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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Coronary computed tomography angiography for the assessment of SYNTAX score

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Abstract

Background: Coronary computed tomography angiography (CCTA) is applied in a growing number of clinical indications. This imaging modality is often regarded as a surrogate of invasive coronary angiography (ICA). In this paper we evaluate the applicability of CCTA alone in the assessment of the SYNTAX score.

Aim: To evaluate the feasibility of calculating the SYNTAX score (SXScore) using CCTA alone instead of ICA.

Methods: Ninety consecutive patients with multivessel or left main (LM) coronary artery disease diagnosed with ICA, in whom prior CCTA scan was available, were included in a post-hoc analysis. First, the SXScore was calculated twice in ten-week intervals by two experienced observers using ICA for each patient. Then the SXScore was calculated twice using CCTA following the same regimen for each patient. Weighted kappa statistic was used to assess the intra-modality and inter-modality reproducibility of the SXScore.

Results: Ninety patients, aged 63.8 ± 8.9 years, 60% male, 64.4% with two-vessel disease, and 35.6% with three-vessel or LM disease met the inclusion criteria. 287 lesions were identified by ICA and 280 by CCTA ($p = 0.56$). Median total SXScore was 11.5 (10.2–14.0) as calculated by ICA and 16.0 (14.3–19.4) by CCTA ($p < 0.001$), and the results were moderately correlated ($R = 0.38$). Inter-modality agreement between ICA and CCTA for SXScore tertiles was moderate (kappa = 0.40). The intra-modality reproducibility of ICA and CCTA for SXScore tertiles was 0.47 and 0.51, respectively.

Conclusions: Inter-modality agreement between CCTA and ICA for calculation of SXSscore is moderate but only slightly worse than intra-modality reproducibility for angiographic alone evaluation. Most of the observed variability can be assigned to the characteristic of the SXScore itself, not to the choice of imaging method. However, the application of CCTA for the assessment of SXScore should be used cautiously.

Key words: coronary computed tomography angiography, SYNTAX score, reproducibility, coronary artery disease

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INTRODUCTION

The SYNTAX score (SXScore), developed in 2005 [1, 2], although not perfect, is a widely used tool for the assessment of coronary artery disease (CAD) complexity in patients with multivessel disease or in cases with left main (LM) stem involved. Five-year follow-up of the patients enrolled to the SYNTAX trial confirmed the role of SXScore in the prediction of adverse effects after percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) [3]. It has been found that the SXScore result correlates with the outcome of patients undergoing elective or acute coronary syndrome-associated PCI [4, 5].

Coronary computed tomography angiography (CCTA) is already a well-established diagnostic method in certain groups of patients [6], and its usefulness has recently been evaluated in new indications, including diagnosis of acute chest pain [7] and in-stent restenosis [8]. The result of a CCTA examination is now available for a significant number of patients scheduled for myocardial revascularisation due to multivessel/LM CAD. Because the results of investigations carried out to-date are

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conflicting [9, 10], in this retrospective study we aimed to define the feasibility of calculating SXScore using CCTA. If it is possible, it might facilitate the decision-making process for the physician performing coronary angiography in this high-risk subgroup of patients. Because inter- and intra-observer reproducibility of the SXScore assessment was reported to be only moderate and varied between studies [11, 12], we also decided to directly compare the intra-modality (invasive coronary angiography [ICA vs. ICA and CCTA vs. CCTA]) and inter-modality (ICA vs. CCTA) reproducibility of the SXScore to determine if the type of diagnostic method or the SXScore algorithm itself is the main source of possible inaccuracy.

METHODS

The study was based on a high-volume single-centre registry. Consecutive patients with at least two-vessel or LM CAD diagnosed with ICA, scheduled for revascularisation between 2009 and 2012, and in whom CCTA was performed for clinical indications within six months before diagnostic ICA, were included in the analysis. All the patients had at least one significant lesion scheduled for revascularisation (at least 50% stenosis assessed by visual estimation) in an epicardial coronary vessel > 1.5 mm in diameter. Patients with previously performed PCI or CABG were excluded.

