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## Original Article

# Residual SYNTAX Score and One-Year Outcome in Elderly Patients With Acute Coronary Syndrome

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## ABSTRACT

**Background:** The residual burden of coronary artery disease after percutaneous coronary intervention (PCI) has been associated with worse ischemic outcome. However, data are conflicting in elderly patients. The aim of our study was to verify the incremental value of the residual Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) score (rSS) over clinical variables and baseline SYNTAX score (bSS) in predicting 1-year mortality or cardiovascular events.

**Methods:** A post hoc analysis of data collected in the Elderly-ACS 2 multicenter randomized trial was performed. We included 630 patients aged > 75 years with multivessel coronary disease undergoing

## RÉSUMÉ

**Contexte :** Le fardeau résiduel de la coronaropathie après une intervention coronarienne percutanée (ICP) a été associé à de moins bons résultats sur le plan ischémique. Les données recueillies chez les patients âgés sont toutefois contradictoires. Cette étude avait donc pour objectif de valider la valeur ajoutée du score SYNTAX (SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery) résiduel (SSr) par rapport aux paramètres cliniques et au score SYNTAX initial (SSi) pour prédire la mortalité à 1 an et les manifestations cardiovasculaires.

**Méthodologie :** Une analyse a posteriori des données de l'étude multicentrique avec répartition aléatoire Elderly-ACS 2 a été effectuée.

Multivessel coronary disease is a common finding in patients admitted to the hospital for an acute coronary syndrome (ACS), particularly at an advanced age.<sup>1</sup> Moreover, optical coherence tomography analyses suggest that secondary plaque

ruptures may occur in approximately 25% of patients with ACS.<sup>2</sup> Current clinical practice guidelines recommend prioritizing the achievement of complete revascularization, whenever possible, using percutaneous coronary intervention (PCI), coronary artery bypass grafting, or their combination.<sup>3</sup>

Recent data suggest that an incomplete revascularization, quantified using the residual Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) score, (rSS), is associated with worse 30-day and 1-year outcomes, including higher mortality, after PCI in patients with moderate- and high-risk ACS.<sup>4-6</sup> The recently published Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for ST-Elevation myocardial infarction (COMPLETE) trial addressed

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See page 7 for disclosure information.

PCI for acute coronary syndrome (ACS). The primary outcome was a composite of death, recurrent myocardial infarction, and stroke at 1-year follow up. Change in c-statistic and standardized net benefit were used to evaluate the incremental value of the rSS.

**Results:** Event rates were significantly higher in patients with incomplete revascularization (rSS > 8). When the rSS was included in a core Cox regression model containing age, previous myocardial infarction, and ACS type, the hazard ratio for patients with score values > 8 was 2.47 (95% confidence interval, 1.51-4.06). However, the core model with rSS did not increase the c-statistic compared with the core model with the bSS (from 0.69 to 0.70) and gave little incremental value in the standardized net benefit.

**Conclusions:** In elderly patients with ACS with multivessel disease undergoing PCI, incomplete revascularization was associated with worse outcome at 1-year follow-up. However, there was no clear incremental value of the rSS in the prediction of 1-year adverse outcome compared with a model including clinical variables and bSS.

this evidence gap in a patient population with a mean age of 62 years, showing a significant benefit of complete revascularization regardless of the intended timing of nonculprit lesion PCI.<sup>7</sup> However, this conclusion needs to be verified in elderly patients who could lose the benefit of complete revascularization because of a potentially higher risk of complications and increased use of contrast agents. Indeed, 3 studies have been published on the role of incomplete revascularization in elderly patients with ACS,<sup>8-10</sup> and the exploration of the rSS as a prognostic factor has led to conflicting results.<sup>8-10</sup>

The aim of this study was to verify the incremental value of the rSS over clinical variables and baseline SYNTAX score (bSS) in predicting 1-year mortality or cardiovascular events in patients aged > 75 years undergoing PCI for an ACS.

