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Commentary: Developing accurate tools for predicting outcomes following coronary artery bypass graft surgery: More data are needed

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The emergence of percutaneous coronary interventions (PCI) as an alternative treatment to coronary artery bypass graft (CABG) surgery for 3-vessel disease (3VD) and left main coronary artery disease (LMCAD) has led to the creation of various tools to assess mortality following coronary revascularization. The SYNTAX score was developed to provide an accurate measurement of the anatomic complexity of CAD.¹ It has subsequently been used to help decide the optimal intervention (PCI vs CABG) for patients with 3VD and has been incorporated into the 2014 American and 2018 European guidelines.^{2,3} However, the original SYNTAX score was based only on the anatomic complexity of CAD and lacked the prognostic effects of concomitant comorbidities known to effect short- and long-term mortality following coronary revascularization. Therefore, the SYNTAX score II was developed to more accurately predict outcomes following coronary revascularization by incorporating 7 clinical variables (ie, age, creatinine clearance, left ventricular ejection fraction, LMCAD, peripheral vascular disease, sex, and chronic obstructive pulmonary disease) in addition to the anatomic complexity of the original SYNTAX score.⁴ SYNTAX score II has been shown to be a better predictor of long-term mortality following either PCI or CABG in patients with 3VD and

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CENTRAL MESSAGE

The SYNTAX score II is more accurate in predicting short- and long-term mortality for patients undergoing coronary revascularization; more data are needed to determine whether PCI or CABG is best.

LMCAD.⁵ Recently, the SYNTAX score II 2020 was developed in which patient sex was removed and diabetes and current smoking history were added as predicted variables.⁶ The SYNTAX score II 2020 has been externally validated for 5-year outcomes using patient-level data from the Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM), Bypass Surgery versus Everolimus-Eluting Stent Implantation for Multivessel Coronary Artery Disease (BEST), Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease (PRECOMBAT), and Evaluation of the Xience Everolimus Eluting Stent vs Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trials.^{6,7}

A unique feature of the SYNTAX score II 2020 is that it can predict not only mortality, but also major adverse cardiovascular events (MACEs) for PCI and CABG in patients with 3VD and LMCAD. Therefore, it was believed that the SYNTAX score II 2020 could provide additional objective data for heart teams to help determine the best approach for coronary revascularization in an individual patient. Hara and colleagues⁸ sought to investigate whether the SYNTAX score II 2020 could be used to identify the benefits of PCI versus CABG in more than 7000 patients with 3VD or LMCAD enrolled in the Japanese Coronary

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Revascularization Demonstrating Outcome Study in Kyoto (CREDO-KYOTO) Registry.⁸ In this study, an absolute risk difference (ARD)—representing the difference between observed and predicted event rates for mortality and MACE following PCI and CABG—was calculated for each patient. In patients with an ARD <4.5%, there was no significant difference between PCI and CABG. However, there was a significant reduction in 5-year mortality in favor of CABG when the ARD was >4.5%. Five-year MACE could not be predicted for either PCI or CABG. The authors concluded that the SYNTAX score II 2020 could be used to help decide the best revascularization strategy for patients with 3VD and LMCAD.

In this edition of the *Journal*, Ram and colleagues⁹ sought to determine the ability of the SYNTAX score II to predict short- and long-term mortality in patients undergoing either PCI or CABG for 3VD or LMCAD using a multicenter national registry derived from 22 hospitals in Israel. The 1112 patients were divided into low (<25), intermediate (25-35), and high (>35) SYNTAX score II groups. The revascularization strategy, PCI versus CABG, was left to the discretion of the treating team. A net reclassification improvement was used to predict the benefit of adding a SYNTAX score II to predict short- and long-term mortality. Patients with a high SYNTAX score II (>35) had significantly higher 30-day mortality (2.8% high vs 0.6% intermediate vs 0% low; $P = .001$) and 6-year mortality (34.9% high vs 11% intermediate vs 3.8% low; $P < .001$) compared with the low and intermediate groups. The addition of the SYNTAX score II, compared with the original SYNTAX score, showed a significant net reclassification improvement of 24.2% ($P = .003$) for predicting 6-year mortality. The authors concluded that in a cohort of real-world patients undergoing coronary revascularization for 3VD or LMCAD, the SYNTAX score II is a better risk-stratification tool for predicting short- and long-term mortality compared with the original SYNTAX score.

Although the authors have demonstrated that the SYNTAX score II may better predict mortality for coronary revascularization, they have not shown how these data can be used by heart teams to determine which revascularization strategy, PCI or CABG, should be used in an individual patient. The authors listed the incidence of postprocedural complications following PCI and CABG, but no direct statistical comparisons were made between the 2 techniques. In addition, no statistical analyses were performed to determine the difference in short- and long-term mortality between PCI and CABG in relation to the severity of their SYNTAX score II, and whether the cause of death—cardiac versus noncardiac—could also be predicted for PCI versus CABG patients. Important data in CABG patients predictive of short- and long-term outcomes were not reported. This included the number of grafts per patient, the use of multiple arterial grafts (MAGs), and whether or not complete revascularization was

achieved. Although the authors reported data on the use of guideline-directed medical therapy (GDMT) on admission, no data was provided on GDMT on either discharge or long-term. Finally, no mention is made regarding the long-term MACE for PCI versus CABG; especially, the incidence of myocardial infarctions (MIs) and the need for repeat revascularization procedures. Thus the value of the SYNTAX score II to determine coronary revascularization by either PCI or CABG by heart teams remains uncertain.

