat revascularization to 8.2%, which is close to those 5.9% in the surgical group (40). In that way, the SYNTAX II study was a positive study due to a significant reduction in MACCE, from 17.4% in the SYNTAX study to 10.6% in the SYNTAX II study (HR 0.58; 95% CI 0.39-0.85; $p=0.006$) (40). As compared to the surgical cohort of patients from the SYNTAX study, in the SYNTAX II study, a similar rate of MACCE was shown: 10.6 vs. 11.2% (HR 0.91; 95% CI 0.59-1.41; $p=0.684$), $p<0.001$ s for non-inferiority (non-inferiority margin for 1 alpha 0.05 was 5%) (40). Finally, using the SYNTAX II strategy (“state of the art” PCI), a similar MACCE rate at 12 months was observed in patients with a SYNTAX score ≤ 22 compared with those with a SYNTAX score >22 (40).

The SYNTAX score II improves on SYNTAX score I by adding clinical variables associated with 4-year all-cause mortality after PCI or CABG to the coronary lesion complexity. Those clinical variables may indicate increased perioperative risk in some patients and suggest that PCI is superior to CABG in terms of all-cause mortality at 4 years.

SYNTAX SCORE II 2020

The major drawbacks of the SYNTAX score II, which was validated to predict only 4-year mortality, only total mortality and not MACE, developed on outdated stents, not on contemporary PCI or CABG techniques and adjunctive imaging or physiology use, having modest predictive accuracy (C-index 0.7) and tendency to over- or under-estimate risk particularly in patients not included in randomised trials, were intended to resolve by introducing the SYNTAX score II 2020 (41, 42), and to offer more robust individualised decision support. The SYNTAX score II 2020 was built on the original SYNTAX score II by incorporating longer follow-up data

and recalibrating the model based on extended survival outcomes. It predicts 10-year all-cause mortality with high accuracy (C-index 0.73-0.79), 5-year MACCE (all-cause death, non-fatal stroke or non-fatal MI) rate with moderate accuracy (C-index 0.65-0.71), and treatment benefit (absolute risk difference) of PCI versus CABG for individual patients, thus helping in guiding personalized decision-making between revascularization strategies and longer-term prognostic information (41,42). The SYNTAX Score II 2020 combines anatomical factors (SYNTAX score, three-vessel disease vs. LMCA disease) and clinical factors (age, diabetes mellitus, creatinine clearance, left ventricular ejection fraction, chronic obstructive pulmonary disease, peripheral vascular disease, and current smoking status) to improve prognostic assessment. It shows better discrimination and calibration across multiple validation cohorts (C-index 0.73 for 10-year mortality for both PCI and CABG, and 0.65-0.71 for 5-year MACCE) and more accurately aligns predicted and observed outcomes (41-44). The SYNTAX score II 2020 explicitly estimates absolute risk differences between PCI and CABG for a specific patient (de novo three-vessel and LM disease), categorizing them into CABG-PCI equipose (small benefit difference) and CABG better (larger predicted benefit with CABG), thus helping personalize decisions (42). The SYNTAX score II 2020 used larger, more contemporary data for derivation and validation: external trial cohorts (FREEDOM, BEST, and PRECOMBAT) and the SYNTAXES extension study to predict longer-term outcome^s (43, 44).

The SYNTAX score II 2020 included variables associated with 10-year all-cause mortality. It provided more accurate, longer-term predictions of clinical outcomes: all-cause mortality at 10 years and MACCE rate at 5 years.

