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LETTER TO THE EDI

Plaque Composit Syntax Score

Combining Angiograph Lipid Burden in Coronary Artery Dise

Angiographic-based Syntax score (SxScore) enables risk stratification of patients in predicting clinical outcomes, according to the complexity of their coronary artery disease (1). However, the luminogram is inherently limited in the identification of coronary plaque vulnerability. On the other hand, evaluation of plaque composition by intracoronary imaging techniques such as intravascular ultrasound, optical coherence tomography and near-infrared spectroscopy (NIRS) may help identify high-risk plaques and estimate risk of periprocedural myocardial necrosis and future adverse events (2). The combined use of angiographic and compositional data on coronary lesions may therefore better assess coronary artery disease and improve risk stratification. We sought to explore the relationship between lipid plaque composition by NIRS and the angiographic severity of coronary artery disease.

From April 2009 until January 2011, NIRS imaging on a nonintervened coronary vessel was performed in 208 consecutive patients. The inclusion/exclusion criteria have been previously published (3). Six patients were excluded from the present analysis due to previous coronary artery bypass graft, which does not allow SxScore quantification. The Lipid Core Burden Index (LCBI) score, summarizing the amount of lipid core plaques in the entire scanned region on

Table 1. Clinical Baseline Characteristics

	Syntax Score ≤5 (n = 67)	Syntax Score >5 to ≤11 (n = 69)	Syntax Score >11 (n = 66)	p Value
Baseline characteristics				
Age, yrs	63.2 ± 10.7	62.3 ± 11.3	64.4 ± 10.1	0.535
Male	45 (67.1)	49 (71.0)	50 (75.8)	0.819
Body mass index, kg/m^2	27.7 ± 4.7	27.7 ± 4.0	27.8 ± 4.7	0.903
Risk factors				
Current smoking	17 (25.3)	17 (24.6)	14 (21.2)	0.530
Hypertension	37 (55.2)	34 (49.3)	40 (60.6)	0.338
Hypercholesterolemia	32 (47.7)	39 (56.5)	39 (59.1)	0.689
Diabetes	7 (10.4)	12 (17.4)	20 (30.3)	0.022
Family history of coronary artery disease	38 (56.7)	40 (58.0)	39 (59.1)	0.743
Cardiac history				
Prior myocardial infarction	24 (35.8)	21 (30.4)	27 (40.9)	0.411
Prior PCI	32 (47.7)	24 (34.8)	19 (28.8)	0.023
Indication to coronary angiography				0.513
Stable angina	36 (53.7)	33 (47.8)	36 (54.5)	
Acute coronary syndromes	31 (46.2)	36 (52.2)	30 (54.5)	
Number of vessels diseased				<0.001
1	40 (59.7)	47 (68.1)	21 (31.8)	
2	8 (11.9)	17 (24.6)	30 (45.4)	
3	3 (4.4)	2 (2.9)	15 (22.7)	
Vessel studied by NIRS				0.203
LAD	29 (43.5)	26 (37.7)	17 (25.8)	
LCX	18 (27.4)	24 (34.8)	30 (45.5)	
RCA	20 (29.1)	19 (27.5)	19 (28.8)	
Medication				
Aspirin	64 (96.8)	67 (97.1)	65 (98.5)	0.805
Beta-blocker	48 (72.6)	51 (73.9)	55 (83.3)	0.285
ACE inhibitor/angiotensin II blockers	49 (74.1)	43 (62.3)	49 (74.2)	0.758
Statin	61 (92.0)	61 (88.4)	57 (86.4)	0.406

Values are mean ± SD or n (%).
ACE = angiotensin-converting enzyme; LAD = left anterior descending artery; LCX = left circumflex artery; NIRS = near-infrared spectroscopy; PCI = percutaneous coronary intervention; RCA = right coronary artery.

a 0-to-1,000 scale, was calculated by NIRS and stratified according to SxScore tertiles per patient. The SxScore was evaluated per vessel and per patient by core laboratory analysts (Cardialysis B.V., Rotterdam, the Netherlands), blinded to NIRS analysis, performed by another team of CoreLab analysts. All variables were stratified according to Syntax score tertiles per patient. Categorical variables were presented as counts and frequency (percentage). Continuous variables (median [interquartile range (IQR)]) were compared using Kruskal-Wallis test with Dunn correction for multiple comparisons between groups. Categorical data were compared using Fisher exact test or the Pearson chi-square test. A linear regression analysis was performed to adjust the relationship between LCBI and the overall Syntax score for age, sex, and traditional risk factors. A 2-sided p value of <0.05 indicated statistical significance. Statistical analyses were performed using SPSS software (version 17.0, SPSS Inc., Chicago, Illinois).

