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Significant association of SYNTAX score on release of cardiac biomarkers in uncomplicated post-revascularization procedures among patients with stable multivessel disease

MASS-V Study group

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Abstract

This study investigated the relationship between angiographic complexities of coronary artery disease (CAD) assessed by SYNTAX Score synergy between percutaneous coronary intervention with taxus and cardiac surgery score (SYNTAX Score) and cardiac biomarker elevation after revascularization procedures.

This is a post-hoc analysis of the medicine, angioplasty or surgery study V study of patients with stable CAD. High-sensitivity troponin 1 (hs-TnI) and creatinine kinase-muscle/brain (CK-MB) were assessed before and after cardiovascular procedures. Baselines SYNTAX Scores (SXScores) were calculated by blinded investigators to patient characteristics.

Of the 202 patients studied, the mean SXScore was 21.25 ± 9.24; 40.10 ± 7.09 in the high SXScore group and 19.06 ± 6.61 in low/mid SXscore group ($P < .0001$). Positive correlations existed between SXScore and median peaks after procedural hs-TnI ($r = 0.18$, $P = .009$) and CK-MB ($r = 0.24$, $P = .001$) levels. In patients with high SXScores (≥33), the median peaks of post-procedural hs-TnI ($P = .034$)and CK-MB ($P = .004$) levels were higher than in low/mid SXScore group (<33).The release of hs-TnI at 6 ($P = .002$), 12 ($P = .008$), and 24 hours ($P = .039$) was higher in high SXScore group than in low/mid SXscore group (<33) as was the release of CK-MB at 6 ($P < .0001$), 12 ($P < .0001$), 24 ($P = .001$), 36 ($P = .007$), 48 ($P = .008$), and 72 hours ($P = .023$). After multivariable analysis, high SXScore was a significant independent predictor of release of CK-MB and hs-TnI peaks higher than the median.

The increase in release of cardiac biomarkers was significantly associated with the extent of atherosclerosis identified by the SYNTAX Score.

Abbreviations: AMI = acute myocardial infarction, CABG = coronary artery bypass grafting, CAD = coronary artery disease, CK-MB = creatinine kinase-muscle/brain, CPB = cardiopulmonary bypass, hs-TnI = high-sensitivity troponin I, LVEF = left ventricular ejection fraction, MASS V = medicine, angioplasty or surgery study V, MI = myocardial infarction, PCI = percutaneous coronary intervention, SXSCore = synergy between percutaneous coronary intervention with taxus and cardiac surgery score, SYNTAX = synergy between percutaneous coronary intervention with taxus and cardiac surgery, URL = upper reference limit.

Keywords: angioplasty, biomarkers, coronary artery bypass, coronary artery disease

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1. Introduction

Synergy between percutaneous coronary intervention with taxus and cardiac surgery score (SYNTAX Score) is available as an anatomical-based tool for objectively determining the complexity of coronary artery disease (CAD), which was initially intended to predict the successfulness of percutaneous coronary intervention (PCI). Subsequently the tool was validated to guide the best revascularization strategy in patients with 3-vessel and left main CAD.[1–3] The SYNTAX trial reported similar survival in patients randomly assigned to PCI with paclitaxel eluting stents versus coronary artery bypass grafting (CABG) after a 5-year follow-up. Recently, the SYNTAXES study evaluated a longer follow-up analysis reporting the 10-year survival after PCI with drug eluting stents versus CABG. In this analysis, mortality rates of PCI and CABG were similar.[4] Since its original usefulness, several different clinical applications for this tool have emerged from stable and unstable subsets of CAD patients.[5] Thus, SXScore has been tested, and it seems to be useful for stratifying the risk of periprocedural complications.[6,7]

Myocardial injury after revascularization procedures is the most common procedural complication and is an important endpoint in trials including patients with CAD.[8] Once periprocedural myocardial infarction (MI), and even modest release of cardiac biomarkers, can be related to mid- and long-term major adverse events, its prediction is clinically relevant.[9] However, the use of only 1 cardiac biomarker and the reduced numbers of blood samples collected after revascularization procedures are important limitations in trials that sought to correlate angiographic complexity and release of biomarkers. Considering lack of data in this field, our purpose was to investigate the correlation between angiographic complexities of CAD as assessed by (SYNTAX Score) (SXScore) and cardiac biomarker elevations after revascularization procedures.

2. Methods

This is a post-hoc analysis of the Medicine, Angioplasty, Surgery V (MASS-V) Study,[8] a single-center, prospective, consecutive study. Details of the MASS-V study design, protocol, patient selection, and inclusion criteria have been previously reported.[10] Briefly, patients with angiographically documented proximal multivessel coronary stenosis of more than 70% by visual assessment and documented ischemia were included. Stress testing or the stable angina assessment of the Canadian Cardiovascular Society (class II or III) was used to document ischemia. All patients were candidates for elective PCI or CABG. A Heart Team including an interventional cardiologist, a clinical cardiologist, and a surgeon decided the revascularization strategies. Patients were excluded if they had undergone any previous interventions, had a recent MI, or other thromboembolic phenomena in the last 3 months, systemic inflammatory disease, or kidney dysfunction (creatinine above 2.0 mg/mL). Present study was approved by the Ethics Committee of the Heart Institute of the University of São Paulo Medical School and was carried out according to Declaration of Helsinki.

