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Incremental value of preprocedural coronary computed tomographic angiography to classical coronary angiography for prediction of PCI complexity in left main stenosis

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ABSTRACT

Introduction: The aim of our study was to assess the incremental value of Coronary Computed Tomography Angiography (CCTA) added to classical coronary angiography, for complex characterization of coronary lesions and prediction of procedural complexity in patients with significant left main (LM) stenoses. Material and Methods: Thirty-six patients with LM disease were enrolled in the study, and each subject underwent CCTA followed by coronary angiography and percutaneous revascularization. Results: Logistic regression analysis indicated a good correlation between the angiographic-calculated and the CCTA-derived Syntax scores for the whole group ($r = 0.87$, $p < 0.0001$) and for the high risk subgroup ($r = 0.86$, $p < 0.0001$), but not for the low and intermediate risk ($r = 0.38$, $p = 0.21$ and $r = 0.62$, $p = 0.07$ respectively). In cases which required complex PCI procedures, both angiographic and CCTA Syntax score were significantly higher than those who did not require complex revascularization procedures (24.5 +/− 11.5 vs 32.2 +/− 14.6, $p = 0.09$ for Angio Syntax, 35.3 +/− 11.5 vs 25.2 +/− 11.3, $p = 0.01$ for CCTA). In the same time, Ca scoring was significantly higher and plaque volumes were significantly larger in cases requiring complex revascularization procedures (299.5 +/− 359.6 vs 917.3 +/− 495.4, $p = 0.04$ for calcium score, 79.7 +/− 28.5 vs 108.7 +/− 25.3 mm^3, $p = 0.002$ for plaque volumes). Multivariate analysis identified the following CCTA parameters as significant predictors of increased risk for complex intervention in LM lesions: plaque volume (OR 8.00, $p = 0.008$), Ca scoring (OR 6.37, $p = 0.02$) and CCTA Syntax score (OR 6.87, $p = 0.01$). Conclusions: CCTA derived parameters provide incremental information to classical coronary angiography for preoperative assessment of lesion severity in complex left main stenosis. CCTA derived Syntax score significantly correlates with the classical Coronary Angiography Syntax score and identifies the subgroup of patients who will be more exposed to procedural complications during the revascularization interventions.

Keywords: Left Main; Syntax Score; Coronary Computed Tomographic Angiography

1. INTRODUCTION

The coronary angiography has become nowadays the gold standard technique for diagnosis of coronary artery stenoses, including those located in the left main (LM) coronary artery.

A positive coronary angiography showing severe narrowing of the LM indicates an urgent need for revascularization, which could improve the tolerance to ischaemic events in other coronary territories and reduce the progression of the associated ventricular dysfunction [1,2]. Percutaneous coronary revascularization has been recently recognized to represent a viable therapeutic alternative in patients with severe left main (LM) stenosis. Despite of the well-known high risk associated with complex interventional procedures in unprotected LM diseases, percutaneous interventions are increasingly used in the treatment of complex LM lesions [3].

Many studies attempted to reveal the role of interventional revascularization in such cases, as an alternative to the traditional coronary artery bypass grafting. The SYNTAX trial (The Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery) in-

cluded 3.075 patients with left main coronary disease or three-vessel disease or both, who were randomized to surgical or percutaneous revascularization [4,5]. The results of the trial revealed the role of percutaneous revascularization in several subsets of patients, especially those with isolated left main disease or left main disease associated with one vessel disease, and led to development of the Syntax score.

Syntax trial led to development of the Syntax score, a complex angiographic score based on characterization of coronary lesions according to specific angiographic parameters, such as tortuosity, bifurcation, the presence of a total occlusion or intracoronary thrombus, calcification, the dominance, type and number of lesions [6,7].

A Syntax score below 22 classifies the lesion in the low-risk category, a score between 22 and 32 is associated with medium risk, while a score above 33 indicates a high-risk lesion.