APPLICATION OF THE SYNTAX SCORE I AND II BY THE HEART TEAM IN MAKING CLINICAL DECISIONS

Heart team meetings at our institution were established in the late 1970s – the SYNTAX score I has been calculated since 2010, when an online calculator became available. The SYNTAX score II has been calculated since the beginning of 2017, and the SYNTAX score II 2020 since 2021. All decisions of the heart team at our institution from June 2017 to July 2018 (N=240) were retrospectively analyzed using both SYNTAX score I and SYNTAX score II. When we assessed CAD severity, 70% of patients had SYNTAX score I ≤ 22 , 17.5% had SYNTAX score I 23-32, and 12.5% had SYNTAX score I ≥ 33 (Figure 1). Overall, the agreement between the recommendations of our heart team and the SYNTAX score was achieved in 72.5% of cases. When comparing the SYNTAX score I in 2014-2015 (N=200) and 2017-2018, we found a slight increase in the severity of CAD (an increase in the SYNTAX score I ≥ 33 from 15% to 20% and a decrease in the SYNTAX score I ≤ 22 from 75% to 65%). Moreover, the more severe the CAD was, the more often the heart team recommended CABG (Figure 2). Interestingly, recommendations for optimal medical therapy by the heart team also increased in patients with higher SYNTAX score I (Figure 2). Finally, when the SYNTAX score II was applied, 75% of patients had an equipose outcome, while PCI was recommended in 5% and CABG in 20% of patients (Figure 3). It means that, in the majority of patients at our institution, as in the SYNTAX II study, either PCI or CABG can be recommended, with similar 4-year mortality rates. Importantly, the heart team at our institution did not recommend both modes of revascularization according to the “either-or” principle, as in cases with an equipose outcome, but selected one option as the

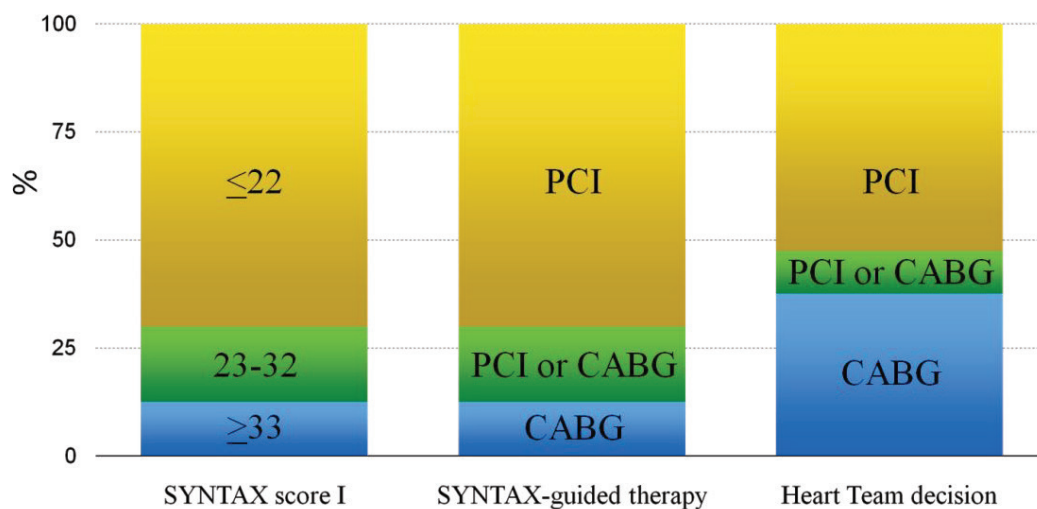


Figure 1. Proportions of patients with the SYNTAX score I, recommended mode of revascularization by using the SYNTAX score I, and recommended therapy by the heart team. Abbreviations: PCI – percutaneous coronary interventions; CABG – aorto-coronary bypass graft surgery.