ICA was performed using a Siemens angiograph (AXIOM Artis DFC; Siemens Medical Systems). Standard multiple projections were acquired and archived on a local server for further off-line analysis.

CCTA data were acquired using a dual source 64-row scanner (Somatom Definition; Siemens Medical Systems, Forchheim, Germany) or 128-row scanner (Somatom Definition Flash; Siemens Medical Systems, Forchheim, Germany). All patients without contraindications received 0.8 mg of nitroglycerin SL prior to image acquisition, and in cases of heart rhythm > 65/min sequential boluses of IV metoprolol (2.5 mg, max. 10 mg) were administered. Images were archived on a local server for off-line analysis using commercially available quantitative CCTA software (Circulation; Siemens Medical Systems).

The acquired images were evaluated by two readers experienced in the assessment of both ICA and CCTA. Calculation of the SXScore was done according to the rules and definitions available online [13]. For CCTA, multiple planar reconstructions (MPR) and maximum intensity projections (MIP) were used for the assessment of number of lesions, severity, and morphology, while three-dimensional volume-rendering reconstructions were used to assess the right/left dominance and angles. Curved-MPR was used for the measurements of lesion length.

Two independent evaluation runs were performed in three-month intervals. In RUN1 SXScore was calculated separately using ICA and CCTA by different readers. In case of any discrepancy a decision was made by consensus. In RUN2 SXScore was calculated in the same way; however, the readers were exchanged (the person who assessed ICA in RUN1 assessed CCTA in RUN2, and vice versa). Additionally, to minimise the potential effect of the learning curve, calculations for the first 40 patients form RUN1 were discarded and images were re-assessed at the end. Data from RUN1 were used for comparison of CCTA and ICA, while data from RUN2 and from RUN1 were used to assess the intra-modality variability. In all analyses ICA was used as a standard reference.

Statistical analysis

Normally distributed continuous data were presented as mean ± standard deviation (SD), and non-normally distributed as medians and inter-quartile range (IQR). Spearman's correlation was used to compare the results of SXScore calculation with ICA and CCTA. The Z statistics were used to compare the Spearman's R coefficients. Cohen's kappa statistic was applied to assess inter-modality (ICA vs. CCTA) as well as intra-modality variability (ICA from RUN1 and RUN2 and CCTA from RUN1 and RUN2) regarding SXScore tertiles and selected morphological features influencing the final result of SXScore calculation. Bland-Altman's plots were generated for comparison of ICA and CCTA. MedCalc version 9.3.8.0 (MedCalc Software, Marierkerke, Belgium) was used for all statistical analyses.

RESULTS

A total of 90 patients (of whom 60% were male) of mean age 63.8 ± 8.9 years filled the inclusion criteria within the study period. Eighty-one (90%) patients were qualified for PCI and nine (10%) for CABG after diagnostic ICA. Fifty-eight (64%) subjects were diagnosed with two-vessel CAD and 32 (36%) with three-vessel or LM disease. Demographic and clinical characteristics of the patients are presented in Table 1.

Table 1. Demographic and clinical characteristics of the study population

Age [years] (mean ± SD)	63.8 ± 8.9
Male	54 (60%)
History of coronary artery disease	76 (84.4%)
Diabetes mellitus	14 (15.6%)
Hypertension	70 (77.8%)
Hypercholesterolaemia	59 (65.6%)
GFR [mL/min] (mean)	70.6
GFR < 60	17 (18.9%)
Calcium score, Agatston (pts.)	442.85
Intervention type:	
PCI	81 (90%)
CABG	9 (105)
Two-vessel disease	58 (64.44%)
Three-vessel/left main disease	32 (35.56%)

CABG — coronary artery bypass grafting; GFR — glomerular filtration rate; PCI — percutaneous coronary intervention