This score system became widely accepted in clinical practice immediately after the Syntax trial and nowadays many cases of left main disease are referred for surgical or interventional treatment based on the calculated Syntax score, the general recommendations being in favor of percutaneous revascularization in cases of low or medium Syntax scores and in favor of surgery in cases with high Syntax scores [8,9].

However, calculation of Syntax score relies only on the information provided by coronary angiography. Despite the recent widespread use of Coronary Computed Tomographyc Angiography (CCTA), key information provided by this technique such as calcium scoring or plaque volumes is rarely taken into consideration when establishing the indication for percutaneous coronary intervention (PCI) in LM diseases [10]. However, CCTA provides incremental value to classical coronary angiography with regard to complex characterization of coronary lesions. As CCTA offers the unique opportunity for assessment of atheromatous plaque burden and calcium content, together with a three-dimensional representation of the lesion, it could predict a more complex interventional procedure in cases with high calcium burden, large plaques or difficult anatomy.

The aim of our study was to assess the incremental value of CCTA on the top of information provided by the classical coronary angiography, for complex characterization of left main stenoses and prediction of procedural complexity in patients with significant LM stenoses.

2. METHODS

2.1. Study Population

This was a single center prospective non-randomized study to evaluate the incremental value of the information provided by CCTA on the top of those obtained by classical coronary angiography in complex characterization of coronary lesions in patients with significant left main disease.

Thirty-six patients with LM disease at the clinical presentation were enrolled in the study, and each subject underwent 64 multi-slice CT followed by coronary angiography and percutaneous revascularization. All patients gave written informed consent, and the study protocol was approved by the ethics committee of the center where the study was conducted.

The inclusion criteria were age >18 years, documented significant (>50%) stenosis of the LM coronary artery and willingness to participate in the study. Patients with contraindications for the repeated administration of contrast agents were excluded from the study.

2.2. CCTA Analysis

All CT acquisitions were made using multi-slice 64 Somatom Sensation CT (Siemens, Germany) with a 64 × 0.5 mm detector collimation. During an inspiratory breath-hold, 60 ml of an iodinated contrast agent (Iopamidol, 370 mg I/ml, Bayer Healthcare, Germany) was infused at a speed of 4.0 ml/sec followed by 20 ml at 2.0 ml/sec. All examinations were preceded by the administration of a short-acting betablocker to achieve the desired heart rate and were conducted only after achieving a stable heart rate below 60 beats/min. All acquired images were transferred to a workstation (Siemens, Germany) for data processing, measurements and interpretation

The following information provided by CCTA have been used for assessing the severity of the lesions and to calculate the CCTA-Syntax score: degree of calcification in the left main lesion, global calcium burden expressed by calcium score, coronary stenosis severity (in the left main and in the rest of the coronary tree), length and diameter of the left main, involvement of the origin of left anterior descending artery and circumflex artery, anatomic distribution (type of dominance), extension of calcification at the origin of the main arteries, involvement of the ostium of the left main, and the plaque volume. All these information have been evaluated by Angio CT multislice 64 using multiplanar 3D reconstructions.

2.3. Coronary Angiography Analysis

Coronary angiography analysis was performed using an Artis Zee Floor Angiograph (Siemens, Germany), using repeated injections of 3 - 5 ml contrast material in the left main coronary lumen and image aquisitions in different incidences, with different angles and tiltings of the X-ray tube.

A significant left main stenosis was defined as a >50%

narrowing of the LM lumen at coronaty angiography in at least one incidence.

Angiographic assessment included the following parameters which served for calculation of Syntax scores, according to the algorhythm available on the web (www.syntaxscore.com): coronary dominance, number and location of lesions, presence of a total occlusion in one coronary artery, bifurcation or aorto-ostial lesion, severe tortuosity, lesion length, presence of calcification or thrombus. All these parameters were assessed for every individual lesion, the final Syntax score being represented by the sum of individual scores of all coronary lesions.

According to their Syntax score, patients were divided into three groups: low risk (Syntax score <22)—12 patients; intermediate risk (Syntax score between 23 and 32)—8 patients, and high risk (Syntax score above 33)—16 patients.