2.1. Coronary angiography and SYNTAX score

All patients underwent coronary angiography with the Judkins technique. Coronary angiography was performed with the standard femoral approach with a 6-F diagnostic catheter. Coronary lesions leading to ≥50% diameter stenosis in ≥1.5-mm vessels were scored separately and added together to provide the cumulative SXScore that was prospectively calculated using the SXScore algorithm on the baseline diagnostic angiogram.[11] Two experienced interventional cardiologists analyzed the SXScore; the opinion of a third analyst was obtained and final judgment was made by consensus in cases of a disagreement. The final score was calculated from individual lesion scores by analysts who were blinded to other information, including patient characteristics, therapies, and clinical outcomes. Intra-observer and interobserver reproducibility were assessed on 40 angiograms. SXScores <33 were categorized as low/mid and SXScores ≥ 33 as high, consistent with prior published reports.[1] Sensitivity analyses were conducted by using specific tertiles of SXScores and analyzing them as continuous variables.

2.2. Cardiac biomarkers

Blood samples were collected for measurement of high-sensitivity troponin I (hs-TnI) and creatine kinase-muscle/brain (CK-MB) mass immediately after PCI and 6, 12, 24, 36, and 48 hours after. For patients undergoing CABG, these cardiac biomarkers were measured immediately after (time 0) and 6, 12, 24, 36, 48, and 72 hours after the operation. The treating surgeon and clinical team were blinded to the CK-MB and hs-TnI data. All samples were centrifuged at 3000 rpm for 20 minutes and analyzed within 2 hours after collection. Analyses of hs-TnI and CK-MB were performed using an ADVIA Centaur immunoassay analyzer (Siemens Health Care Diagnostics, Tarrytown, NY). According to the manufacturer, lower limit of detection of hs-TnI using the high-sensitivity Ultra kit is 0.006 ng/mL, and the 99th percentile upper reference limit (URL) is 0.04 ng/mL. The assay precision represented by the percentage coefficient of variation was 10% at 0.03 ng/mL. The detection limit of the CK-MB mass kit was 0.18 ng/mL. Cutoff values at the 99th percentile were 3.8 ng/mL for women and 4.4 ng/mL for men. The coefficients of variations for CK-MB mass, as specified by the manufacturer, were 3.91% at 3.55 ng/mL and 3.67% at 80.16 ng/mL. These measurements are in accordance with the recommendations of the Study Group on Biomarkers in Cardiology of the European Society of Cardiology Working Group on Acute Cardiac Care.[12]

2.3. Cardiac magnetic resonance and late gadolinium enhancement (CMR)

All patients in this trial were forwarded to CMR 2 days before the intervention and 6 days after each invasive procedure during the hospitalization period. The patients were studied in a 1.5-T Achieva MR scanner (Philips Healthcare, Andover, MA). Steady-state free precession cine images were acquired in 2 long-axis (2 and 4 chambers) views and 8 to 10 short-axis views of the left ventricle. Contrast-enhanced images were acquired in long- and short-axis planes identical to the cine images. Typical voxel size was 1.6 2.1 8 mm, with a reconstruction matrix of 528 and a reconstructed voxel size of 0.6 mm. MI was defined as the identification of hyper-enhancement in the myocardium on CMR. Infarcted regions exhibit this phenomenon, which might be due to an increased volume of distribution of the contrast agent because of rupture of myocyte membranes and slow contrast washout. All areas of late gadolinium-diethylene triamine penta- acetic acid hyperenhancement were quantified by 2 experienced observers who interpreted the LGE while blinded to the interventional technique and biochemical data. When measurements differed, a third observer

performed a review, and a consensus was obtained. Hyper-enhanced pixels were defined as those with image intensities exceeding 2 standard deviations greater than the mean of image intensities in a remote myocardial region in the same image. Pre-intervention and post- intervention scans were read side by side in both surgical techniques, with and without extracorporeal circulation.

2.4. Statistical analysis

Categorical data are presented as percentages and continuous data as means ± standard deviations, or as medians and interquartile ranges, as appropriate. Categorical data were compared using the chi-square. Continuous variables were tested regarding their distribution with the Shapiro–Wilk test. Those normally distributed were compared using the unpaired *t* test and if not normally distributed by Wilcoxon rank-sum test. Analyses of correlations were performed among SXScore and each biomarker and nonparametric Spearman's correlation coefficients were calculated with their 95% confidence intervals. Intraobserver and interobserver variability were evaluated using kappa statistics. Univariable logistic regression analyses were performed to assess the relationship between the SXScore and occurrence of late gadolinium enhancement in cardiac magnetic resonance. Multivariable logistic regression analyses were performed to assess the relationship between the SXScore and cardiac biomarker peaks as dichotomous variables (higher than median of population). Demographic and clinical variables were included in this analysis. Other variables were also tested for significance, including left ventricular ejection fraction (LVEF), metabolic profile, arterial pattern, smoking status, cardiopulmonary bypass (CPB) time, and renal function. To construct the multivariable model, we first examined univariate models; variables at least marginally associated with the endpoint ($P < .10$) were included in a model in which stepwise selection was used for predictor selection at each step. Additional candidate variables were included in the multivariable model if there was significant treatment by predictor interactions ($P \leq .05$). A secondary analysis was performed to compare incidence of clinical events in different SXScore groups. In this analysis we considered as endpoints, overall death, non-procedural acute MI (AMI), and a combination of these 2 components. Event rates were estimated using the Kaplan-Meier method, and differences among groups were assessed by means of the log-rank test. Hazard ratios were estimated by Cox proportional hazards analysis. Finally, the effects of treatment strategies according the SXScore were estimated using a contrast of main effects and interaction effects for treatment without further covariate adjustment. The statistical significance of differences in the effect of treatment modalities on each endpoint was evaluated using the full population and a multiplicative interaction term.