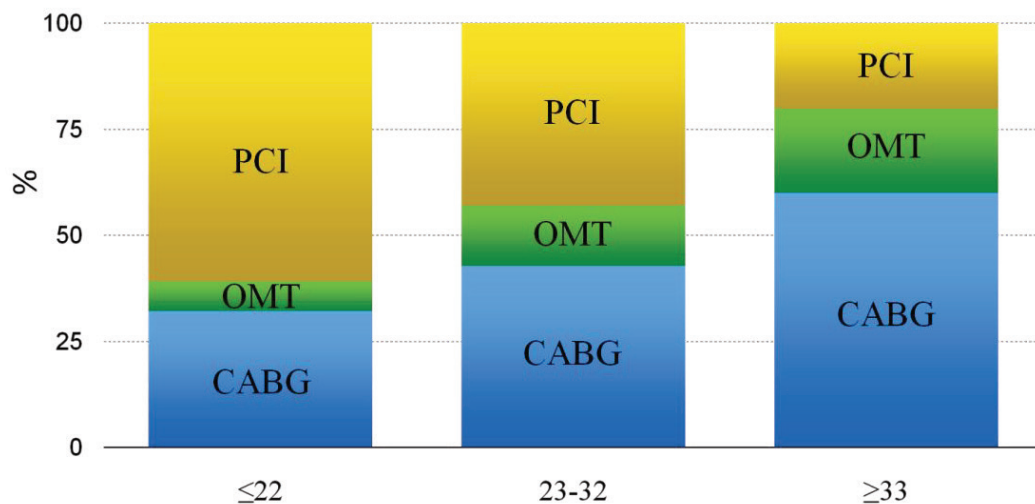


Figure 2. The heart team’s recommendations for the mode of revascularization, including OMT, according to tertiles of the SYNTAX score I. Abbreviations: PCI – percutaneous coronary interventions; CABG – aorto-coronary bypass graft surgery; OMT – optimal medical therapy.

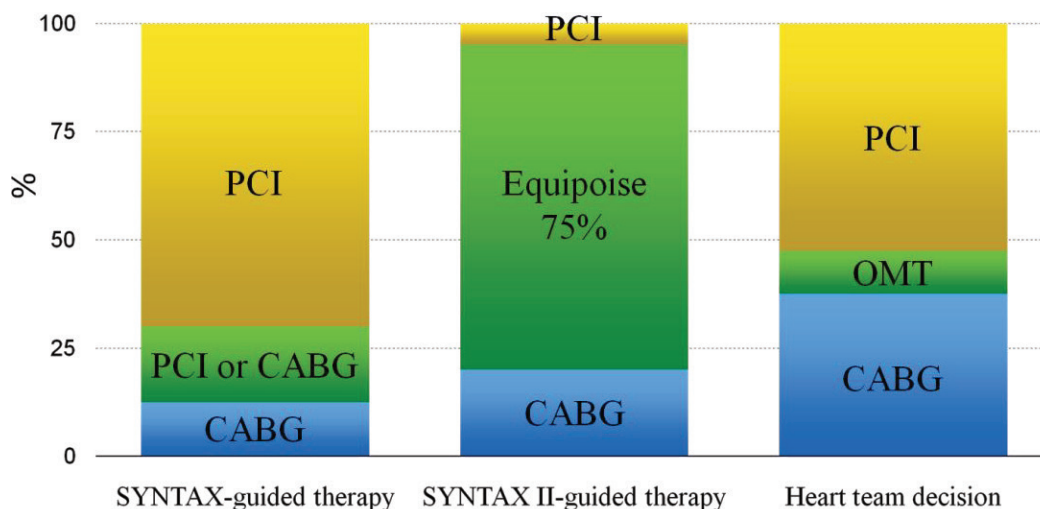


Figure 3. Recommended mode of revascularization by application of the SYNTAX score I, the SYNTAX score II, and by decision of the heart team. A substantial proportion of patients were deemed candidates for CABG by the heart team in this moderately complex cohort. Abbreviations: PCI – percutaneous coronary interventions; CABG – aorto-coronary bypass graft surgery; OMT – optimal medical therapy.

optimal option for an individual patient (Figure 3). Recently, in cases with equipoise outcomes, the heart team at our institution has begun to involve patients in the decision-making process, taking into account patients’ preferences.

This analysis is limited to the use of the SYNTAX scores I and II only. The majority of patients’ records were destroyed in the fire that affected the archive in an old building under reconstruction at the time. However, it illustrates the evolution of our heart team’s efforts to objectively assess the anatomical and clinical complexity of the evaluated patients using the SYNTAX scores I and II.