2.4. Percutaneous Coronary Intervention

All PCI procedures were performed according to standard practice and the complexity of PCI was retrospectively assessed immediately after the intervention. A complex PCI was defined when each of the following parameters were recorded during the procedure: use of kissing balloon, use of high-pressure balloons or postdilatation, radiation time >25 min or usage of >400 ml contrast media. Complex PCI was required for 20 patients, while 16 patients underwent non-complex PCI.

The study objectives were as follows:

1) To demonstrate the correlation between CCTA—derived Syntax score and coronary angiography-derived Syntax score in significant LM lesions, in the global population of the study and in the subsets of patients with low, medium and high risk lesions.

2) To demonstrate the correlation between Ca scoring determined by CCTA and Syntax score determined by CCTA and Coronary Angiography.

3) To identify the significant CCTA and angiographic-derived predictors of complex PCI procedures in significant LM stenoses.

2.5. Statistical Analysis

All statistical analyses were performed using the Graph Pad InStat software, version 3.1, (GraphPad software Inc., San Diego, California, MA, USA). Categorical variables are expressed as percentages. Fisher's exact test was used for comparing the categorical variables. Continuous values are expressed as the mean and standard deviation, and statistical significance was determined using the Mann-Whitney test. Multivariate logistic regression was used to assess the predictors for need of complex PCI intervention. Statistical significance was considered for a p value <0.05, and all p values were 2-sided.

3. RESULTS

Baseline characteristics of the 36 patients with LM diseased included in the study are listed in **Table 1**. We recorded the predominance of gender male (67.4%) and a significant presence of risk factors: hypertension in 58.3%, hyperlipidemia in 41.6%, diabetes in 33.33% and smoking in 36.1% of cases. CCTA characteristics at baseline indicated an average calcium score of 784.9 +/− 77.6 and a mean LM plaque burden of 96.6 +/− 30.0 mm^3.

3.1. Correlation between CCTA—Derived Syntax Score and Coronary Angiography-Derived Syntax Score in Significant LM Lesions

There were no significant differences between the mean Syntax score calculated by angiography and those calculated by CCTA.

Angio Syntax score was slightly lower than the one calculated by CCTA in the global population of the study (29.1 +/− 13.9 versus 31.6 +/− 12.6, p = 0.4), however this difference was not statistically significant. We per-

Table 1. Baseline characteristics of study population (n = 36).

Characteristic	Values n (%)
Age, years	62.9 +/− 9.5
	95% CI 59.7 - 69.2
Gender, male	29 (67.4)
Left Ventricular Ejection Fraction	49.2 +/− 7.2
	95% CI 46.7 - 51.7
Cardiovascular risk factors	
Hypertension	21 (58.3)
Hyperlipidemia	15 (41.6)
Diabetes	12 (33.3)
Smoker*	13 (36.1)
Obesity (BMS > 25 km/m^2)	11 (30.5)
CCTA analysis	
Calcium scoring	784.9 +/− 77.6
	95% CI 627.1 - 942.7
LM plaque burden	224.3 +/− 45.0
	95% CI 132.8 - 315.8

*Past or present; Data are represented as mean+/− standard deviation or as number (percentage).

formed a subgroup analysis of Angio versus CCTA Syntax score in the subgroups with low, intermediate and high risk. We found that in the low risk subgroup coronary angiography seems to underestimate the severity of the lesions as compared to CCTA (Angio Syntax score 13.0 +/− 4.8 compared with CCTA Syntax score 18.9 +/− 7.6, p = 0.03). However, we did not find any statistically significant difference in Angio versus CCTA Syntax scores for the intermediate risk (28.2 +/− 4.1 vs 30.7 +/− 8.1, p = 0.4) and high risk subgroups (42.4 +/− 5.9 vs 43 +/− 8.2, p = 0.8) **Table 2**.

Similarly with the observation recorded in the global population of the study, in all the subgroups the Coronary Angiography Syntax score seems to underestimate the severity of coronary lesions as compared with CCTA Syntax score.