All tests were 2-sided; $P < .05$ was considered statistically significant. All statistical analyses were performed with SPSS version 21.0 (SPSS. Inc).

3. Results

Between March 2012 and March 2014, 326 nonrandomized, prospective, consecutive patients with documented stable CAD were eligible for revascularization procedures. All patients had severe obstructive lesions in at least 2 epicardial arteries, associated with angina pectoris and preserved ventricular function. A total of 148 patients were referred for CABG and 71 for PCI. Of these, 202 patients completed the study and were included in main analysis. SXScore and cardiac biomarkers were available in all patients included in the main analysis (Fig. 1).

Baseline characteristics were similar between patients who had high SXScore versus low/mid SXScore, including LVEF, 3-vessel disease patients, and baseline cardiac biomarkers (Table 1). However, a higher proportion of hypertensive patients were in the high SXScore group ($P = .03$). Furthermore, there was a significant difference regarding treatment comparing high SXScore with low SXScore patients ($P = .001$). As expected, patients with high SXScores presented higher proportion of CABG.

3.1. Cardiac biomarkers and SYNTAX score

SXScores were calculated for 202 patients (100%) with excellent intraobserver (0.87) and interobserver (0.84) kappa statistics, as in previous studies.[13,14] The mean SXScore in the 202 study patients was 21.25 ± 9.24. Of the patients, 181 had low/mid SXScores and 21 had high SXScores. The mean SXScore was significantly higher in the high SXScore group compared with the low/mid SXScore (40.10 ± 7.09 vs 19.06 ± 6.61, $P < .001$).

Serum hs-TnI peak was significantly and positively correlated with the SXScore (Spearman correlation: $r = 0.18$, $P = .008$).CK-MB peak was also significantly and positively correlated with SXScore (Spearman correlation: $r = 0.24$, $P = .001$).

The median peak post-procedural hs-TnI (Fig. 2) levels in patients in the high SXScore group was significantly higher compared with that in the low/mid SXScore group (3.00; interquartile range[IQR]: 2.19–9.04 ng/dL vs 1.99 [IQR: 0.47–5.17 ng/dL], $P = .034$),and the median CK-MB peak in patients in the high SXScore group was also significantly higher compared with that in the low/mid SXScore group (27.83 [IQR: 14.3–69.76 ng/dL] vs 12.98 [IQR: 4.09- 28.11 ng/dL], $P = .004$).The median peak of hs-TnI after myocardial revascularization was higher in the SXScore high group compared with the low/mid group at 6 hours ($P = .002$), 12 hours ($P = .008$) and 24 hours ($P = .039$) after the procedure. In addition, median peak CK-MB after myocardial revascularization was higher in the SXScore high group compared with the low/mid group at 6 hours ($P < .001$), 12 hours ($P < .001$), 24 hours ($P = .001$), 48 hours ($P = .008$) and 72 hours ($P = .02$) after the intervention (Fig. 3).

After multivariable analysis and adjustment for covariates (systemic arterial hypertension, diabetes, age, and creatinine), SXScore was an independent and significant predictor for peaks CK-MB and hs-TnI releases above the median (Table 2). Considering treatment modality and including this variable in the model, SXScore presented an adjusted [OR]: 1.01; 95% confidence interval [CI] 0.98–1.05; $P = 0.345$ for troponin above median; and adjusted [OR]:1.00; 95% CI 0.96–1.04; $P = 0.76$ for CK-MB above median. Analyzing only surgical subjects and adding CPB time in the model (Table 3), we found that CPB time was an independent predictor for release of cardiac biomarkers above median (odds ratio [OR] adjusted 1.02, 95% CI 1.01–1.03; $P = .001$ for CK-MB above median and an OR adjusted 1.01, 95% CI: 1.01–1.02; $P = 0.03$ for hs-TnI above median). Moreover, when we analyzed in detail the characteristics of patients with elevations of biomarkers above and below the median, we identified that only SXScore and the treatment received had significant differences, reinforcing the impact of angiographic complexity on the release of cardiac biomarkers