Table 2. Comparison of SXScore calculation — ICA vs. CCTA

Variable	ICA	CCTA	P	kappa
Disease location and extent				
Number of lesions	287	280	0.55	0.14
Number of lesions/patient:				
Mean ± standard deviation	3.19 ± 1.20	3.11 ± 1.33	0.65	
Median (IQR)	3 (2–4)	3 (2–4)	0.56	
Two-vessel disease	58	52		0.35
Three-vessel disease/LM	32	38		0.35
Left dominance	18	27	0.02	0.27
LM/LAD/IM lesions:	112	116		0.29
Mean ± SD	1.24 ± 0.72	1.29 ± 0.78	0.63	
Median (IQR)	1 (1–2)	1 (1–2)	0.68	
LCx lesions:	80	63		0.29
Mean ± SD	0.89 ± 0.69	0.7 ± 0.64	0.02	
Median (IQR)	1 (0–1)	1 (0–1)	0.04	
RCA lesions:	95	101		0.5
Mean ± SD	1.06 ± 0.84	1.12 ± 0.83	0.42	
Median (IQR)	1 (1–2)	1 (1–1)	0.43	
Median SYNTAX score	11.5 (10.2–14.0)	16 (14.3–19.4)	< 0.001	
SYNTAX score tertiles				
< 23	77	63		0.38
23–32	10	23		0.32
> 32	3	4		–0.04
SYNTAX score deciles				
0–10	36	23		0.19
11–20	38	35		0.06
21–30	16	26		0.39
31–40	3	5		–0.04
41–50	0	2		0
Lesion characteristics				
Bifurcations	48	59		0.12
Long lesions	18	36		0.41
Total occlusions	18	25		0.64
Calcified lesions	0	31		–
Ostial lesions	2	6		0.03
Diffusely diseased segment	4	8		0.12

ICA — invasive coronary angiography; IM — intermediate branch; IQR — inter-quartile range; CCTA — coronary computed tomography angiography; LM — left main; LAD — left anterior descending, LCX — left circumflex; RCA — right coronary artery

In total, 287 lesions were identified by ICA and 280 by CCTA ($p = 0.56$). Median total SXScore was 11.5 (10.2–14.0) as calculated from ICA and 16.0 (14.3–19.4) when calculated from CCTA; the difference was significant with $p < 0.001$ (Table 2). There was only moderate inter-modality correlation between total SXScore calculated from ICA and CCTA (Spearman's R = 0.36). Intra-modality correlation between total SXScore obtained in RUN1 and RUN2 for ICA and for CCTA was 0.63 ($p < 0.001$) and 0.53 ($p < 0.001$), respectively. The difference between correlation coefficients was statistically significant only for ICA and CCTA correlation vs. ICA RUN1 and ICA RUN2 correlation (Z-statistic $p = 0.02$, Fig. 1).

Bland-Altman plots for inter- and intra-modality correlation in the estimation of total SXScore revealed the best