Similarly, logistic regression analysis indicated a good correlation between the Angiography-derived and the CCTA-derived Syntax scores for the whole group (r = 0.87, p < 0.0001) and for the high risk subgrouo (r = 0.86, p < 0.0001), but not for the low and intermediate risk (r = 0.38, p = 0.21 and r = 0.62, p = 0.07 respectively) **Figure 1**.

3.2. Correlation between Ca Scoring Determined by CCTA and Syntax Score Determined by CCTA and Coronary Angiography

Calcium score is a CCTA-derived parameter useful for prediction of coronary lesions severity. We found a good correlation between the calcium score determined by CCTA and the Syntax scores, either as determined by Coronary Angiography (r = 0.72, p < 0.0001) or by CCTA (r = 0.69, p < 0.0001) **Figure 2**.

CCTA and angiographic-derived predictors of complex PCI procedures in significant LM stenoses.

Another objective of the study was to identify CCTA and coronary angiography-derived predictors of complex PCI procedures. In cases which required complex PCI procedures, both angiographic and CCTA Syntax score were significantly higher than in those who did not require complex revascularization procedures (24.5 +/− 11.5 vs 32.2 +/− 14.6, p = 0.09 for Angio Syntax, 35.3 +/− 11.5 vs 25.2 +/− 11.3, p = 0.01 for CCTA Syntax). In the same time, Ca scoring was significantly higher and plaque volumes significantly larger in cases requiring complex revascularization procedures (299.5 +/− 359.6 vs 917.3 +/− 495.4, p = 0.04 for calcium score, 79.7 +/− 28.5 vs 108.7 +/− 25.3 mm^3, p = 0.002 for plaque volumes) (**Figure 3**).

Figure 4 is an exemplification of a significant LM stenosis with high calcium content and a large volume atheromatous plaque in the LM, visualized by 3D CCTA (A), multiplanar reconstruction CCTA (B) and angiographic aspect before (C) and after PCI (D), the lesion appearing much more severe in CCTA than in conventional angiography.

On the other hand, clinical parameters such as ejection fraction did not show any statistically significant difference between the subgroup of patients necessitating complex PCI procedures and those who did not **Table 3**.

Multivariate analysis identified the following CCTA-derived parameters as significant predictors of increased risk for complex intervention in LM lesions: plaque volume (Odds Ratio 8.00, p = 0.008), Ca scoring (Odds Ratio 6.37, p = 0.02) and CCTA Syntax score (Odds Ratio 6.87, p = 0.01). Angiography-derived Syntax score

Table 2. Low CT-attenuation plaques and IVUS-derived markers of vulnerability in culprit lesions.

	Angiographic Syntax score	CCTA Syntax score	p value
Global population of the study			**0.4**
Mean +/− SD	29.1 +/− 13.9	31.6 +/− 12.6	
95% *confidence interval*	24.4 - 33.8	27.3 - 35.9	
Low risk group (Syntax score < 22), n = 12			**0.03**
Mean +/− SD	13.0 +/− 4.8	18.9 +/− 7.6	
95% *confidence interval*	9.9 - 16.1	14.1 - 23.7	
Medium risk group (Syntax score 23 - 32), n = 8			**0.4**
Mean +/− SD	28.2 +/− 4.1	30.7 +/− 8.1	
95% *confidence interval*	25.1 - 31.4	24.6 - 37.0	
High risk group (Syntax score > 33), n = 16			**0.8**
Mean +/− SD	42.4 +/− 5.9	43 +/− 8.2	
95% *confidence interval*	39.2 - 45.7	38.5 - 47.5	