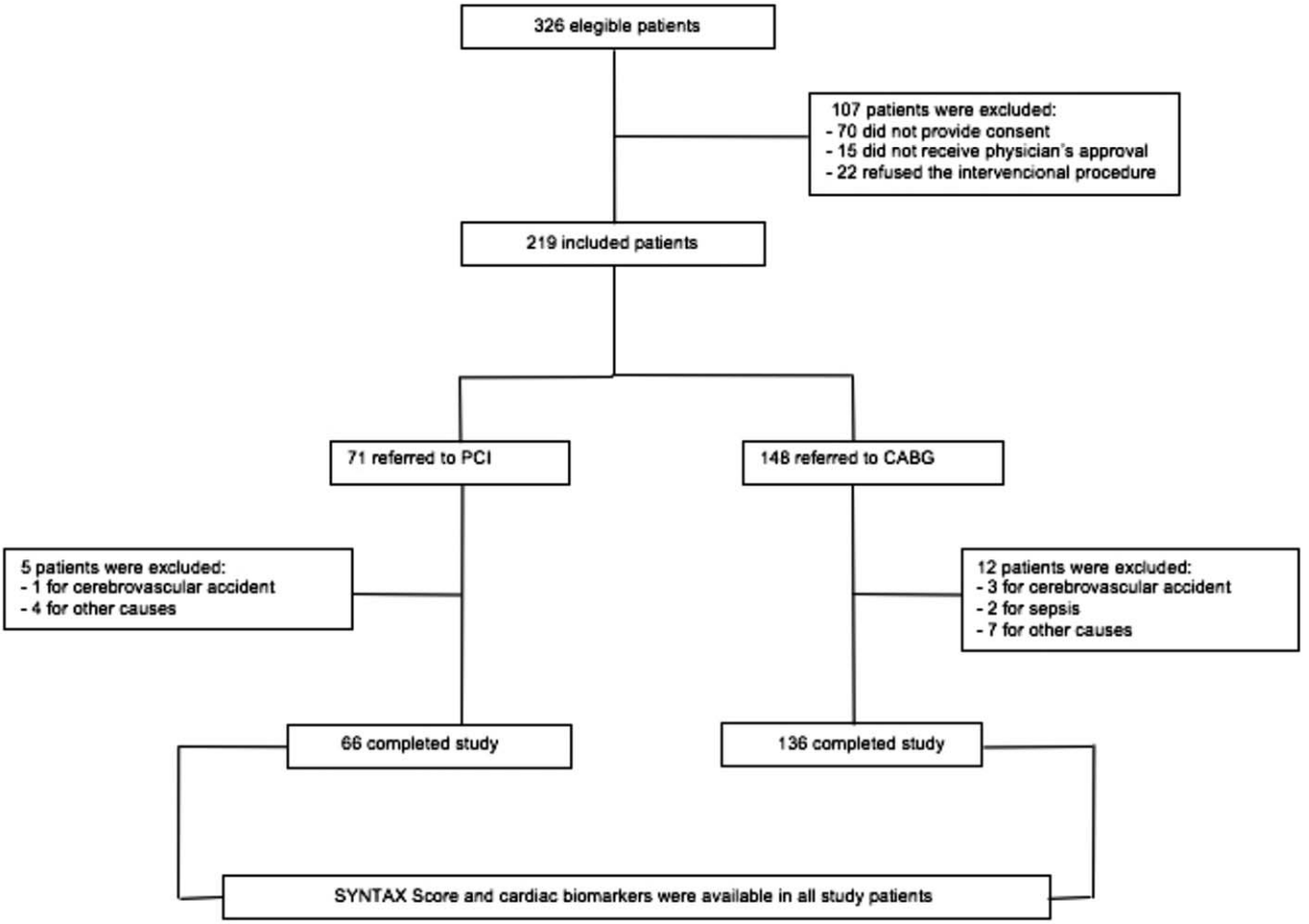

Figure 1. Consolidated standards of reporting trials (CONSORT) diagram of trial participants. CABG = coronary artery bypass grafting, PCI = percutaneous coronary intervention, SYNTAX = Synergy Between Percutaneous Coronary Interventions with Taxus and Cardiac Surgery.

Table 1

Demographic, laboratory, clinical, and angiographic characteristics of patients by SXScore groups.

Characteristics*	High SXScore (n = 21)	Low/mid SXScore (n = 181)	*P* value
Demographic profile			
Age, yr	64.9 ± 7.64	61.81 ± 9.29	.88
Male (%)	66.7	67.4	.94
Current or past smoker (%)	81.0	81.2	1.00
Myocardial infarction (%)	14.3	34.3	.06
Hypertension (%)	100.0	82.9	.03
Diabetes mellitus (%)	42.9	44.8	.86
Angina (CCS II or III)(%)	76.1	64.6	.64
Laboratory values			
Total cholesterol, mg/dL	173.7 ± 57	170.6 ± 44	.77
LDL cholesterol, mg/dL	100 ± 42	100 ± 35	.95
HDL cholesterol, mg/dL	39 ± 10	37 ± 11	.60
Triglycerides, mg/dL	185 ± 191	165 ± 106	.45
Plasma glucose, mg/dL	136 ± 57	129 ± 48	.52
Creatinine, mg/dL	1.07 ± 0.3	1.05 ± 0.2	.53
Baseline Troponin†, ng/dL	0.01 (0.006–0.013)	0.01 (0.006–0.018)	.74
Baseline CK-MB†, ng/dL	1.24 (0.83–1.64)	1.04 (0.65–1.60)	.46
Angiographic findings			
Double-vessel disease (%)	14.3	34.3	.14
Triple-vessel disease (%)	85.7	64.6	.14
LVEF (%)	67 ± 9.2	69 ± 10.8	.57
Treatment			
CABG on pump	71.4	29.8	.001
CABG off pump	19.0	34.8	
PCI	9.5	35.4	

CABG = coronary artery bypass grafting, CK-MB = creatinine phosphokinase fraction MB, LDL = low-density lipoprotein, LVEF = left ventricular ejection fraction, PCI = percutaneous coronary intervention, SXScore = SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) Score.