ADVANTAGES AND LIMITATIONS OF SYNTAX SCORE I, II, AND II 2020 IN CLINICAL PRACTICE

In the SYNTAX study, the SYNTAX score I disclosed that angiographic complexity of coronary disease had

predictive value for PCI and CABG. Patients with intermediate (23-32) and high SYNTAX score (≥33) can benefit more from CABG compared to PCI, if they do not have severe comorbidities associated with high perioperative mortality. The SYNTAX score II was developed by incorporating clinical variables associated with 4-year mortality, either after PCI or after CABG, in patients enrolled in the SYNTAX study. The SYNTAX score II potentially can change the recommendation for myocardial revascularization based on the SYNTAX score I alone. The SYNTAX score II may overestimate the mortality rate after contemporary PCI (first-generation DES was used in the SYNTAX study, rare use of IVUS, lower success in CTO recanalization in the SYNTAX study as compared with the SYNTAX II study), as well as after CABG (if it is applied in patients with low SYNTAX score I). However, the greatest limitation of the SYNTAX score II is the absence of physiologic assessment of coronary stenosis, the lack of recommendations for medical therapy, and the short-term

prediction of clinical outcome after either PCI or CABG. The SYNTAX score II indicated equipoise outcomes in the majority of patients (75%) after PCI or CABG, not only in the SYNTAX II study but also in daily clinical practice at our institution. The SYNTAX score II 2020 amended the SYNTAX score II by extending the prediction of mortality rate at 10 years and MACCE at 5 years, and increasing the accuracy for predicting outcomes in female patients. Final decision, however, about the mode of myocardial revascularization or optimal medical therapy, is made by the heart team consisting of non-invasive cardiologist, an interventional cardiologist, a cardiac surgeon, and an anesthesiologist who routinely include SYNTAX scores in the recommendation-making process.

The heart team at our institution initially assessed mainly patients with low SYNTAX scores, but over the years, the proportion of patients with more complex CAD increased. Interestingly, the percentage of patients with more complex CAD who received optimal medical therapy recommended by the heart team also increased. The majority of patients with an equipoise clinical outcome, as assessed by the SYNTAX score II, were indicated for PCI by our heart team. The smallest proportion of these patients were recommended for optimal medical therapy. Finally, all three SYNTAX scores serve as useful tools for deciding on the mode of myocardial revascularization, but any such decision cannot be based solely on these scores.

CONCLUSION

The SYNTAX score I is a solely angiographic tool that considers CABG as the gold standard for myocardial

revascularization, with PCI considered inferior or non-inferior, but never superior. However, it is a relevant clinical tool recommended for decision-making in the current European guidelines on myocardial revascularization. The SYNTAX score II identifies patients at similar or higher risk of 4-year mortality after PCI compared to CABG, but also those at lower risk of all-cause death after PCI compared to CABG. The SYNTAX score II 2020, which predicts 10-year mortality and 5-year MACE, can help identify patients with CCS and three-vessel disease or LM disease who will benefit more from PCI or CABG in the long term. The SYNTAX score II 2020 offers a highly accurate 10-year prediction of all-cause mortality and moderately accurate 5-year prediction of major adverse cardiac and cerebral events after percutaneous or surgical myocardial revascularization, which makes it a strong candidate as a reliable decision-making tool for the heart team when recommending percutaneous or surgical myocardial revascularization for an individual patient with multivessel disease and CCS.

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References:

1. Thomas JL. Vineberg legacy: Internal mammary artery implantation from inception to obsolescence. *Tex Heart Inst J* 1999;26(2):107-113. PMID: 10397432; PMCID: PMC325613.
2. Brian Buxton, Galvin SD. The history of arterial revascularization: from Kolesov to Tector and beyond. *Ann Cardiothorac Surg* 2013;2(4):419-442. doi: 10.3978/j.issn.2225-319X.2013.07.24. PMID: 23977617.
3. Reul GJ. Present status of the internal mammary artery as a coronary artery bypass conduit at the Texas Heart Institute. *Tex Heart Inst J* 1985;12(3):211-219. PMCID: PMC341859. PMID: 15227007.
4. Sowton E, Yates AK, Curry PVL, Deverall PB, Jackson G, Pumphrey CW, et al. Coronary angioplasty versus coronary artery bypass surgery: the Randomised Intervention Treatment of Angina (RITA) trial. RITA trial participants. *Lancet* 1993;6:341(8845): 573-880. doi: 10.1016/0140-6736(93)90348-K.
5. Hamm CW, Reimers J, Ischinger T, Rupprecht HJ, Berger J, Bleifeld W. A randomized study of coronary angioplasty compared with bypass surgery in patients with symptomatic multivessel coronary disease. German Angioplasty Bypass Surgery Investigation (GABI). *N Engl J Med* 1994;331(16):1037-1043. doi: 10.1056/NEJM199410203311601. PMID: 8090162.
6. Rodriguez A, Mele E, Peyregne E, Bullon F, Perez-Baliño N, Liprandi MI, Palacios IF. Three-year follow-up of the Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease (ERACI). *J Am Coll Cardiol* 1996;27(5):1178-1184. doi: 10.1016/0735-1097(95)00592-7. PMID: 8609339.
7. King SB, Lembo NJ, Weintraub WS, Kosinski AS, Barnhart HX, Kutner MH, et al. A randomized trial comparing coronary angioplasty with coronary bypass surgery. Emory Angioplasty versus Surgery Trial (EAST). *N Engl J Med* 1994;331(16):1044-1050. doi: 10.1056/NEJM199410203311602. PMID: 8090163
8. CABRI Trial Participants. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularization Investigation). CABRI Trial Participants. *Lancet* 1995; 346(8984):1179-1184. PMID: 7475656. doi: 10.1016/S0140-6736(95)91800-4.
9. Alderman EL, Andrews K, Bost J, Bourassa M, Chaitman BR, Detre K, et al. Comparison of Coronary Bypass Surgery with Angioplasty in Patients with Multivessel Disease. The BARI Investigators. *N Engl J Med* 1996;335:217-225. doi: 10.1056/NEJM199607253350401.
10. Morrison DA, Sethi G, Sacks J, Henderson W, Grover F, Sedlis S, et al. Percutaneous coronary intervention versus coronary artery bypass graft surgery for patients with medically refractory myocardial ischemia and risk factors for adverse outcomes with bypass: a multicenter, randomized trial. Investigators of the Department of Veterans Affairs Cooperative Study #385, the Angina With Extremely Serious Operative Mortality Evaluation (AWESOME). *J Am Coll Cardiol* 2001;38(1):143-149. doi: 10.1016/s0735-1097(01)01366-3. PMID: 11451264