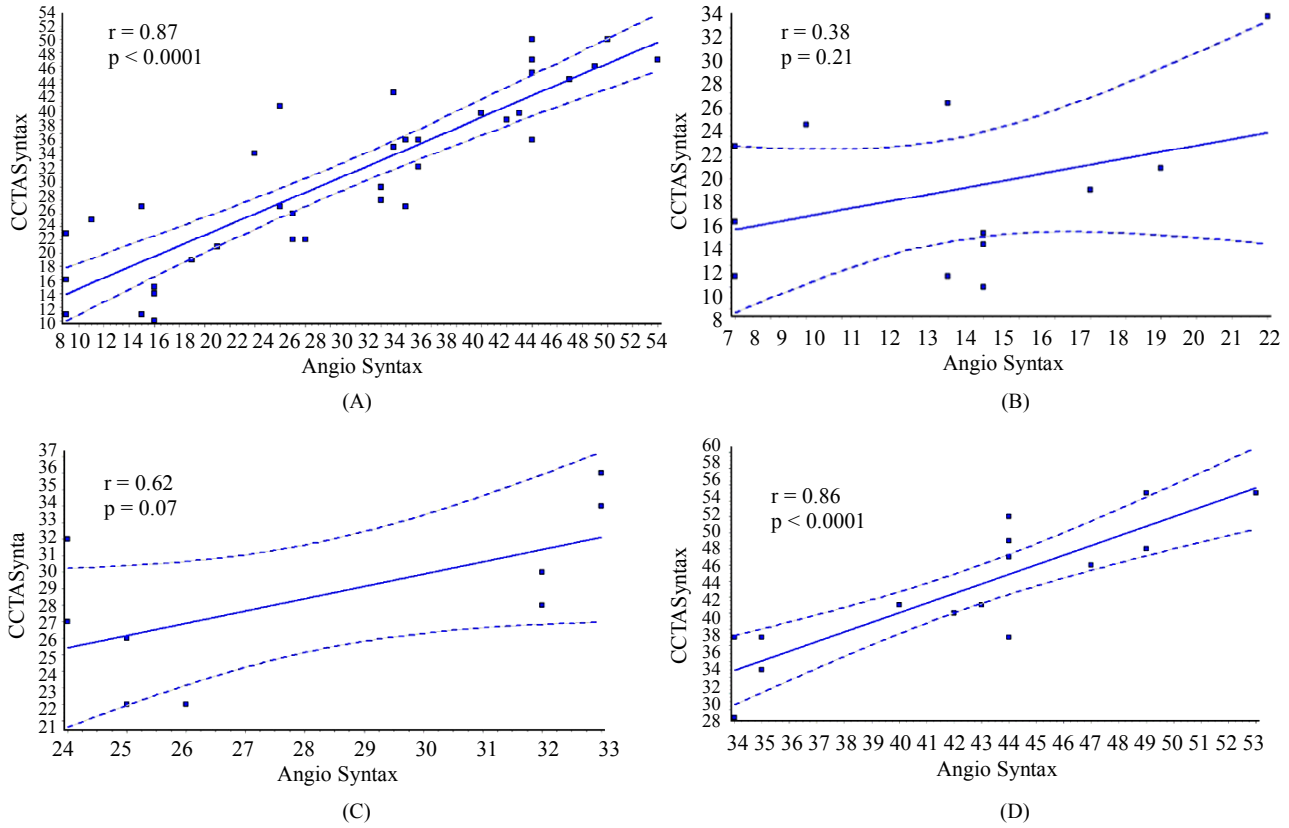

Figure 1. Correlation between angiography-derived and CCTA-derived Syntax scores in the global population (A) and in the low risk (B), intermediate risk (C) and high risk (D) lesions. (A) Global population of the study; (B) Low risk; (C) Intermediate risk; (D) High risk.