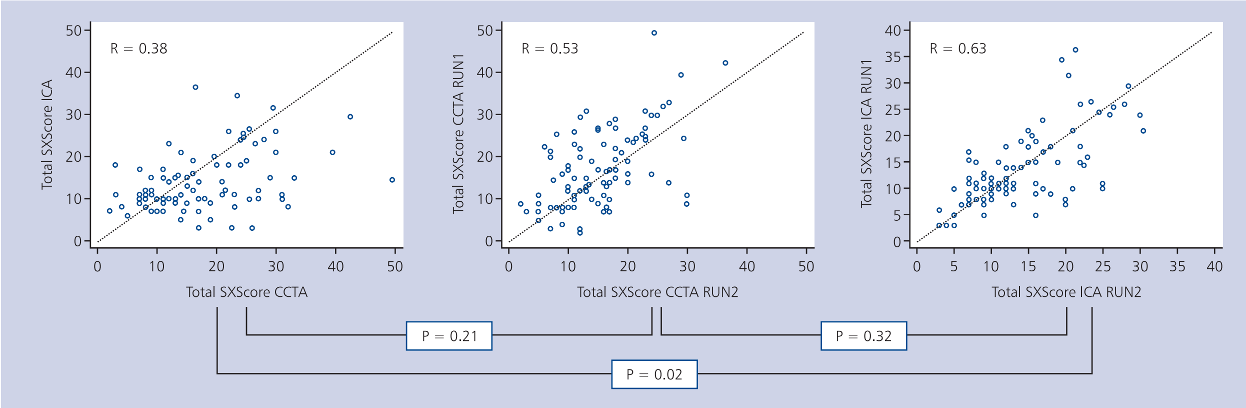

Figure 1. Inter- and intra-modality correlation for coronary computed tomography angiography (CCTA) and invasive coronary angiography (ICA) in total SYNTAX score calculation; p-values for Z-statistic comparison of two correlation coefficients

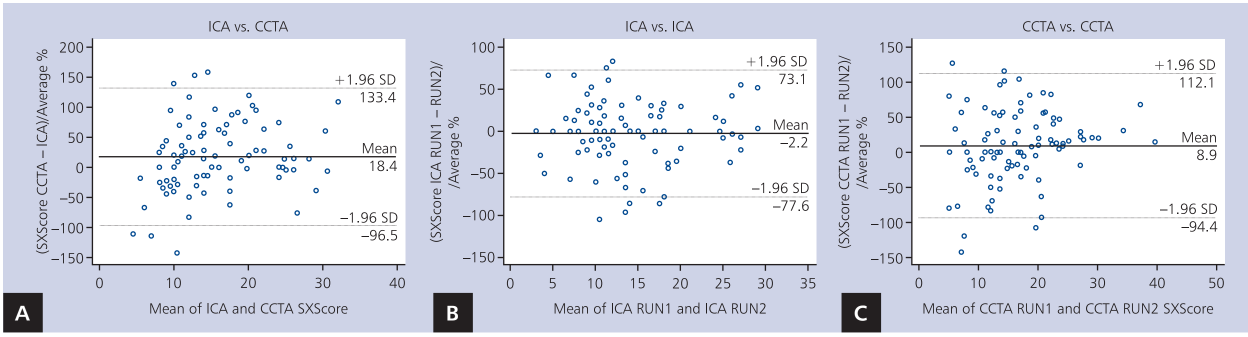

Figure 2. Bland-Altman plot for comparison of: **A**. Coronary computed tomography angiography (CCTA) and invasive coronary angiography (ICA); **B**. ICA RUN1 and RUN2; **C**. CCTA RUN1 and RUN2 in calculation of total SYNTAX score

reproducibility between ICA RUN1 and RUN2 (mean –2.2), followed by CCTA RUN1 and CCTA RUN2 (mean 8.9) and ICA and CCTA (mean 18.4) (Fig. 2).

To determine if SXScore calculation with CCTA would change the patients' qualification into tertiles validated in the SYNTAX trial (< 23; 23–32 and > 32 points calculated by ICA) [2] kappa values were calculated. Similar reproducibility in terms of patients' assignment into tertiles was observed for ICA vs. CCTA (k = 0.4), CCTA RUN1 and RUN2 (k = 0.51) and ICA RUN1 and RUN 2 (k = 0.47). For example, from 78 patients qualified to the lowest SXScore tertile (< 23 points) based on ICA, 16 (20.5%) patients were classified to the intermediate tertile (23–32 points) and two patients to the highest tertile (> 32 points) after calculation of SXScore based on CCTA, which would have important clinical implications. Due to gte low mean SXScore in the analysed cohort, additional total SXScore quantification into quintiles was made (< 10; 11–20; 21–30; 31–40, and > 40 points calculated by ICA). The inter-modality reproducibility in patients' assignment into quintiles (k = 0.17) was lower in comparison to intra-modality reproducibility of CCTA (k = 0.34) and ICA (k = 0.43) (Fig. 3).