### Study Design

We conducted a post hoc analysis of data collected in the Elderly-ACS 2 multicenter randomized trial of patients aged > 75 years with an ACS undergoing PCI during index admission.<sup>11</sup> Included in the present analysis were patients with multivessel coronary disease and available data for bSS and rSS. To reduce variability in acquisition methods, we collected data from centers having enrolled at least 25 patients in the original study.

The study protocol complies with the Declaration of Helsinki and was approved by local Ethics Committees. Informed consent was obtained from the subjects originally enrolled in the Elderly-ACS 2 trial.

### Baseline and residual SYNTAX score

The bSS and rSS were analyzed by a panel of interventional cardiologists blinded to the clinical outcomes. The SYNTAX

Pour ce faire, 630 patients âgés de plus de 75 ans, atteints d'une coronaropathie multitrunculaire et ayant subi une ICP pour traiter un syndrome coronarien aigu (SCA) ont été retenus. Le critère d'évaluation principal était composé du décès, de l'infarctus du myocarde récurrent et de l'accident vasculaire cérébral (AVC) au moment du suivi à 1 an. La variation de la statistique C et le bénéfice net normalisé ont servi à évaluer la valeur ajoutée du SSr.

**Résultats :** Les manifestations étaient significativement plus fréquentes chez les patients dont la revascularisation était incomplète (SSr > 8). Lorsque le SSr a été pris en compte dans un modèle de régression de Cox de base ayant pour facteurs l'âge, les antécédents d'infarctus du myocarde et le type de SCA, le rapport des risques instantanés pour les patients ayant un score > 8 était de 2,47 (intervalle de confiance à 95 % : 1,51-4,06). L'intégration du SSr dans le modèle de base n'a toutefois pas donné lieu à une statistique C plus élevée que celle du SSI (0,70 vs 0,69) et conférait peu de valeur ajoutée sur le plan du bénéfice net normalisé.

**Conclusions :** Chez les patients âgés présentant un SCA et une atteinte multitrunculaire, et subissant une ICP, la revascularisation incomplète a été associée à de moins bons résultats au moment du suivi à 1 an. Le SSr n'a toutefois pas été clairement associé à une valeur ajoutée pour prédire une issue défavorable à 1 an comparativement à un modèle reposant sur des paramètres cliniques et le SSI.

score was computed using the SYNTAX score algorithm<sup>12,13</sup> available at the SYNTAX score website.<sup>14</sup> The rSS was defined as the SYNTAX score at the end of the index procedure or at the end of the last planned procedure performed during the index admission. For patients with ST-elevation myocardial infarction (STEMI), the SYNTAX score was calculated using the angiographic views of the infarct-related artery before any intervention.<sup>15</sup> Patients with prior coronary artery bypass were excluded because the SYNTAX score had not been validated in this cohort.<sup>16</sup> All data were entered into a dedicated computerized database.

The primary study outcome was a composite of death, recurrent myocardial infarction (MI), and stroke at 1-year follow-up. All events included in the study database had been adjudicated by an independent Event Adjudication Committee.<sup>11</sup>

### Statistical analysis

Baseline characteristics were compared between patients with complete and incomplete revascularization using the anatomic definition of incomplete revascularization adopted in other studies: rSS > 8.<sup>5,17</sup> Continuous data are presented as mean ± standard deviation or median (interquartile range [IQR]) and were compared between groups (complete vs incomplete revascularization) using the Student *t* test or Mann–Whitney test, as appropriate. Categorical variables were compared between groups using the chi-square test. Correlation between the bSS and rSS was assessed through the Spearman's coefficient of correlation.

We estimated the cumulative incidence of the composite outcome across strata of rSS (<8 vs >8) using the Kaplan–Meier method and assessed the univariate association between the rSS and the event rate using the log-rank test.