Patients in the highest SxScore tertile had higher incidence of diabetes ($p = 0.022$), more frequently had 3-vessel disease ($p < 0.001$), and had lower rates of previous percutaneous coronary intervention ($p = 0.023$). No differences were observed for other clinical or angiographic variables (Table 1). Overall, the median SxScore was 8 (IQR: 4 to 14); the left anterior descending artery (LAD) contributed to the median SxScore the most (LAD: 6 [IQR: 0 to 9] vs. left circumflex artery: 0 [IQR: 0 to 3] vs. right coronary artery: 0 [IQR: 0 to 3], $p < 0.001$). The SxScore of the vessel analyzed by NIRS was 0 (IQR: 0 to 4). Overall, the median LCBI was 43 (IQR: 16 to 83) and was not different between the various coronary arteries analyzed (LAD: 36 [IQR: 12 to 67] vs. left circumflex artery: 48 [IQR: 25 to 83] vs. right coronary artery: 45 [IQR: 15 to 103], $p = 0.247$). Within the vessel imaged by NIRS, there was no relationship between LCBI and SxScore (Spearman rho = 0.004, $p = 0.954$), but there was a modest relationship between LCBI and the overall SxScore (Spearman rho = 0.330, $p < 0.001$). Upon linear regression analysis, LCBI and age were the only independent predictors of the overall SxScore ($p = 0.004$ and $p = 0.045$, respectively). The LCBI was significantly different distributed across patients categorized by SxScore tertiles ($p = 0.009$) (Fig. 1). Patients with the highest SxScore, in particular, exhibited the highest LCBI, as compared to patients with the lowest SxScore ($p < 0.001$). The LCBI was also numerically higher in presence of 3-vessel disease, although its distribution was not statistically different (no disease: median: 17 [IQR: 7 to 48]; 1-vessel disease: median: 34 [IQR: 14 to 78]; 2-vessel disease: median 54 [IQR: 21 to 111]; 3-vessel disease: median: 63 [IQR: 44 to 80], $p = 0.275$).

Attempts have been made to combine SxScore with clinical or functional data to overcome limitations of angiography and to improve its prognostic value. In particular, fractional flow reserve has been incorporated into SxScore to form the "functional SxScore." This score exhibited better patient risk stratification than the conventional angiographic-based SxScore (4). Similarly, the carotid intima-media thickness has demonstrated an incremental predictive value for coronary SxScore (5). However, all such combinations and permutations do not evaluate the presence of high-risk lipid-rich plaques, which are prone to rapid progression and rupture with coronary events (4). Our analysis demonstrated that the presence of lipid-rich plaques in 1 coronary artery parallels the increase of the global angiographic complexity of the disease in the 3 major epicardial vessels. It is noteworthy that the LCBI was analyzed in only 1 non-culprit coronary vessel with a very low SxScore. Within this imaged vessel, there was no relationship between the LCBI and the SxScore. This finding is not surprising given the limitations of angiography to detect high-risk plaques. NIRS may overcome these limitations, identifying high-risk plaques not discernible in patients with low angiographic complexity. We believe that the LCBI would be higher in angiographically more significant complex coronary artery disease, as a positive correlation between plaque burden and its lipid content has been previously demonstrated and that angiography has low rate of false-positive results in identifying coronary plaques (4).

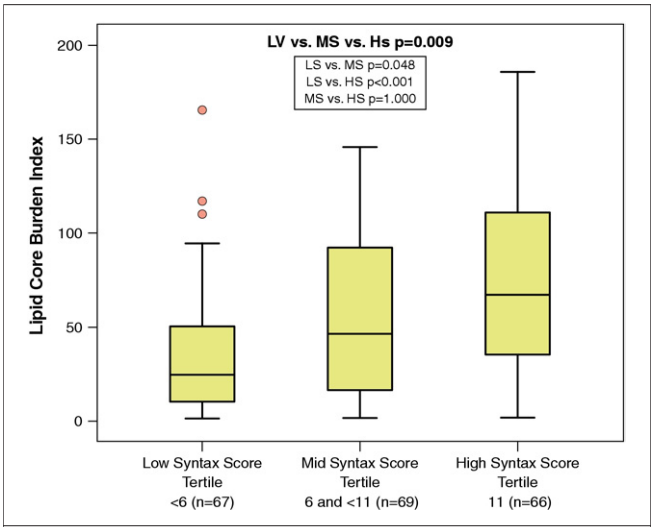

Figure 1. LCBI Is Significantly Different Distributed Across the 3 SxScore Tertiles

In particular, patients in the highest Syntax score (SxScore) tertile have higher Lipid Core Burden Index (LCBI) compared with patients in the low SxScore tertile. LS = low Syntax score tertile; MS = mid Syntax score tertile; HS = high Syntax score tertile.

These findings support the development of a compositional Syntax score by combining plaque lipid burden and angiographic measurements for better prediction of adverse coronary events and decision-making process during revascularization.

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