To determine the variables of SXScore that were best and worst reproduced by CCTA, a subanalysis was performed. Variables selected for analysis were: total number of lesions, number of bifurcation lesions, long lesions (> 20 mm), aorto-ostial lesions, heavily calcified lesions, and chronically occluded vessels (CTOs). The best reproduced variable by CCTA in comparison to ICA was the number of CTOs (k = 0.64) and number of long lesions (k = 0.41), while poor reproducibility was observed for the number of bifurcations (k = 0.12) and ostial lesions (k = 0.03) (Fig. 3).

DISCUSSION

The number of patients who undergo CCTA before ICA and even instead of ICA is continuously growing. This is apparently because of improvements in CT-scanner construction and the growing experience of medical staff in interpreting images, which results in good reproducibility in detection of coronary lesions [14, 15]. Good accessibility and low-invasiveness encourage physicians to precede invasive procedures in cases of stable CAD and sometimes of acute chest pain with CCTA.

Assuming that the calculation of SXScore may be performed reliably using CCTA alone, the decision-making pro-

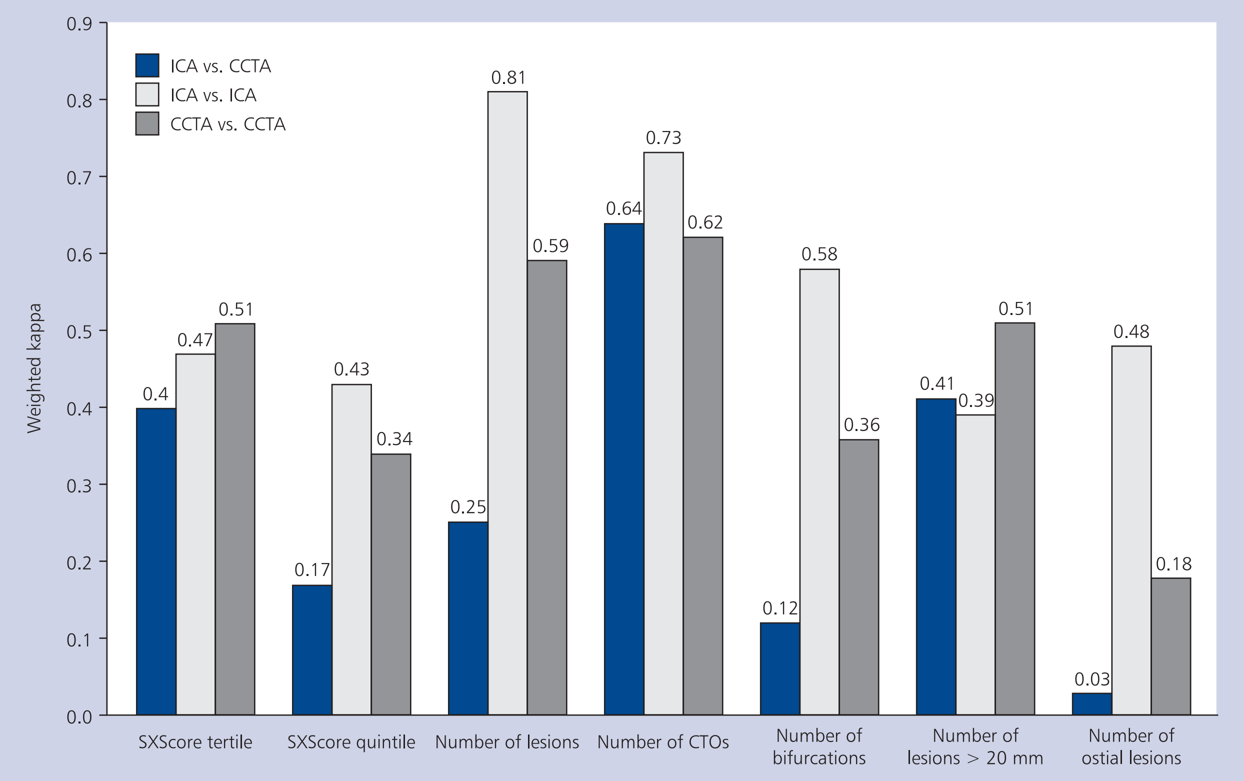

Figure 3. Inter- and intra-modality reproducibility for coronary computed tomography angiography and invasive coronary angiography for SYNTAX score (SXScore) tertiles and selected parameters of the SYNTAX score; ICA — invasive coronary angiography; CCTA — coronary computed tomography angiography; CTO — chronically occluded vessels

