The Rate of Discordance between Syntax Score II and Cardiologist Decision as a Guide for Mode of Revascularization in Patients with Complex Coronary Artery Disease

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Abstract:

**Background:** The SYNTAX score (SS) II is an objective tool for predicting 4-year mortality and guiding treatment decisions for percutaneous coronary intervention (PCI) and/or coronary artery bypass graft (CABG) in patients with complex coronary artery disease (CAD) and/or unprotected left main stem disease (ULMSD).

**Objectives:** To assess the agreement between the clinical decisions of the cardiologist and the SS II recommendation regarding the revascularization strategies in patients with complex CAD and/or ULMSD.

**Patients and Methods:** Prospective data from patients who presented to Baghdad Medical City Catherization Labs for coronary angiography and were followed up between January 2014 and November 2015 were analyzed. For these patients, SS II was assessed by the two anatomical variables (SS and presence of ULMSD) and six clinical variables (age, creatinine clearance, left ventricular ejection fraction, sex, chronic obstructive pulmonary disease, and peripheral vascular disease) to predict 4-year mortality after revascularization with PCI and/or CABG. These scores were then compared with the clinical decisions of cardiologists. After 1 year of data collection, we followed up the patients by phone to assess their mortality status. Patients were categorized into three groups according the interventional procedures: Group 1 (for PCI), Group 2 (for CABG), and Group 3 (for PCI vs. CABG).

**Results:** Two hundred patients were enrolled. Their mean age was 60.23 ± 9.836 years, and 157 (78.5%) were men. Depending on the clinical judgment of the cardiologist, 71 (35.5%) patients were referred for PCI (Group 1), 119 (59.5%) patients for CABG (Group 2), and the remaining 10 (5%) patients for PCI vs. CABG (Group 3). Based on an assessment of 4-year mortality by the SS II, CABG would have been the treatment of choice in 67 (33.5%) patients, PCI in 30 (15%) patients, and both the treatments in 103 (51.5%) patients. There was a concordance between the clinical decision of the cardiologist and SS II in 67 (33.5%) patients and discordance in 133 (66.5%) patients. Six patients died within 1 year, most of whom were from the discordant group.

**Conclusion:** There was a statistically significant discordance between the SS II recommendation and clinical judgment of the interventional cardiologist. SS II proved to be a useful objective tool to assist experienced clinical judgment in determining appropriate revascularization strategy for CAD patients.

**Keywords:** SYNTAX score, complex coronary artery disease, coronary revascularization.

Introduction:

The SYNTAX Score II (SS II) was recently developed to guide better decision-making between percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) compared to the anatomical SYNTAX score (SS) in patients with complex coronary artery disease (CAD). The SS II merges the anatomical SS and clinical variables [age, creatinine clearance (CrCl), left ventricular ejection fraction (LVEF), presence of unprotected left main stem disease [ULMSD], peripheral vascular disease (PVD), female sex, and chronic obstructive pulmonary disease (COPD)] to upgrade the threshold value of the anatomical SS by individual assessment of long-term mortality in patients with left main/multivessel CAD undergoing either PCI or CABG (Fig. 1).1,2 There are specific points assigned to each factor of SS II. A total of 8 points can be used for accurately predicting the 4-year mortality of an individual patient proposing to undergo PCI or CABG. Younger age, reduced LVEF, and female sex favors CABG over PCI based on long-term prognosis. Thus, in such patients, a lower anatomical SS would be required for similar long-term mortality risk for PCI and CABG. In contrast, older age, ULMSD, and COPD favors PCI over CABG. Thus, in these types of patients, a higher anatomical SS would be needed for the long-term mortality risks to be similar. For example, a 60-year-old man with an anatomical SS of 30, LVEF of 50%, presence of ULMSD, CrCl of 60 ml/min, and COPD would have 41 points (predicted 4-year mortality: 16.3%) and 33 points (predicted 4-year mortality: 8.7%) to undergo CABG and PCI, respectively. In the same example,
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exclusion of COPD would lead to identical points (29 points) and 4-year mortality predictions (6.3%) for CABG and PCI. In this study, we aimed to assess the agreement between clinical decisions of the cardiologist and the SS II recommendation regarding revascularization strategies in patients with complex CAD and/or ULMSD.

COPD, chronic obstructive pulmonary disease; F, female; LVEF, left ventricular ejection fraction; Left main, unprotected left main coronary artery disease; M, male; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease.

Patients and methods:
Prospective data from patients who presented to Baghdad Medical City Catheterization Labs for coronary angiography (CA) and were followed up between January 2014 and November 2015 were analyzed. All patients were evaluated considering age, history of diabetes, high blood pressure, smoking status, hypercholesterolemia, COPD, PVD, myocardial infarction (MI), cerebrovascular accident (CVA), and family history of premature cardiovascular diseases. Blood urea and serum creatinine, and electrocardiographic and echocardiographic assessments were performed for all patients before CA. All patients underwent diagnostic CA. The baseline anatomical SS for each angiogram was assessed by the interventional cardiologist using a manual method or a computer program (each coronary lesion causing stenosis of ≥50 percentage diameter of a vessel with a caliber ≥1.5 mm).

