

Peer Review File

Article Information: <https://dx.doi.org/10.21037/cdt-22-172>

Reviewer A:

In presented study Authors compared SYNTAX score to coronary angiogram standard evaluation I terms of future MACE. As per Authors SYNTAX score due to its complexity is not as often used as it should be, thus the proposition of the easier system. In general the study is well written and I could not find any significant mistakes. That said, I have only few comments:

Comment 1: What kind of stents did patients have implanted: BMS, DES, were there any BVS? An in CABG group how many of the patients had venous bypass grafts and how many arterial?

Reply: At the time of baseline data collection patients submitted to PTCA were treated with first generation DES and BMS; none were treated with BVS. In the surgery cohort, 4 patients got only venous grafts, 7 only arterial grafts and the remaining were treated with both kind of grafts. We added this information to methods (see Page 07, line 127 to 129).

Changes in the text: "Patients submitted to PCI were treated with first generation drug eluting and bare metal stents. Almost all patients treated by CABG received an arterial graft."

Comment 2: How many patients were followed for less than 2 years?

Reply: Just 2 patients.

Changes in the text: N/A

Comment 3: Patients with previous PCI were excluded, yet there were more than 50% of patients after previous ACS in both CABG and PCI groups. Does it mean all of them had OMT after ACS?

Reply: Most participants with a previous ACS were using drugs for secondary prevention, and therefore more patients that were submitted to CABG and PCI (table 1). Because the treatment was modified after the diagnostic angiogram, we believe that the previous treatment did not influence the incidence of outcomes.

Changes in the text: N/A

Comment 4: Study is quite small however it concentrates on one of the problems of SYNTAX score, the idea is interesting and could be repeated in bigger study.

Reply: We agree, and recognized this limitation, and encourage larger studies to be carried out to corroborate our results.

Changes in the text: N/A

Reviewer B:

Comment: Retrospective analysis of risk stratification by the SYNTAX score vs. "conventional" CAD assessment in 454 patients at a single center followed 6 years for MACE.

Originality: Few studies looked at comparative effectiveness for CAD grading and patient outcome.

Accuracy: Further details are required to assess the adequacy of methods. Foremost, the "conventional"

CAD grading is not well explained. "Conventional" CAD grading, in this reviewer's mind, is nonobstructive, 1, 2, 3-vessel obstructive CAD, LM disease. High-risk CAD is typically defined as 50% or greater LM disease; traditionally (before ISCHEMIA) also 3 v CAD and 2 v CAD including the prox LAD. The authors need to explain their rationale for using their grading and include above grading. They may want to discuss CAD grading before and after ISCHEMIA (see Ferraro R et al, JACC 2020).

Importantly, SYNTAX was NOT design to predict MACE but to predict procedural outcome for PCI vs. CABG (NOT OMT!). Nevertheless, folks incorrectly apply SYNTAX in this context and the authors' data may be useful to address this issue. The authors may discuss this issue also.

Relevance: Risk stratification is critical for patient management. The authors may elaborate on this issue.

The authors pursue a good idea and have a decent data set including follow up to analyze. They need to revise for clarify and add analyses which truly are consistent with "conventional" CAD grading. With adequate revisions, I do see merit in this study.

Reply: This is an important comment, and gave us the opportunity to comment the changing of paradigm for investigation and treatment of CHD after the findings of the COURAGE and mainly of the ISCHEMIA trials. The Ms by Richard Ferraro and collaborators highlights the changing of paradigm and was now cited in discussion (see Page 13, line 247 to 250). The information that the SYNTAX was proposed to predict outcomes after PCI or CABG and not OMT was also commented in the discussion about the Sxscore (see Page 13, lines 260 and 261). We do not believe that there is a substantial difference in regard to the grading of CAD by the reviewer's mind the one used by us: less than 50%, nonobstructive, more than 50% in left main or multivessel, intermediate or high risk (before the Ischemia trial).

Changes in the text: "The assessment of the predictive performance of anatomical criteria is particularly important since the publication of the results of the ISCHEMIA trial (28), that together with other studies demonstrated that testing for inducible myocardial ischemia is inferior to anatomic assessment for risk stratifying and managing patients with CHD" (see Page 13, line 247 to 250).

"It was originally designed to predict procedural outcome for PCI vs. CABG, and not medical therapy." (see Page 13, lines 260 and 261).

Reviewer C:

The authors have done a commendable job in looking into the outcomes of chronic stable CAD management based on syntax score versus an angiographic assessment that is the LMMCAD method and has shown that both methods and almost similar prognostication values.

Comment 1: The main drawback of the study is a very small sample of the patients with intermediate to high syntax scores. The overwhelming majority of patients have overall low syntax scores, only 53 patients ~ 11.7% have intermediate to high syntax scores. This will reduce the power of the study.

Reply: We agree, and this limitation was already recognized in discussion. Please, note that the following phrase provided our interpretation, i.e., that despite de low power, the magnitude of differences including the confidence limits are not clinically relevant. For the purpose of our study, however, the risks were identified for higher scores in both methods and were not substantially different between them.

Changes in the text: N/A

Comments 2: Authors need to provide information on how many were left main diseases, multi-vessel, and proximal LAD lesions. PCI group 93.6% have low Syntax score but at the same time in 29.9% patients of the PCI group patient had LMMCAD, which suggests a discrepancy in calculating syntax score or defining lesions. Overall the study population has 34.48% of patients with LMMCAD but as mentioned above only 11% of patients have syntax scores that are intermediate to high.

Reply: Patients with lesions higher than 50% in one or two major coronaries were classified as intermediate or high risk by the LMMCAD criterion, but may be classified as low risk by SXscore.

Changes in the text: N/A