11. Morrison DA, Sethi G, Sacks J, Henderson WG, Grover F, Sedlis S, et al. Percutaneous coronary intervention versus repeat bypass surgery for patients with medically refractory myocardial ischemia: AWE-SOME randomized trial and registry experience with post-CABG patients. *J Am Coll Cardiol* 2002;40(11):1951-1954. doi: 10.1016/s0735-1097(02)02560-3.
12. Rodriguez A, Bernardi V, Navia J, Baldi J, Grinfeld L, Martinez J, et al. Argentine Randomized Study: Coronary Angioplasty with Stenting versus Coronary Bypass Surgery in patients with Multiple-Vessel Disease (ERACI II): 30-day and one-year follow-up results. ERACI II Investigators. *J Am Coll Cardiol* 2001;37(1):51-58. doi: 10.1016/s0735-1097(00)01052-4.
13. Rodriguez AE, Baldi J, Fernández Pereira C, Navia J, Rodriguez Alemparte M, Delacasa A, et al. ve-year follow-up of the Argentine randomized trial of coronary angioplasty with stenting versus coronary bypass surgery in patients with multiple vessel disease (ERACI II). ERACI II Investigators. *J Am Coll Cardiol* 2005;46(4):582-588. doi: 10.1016/j.jacc.2004.12.081.
14. Serruys PW, Unger F, Sousa JE, Jatene A, Bonnier HJ, Schönberger JP, et al. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. *N Engl J Med* 2001;344(15):1117-1124. doi: 10.1056/NEJM200104123441502.
15. SoS Investigators. Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the Stent or Surgery trial): a randomised controlled trial. *Lancet* 2002;360(9338): 965-970. doi: org/10.1161/CIRCULATIONAHA.109.9116.
16. Hueb W, Soares PR, Gersh BJ, César LAM, Luz PL, Puig LB, et al. The medicine, angioplasty, or surgery study (MASS-II): a randomized, controlled clinical trial of three therapeutic strategies for multivessel coronary artery disease: One-year results. *J Am Coll Cardiol* 2004;43:1743-1751. doi: 10.1016/j.jacc.2004.01.034.
17. Hueb W, Lopes NH, Gersh BJ, Soares P, Machado LAM, et al. Five-Year Follow-Up of the Medicine, Angioplasty, or Surgery Study (MASS II). A Randomized Controlled Clinical Trial of 3 Therapeutic Strategies for Multivessel Coronary Artery Disease. *Circulation* 2007;115:1082-1089. doi: 10.1161/CIRCULATIONAHA.
18. Hueb W, Lopes NH, Gersh BJ, Soares P, Ribeiro EE, Pereira AC, et al. Ten-Year Follow-Up Survival of the Medicine, Angioplasty, or Surgery Study (MASS II) A Randomized Controlled Clinical Trial of 3 Therapeutic Strategies for Multivessel Coronary Artery Disease. *Circulation* 2010;122:949-957. doi: 10.1161/CIRCULATIONAHA.109.911669.
19. Serruys PW, Morice MC, Kappetein P, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease. *N Engl J Med*. 2009;360:961-972. doi: 10.1056/NEJMoa0804626.
20. Serruys PW, Onuma Y, Garg S, Vranckx P, De Bruyne B, Morice MC, et al. 5-year clinical outcomes of the ARTS II (Arterial Revascularization Therapies Study II) of the sirolimus-eluting stent in the treatment of patients with multivessel de novo coronary artery lesions. 5-year clinical outcomes of the ARTS II (Arterial Revascularization Therapies Study II) of the sirolimus-eluting stent in the treatment of patients with multivessel de novo coronary artery lesions. ARTS II Investigators. *J Am Coll Cardiol* 2010;55(11):1093-1101. doi: 10.1016/j.jacc.2009.11.049.
21. Hlatky MA, Boothroyd DB, Bravata DM, Boersma E, Booth J, Brooks MM, et al. Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials. *Lancet* 2009;373(9670):1190-1197. doi: 10.1016/S0140-6736(09)60552-3.
22. Colombo A, Orlic D, Stankovic G, Corvaja N, Spanos V, Montorfano M, Liistro F, Carlino M, Airolidi F, Chieffo A, Di Mario C. Preliminary observations regarding angiographic pattern of restenosis after rapamycin-eluting stent implantation. *Circulation* 2003;107(17):2178-80. doi: 10.1161/01.CIR.0000070592.04766.36.
23. Orlic D, Bonizzoni E, Stankovic G, Airolidi F, Chieffo A, Corvaja N, Sangiorgi G, Ferraro M, Briguori C, Montorfano M, Carlino M, Colombo A. Treatment of multivessel coronary artery disease with sirolimus-eluting stent implantation: immediate and mid-term results. *J Am Coll Cardiol* 2004;43:1154-60. doi: 10.1016/j.jacc.2003.10.052.
24. Chieffo A, Bonizzoni E, Orlic D, Stankovic G, Rogacka R, Airolidi F, et al. Intraprocedural stent thrombosis during implantation of sirolimus-eluting stents. *Circulation* 2004;109:2732-6. doi.org/10.1161/01.CIR.0000131890.83839.5B.
25. Vrints C, Andreotti F, Koskinas KC, Rossello X, Adamo M, Ainslie J, et al.; ESC Scientific Document Group. 2024 ESC Guidelines for the management of chronic coronary syndromes. *Eur Heart J* 2024 Sep 29;45(36):3415-3537. doi: 10.1093/eurheartj/ehae177. PMID: 39210710.
26. Orlic D, Vitrella G, Corvaja N, Colombo A. New technique to seal a long giant coronary aneurysm with PTFE-covered stents: a case report. *Catheter Cardiovasc Interv* 2006;67:41-5. doi: 10.1002/ccd.20523.
27. Mehmedbegovic Z, Vukcevic V, Stojkovic S, Beleslin B, Orlic D, Tomasevic M, et al. Long-term follow-up optical coherence tomography assessment of primary percutaneous coronary intervention for unprotected left main. *Rev cardiovasc Med* 2024;25(12):445. doi: 10.31083/j.rcm2512445.
28. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease, *EuroInterv* 2005;1:219-227. doi: 10.4244/VII12A31.
29. Leaman DM, Brower RW, Meester GT, Serruys P, van den Brand M. Coronary Artery Atherosclerosis: Severity of the Disease, Severity of Angina Pectoris and Compromised Left Ventricular Function. *Circulation* 1981;63(2):285-299. doi: 10.1161/01.cir.63.2.285.
30. Serruys PW, Morice M-C, Kappetein P, Colombo A, Holmes DR, Mack M, Stahle E. et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med* 2009;360:961-972. doi: 10.1056/NEJMoa0804626.
31. Mohr FW, Morice M-C, Kappetein PA, Feldman TE, Stahle E, Colombo A, et al. Coronary artery bypass surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *Lancet* 2013;381:629-38. doi: 10.1016/S0140-6736(13)60141-5.
32. Morice M-C, Serruys PW, Kappetein AP, Feldman TE, Stahle E, Colombo A, et al. Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the synergy between percutaneous coronary intervention with Taxus and cardiac surgery trial. *Circulation* 2014;129:2388-2394. doi: 10.1161/CIRCULATIONAHA.113.006689.
33. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, et al. The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). 2014 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J* 2014;35:2541-2619. doi: 10.1093/eurheartj/ehu278.
34. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS). 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J* 2018;00:1-96. doi: 10.1093/eurheartj/ehz507.
35. Escaned J, Banning A, Farooq V, Echavarría-Pinto M, Onuma Y, Ryan N, et al. Rationale and design of the SYNTAX II trial evaluating the short to long-term outcomes of state-of-the-art percutaneous coronary revascularisation in patients with de novo three-vessel disease. *EuroIntervention* 2016;12:e224-e234. doi: 10.4244/EIJV12I2A36.
36. Garg S, Sarno G, Garcia-Garcia HM, Giris C, Wykrzykowska J, Dawkins KD, et al. A New Tool for the Risk Stratification of Patients With Complex Coronary Artery Disease. The Clinical SYNTAX Score. *Circ Cardiovasc Interv* 2010;3:317-326. doi: 10.1161/CIRCINTERVENTIONS.109.914051.
37. Farooq V, van Klaveren D, Steyerberg EW, Meliga E, Vergouwe Y, Chieffo A, et al. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percu-