We fitted multivariable Cox proportional hazard models to estimate the hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) for each potential predictor of the 1-year composite outcome. We first defined a core model by selecting all predictors that had an HR < 0.8 or > 1.2 (for binary variables) and a *P* value < 0.10 among a set of potential predictors, including sex, age, prior MI, type of ACS, left ventricular ejection fraction, diabetes, chronic obstructive pulmonary disease, peripheral vascular disease, glomerular filtration rate, blood haemoglobin, and body mass index. Then, we compared 3 prediction models including (1) the predictors of the core model plus the bSS; (2) only the rSS; and (3) the predictors of the core model plus the rSS.

In the main analysis, bSS and rSS were included in the models as continuous variables, whereas in a secondary analysis we categorized both scores. Categories for bSS were defined by tertiles of the frequency distribution, whereas rSS was used as binary variable (<8 vs >8).

To replace missing values for left ventricular ejection fraction, glomerular filtration rate, hemoglobin, and body mass index, we used multiple imputation with chained equations.<sup>18</sup> We carried out 5 imputations and used the Rubin's rules to combine the results across the imputed datasets.

We computed the c-statistic to evaluate the discrimination ability of the models. For internal validation, the optimism of the models was estimated by using 300 bootstrapping samples.<sup>19</sup> The estimated optimism was then subtracted from the c-statistic calculated in the original cohort to obtain the optimism-corrected c-statistic. We assessed the model calibration by comparing the predicted probabilities at 1 year and the corresponding Kaplan–Meier estimate, stratifying on intervals of predicted probabilities. To obtain the predicted probabilities, we combined the regression coefficients with the baseline survival function. The baseline survival function was based on zero values for centered continuous variables with all binary predictor set to zero.

According to the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis statement,<sup>20</sup> the change in net benefit (NB) was calculated to evaluate the clinical utility of including the rSS in a prediction model.

The NB is a simple indicator that can be used to evaluate the clinical utility of a prediction model when it is designed to make clinical decisions, for instance, to refer patients predicted to be at high risk of worse outcome to a more intensive treatment. The indicator balances benefits and harms, and puts them on the same scale so that they can be compared directly.<sup>21,22</sup>

We calculated the NB obtained from the application of each prediction model as

$$NB = \frac{TP}{N} - \frac{FP}{N} \cdot \frac{p}{1-p} \quad (1)$$

Where TP are the true-positives, that is, the patients classified at high risk who developed the event, FP are the false-positives, that is, the patients classified at high risk but who did not have the event, *p* is the decision threshold or cutoff used to classify the patient at high risk, and *N* is the total sample size. TP and FP were obtained according to the method described by Vickers et al.<sup>23</sup> The NB was then divided by the proportion of patients who experienced the

composite outcome to obtain the standardized NB (sNB).<sup>21</sup> This facilitates the interpretation of the NB because the sNB represents the proportion of the maximum clinical utility than can be achieved when all patients who had the event and no patients without the event are classified in the high-risk category.

We computed the sNB and the change in the sNB resulting from the inclusion of the rSS in prediction models at 3 different prespecified plausible thresholds of 1-year event rate of 0.10, 0.20, and 0.30, that is, patients were classified at high risk if their predicted probability of 1-year death or cardiovascular event exceeds the threshold. The 95% CIs for the change in the sNB were obtained by bootstrap with 1000 replications.<sup>23</sup>

Decision curves were also drawn to show the sNB for decision thresholds up to 0.50. The analyses were performed using STATA version 14 (StataCorp LP, College Station, TX) and R software version 3.5.1.

## Results

Among the 25 centers enrolling 1443 patients in the Elderly-ACS 2 trial, 15 contributed with > 25 patients each, for a total of 1085 subjects (75.2% of the whole study population). Among them, 630 patients (58%) had multivessel coronary artery disease. The median bSS was 18 (IQR, 12-25; range, 2-68), and the median rSS was 6 (IQR, 2-11; range, 0-51). The correlation between bSS and rSS was 0.68 (*P* < 0.001). An rSS = 0 was achieved in 116 patients (18.4%).