* Values are expressed as means (standard deviation) or percentage (number).

† Values are expressed as median (interquartile range).

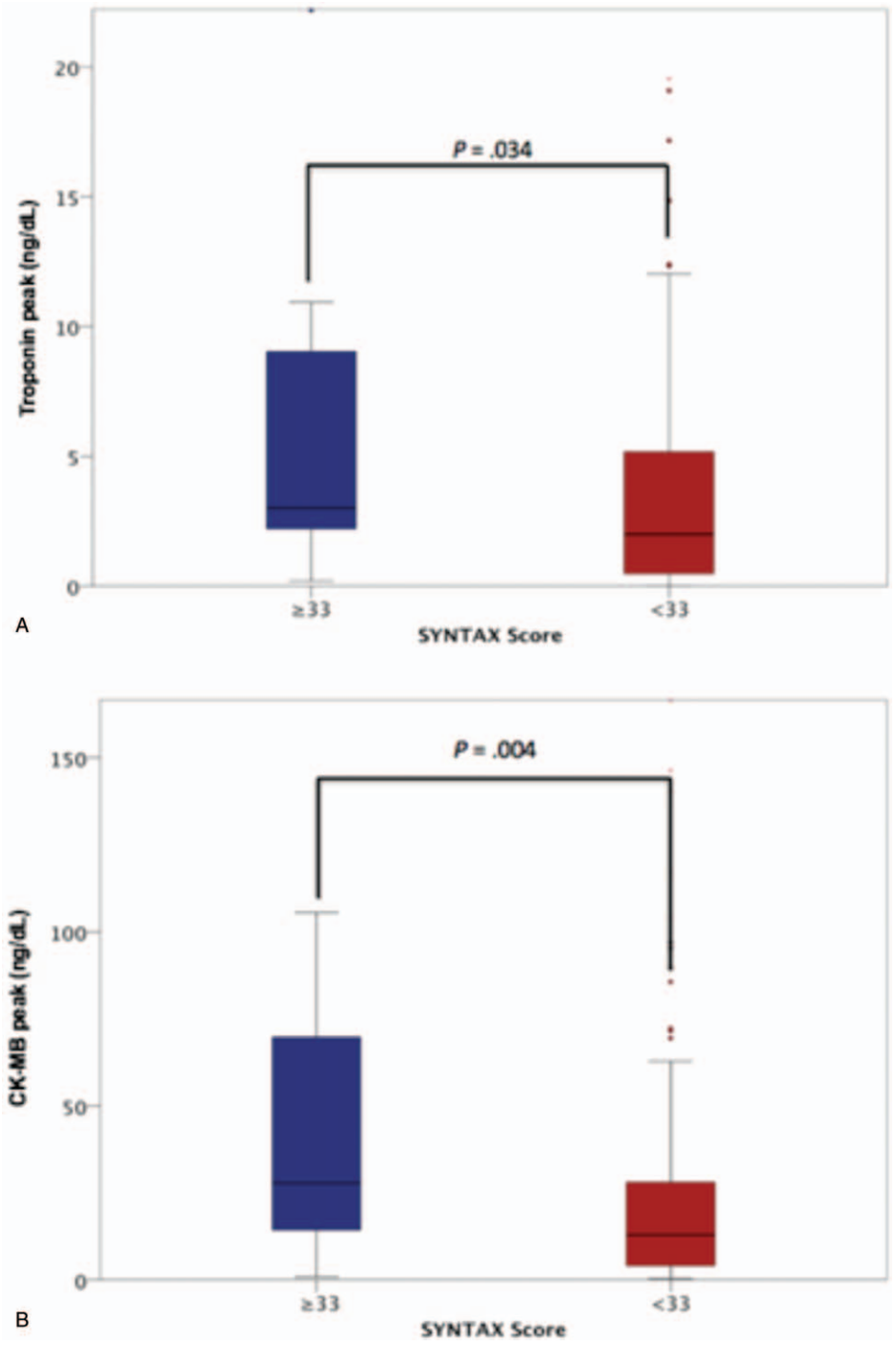

Figure 2. Box plot of patient troponin (A) and creatine kinase-MB (B) peaks for patients with high SXScore (blue box) and low/ mid SXScore (red box).

(Tables 4 and 5). Among those on PCI arm (Table 6), SXScore was not a predictor of troponin (OR adjusted 1.01, 95% CI: 0.97–1.08; $P=0.87$) or CK-MB (OR adjusted 0.98, 95% CI: 0.88–1.08; $P=0.74$) above the median in model adjusted for covariates (systemic arterial hypertension, diabetes, age, and creatinine).

It is noteworthy that despite higher proportion of surgical patients in the high SXScore group (Table 1), the treatment chosen, PCI or CABG, did not modify the SXScore effect on troponin ($P_{interaction}=.69$) and CKMB ($P_{interaction}=.95$) above the medians.