SS II uses two anatomical variables (SS and presence of ULMSD) and six clinical variables (age, CrCl, LVEF, sex, COPD, and PVD) to predict 4-year mortality after revascularization with PCI or CABG. The Cockcroft–Gault formula was used to estimate CrCl. Using the baseline clinical and angiographic data, SS II was calculated for each patient using a nomogram of SS II (Fig. 1). In the assessment of each patient, SS II generates different scores and distinct predicted mortalities according to the potentially applied mode of revascularization, percutaneous or surgical intervention. SS II recommends CABG if the difference in the predicted mortality risk favors CABG with 95% confidence, or PCI if the difference favors PCI with 95% confidence. Conversely, the SS II recommends PCI vs. CABG if mortality risk predictions were within the 95% confidence interval of the difference in mortality risk prediction. Patients were categorized into three groups according the interventional procedures: Group 1 (for PCI), Group 2 (for CABG), and Group 3 (for PCI vs. CABG).

SS II recommendations were compared with the clinical judgments of cardiologists and the concordance vs. discordance between the two was assessed. After 1 year of data collection, we followed up the patients by phone to assess their mortality status; however, this communication was successful in 92 patients only.

The study was approved by the Research Ethics Committee of Baghdad Medical City Catheterization Lab, and performed in accordance with the ethical standards of the Declaration of Helsinki. In addition, all patients signed an informed consent form before
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Results:
Two hundred patients were included in the current study. SS II baseline demographic data are presented in Table 1. The patient ages ranged from 33-80 years (mean 60.23 ± 9.836 years). There were more men than women (78.5% vs. 21.5%). The risk factors noted were hypertension (56.5%), diabetes mellitus (45.5%), currently smoking (26%), and hypercholesterolemia (8%). There were statistically significant differences in age, female gender, diabetes mellitus, smoker, COPD, family history, dyslipidemia, CrCl, and LVEF between the groups.

The PCI recommended group (Group 1) was older, with better LVEF, a higher prevalence of COPD, and a lower anatomical SS. On the contrary, patients recommended for CABG (Group 2) were younger, male, with higher anatomical SS, and lower LVEF.

Table 1: Baseline characteristics according to SYNTAX score II

| Characteristic          | Total (n=200) | Group 1 (n=30) | Group 2 (n=67) | Group 3 (n=103) | p-value |
|-------------------------|---------------|----------------|----------------|-----------------|---------|
| Age (years) ± SD        | 60.23 ± 9.836 | 69.5 ± 7.695   | 61.54 ± 9.161  | 56.78 ± 8.969   | 0.001*  |
| Male %                  | 157 (78.5%)   | 29 (96.7%)     | 33 (49.3%)     | 95 (92.1%)      | 0.061   |
| Female %                | 43 (21.5%)    | 1 (3.3%)       | 15 (25.7%)     | 5 (7.9%)        | 0.042*  |
| Hypertension %          | 113 (56.5%)   | 18 (60.0%)     | 42 (62.7%)     | 53 (51.5%)      | 0.416   |
| Diabetes mellitus %     | 91 (45.5%)    | 8 (28.5%)      | 44 (62.8%)     | 39 (38.2%)      | 0.001*  |
| Current smoker %        | 52 (26%)      | 8 (26.7%)      | 13 (19.4%)     | 31 (30.1%)      | 0.003*  |
| COPD %                  | 24 (12%)      | 14 (46.7%)     | 2 (2.9%)       | 8 (7.8%)        | 0.001*  |
| PVD %                   | 9 (4.5%)      | 2 (7.1%)       | 5 (7.7%)       | 2 (1.96%)       | 0.210   |
| Previous MI %           | 56 (28%)      | 4 (14.2%)      | 25 (35.7%)     | 27 (26.4%)      | 0.06    |
| CVA, TIA %              | 6 (3%)        | 1 (3.6%)       | 3 (4.2%)       | 2 (1.96%)       | 0.6     |
| Family history %        | 22 (11%)      | 0              | 6 (8.5%)       | 16 (15.7%)      | 0.04*   |
| Dyslipidemia %          | 16 (8%)       | 0              | 3 (4.2%)       | 13 (12.7%)      | 0.012*  |
| CrCl ml/min ± SD        | 87.8 ± 31.23  | 80.64 ± 20.8   | 74.4 ± 28.632  | 98.5 ± 31.529   | 0.001*  |
| LVEF by M-mode          | 54.95 ± 10.33 | 56.89 ± 7.3    | 49.29 ± 12.33  | 54.94 ± 10.33   | 0.001*  |
| ULMSD ± 3 CAD %         | 24 (12%)      | 3 (10.7%)      | 8 (11.4%)      | 13 (12.7%)      | 0.006*  |
| SYNTAX Score ± SD       | 24.6 ± 8.489  | 19.64 ± 5.78   | 28.91 ± 8.267  | 24.87 ± 8.368   | 0.001*  |