### Baseline characteristics

Patients with incomplete revascularization (rSS > 8) were older and had a higher burden of several cardiovascular risk factors (hypertension, dyslipidemia, decreased kidney function, decreased hemoglobin value) and a higher rate of MI in their medical history (Table 1). Left main disease was more common in patients with incomplete revascularization, whereas the other angiographic characteristics were comparable. Patients with incomplete revascularization were more likely to receive anti-ischemic therapy and diuretics at discharge (Table 2).

### One-year outcome

At 1-year follow-up, 68 patients experienced the composite event of mortality, MI, and stroke, with an estimated cumulative incidence of 12.9% (95% CI, 9.8-16.0). All-cause mortality occurred in 41 patients (6.5%), 18 (4.6%) in patients with rSS score ≤ 8 and 23 (9.7%) in those with higher rSS. Recurrent MI occurred in 20 patients (3.17%), 6 (1.5%) in patients with rSS score ≤ 8 and 14 (5.6%) in patients with higher rSS. Stroke occurred in 14 patients (2.2%), 7 (1.8%) in patients with rSS score ≤ 8 and 7 (2.9%) in the group with higher rSS. Other clinically meaningful events were higher in patients with rSS > 8 as shown in (Supplemental Table S1).

### Predictors of 1-year outcome

Figure 1 shows the cumulative incidence function for patients with rSS less than and greater than 8. An rSS > 8 was associated

**Table 1. Baseline clinical characteristics**

	rSS 0-8 (n = 392)	rSS > 8 (n = 238)	P value
Age, y	79 (76-83)	81 (78-85)	< 0.001
Male sex	250 (63.8)	146 (61.3)	0.540
Body mass index (kg/m <sup>2</sup> )	25.5 (23.5-27.8)	25.7 (23.6-28.4)	0.485
Family history of cardiovascular disease	63 (16.1)	20 (8.4)	0.006
Diabetes	111 (28.3)	74 (31.1)	0.458
Hypertension	292 (74.5)	194 (81.5)	0.042
Hypercholesterolemia	154 (39.3)	113 (47.5)	0.044
Current smoker	30 (7.6)	19 (7.9)	0.881
Chronic respiratory failure	16 (4.1)	11 (4.6)	0.745
Liver disease	5 (1.3)	4 (1.7)	0.678
eGFR at admission (mL/min)*	69.3 (53.6-85.1)	61.7 (48.9-80.8)	0.005
Hemoglobin at admission (g/dL)			
Males	14 (13-15)	13.8 (12.6-14.6)	0.055
Females	12.5 (11.7-13.8)	12.2 (11.7-13.2)	0.070
Neurological disorders	15 (3.8)	4 (1.7)	0.127
Malignancies	9 (2.3)	6 (2.5)	0.857
Previous cardiovascular events			
Myocardial infarction	54 (13.8)	52 (26.0)	< 0.001
PCI	61 (15.6)	45 (18.9)	0.276
Peripheral vascular disease	32 (8.2)	24 (10.1)	0.411
Atrial fibrillation	13 (3.3)	9 (3.8)	0.758
Ongoing cardiovascular medications			
Aspirin	184 (46.9)	119 (47.2)	0.133
Clopidogrel	92 (11.9)	42 (13.6)	0.161
Beta-blockers	121 (30.8)	89 (37.4)	0.078
Calcium antagonists	99 (25.3)	66 (27.3)	0.088
ACEIs or ARBs	200 (51.0)	137 (57.6)	0.117
Diuretics	109 (27.8)	65 (27.3)	0.109
Nitrates	39 (9.9)	49 (20.6)	< 0.001
Statins	111 (28.3)	102 (42.9)	0.001

Data are no. (%) for categorical variables and median (IQR) for continuous variables.

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor antagonist; eGFR, estimated glomerular filtration rate; PCI, percutaneous coronary intervention; rSS, residual SYNTAX score.