In this sample, we observed 14 combined events, 8 all-cause deaths and 6 AMI in a median follow-up of 4 years (IQR:3.2–4.6). Among subjects with low/mid SXScore it was observed 10 events, 6 deaths and 4 AMI, while in high SXScore group 4 events, 2 deaths and 2 AMI. Combined event rates were 5.5% and 19% for low/mid SXScore and high SXScore respectively (Log-rank *P*: .938; HR:2.40 95%IC 0.74–7.80; $P=.147$). No

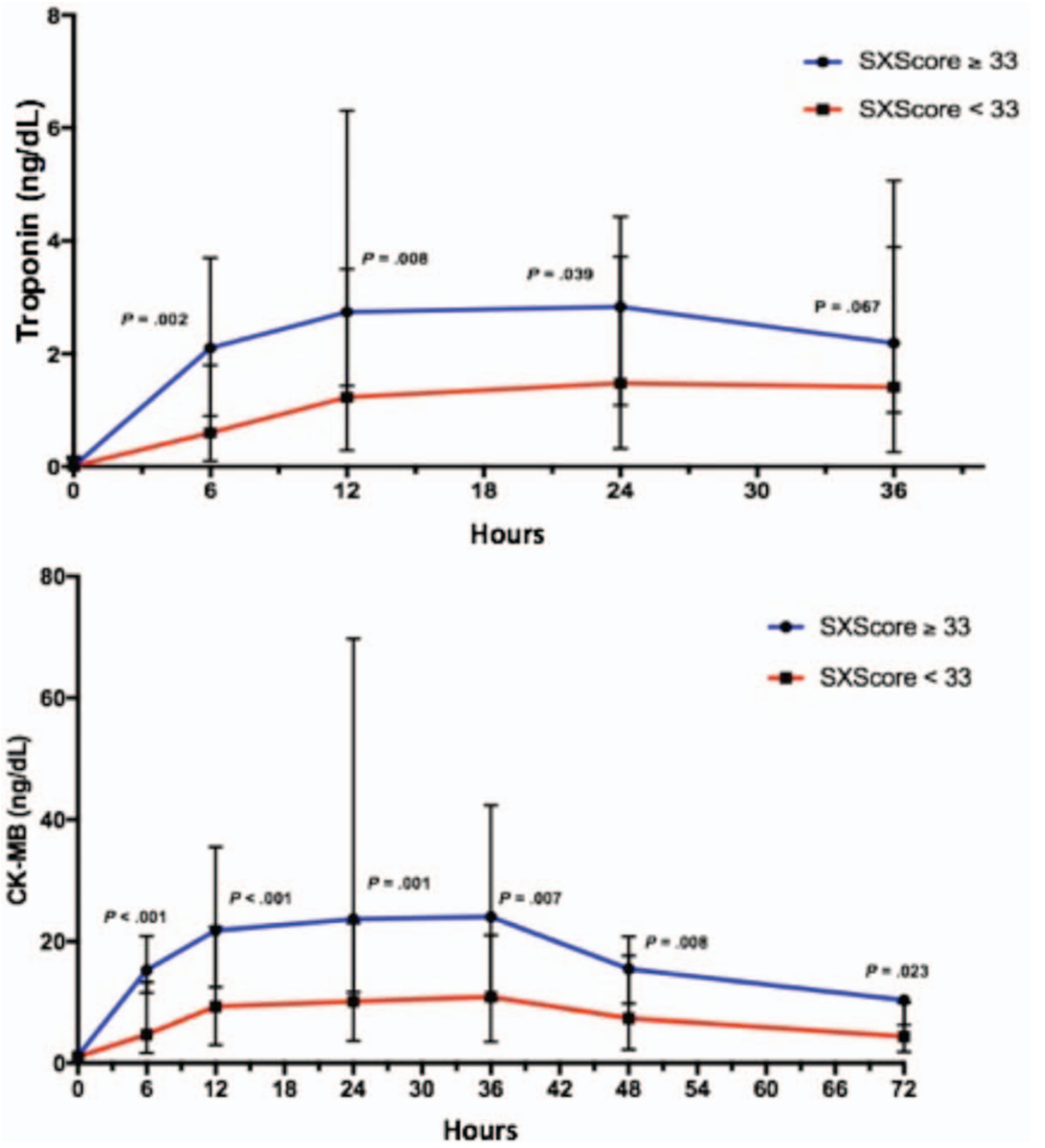

Figure 3. Release of biomarkers after revascularization procedure is compared between high SXScore (blue lines) and low/ mid SXScore (red lines) for (A) cardiac troponin I and (B) creatine kinase-MB.

Table 2

Multivariable analysis including SYNTAX Score as well as clinical variables (age, creatinine, hypertension, and diabetes) with post procedural cardiac biomarkers release, troponin, and creatine kinase-MB, higher than median.

Clinical variable	Odds ratio (95% CI) CK-MB peak >median	*P* value	Odds ratio (95% CI) troponin peak > median	*P* value
SYNTAX Score*	1.04 (1.01–1.08)	.01	1.04 (1.01–1.08)	.01
Diabetes mellitus	1.11 (0.63–1.97)	.72	1.15 (0.65–2.03)	.63
Hypertension	0.85 (0.38–1.88)	.69	1.21 (0.55–2.66)	.64
Creatinine (for each 1mg/dL)*	0.91 (0.31–2.68)	.86	0.97 (0.33–2.87)	.96
Age (for each yr)*	0.99 (0.96–1.02)	.66	1.00 (0.97–1.03)	.95

CI = confidence interval, CK-MB = creatinine phosphokinase fraction MB.
* Analyzed as a continuous variable.