cess in patients with complex CAD would be faster. Obtaining information about SXScore before invasive diagnosis would give useful information on long-term risk stratification [3–5, 16] and therefore possibly reduce the number of required invasive procedures. In selected cases with high SXScore and convenient anatomy the decision to perform CABG might even be made without ICA.

To our knowledge, direct comparison of CCTA and ICA in the calculation of the SXScore was already described in two papers [9, 10]. The results of those studies were not concordant.

Popadopoulou et al. [9] calculated SXScores for 80 patients, only 45% of whom had two- or three-vessel CAD. Median SXScore for ICA and CCTA was 10.5 and 13.0, respectively, and there was significant correlation (Spearman's R = 0.73) between calculated results. Very good reproducibility in terms of patient classification into tertiles was found (k = 0.8); however, the tertiles were different form the standard thresholds used in the SYNTAX trial.

In the second study of Kerner et al. [10] 104 patients were analysed, of whom 38 (36.5%) had one-vessel disease. Here the median SXScore calculated in CCTA was lower than in ICA (10.3 vs. 14.2) and significantly underestimated the complexity of CAD. CCTA identified fewer lesions per patient (1.7 vs. 2.2, $p < 0.001$). Reproducibility of CCTA in comparison to ICA was only fair (k = 0.33). The intra-modality reproducibility for total SXScore was moderate in CCTA (k = 0.51) and very good in ICA (k = 0.84).

To our study only patients with multivessel or LM-involved CAD were included, to allow comparability with the SYNTAX trial population. Also, standard SXScore tertiles (< 23; 23–32, > 32 points) were used to compare reproducibility; however, the median ICA SXScore in our study was low (11.5; IQR 10.2–14.0). In our setting, in contrast to the results of Kerner et al. [10], CCTA significantly overestimated total SXScore. However, we confirmed the conclusion of Kerner et al. [10] that performance of CCTA is good for recognising CTOs and is low for bifurcations. We found higher reproducibility in long lesions (> 20 mm; k = 0.41 vs. k = 0.12 by Kerner et al. [10]).

However, reproducibility of SXScore was only moderate (k = 0.4) and lower in comparison to intra-modality reproducibility for ICA and CCTA (k = 0.63 and k = 0.53, respectively), the differences were reduced when patients' allocation into SXScore tertiles was analysed (k = 0.4; 0.47 and 0.51), respectively, for CCTA vs. ICA, ICA vs. ICA, and CCTA vs. CCTA, which is consistent with the results of Garg et al. [12], who showed that SXScore itself has only moderate inter-observer reproducibility.

In our study CCTA had good reliability in detection of significant lesions, since there was no statistical difference in the mean ($p = 0.65$) and median ($p = 0.56$) number of lesions per patient. The main source of difference in the total number of lesions detected in CCTA in comparison to ICA (280 vs. 287) was underdetection of lesions in the circumflex (63 vs. 80, $p = 0.04$ for median number of lesions per patient), while differences in the number of lesions in LAD/intermediate branch/LM and right coronary artery were not significant. We found a substantial difference in the assessment of left coronary artery dominance between CCTA and ICA (27 vs. 18, $p = 0.02$). Since the performance of CCTA in patients' allocation to I and II SXScore tertile was acceptable, the divergence of results in patients with the highest score (> 32) was inacceptable ($k = -0.04$). One possible reason is the low number of patients (only three as found by ICA).