\*eGFR by the Cockcroft–Gault formula.

with higher 1-year event rates. [Supplemental Table S2](#) shows the results of the Cox regression model including sex, age, and all potential clinical predictors. Sex, ventricular ejection fraction, glomerular filtration rate, hemoglobin, diabetes, peripheral vascular disease, and chronic obstructive pulmonary disease were not significantly associated with the event rate and therefore were not included in the core model.

[Table 3](#) shows the HRs and corresponding 95% CIs estimated from the 3 prediction models. The HR for 1-point increase in the rSS was 1.06 (1.03-1.08) when the rSS was the only predictor of the model and 1.05 (1.02-1.07) in the multivariable model. [Supplemental Table S3](#) shows the results of the models with bSS and rSS used as categorical variables. When the rSS was considered as categorical variable, patients with values > 8 had a higher cumulative incidence of events with an adjusted HR of 2.47 (95% CI, 1.51-4.06).

### Performance of prediction models and clinical utility

As shown by the c-statistic, the inclusion of the rSS instead of the bSS in the core model did not materially change the discrimination ability ([Table 3](#)). The discrimination ability of the model including the rSS as the only predictor was lower compared with the other models. All models were well calibrated ([Supplemental Fig. S1](#)).

[Table 4](#) gives the sNB obtained from each prediction model when used to classify patients at high or low risk of the composite outcome based on 3 selected decision thresholds

with estimated event rates of 0.10, 0.20, and 0.30. The inclusion of the rSS in the core model resulted in little improvement in the sNB only for the decision threshold of 0.10. For this threshold, the core model including the rSS would correctly identify 4 additional cases and yield 63 less false-positives compared with the core model with the bSS in a population of 1000 patients with a cumulative incidence of the composite event of 12.9%.

[Figure 2](#) shows the decision curves with the sNB estimated for decision thresholds up to 0.50. No clear improvement in risk prediction emerged from the model with the rSS. Results were similar when the bSS and the rSS were included in the model as categorical variables ([Supplemental Table S4](#) and [Fig. S2](#)).

### Discussion

The present analysis, performed in a cohort of elderly and very elderly patients admitted to the hospital for an ACS and treated with PCI, provides relevant insight on the prognostic role of residual critical coronary artery disease, as quantified by the rSS, after ACS treatment. The main findings are the following: In elderly patients with ACS, the residual burden of untreated coronary artery disease is associated with worse outcome at 1-year follow up; however, the rSS does not substantially improve risk prediction when added to a core prediction model including selected clinical variables and bSS. This information may assist clinicians in deciding whether to



**Table 2. Characteristics of index ACS event**

	rSS 0-8 (n = 392)	rSS > 8 (n = 238)	P value
Left ventricular ejection fraction	50 (45-55)	50 (40-55)	0.548
Coronary angiography			
Radial access	320 (81.6)	180 (75.6)	0.071
Left main	77 (19.6)	63 (26.5)	0.046
Procedural treatment			
Stenting	381 (97.4)	222 (94.9)	0.035
Drug-eluting balloons	8 (2.1)	4 (1.7)	0.760
Plain balloon angioplasty	6 (1.5)	10 (4.3)	0.037
Procedural success	378 (96.4)	227 (95.4)	0.794
Length of hospital stay (d)	6 (5-8)	6 (5-10)	0.183
Periprocedural medications			
Aspirin	359 (91.6)	223 (93.7)	0.557
Glycoprotein IIb/IIIa antagonists	77 (19.6)	43 (18.1)	0.880
Unfractionated heparin	330 (84.2)	176 (73.9)	0.005
Low-molecular-weight heparin	65 (16.6)	60 (25.1)	0.031
Bivalirudin	24 (6.1)	17 (7.1)	0.878
Medications at discharge			
Aspirin	385 (98.2)	228 (95.8)	0.117
Proton pump inhibitors	362 (92.3)	209 (97.8)	0.068
Beta-blockers	304 (77.5)	191 (80.2)	0.040
Calcium antagonists	87 (22.2)	51 (21.4)	0.117
ACEIs or ARBs	329 (83.9)	184 (77.3)	0.039
Diuretics	135 (34.4)	103 (43.3)	0.005
Nitrates	42 (10.7)	37 (15.5)	0.019
Statins	365 (93.1)	221 (92.8)	0.056
Oral anticoagulant	8 (2.0)	9 (3.8)	0.047

