Paradigm Has Already Shifted to Ischemia-Guided Functional Approach

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The anatomical SYNTAX (Synergy between percutaneous coronary intervention with TAXUS and Cardiac Surgery) score is a stratification score illustrating the complexity of angiographic stenosis. It was considered a surrogate for poor prognosis following percutaneous coronary intervention (PCI). Accordingly, in patients with a high baseline SYNTAX score (bSS) requiring coronary revascularization, coronary artery bypass graft (CABG) surgery was chosen over PCI in the current guidelines. The mechanism by which bSS is a good surrogate for long-term prognosis is evident. Patients with a high bSS compared to those with a low bSS have more complex comorbidities, such as old age, diabetes, multiple stenoses, and low left ventricular function. Subsequently, they receive more complex procedures using multiple stents and devices.

Since revising the SYNTAX score II by taking into consideration clinical risk factors, the function of the scoring model in choosing between PCI and CABG and prognosis prediction has improved. The residual SYNTAX score (rSS), which is a variant of the SYNTAX score, was recently constructed to represent the extent of untreated coronary lesions after revascularization treatment. In the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) study, comprised of patients with acute coronary syndrome (ACS), there was a stepwise increase in the rate of major adverse cardiac events, including death, myocardial infarction (MI), and unplanned revascularization in patients with an rSS of 0 (16.3%), >0–2 (18.0%), >2–8 (20.0%), and >8 (22.4%). In particular, for patients with an rSS >8, indicating incomplete revascularization (ICR) of multiple lesions after PCI, the mortality rate was significantly higher than in patients with an rSS ≤8. It is worth noting that subjects in the ACUITY study were not suitable to validate the predictive ability of rSS. ACS patients enrolled in the ACUITY study may have been intentionally treated with a culprit angioplasty, without the goal of complete revascularization.
A retrospective angiographic analysis of the SYNTAX study by Farooq et al. provides important information on whether the rSS has a good discriminatory power for predicting outcomes in patients presenting with relatively stable symptoms. Patients with an rSS of >8 had a higher risk of 5-year mortality (35.3%) compared to those with an rSS of 0 (8.5%), >0–4 (8.7%), and >4–8 (11.4%). Given these findings, rSS appears to be a validated angiographic score to represent the degree of ICR and predict outcomes following PCI. Combined with the predictive role of bSS before PCI, simulation of post-procedural rSS may synergistically help the Heart team decide the best revascularization approach. For a patient with multiple stenoses who is expected to have an rSS >8 after using PCI, CABG may be a more appropriate approach regardless of the bSS. On the other hand, if a reasonable ICR with a low rSS is expected, PCI may be an alternative approach to surgery, even for patients with a relatively high bSS.

Despite the conceptual usefulness and related evidence, the clinical relevancy and application of rSS is still debatable. First, the anatomical rSS still has an inherent limitation on the lack of considering clinical risk factors. Second, marked variability in the prognostic value of angiographic CR across studies has been observed. Some studies showed favorable results after CR compared with ICR, in patients receiving PCI with bare-metal or drug-eluting stents (DES). In 3,803 propensity-score matched pairs who received PCI with DES, the 8-year survival rate was higher after CR than ICR (80.8% vs. 78.5%; hazard ratio [HR], 1.12; 95% confidence interval [CI], 1.01 to 1.26; p=0.04). By contrast, another recent study failed to show an association between CR and long-term clinical outcomes. Out of 1,400 patients with multivessel disease receiving DES, CR was performed in 573 (40.9%) patients with a similar 5-year incidence of major adverse cardiac or cerebrovascular events (MACCE), comprising death, MI, stroke, or target vessel revascularization compared with ICR patients (24.0% vs. 29.3%);
adjusted HR, 0.94; 95% CI, 0.75 to 1.18; p=0.61). The discrepancy across studies may indicate that CR rate and its clinical impact may be diverse according to geographical and temporal variations. ICR is often performed intentionally by surgeons taking into consideration the clinical presentation, comorbidity, anatomical complexity, functional ischemia, economical status, reimbursement regulation, or institutional policies. In fact, a high rSS caused by multiple residual stenoses may be a consequence of unsuccessful PCI, not an independent covariate influencing outcomes. Due to the multifactorial mechanisms influencing residual lesions following PCI, rSS may be limited to generalized applications in daily practices. In fact, small lesions up to 1.5 mm, which is the threshold for calculating rSS, are often unrevascularized in the procedures.

Third, another serious limitation of rSS is the lack of information on functional ischemia in the scoring model. Inducible myocardial ischemia during functional testing has a crucial prognostic significance in determining whether or not to treat anatomical stenosis. The FAME (Flow Reserve versus Angiography for Multivessel Evaluation) study, which compared fractional flow reserve (FFR)-guided PCI to angiography-guided PCI for stable patients, showed that in lesions with a stenosis between 50–70%, 71–90%, and 91–99%, 65%, 20%, and 4% were found to be functionally insignificant lesions with FFR >0.80, respectively. Patients assigned to ischemia-guided PCI using FFR received fewer stents (1.9 vs. 2.7, p<0.001) and showed a lower 2-year incidence of death or MI (8.4% vs. 12.9%, p=0.02) compared with angiography-guided PCI. Kim et al. also reported that ischemia-guided revascularization using single photon emission computed tomography reduced the incidence of MACCE compared to non-ischemia-guided revascularization (17.4% vs. 22.8%; adjusted HR, 0.59; 95% CI, 0.43–0.81; P=0.001), driven by a lower incidence of repeat revascularization (9.9% vs. 14.8%; adjusted HR, 0.53; 95% CI, 0.35–0.80; P=0.003) in a single center registry comprising 2,587 patients. Therefore, the
integration of clinical and functional information on the anatomical rSS may be warranted for a better performance as a prognostic surrogate. The ongoing ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trial, comparing the effectiveness of initial optimal medical treatment vs. revascularization for patients with moderate to severe ischemia, may clarify the differential clinical impact of residual anatomical stenosis versus functional stenosis for stable coronary disease patients.

In conclusion, Farooq et al. have validated the angiographic score model of rSS that accurately predicts a long-term prognosis following PCI with DES for multivessel or left main stenosis. The score has advantages and disadvantages for general use in coronary revascularization. Because the bSS and rSS are closely related and easily calculated, the two scores improve the predictability of PCI prognosis and help physicians select optimal revascularization strategies. However, the absence of functional data in scoring is a disadvantage to guiding an appropriate revascularization approach. Given this, with the application of these scoring systems, physicians need to re-emphasize the importance of adhering to guidelines recommending ischemia-guided revascularization.\textsuperscript{2,3} An approach of ‘reasonable incomplete revascularization’ for stable patients is necessary for optimal outcomes.\textsuperscript{3,11,17} Future research to construct a better scoring model is required in order to comprehensively address patients’ clinical, anatomical, and functional complexities and predict subsequent prognosis.

**Conflict of Interest Disclosures:** None.

**References:**


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