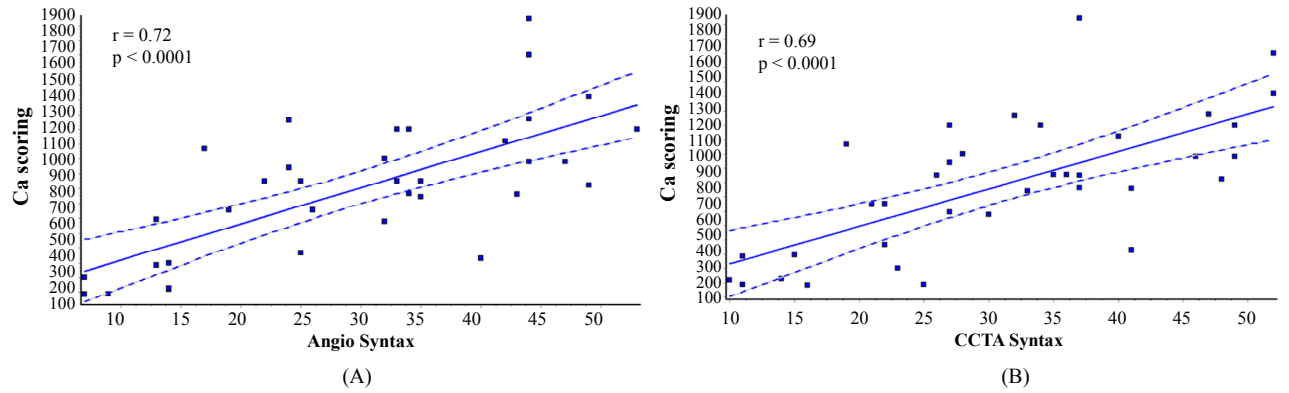

Figure 2. Correlation between calcium score determined by CCTA and Angio-derived (A) or CCTE-derived (B) Syntax score.

was also associated with a high risk for complex LM intervention, however with a lower statistical significance than the CCTA-derived parameters (Odds Ratio 4.47, p = 0.04) **Table 4**.

The SYNTAX trial results suggest that CABG remains the standard of care for patients with complex disease as expressed by a high Syntax score; however, PCI could represent a superior alternative for revascularization in certain subgroup of patients, mainly those with less complex disease and lower Syntax scores [1,11].

Incorporating the CCTA information into the Syntax algorythm could provide a more complex set of information, thus serving for selection of a more appropriate therapeutic strategy in complex LM cases. The main advantage of the CCTA against standard coronary angiography is the ability to visualise exactly the extent, distribution and severity of calcifications at the level of the lesion, which is of particular importance at the level of the left main [12]. In the same time, the CCTA technique provides the unique opportunity of plaque quan-