Data are no. (%) for categorical variables and median (IQR) for continuous variables.

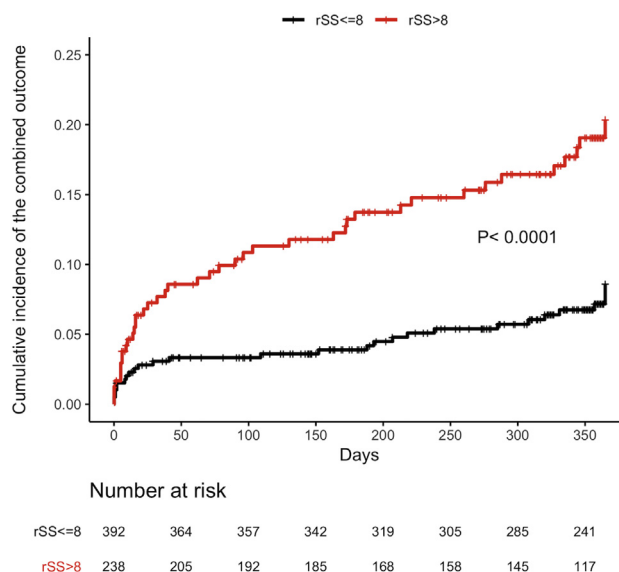
ACEI, angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; ARB, angiotensin-receptor antagonist; rSS, residual SYNTAX score.

pursue complete revascularization in elderly patients with ACS after PCI of the presumably culprit artery.

Our study provides unique data on an elderly population, 20 years older, and with a higher representation of women compared with the recent COMPLETE trial, which showed the superiority of complete vs incomplete revascularization in patients with STEMI.<sup>7</sup>

Despite the differences across the existing observational studies and various definitions adopted (anatomy-based definition vs functional/physiological approach), meta-analyses have suggested significant benefit from complete revascularization over incomplete revascularization with an 18% to 30% difference in long-term mortality and 22% to 33% decrease in MI incidence.<sup>24,25</sup> The overall benefit of complete revascularization was finally shown in the COMPLETE trial of patients with STEMI, but without mortality benefit for which the study was not powered.

We assessed the incremental value of rSS over key clinical predictors and bSS with regard to a hard end point such as the composite of all-cause death, postdischarge MI, and stroke, which we consider of the highest importance in elderly patients, although not necessarily affected by the completeness of revascularization. Mortality was not affected by complete revascularization in the COMPLETE trial,<sup>7</sup> MI at 1-year follow-up was very low in the Elderly-ACS 2 study,<sup>10</sup> and stroke is not likely to be affected by the extent of PCI-corrected coronary disease. The importance of combining



**Figure 1.** Kaplan–Meier estimates of the cumulative incidence functions of the combined outcome (cardiovascular event or death) according to residual Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) score (rSS). Log-rank test P value for comparison between cumulative incidence functions.

clinical and anatomic variables to help decision making in ACS and PCI has been described.<sup>26-28</sup>

Our results are consistent with data drawn from the all-comers SYNTAX trial and other cohort studies, which confirm the prognostic role of rSS in patients with stable coronary artery disease, ACS, and cardiogenic shock.<sup>4-6,26-29</sup> However, they add relevant information assessing the specific and incremental role of residual coronary artery disease in elderly patients with ACS, evaluated throughout the decision curves analysis. This approach has recently been considered the best to describe and compare different prediction models,