Table 3

Multivariable analysis including SYNTAX Score as well as clinical variables (age, creatinine, hypertension, and diabetes) and cardiopulmonary bypass time in patients who underwent coronary artery bypass grafting with cardiac biomarkers release, troponin, and creatine kinase-MB, higher than median.

Clinical variable	Odds ratio (95% CI) CK-MB peak >median	*P* value	Odds ratio (95% CI) troponin peak > median	*P* value
SYNTAX Score*	0.99 (0.94–1.03)	.55	1.00 (0.96–1.04)	.96
CPB time (for each minute)*	1.02 (1.01–1.03)	.001	1.01 (1.01–1.02)	.03
Diabetes mellitus	1.52 (0.68–3.38)	.31	1.07 (0.51–2.23)	.86
Hypertension	1.22 (0.39–3.83)	.74	1.45 (0.48–4.35)	.51
Creatinine (for each 1mg/dL)*	0.89 (0.20–3.96)	.88	1.40 (0.35–5.60)	.63
Age (for each year)*	0.99 (0.95–1.04)	.74	1.00 (0.96–1.04)	.96

CI = confidence interval, CK-MB = creatinine phosphokinase fraction MB, CPB = cardiopulmonary bypass.
* Analyzed as a continuous variable.

difference was observed regarding death or AMI rates among SXScore groups (Log-rank $P = .235$ and .732, respectively). Additionally, we found no association between SXS score and occurrence of late gadolinium enhancement in cardiac magnetic resonance (OR 1.04, 95% CI: 0.99–1.08; $P = .07$).

4. Discussion

To the best of our knowledge, this is the first study to analyze the relationship between the degree and complexity of atherosclerotic disease burden of coronary arteries, evaluated by the SXScore, and the release of cardiac biomarkers, troponin, and CK-MB, in pre-specified serial dosages, after myocardial revascularization procedures. Our findings indicate that the complexity of CAD, as defined by SXScore, could predict myocardial injury after adjustment for traditional risk factors for CAD.

Patients in the highest tertile of the SXScore, compared with the low/mid tertiles, had significantly higher median peaks hs-TnI and CK-MB levels. Furthermore, the release of cardiac biomarkers in patients in the high SXScore group compared with the low/mid SXScore group was also higher in predefined periods after revascularization procedures. After multivariable analysis and adjustment for covariates, SXScore was an independent and significant predictor of cardiac biomarkers releases above the median.

In our study, alterations in biomarkers were not negligible; the high SXScore group had median peaks of 75 times and around 7 times the 99th percentile URL for hs-TnI and CK-MB, respectively. A large patient-level meta-analysis demonstrated a doubling of short- and long-term mortality in patients in whom cardiac biomarker measurements within 24 hours after CABG rose to ≥4 to 5 of the 99th percentile URL,[9] as was observed in our trial.

Table 4

Demographic, laboratory, clinical, and angiographic characteristics of patients with release of CK-MB below and above of median.

Characteristics*	Below of median (CK-MB ≤ 14.1 ng/dL)	Above of median (CK-MB > 14.1ng/dL)	*P* value
Demographic profile			
Age (yr)	62.3 ± 8.9	61.9 ± 9.4	.76
Male (%)	67.3	67.3	1.00
Current or past smoker (%)	79.2	83.1	.66
Myocardial infarction (%)	36.6	27.7	.18
Hypertension (%)	83.2	86.1	.56
Diabetes mellitus (%)	44.6	44.6	1.00
Laboratory values			
Total cholesterol, mg/dL	174.6 ± 43	167.0 ± 46	.13
LDL cholesterol, mg/dL	102.1 ± 35	98.9 ± 37	.48
Plasma glucose, mg/dL	129.3 ± 47	130.5 ± 52	.97
Creatinine, mg/dL	1.05 ± 0.2	1.05 ± 0.2	1.00
Baseline troponin†, ng/dL	0.01 (0.006–0.021)	0.01 (0.006–0.015)	.18
Baseline CK-MB†, ng/dL	1.03 (0.64–1.70)	1.11 (0.68–1.60)	.85
Angiographic findings			
SYNTAX Score†	19 (12–25)	21 (17–28)	.011
Triple-vessel disease (%)	59.4	74.3	.07
LVEF (%)	67 ± 9	65 ± 12	.41
Treatment			
CABG on pump	14.9	53.5	<0.001
CABG of pump	28.7	37.6	
PCI	56.4	8.9	

CABG = coronary artery bypass grafting, CK-MB = creatinine phosphokinase fraction MB, LDL = low-density lipoprotein, LVEF = left ventricular ejection fraction, PCI = percutaneous coronary intervention, SXScore = SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) Score.
* Values are expressed as means (standard deviation) or percentage (number).
† Values are expressed as median (interquartile range).

Table 5

Demographic, laboratory, clinical, and angiographic characteristics of patients with release of troponin below and above of median.