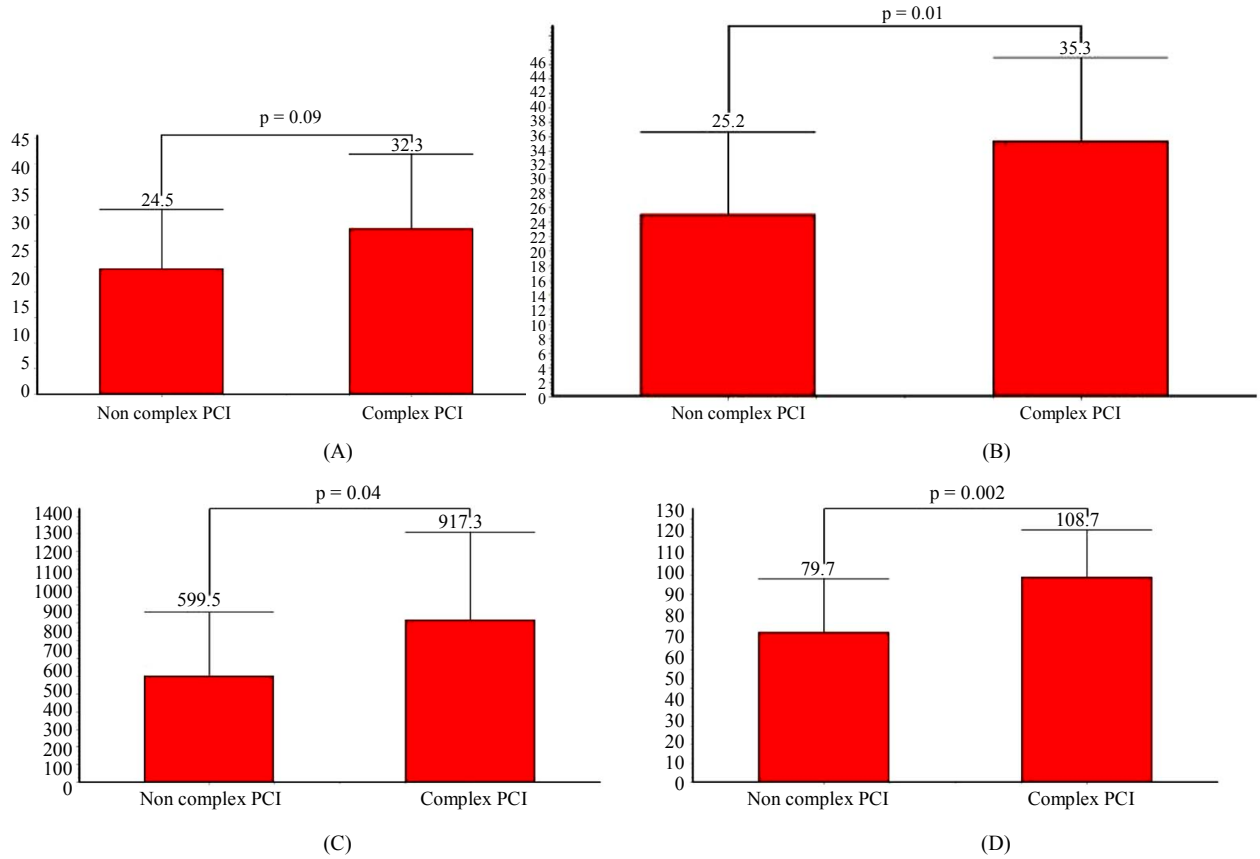

Figure 3. Association between the need for complex PCI procedures and Angio Syntax score (A), CCTE Syntax score (B), CCTA Ca score (C) and Left Main plaque volume (D). (A) Angio Syntax; (B) CCTA Syntax; (C) CCTA Ca score; (D) LM Plaque volume (mm^3).

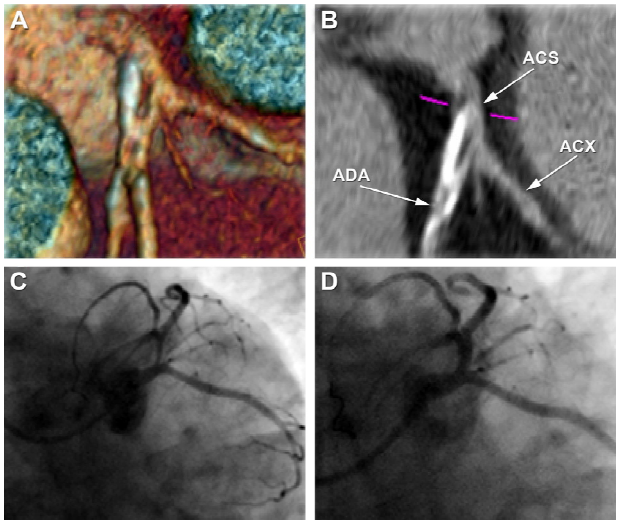

Figure 4. Significant LM stenosis with high calcium content and a large volume atheromatous plaque in the LM, visualized by 3D CCTA (A), multiplanar reconstruction CCTA (B). Angiographic aspect before (C) and after PCI (D), showing that the lesion appeares less severe in conventional angiography than in CCTA, due to the lack of appropriate calcium visualization by angiography. The severity of the lesion is underestimate by angiography.

tification, allowing the determination of plaque volume. LM plaques are usually large volume plaques which rupture and embolise frequently during the percutaneous revascularization procedure, therefore the preoperative assessment of plaque volume by CCTA and characteristics could help to prevent the procedure-related complications [13,14].

In this study we demonstrated that use of CCTA Syntax score may better stratify the patients with significant LM stenosis according to their risk than does the stratification based only on angiography-derived Syntax score. We found a good correlation between the angiography derived and CCTA-derived Syntax scores especially for cases with high Syntax scores. As in the rest of the cases angiography seems to underestimate the severity of the lesions, we can conclude that the incremental role of CCTA to coronary angiography is more obvious especially in high risk lesions. These are usually heavily calcified lesions, with high atheromatous burden, coronary calcification and plaque burden being exactly the parameters easily assessed by the CCTA [15].