**Table 3. HRs and 95% CIs of 1-year mortality or cardiovascular event estimated from multivariable Cox regression models**

Predictors	Core model* + bSS	Model including only rSS	Core model* + rSS
Age (y)	1.08 (1.03-1.13)	-	1.08 (1.03-1.14)
Prior MI	2.15 (1.25-3.69)	-	2.02 (1.17-3.49)
STEMI	1.87 (1.14-3.06)	-	1.88 (1.14-3.09)
bSS	1.04 (1.01-1.06)	-	-
rSS	-	1.06 (1.03-1.08)	1.05 (1.02-1.07)
AIC	822	832	819
c-statistic	0.690	0.644	0.700
Optimism	0.681	0.643	0.691
-corrected c-statistics			

AIC, Akaike information criterion; BMI, body mass index; bSS, baseline SYNTAX score; CI, confidence interval; HR, hazard ratio; MI, myocardial infarction; rSS, residual SYNTAX score; SE, standard error; STEMI, ST-elevation myocardial infarction.

\*The core model included only the predictors that had an HR < 0.8 or > 1.2 (for binary variables) and a P value < 0.10 in a starting model including terms for sex, age, previous myocardial infarction, type of acute coronary syndrome, diabetes, peripheral vascular disease, and chronic pulmonary disease.

**Table 4. Clinical utility of the prediction models at different plausible threshold probabilities of 1-year mortality or cardiovascular event**

Threshold probability	Core model* + bSS (Model 1)	sNB		Change in sNB (95% CI)	
		Model including only rSS (Model 2)	Core model* + rSS (Model 3)	Model 2 vs Model 1	Model 3 vs Model 1
0.10	0.38	0.36	0.47	-0.02 (-0.16 to 0.11)	0.09 (0.02-0.16)
0.20	0.17	0.05	0.11	-0.12 (-0.28 to 0.04)	-0.06 (-0.19 to 0.07)
0.30	0.05	0.02	0.07	-0.03 (-0.13 to 0.06)	0.02 (-0.06 to 0.09)

bSS, baseline SYNTAX score; rSS, residual SYNTAX score; sNB, standardized net benefit.

\*The core model included age, prior myocardial infarction and type of acute coronary syndrome as predictors.

allowing considerations related to the clinical value of a specific risk-stratification tool.<sup>20</sup> According to this analysis, the model including rSS on top of core variables (age, prior MI, and ACS type) and bSS did not significantly improve patients' risk stratification.

This finding is not surprising, considering the heterogeneity of the elderly population. Clinical characteristics associated with aging, such as comorbidities, polypharmacy, frailty, cognitive status, and socioeconomic features, are difficult to be completely addressed and further discriminate patient's risk beyond age.<sup>30</sup> In the LONGEVO-SCA registry, which included a cohort of 531 octogenarians with ACS with geriatric assessment at admission, frailty was an effect modifier in the association between invasive management and outcome. Whereas a conservative management was associated with worse outcome in nonfrail patients, this did not occur in frail patients.<sup>31</sup>

Similar results were reported by Sanchis et al.,<sup>32</sup> who randomized 106 elderly patients with ACS to a routine invasive or a selective invasive strategy. Patients enrolled had to have at least 2 requisites to be considered comorbid patients (peripheral artery disease, cerebral vascular disease, dementia,

chronic pulmonary disease, chronic renal failure, or anemia). Although an advantage in decreasing mortality and ischemic events was observed at 3 months, the benefit was lost at longer-term follow-up.

We could argue that in elderly patients, a more extensive revascularization should be balanced, case by case, with the excess of contrast medium, the risk of vascular complications, and the prolonged hospital stay in patients with staged procedures, and the impact of comorbidity and frailty should always be considered.