- taneous coronary intervention for individual patients: development and validation of SYNTAX score II *Lancet* 2013;381:639-650. doi: 10.1016/S0140-6736(13)60108-7. doi: 10.1016/S0140-6736(13)60108-7.
38. Chieffo A, Meliga E, Latib A, Park SJ, Onuma Y, Capranzano P, et al. Drug-Eluting Stent for Left Main Coronary Artery Disease The DELTA Registry: A Multicenter Registry Evaluating Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting for Left Main Treatment. *J Am Coll Cardiol Intv* 2012;5:718-727. doi: 10.1016/j.jcin.2012.03.022.
 39. Campos CM, van Klaveren D, Iqbal J, Onuma Y, Zhang YJ, Garcia-Garcia HM, et al. Predictive Performance of SYNTAX Score II in Patients With Left Main and Multivessel Coronary Artery Disease - analysis of CREDO-Kyoto registry. *Circ J* 2014;78:1942-1949. doi: 10.1253/circj.cj-14-0204.
 40. Escaned J, Collet C, Ryan N, De Maria GL, Walsh S, Sabate M, et al. Clinical outcomes of state-of-the-art percutaneous coronary revascularization in patients with de novo three vessel disease: 1-year results of the SYNTAX II study. *Eur Heart J* 2017;00: 1-11. doi: 10.1093/eurheartj/ehx547.
 41. Takahashi K, Serruys PW, Fuster V, Farkouh ME, Spertus JA, Cohen DJ, et al. Redevelopment and validation of the SYNTAX score II to individualise decision making between percutaneous and surgical revascularisation in patients with complex coronary artery disease: secondary analysis of the multicenter randomised controlled SYNTAXES trial with external cohort validation. *The Lancet* 2020;396:10260, 1399-1412. doi: 10.1016/S0140-6736(20)32114-0.
 42. Thuijs DJFM, Kappetein PA, Serruys PW, Mohr FW, Morice M-C, Mack MJ, et al. Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. *Lancet* 2019; 394: 1325-1334. doi: 10.1056/NEJMoa0804626.
 43. Hara H, Shiomi H, van Klaveren D, Kent DM, Steyerberg EW, Garg S, et al. External validation of the SYNTAX Score II 2020. *J Am Coll Cardiol* 2021;78:1227-1238. doi: 10.1016/j.jacc.2021.07.027.
 44. Squiers JJ and DiMaio JM. SYNTAX score II 2020: a remake worth the price of admission? *J Am Coll Cardiol* 2021, 78, 12: 1239-1241. doi: 10.1016/j.jacc.2021.07.028.
 45. Hamilos MI, Ostojic M, Beleslin B, Sagic D, Mangovski Lj, Stojkovic S, et al. on behalf of the NOBORI CORE Investigators. Differential Effects of Drug-Eluting Stents on Local Endothelium-Dependent Coronary Vasomotion. *J Am Coll Cardiol* 2008;51:2123-9. doi: 10.1016/j.jacc.2007.12.059.