What can be done to improve the prognostic accuracy for determining short- and long-term mortality and MACE following PCI or CABG for patients with 3VD and LMCAD? To develop more accurate tools to predict outcomes following PCI and CABG, more data are needed. Both CABG and PCI outcomes are determined by preprocedure comorbidities and coronary anatomy, procedure-related techniques, and postrevascularization complications. Although preprocedural comorbidities and coronary anatomy are well documented by SYNTAX score II, they fail to take into account the techniques used during the procedure and the immediate postrevascularization complications following PCI and CABG that have a significant effect on mortality and MACE. This explains why both SYNTAX score I and II failed to predict long-term MACE.⁸ A new scoring system needs to be developed to include data during the revascularization procedure and the immediate postrevascularization period for both PCI and CABG to more accurately reflect the benefits of both techniques in patients with 3VD and LMCAD. The new scoring system should include the following:

ABILITY TO ACHIEVE COMPLETE REVASCULARIZATION

Incomplete revascularization has been associated with decreased late survival following both PCI and CABG.^{10,11} Farooq and colleagues¹¹ reported that following PCI, a residual SYNTAX score I >8 was associated with a 35% all-cause mortality at 5 years ($P < .001$). Therefore, if a complete revascularization could not be achieved with PCI, CABG would be a more appropriate revascularization procedure in patients with 3VD in whom a residual SYNTAX score >8 after PCI is expected regardless of the baseline SYNTAX score II.

REVASCULARIZATION WITH MAG

MAG has been associated with improved long-term survival, but in the New York State database, the survival curves began to diverge only after 7 years.¹² Therefore, new scoring systems need to take into account that survival and MACE should be based on both 5- and 10-year follow-up. In the current SYNTAX score II, low-risk, younger patients would have lower scores suggesting no difference in 30-day mortality between PCI and CABG. These patients would more likely be referred for PCI, despite the fact

that CABG with MAG would have the potential for better long-term survival and a decreased incidence of revascularization, recurrent MI, and recurrent angina.

TREATMENT OF CONCOMITTENT COMORBIDITIES DURING CORONARY REVASCULARIZATION

Significant but asymptomatic valve disease and preprocedure atrial fibrillation can increase both short- and long-term mortality and MACE if they are not addressed at the time of the coronary revascularization procedure. A concomitant ablation procedure and left atrial appendage closure at the time of CABG in patients with preoperative atrial fibrillation has been associated with a decreased incidence of strokes, systemic embolization, and improved long-term survival.¹³ The ability to treat coexisting comorbidities at the time of coronary revascularization should be reflected in future scoring models.

COMPLIANCE WITH GDMT

Noncompliance with GDMT following both PCI and CABG has been shown to decrease long-term survival, freedom from MI, and the need for repeat coronary revascularization procedures.^{14,15} The lack of compliance with GDMT is especially detrimental for CABG patients. The beneficial advantages of CABG over PCI with 3VD and LMCAD have been found to be negated in those CABG patients who are noncompliant with GDMT.^{14,15} Therefore, compliance with GDMT should be factored into new scoring systems to more accurately reflect long-term mortality and MACE.

POTENTIAL NEED FOR FUTURE REVASCULARIZATION PROCEDURES

Currents scoring systems do not take into account the morbidity and mortality involved when a future revascularization procedure is required. This is especially true for younger patients with low SYNTAX scores who are more likely to receive a multivessel PCI. However, patients with previous multivessel stenting who subsequently undergo CABG have an increased risk for hospital mortality, MACE, and decreased long-term survival compared with patients without a previous PCI, especially in patients with diabetes.¹⁶⁻²⁰ This should be reflected in future scoring systems and be discussed more thoroughly in heart teams; especially in relation to younger patients with lower SYNTAX scores.

Because of the shortcomings of the current scoring systems, heart teams must continue to take into account not only preoperative comorbidities and coronary anatomy, but also the ability to achieve a complete revascularization, the durability of the conduits and the stents used, and the ability to treat other comorbidities at the time of revascularization such as atrial fibrillation and valve

disease. Furthermore, it is important to note that compared with PCI, although CABG mortality may be slightly higher during the first year following revascularization, CABG results in a significant increase in freedom from recurrent angina and the need for repeat revascularization in the long term. This is similar to the findings from the Placement of Aortic Transcatheter Valves 3 (PARTNER 3) trial comparing surgical aortic valve replacement with transcatheter aortic valve replacement in low-risk patients where the advantages seen in mortality and stroke at 1 year in the transcatheter aortic valve replacement group were no longer seen after 2 years.²¹

The SYNTAX score II has been shown to be more accurate than its predecessor, but to better predict short- and long-term mortality and MACE in order to better determine the role of PCI versus CABG in individual patients, more data are needed.

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