SD, standard deviation; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; MI, myocardial infarction; CVA, cerebrovascular accident; TIA, transient ischemic attack; CrCl, creatinine clearance; LVEF, left ventricular ejection fraction; ULMSD, unprotected left main stem disease; CAD, coronary artery disease

P values were calculated by ANOVA. *statistically significant

A summary of the distribution of the total patient cohort is shown in Fig. 2.
PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; SS II, SYNTAX score II; CD, cardiologist’s decision

The recommendations for PCI or CABG according to SS II in complex CAD and ULMSD are shown in Table 2. No significant differences were observed.

Table 2: SYNTAX score II based treatment recommendations in complex coronary artery disease and unprotected left main stem patients

| SYNTAX Score II | Complex CAD | ULMSD | Total | p-value |
|----------------|-------------|-------|-------|---------|
|                | (n=176)     | (n=24) | (n=200)|         |
| Group 1        | 27 (15.3%)  | 3 (12.5%) | 30 (15%) | 0.067 |
| Group 2        | 59 (33.6%)  | 8 (33.3%) | 67 (33.5%) | 0.068 |
| Group 3        | 90 (51.1%)  | 13 (54.2%) | 103 (51.5%) | 0.069 |

ULMSD, unprotected left main stem disease; CAD, coronary artery disease

The clinical judgment of cardiologists for the interventional procedure is shown in Table 3. Of the 67 patients who were referred for CABG based on their SS II, the cardiologist’s recommendation was concordant in 47 (70.1%) patients referred for CABG and discordant in 19 (28.35%) patients planned for PCI, as well as 1 patient referred for PCI vs. CABG, with a significant p-value. The concordance of clinical judgment and SS II recommendations is shown in Table 4.

Table 3: Distribution of the clinical decisions according to SYNTAX score II recommendations

| Variables | SYNTAX Score II Total | p-value |
|-----------|----------------------|---------|
|           | Group 1 | Group 2 | Group 3 |
| Clinical decision of cardiologist | 11 | 19 | 41 | 71 | 0.04* |
| Group 1 | 19 | 47 | 53 | 119 |
| Group 2 | 0 | 1 | 9 | 10 |
| Total | 30 | 67 | 103 | 200 |

*statistically significant

Table 4: Concordance of clinical judgment and SYNTAX Score II recommendations

| Clinical decision of cardiologist | SYNTAX Score II p-value |
|----------------------------------|-------------------------|
|                                  | Group 1 | Group 2 | Group 3 | Total |
| Concordance (n=97)               | 11 | 47 | 9 | 67 | 0.001* |
| Discordance (n=133)             | 19 | 20 | 94 | 133 |
| Total (n=200)                   | 30 | 67 | 103 | 200 |

*statistically significant

After 1 year, the clinical outcomes of 92 patients were checked by phone follow-up. The mortality rate was 6.25%, as shown in Table 5. A significant difference was observed between patients with and without concordance (p-value = 0.0286).

Table 5: Mortality rate according to the concordance and discordance groups

| Clinical decision of cardiologist | Mortality after 1 year p-value |
|----------------------------------|--------------------------------|
| Concordance (n=44)               | 2 (4.6%)                      | 0.0286* |
| Discordance (n=48)               | 4 (8.3%)                      |        |
| Total (n=92)                     | 6 (6.52%)                     |        |

*statistically significant

Distribution of the anatomical SS according to the SS II recommendation is shown in Table 6. Anatomical SS was classified as low anatomical SS (<22) and PCI was recommended, whereas patients with high anatomical SS (>33) were referred for CABG (p-value = 0.001).

Table 6: Distribution of the SYNTAX score II treatment recommendation

| Score | SYNTAX Score II | Total | p-value |
|-------|-----------------|-------|---------|
|       | Group 1 | Group 2 | Group 3 |       |
| Anatomical SYNTAX Score | 22 | 16 | 34 | 34 | 60 | 0.0001* |
|        | 23 | 13 | 36 | 36 | 72 |        |
|        | 32 | 1 | 3 | 3 | 68 |        |
| Total | 30 | 67 | 103 | 200 |