The very low number of patients with high SYNTAX score is probably the main limitation of the study. Therefore, any reasoning concerning this particular subgroup of patients should be very careful.

CONCLUSIONS

The results of our study, which compared the CCTA-derived SXScore with SXScore derived from ICA, show moderate inter-modality agreement between CCTA and ICA for SXSscore calculation. However, the observed agreement is only slightly worse than intra-observer agreement for angiographic SXScore evaluation. Most of the observed variability can be assigned to the characteristic of the SXScore itself, not to the choice of imaging method. Overall, the use of CCTA to assess the SXScore should be cautious.

Conflict of interest: *none declared*

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Ocena SYNTAX score na podstawie tomografii komputerowej tętnic wieńcowych

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Streszczenie

Wstęp: Wskazania do stosowania tomografii komputerowej (CT) tętnic wieńcowych systematycznie się rozszerzają, coraz częściej badanie to stanowi substytut klasycznej koronarografii.

Cel: Niniejsza praca ma na celu ocenę użyteczności CT tętnic wieńcowych do obliczania wyniku w skali SYNTAX score (SXScore) w porównaniu z wynikiem obliczonym na podstawie koronarografii.

Metody: Dziewięćdziesięcioro kolejnych pacjentów z wielonaczyniową chorobą wieńcową lub z zajęciem pnia lewej tętnicy wieńcowej, rozpoznanymi na podstawie koronarografii, u których dostępne było wykonane uprzednio badanie CT tętnic wieńcowych, zostało włączonych do analizy *post-hoc*. Najpierw wynik w skali SXScore został obliczony 2-krotnie w 10-tygodniowym odstępnie czasowym przez 2 lekarzy doświadczonych w ocenie koronarografii. Następnie 2-krotnie w ten sam sposób obliczono SXScore na podstawie dostępnych obrazów z CT tętnic wieńcowych. Zastosowano statystyczną metodę kappa dla oceny powtarzalności wyników w skali SXScore dla każdej z metod obrazowania oraz pomiędzy obiema metodami.

Wyniki: Dziewięćdziesięcioro pacjentów, w wieku średnio 63,8 ± 8,9 roku, w tym 60% osób płci męskiej, 64,4% z dwunaczyniową chorobą wieńcową i 35,6% z trójnaczyniową chorobą wieńcową lub zajęciem pnia lewej tętnicy wieńcowej, spełniło kryteria włączenia do analizy. W koronarografii zidentyfikowano 287 zwężeń, w CT tętnic wieńcowych — 280 zwężeń ($p = 0{,}56$). Mediana wyniku SXScore wyniosła 11,5 (10,2–14,0) wg obliczeń na podstawie koronarografii i 16,0 (14,3–19,4) wg obliczeń na podstawie CT tętnic wieńcowych ($p < 0{,}001$). Korelacja otrzymanych wyników była umiarkowana ($R = 0{,}38$). Powtarzalność wyników obliczeń SXScore w zakresie standardowych tercyli (< 23; 23–32 i > 32 punktów) między koronarografią i CT tętnic wieńcowych była umiarkowana (kappa = 0,40). Powtarzalność wyników wewnątrz każdej z metod wyniosła 0,47 i 0,51, odpowiednio dla koronarografii i CT tętnic wieńcowych.

Wnioski: Korelacja wyników obliczonych na podstawie CT tętnic wieńcowych i koronarografii w skali SXScore jest umiarkowana, jednak jedynie nieznacznie gorsza niż powtarzalność kolejnych wyników uzyskiwanych przez jednego obserwatora na podstawie koronarografii. Za wykazaną w badaniu zmienność odpowiada przede wszystkim sama charakterystyka skali SYNTAX, nie zaś wybrana metoda obrazowania. Mimo to wydaje się, że należy zachować ostrożność podczas szacowania wyniku w skali SXScore na podstawie CT tętnic wieńcowych.

Słowa kluczowe: tomografia komputerowa tętnic wieńcowych, SYNTAX score, powtarzalność, choroba wieńcowa

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