EVOLUCIJA SYNTAX SKORA (I, II AND II 2020): RAZVOJ, PRIMENA I OGRANIČENJA U SVAKODNEVNOJ KLINIČKOJ PRAKSI

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Sažetak

Hirurška revaskularizacija miokarda je zlatni standard za revaskularizaciju miokarda u hroničnom koronarnom sindromu (CCS). Prve randomizovane studije koje su poredile implantaciju običnog metalnog stenta (BMS) sa aorto-koronarnom by-pass hirurgijom (CABG) pokazale su sličnu učestalost smrti i infarkta miokarda, a ređu pojavu ponovne revaskularizacije miokarda nakon CABG u odnosu na implantaciju BMS, što je dovelo do razvoja stentova sa oslobađanjem leka (DES) sa manjom učestalošću kliničke restenoze. Tokom godina, pojavila se potreba za objektivnom procenom i izračunavanjem rizika i koristi od hirurške ili perkutane revaskularizacije miokarda, davanje prednosti jednoj od ove dve metode, ili njihovom sličnom ishodu kod pojedinih bolesnika. SYNTAX skor I je korišćen za kvantitativnu procenu kompleksnosti koronarne stenozе kod bolesnika sa CCS. Ipak, dva glavna nedostatka SYNTAX skora I, 1) odsustvo procene funkcionalne značajnosti koronarne stenozе i 2) odsustvo kliničkih varijabli koje mogu da utiču na

perioperativnu smrtnost, su delimično prevaziđene razvojem SYNTAX skora II. SYNTAX skor II sadrži kliničke varijable koje su pokazale najveću udruženost sa smrtnošću (uzrast, klirens kreatinina, ejekciona frakcija leve komore, aterosklerotska bolest glavnog stabla leve koronarne arterije, ženski pol, periferna vaskularna bolest i hronična opstruktivna bolest pluća). SYNTAX skora II 2020 predstavlja ekstenziju SYNTAX skora II u kliničkom praćenju za desetogodišnju smrtnost. SYNTAX skor II i II 2020 potencijalno mogu da promene preporuku za revaskularizaciju miokarda koja je zasnovana samo na vrednosti SYNTAX I skora. Ovaj revijalni pregled ima za cilj da prikaže razvoj ova tri skora, njihovu pouzdanost, prediktivni značaj i ograničenja u praktičnoj primeni kod pojedinih bolesnika sa CCS.

Primarni cilj: prikazati razvoj SYNTAX skorova I, II i II 2020, njihov prognostički značaj i ograničenja u svakodnevnoj kliničkoj praksi pri izboru optimalne metode revaskularizacije miokarda kod pojedinih bolesnika sa HKS.

Ključne reči: SYNTAX skor, revaskularizacija miokarda, prognoza

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