This superior value of CCTA relies mainly in providing incremental information to coronary angiography

Table 3. Clinical, CCTA and angiographic parameters for prediction of intervention complexity in LM diseases.

	Non Complex PCI n = 20	Complex PCI N = 16	p value
Ejection Fraction			**0.6**
Mean +/− SD	50 +/− 7.9	48.6 +/− 7.2	
95% *confidence interval*	45.6 - 54.4	45.4 - 51.9	
Angio Syntax score			**0.09**
Mean +/− SD	24.5 +/− 11.5	32.3 +/− 14.6	
95% *confidence interval*	18.1 - 30.9	25.7 - 38.9	
CCTA Syntax score			**0.01**
Mean +/− SD	25.2 +/− 11.3	35.3 +/− 11.5	
95% *confidence interval*	18.9 - 31.5	30.1 - 40.5	
Ca scoring			**0.04**
Mean +/− SD	599.5 +/− 359.6	917.3 +/− 495.4	
95% *confidence interval*	400.4 - 798.7	691 - 1142.8	
LM plaque volume			**0.002**
Mean +/− SD	79.7 +/− 28.5	108.7 +/− 25.3	
95% *confidence interval*	63.9 - 95.5	97.2 - 120.2	

Table 4. Multivariate predictors of intervention complexity in patients with left main disease.

	Odds Ratio (95% CI)	p value
Smoker	0.55 (0.14 - 2.17)	0.5
Diabetes	1.36 (0.35 - 5.21)	0.74
Dyslipidemia	1.65 (0.43 - 6.31)	0.51
Left Ventricular Ejection Fraction	2.43 (0.62 - 9.47)	0.3
Angio Syntax score	4.47 (1.05 - 18.9)	0.04
CCTA Syntax score	6.87 (1.55 - 30.4)	0.01
Ca scoring	6.37 (1.42 - 28.61)	0.02
LM plaque volume	8.00 (1.68 - 37.9)	0.008

with regard to lesion characterization and complex 3D visualization of coronary plaques in the same time with plaque quantification and determination of calcium content within the coronary arteries [15,16].

In this study we found that the most significant predictors for complex procedures in LM stenoses were the CCTA derived parameters: Ca score, CCTA Syntax score and plaque volume, all of them having a prediction power superior to the conventional angiography-derived Syntax score. We found that patients with high calcium content in the coronary arteries, large volumes of LM coronary plaques or high Syntax scores by CCTA were more likely to necessitate a complex PCI procedure, either lasting longer than usual or necessitating complex techniques (bifurcation kissing, postdilatation, high pressure balloons, more contrast, longer X-ray exposure, etc.). This underlines the role of CCTA in providing complex information necessary for a complex preprocedural evaluation in LM lesions.

3.3. Study Limitations

The CT analysis was not able to distinguish between different low density components of coronary plaques, which are considered as markers of vulnerability—low density atheroma, necrotic core or thrombus. However, identifying a high burden with coronary plaque significantly associated with the need of complex revascularization procedure, irrespective of the differentiation between thrombus, necrotic core or very low density cholesterol-rich atheroma. A high calcium score could preclude a good quality CT image and this could be reflected in Syntax CCTA calculations. Finally, the number of patients included in the study is not extensive.

4. CONCLUSIONS

CCTA derived parameters provide incremental information to classical coronary angiography for preoperative assessment of lesion severity in complex left main stenosis. CCTA derived Syntax score significantly correlates with the classical Coronary Angiography Syntax score and identifies the subgroup of patients who will be more exposed to procedural complications during the revascularization interventions.

Based on these findings, CCTA could represent a new noninvasive clinical tool, useful for preoperative evaluation of patient risk and for selection of the best therapeutic strategy in these cases.

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