Characteristics*	Below of median (troponin ≤ 2.19 ng/dL)	Above of median (troponin > 2.19 ng/dL)	*P* value
Demographic profile			
Age (yr)	62.04 ± 8.4	62.23 ± 9.8	.99
Male (%)	64.4	70.3	.37
Current or past smoker (%)	78.2	84.1	.53
Myocardial infarction (%)	32.7	31.7	.88
Hypertension (%)	85.1	84.2	.85
Diabetes mellitus (%)	45.5	43.6	.78
Laboratory values			
Total cholesterol, mg/dL	172.1 ± 43	169.6 ± 46	.66
LDL cholesterol, mg/dL	99.7 ± 35	101.4 ± 37	.71
Plasma glucose, mg/dL	133.1 ± 46	126.8 ± 52	.12
Creatinine, mg/dL	1.04 ± 0.2	1.06 ± 0.2	.70
Baseline Troponin†, ng/dL	0.01 (0.006–0.022)	0.01 (0.006–0.015)	.27
Baseline CK-MB†, ng/dL	1.08 (0.68–1.87)	1.01 (0.66–1.47)	.38
Angiographic findings			
SYNTAX Score†	19 (13–25)	21 (17–27)	.03
Triple-vessel disease (%)	63.4	70.3	.17
LVEF (%)	68 ± 9	64 ± 11	.10
Treatment			
CABG on pump	20.8	47.5	<.001
CABG of pump	29.7	36.6	
PCI	49.5	15.8	

CABG = coronary artery bypass grafting, CK-MB = creatinine phosphokinase fraction MB, LDL = low-density lipoprotein, LVEF = left ventricular ejection fraction, PCI = percutaneous coronary intervention, SXScore = SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) Score.

* Values are expressed as means (standard deviation) or percentage (number).

† Values are expressed as median (interquartile range).

The relationship between a high SXScore and elevation of cardiac biomarkers may be associated with the surgical or percutaneous procedure per se. Patients with higher SXScores have greater anatomical complexity, usually requiring more time for revascularization procedures and, subsequently, elevated risk for myocardial injury. Furthermore, a strong association exists between postprocedural cardiac biomarker release and components of SXScore, such as large atherosclerotic plaque burden, large thrombus burden, coronary calcification, and lesion eccentricity, as detected by angiography and intravascular ultrasound imaging.[7,15] In surgical patients, higher release of cardiac biomarkers, in the highest tertile of the SXScore, may be related to greater risk of incomplete myocardial protection with transient ischemia, reperfusion injury, and a systemic inflammatory state in this group of subjects with documented higher angiographic complexity. Furthermore, the longer CPB time is directly related to the anatomic complexity or number of grafts used, thus providing greater release of cardiac biomarkers. In our analysis, CPB time was an independent predictor of the release of cardiac biomarkers in the model including SXScore probably by the mechanisms referred above. As documented by trials comparing CAGB with or without CPB, presence of CPB is a decisive factor in myocardial injury after surgical revascularization procedures. Despite similar mortality between off-pump and on-pump CABG, myocardial injury is higher in on-pump CABG patients.[8,16]

In our study, we found no association between SXSscore and occurrence of late gadolinium enhancement in cardiac magnetic resonance, probably because angiographic complexity is associated with the release of biomarkers and not the presence of AMI, as shown by the gold standard, which is cardiac magnetic resonance. In addition, the medicine, angioplasty or surgery study V (MASS V) study made it clear that cutoff values that best correlated with late enhancement were even higher than those found in patients with high SXScore.[8]

The following limitations of this study should be considered in the interpretation of our findings. The present study is a post-hoc analysis of the MASS V trial, and the results should be considered

Table 6

Multivariable analysis including SYNTAX Score as well as clinical variables (age, creatinine, hypertension, and diabetes) with post procedural cardiac biomarkers release, troponin, and creatine kinase-MB, higher than median in patients undergoing percutaneous coronary intervention.

Clinical variable	Odds ratio (95% CI) CK-MB peak >median	*P* value	Odds ratio (95% CI) troponin peak > median	*P* value
SYNTAX score*	0.98 (0.88–1.08)	.74	1.01 (0.97–1.08)	.87
Diabetes mellitus	5.83 (0.62–54.47)	.12	3.29 (0.75–14.47)	.11
Hypertension	1.11 (0.18–6.84)	.91	0.60 (0.10–3.41)	.57
Creatinine (for each 1mg/dL)*	3.38 (0.18–63.09)	.41	1.65 (0.15–17.55)	.67
Age (for each yr)*	1.01 (0.93–1.10)	.74	1.02 (0.96–1.10)	.42

CI = confidence interval, SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

* Analyzed as a continuous variable.

as hypothesis generating, and not design to establish causality and mechanistic statements. Our results cannot be generalized to other hs-TnI assays given that different hs-TnI assays are not biologically equivalent because manufacturers use different reference populations to determine the 99th percentile URL. Our study was not intended to create new cut-offs for biomarkers and the dichotomization using the median as a cut-off was based in the distribution of these variables in our sample. Size of our sample limits interpretation of data within each therapeutic approach. Besides, different distribution of SXScore among different therapeutic strategies may difficult to measure the specific impact of treatment on biomarkers. Furthermore, as expected for this population of stable CAD patients after revascularization procedures, a low rate of events was observed in the follow-up. Thus, differences regarding event rates among SXScore groups must be interpreted with caution, and specific analysis dedicated to study predictors of clinical events will be needed.

5. Conclusions

An increase in post procedural hs-TnI and CK-MB levels showed a significant association with angiographic atherosclerotic extent and burden, as assessed by SXScore. In addition, SXScore remained an independent predictor of biomarker levels above the median even when adjusted for covariates.

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