In the present study, the rSS showed only a potential modest incremental clinical utility when a plausible decision threshold of 0.10 was used to define patients at high risk of death, recurrent MI, or stroke. In clinical terms, this would imply a potential utility of achieving complete revascularization in patients at overall lower risk, as estimated by the prediction model including age, prior MI, type of ACS, and bSS.

## Limitations

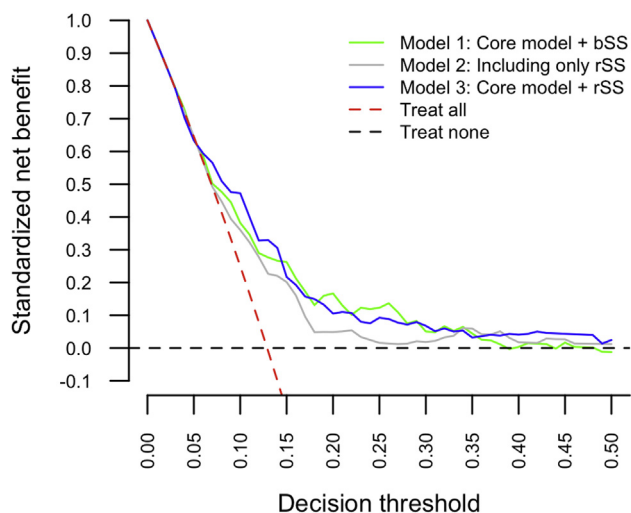
A possible limitation of the study is its design with data collected in an experimental setting with strict monitoring and aggressive management of risk factors and complications. This may reduce the generalizability of the results to real life. However, this may also be a strength, considering the standardized approach toward patients' management and follow-up.

The partial predictive ability of the models may result from unmeasured factors, such as poor social network, impaired cognitive function, dementia, and depression symptoms, which were not assessed in the Elderly-ACS 2 study but may have a significant impact on the prognosis of this elderly population with a high burden of comorbidities.

Ejection fraction and eGFR did not show a significant association with outcome, and we decided not to force these otherwise key variables in the final model. Prior studies have shown the relevant prognostic role of prior MI and ACS type,<sup>33</sup> which are clinically correlated with ejection fraction. These stronger predictors could have potentially overcome the prognostic role of ejection fraction in our study population. On the other side, we cannot exclude that there was a sort of hidden selection bias in an Elderly-ACS study of patients' candidates to an invasive strategy.

We have evaluated only the anatomic rSS. Further studies could clarify if the evaluation of functional rSS could be useful in selecting the best approach in this high-risk population.

Finally, we considered the benefit of achieving a complete revascularization only in terms of coronary anatomy jeopardized



**Figure 2.** Decision curves with standardized net benefit (sNB) computed using the predictions obtained from 3 different models: (1) a core model plus the baseline Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) score (bSS); (2) a model including only the rSS; (3) a core model plus the rSS. The core model included age, prior myocardial infarction (MI), and type of acute coronary syndrome. The sNB is also shown for the 2 extreme conditions, that is, all patients assumed to be at high risk and all patients assumed to be at low risk.

analytics. Other important aspects (e.g., myocardial viability of regions proposed for incomplete revascularization, extent and stability of regional collateral support, and technical revascularization suitability of each individual diseased vessel) should always be evaluated. Unfortunately, these important details, albeit relevant, were not available.

## Conclusions

Recent randomized controlled trials, such as the Elderly-ACS 2<sup>11</sup> and PopularAge<sup>34</sup> studies, have suggested that results drawn from younger patients with ACS are not generalizable to the elderly population. In the present study, a lower degree of residual critical coronary disease after PCI was associated with better 1-year outcome in an elderly population with ACS, but did not substantially improve risk prediction. Elderly patients are a heterogeneous, complex, and often high-risk group for whom cardiovascular risk prediction requires a multidimensional clinical approach beyond coronary anatomic variables.

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The authors have no conflict of interest to declare.

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### Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at <https://www.cjopen.ca/> and at <https://doi.org/10.1016/j.cjco.2020.03.005>.