*statistically significant

Discussion:
The SS II demonstrated that certain anatomical and clinical characteristics could have different impact on the preferred type of treatment. This provides the cardiologist vital information for decision-making; i.e. younger women, those with lower CrI, lower LVEF, and higher anatomical SS should undergo CABG. On contrary, older people, with lower SS, and COPD should undergo PCI. Campos et al.2 and Farooq et al.10 have reported similar recommendations. However, the presence of diabetes favored CABG in the current study, which is different from the findings by Campos et al. who favored PCI.2 In the study by Farooq et al., diabetes was not a significant risk factor.10
In the current study, the treatment recommendations for CABG and PCI in the complex CAD group were 33.6% and 15.3%, respectively. For ULMSD, CABG was recommended in 33.3% of patients and PCI recommended in 12.5% of patients, with no significant difference. This result is similar to the results obtained by Farooq et al.10 and Escaned et al.11 In the SYNTAX II trial1, the treatment recommendations for CABG and PCI in the complex CAD group were 40.7% and 0.5%, respectively (the remaining 58.8% were scheduled for PCI vs. CABG). For the left main cohort, CABG was recommended in 11.5% of patients and PCI in 8.8% of patients.2 There was a difference in treatment recommendations between the current study and the findings of Farooq et al.10 in the complex CAD group, but the recommendations were very similar in the ULMSD group.

Our study showed that SS II recommendations resulted in 33.5% for CABG and 15% for PCI, while the remaining 51.5% of patients were recommended for CABG vs. PCI (Table 3). Comparison between the current study and the international studies according to SYNTAX II recommendations shown is figure 3, in the Bojan et al. study12. PCI was suggested in 1%, CABG in 41.4%, and PCI vs. CABG in 58% of the patients. In the SYNTAX II trail, PCI and CABG were recommended in 2% and 24% of the patients, respectively, whereas the remaining 74% were recommended for PCI vs. CABG.1 Campos et al.2 undertook a large study with 5433 patients that showed CABG and PCI recommendations of 1% and 5%, respectively, while the remaining (96%) patients were recommended for PCI vs. CABG. In the study by Salvatore et al.13, which included 217 patients, PCI was recommended by SS II in 46.1% of the patients. The difference in these proportions of treatment recommendations confirms that the present group in the current study had a lower risk profile for PCI compared to the SYNTAX trial and to the study by Campos et al.2 Moreover, the difference in recommendations dependent on the SS II calculation, which includes several clinical factors, means that a change in each factor may lead to significant variations in the SS II recommendation.

Figure 3: Comparison between the current study and the international studies according to SYNTAX II recommendations.

PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.

The decision-making process to establish the optimum revascularization strategy and evaluation of the expected benefits vs. procedural (interventional or surgical) risk depends on clinical judgment of the interventional cardiologist. In the current study, 35.5% patients were recommended for PCI and 59.5% for CABG, while the rest (5%) were recommended for PCI vs. CABG. Compared to our SS II recommendation (Table 3), there was a low agreement between the clinical judgment and SS II recommendation with concordance in 33.5% of patients and discordance in the remaining 66.5% of patients. In the study by Bojan et al., there was high agreement between the SS II treatment recommendation and clinical judgment, with concordance in 76.1% of patients.12 The low concordance between clinical judgment and SS II recommendation in the current study may be due to: 1) the decision depended mostly on the anatomical SS regardless of other clinical risk factors, 2) the decision of the heart team was the final clinical decision in the study by Campos et al.,2 but in our study, the decision was dependent on the interventional cardiologist, and/or 3) the discordance in SS II CABG recommendations may be explained by the refusal of the patient to undergo CABG. The mortality observed at the 1-year follow-up was 6.25% and a significant difference in the observed mortality was found between patients with and without concordance (4.6% vs. 8.3%, respectively). All deceased patients died due to cardiac causes. The presence of ULMSD, diabetes, or the presence of a high SS II with a CABG recommendation but PCI treatment, were the best predictors of mortality at 1-
year. These results are similar to those reported by Salvatore et al.13 and Escand et al.11 These findings emphasize the importance of the SS II in providing objective individual risk stratification for decision-making. Since the anatomical SS is one of the components of the SS II, the other clinical factors clearly impacted the treatment recommendations with a significant difference, and this finding was comparable with that obtained by Cavalcante.14 There were patients with a low anatomical SS (<22) recommended for PCI and patients with a high anatomical SS (>33) in whom CABG could be considered. These results are compatible with those obtained by Farooq et al., Campos et al., and Cavalcante.14

**Limitations:** There was no 4-year follow-up to correlate with 4-year predictions in this study. This was a single center study, so the generalizability of our findings to other study populations may be limited.

**Conclusions:**
There was a statistically significant discordance between the SS II recommendation and clinical judgment of the interventional cardiologist. SS II proved to be a useful objective tool to assist experienced clinical judgment in determining appropriate revascularization strategy for CAD patients. This tool can be used in daily clinical practice in the catheterization lab to guide the optimization of revascularization strategies in patients with complex CAD and/or ULMSD in order to reduce mortality rates.

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