Significant coronary artery disease (CAD) is present in up to 50% of patients with symptomatic aortic stenosis (AS). Although numerous databases have shown that the addition of bypass grafting to an aortic valve replacement (AVR) nearly doubles the mortality, surgical series have shown that leaving significant coronary stenosis untreated increases AVR mortality.1–4 Thus, the standard of care for this population has been concomitant coronary artery bypass grafting along with surgical aortic valve replacement.

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Several groups have been investigating the role of hybrid procedures for the treatment of concomitant CAD and AS. Percutaneous coronary intervention either immediately preceding or simultaneously with surgery has been shown in limited series to be safe.5 Admittedly, there may be a strong publication bias favoring studies with superior outcomes, and larger studies are underway. The goal of hybrid procedures is to reduce a higher-risk coronary artery bypass grafting (CABG)/AVR to 2 potentially lower-risk and less morbid procedures. There are at least 2 important considerations raised by this concept. First, can PCI be performed safely in the setting of AS, and if so what is the best timing for it? Second, what is the impact of the necessary dual antiplatelet therapy on bleeding with surgery?

There are very limited data evaluating the safety of PCI in the setting of AS. Although several studies noted that PCI could be performed safely without increased procedural risk, these studies were small and uncontrolled.6–7 The study by Kapadia et al in this issue of Circulation adds significantly to our understanding of the safety and efficacy of PCI in the setting of AS.8 It compares the outcomes of 254 patients with severe aortic stenosis who underwent PCI at the Cleveland Clinic over an 11-year period with the outcomes of a propensity-matched cohort without AS. Although there was no difference in mortality between matched controls, the short-term mortality of 4.3% is sobering and attests to the high-risk nature of this population.

Subgroup analyses demonstrated 2 potential reasons for this increased mortality, namely the inclusion of patients with Society of Thoracic Surgery (STS) risk scores >10 and those with low ejection fractions. The higher–STS-risk-score patients may have included a significant proportion of acute coronary syndrome patients because this risk score is influenced significantly by factors such as acute coronary syndrome and need for an urgent procedure. The other subgroup with poor outcomes was those with an EF <30%. The post-PCI mortality in this group was 15.4%, and in part driven by acute complications. The latter raises the issue of whether balloon aortic valvuloplasty (BAV) should be performed in these patients preceding PCI to reduce risk. Although data are limited, several small series have shown that BAV, either concomitantly or staged, can be performed safely in patients with AS and CAD.9,10 This strategy may mitigate some of the risk of PCI in the setting of AS and may be especially important in those patients with depressed left ventricular function and heart failure.

The larger and mostly untested issue relative to CAD and AS relates to transcatheter AVR in high-risk patients. Current published US randomized trials systematically excluded patients with the need for revascularization (though antecedent PCI was occasionally performed to qualify for eligibility) and did not demonstrate any interaction between CAD and mortality.11 However, with increased clinical availability and expanded use of TAVR, the issue of concomitant CAD has become one of increasing interest. A study by Dewey et al indicated that CAD was present in 49% of patients undergoing TAVR.12 The 30-day mortality in patients with CAD was >10-fold higher compared to patients without CAD (13.1% versus 1.2%). Also, long-term mortality was significantly higher in patients with CAD.

There are several key limitations to the study by Dewey et al. First, it represented the earliest experience in both the United States and Europe with TAVR. Second, CAD was defined simply as prior revascularization (CABG or PCI)
and there was no information about degree of ischemic burden. A subsequent study published by Masson et al characterized patients by degree of unrevascularized territory.\textsuperscript{13} The prevalence of CAD was 75.6\% of this study. The 30-day mortality was not different between patients with and without CAD (11.5\% versus 6.3\%), but this may have been due to limited sample size. Nevertheless, this study did not demonstrate significant differences in either 30-day or 1-year survival on the basis of presence or absence of CAD. A recent publication from France also failed to demonstrate differences in short- or long-term survival on the basis of CAD.\textsuperscript{14} In this study of 145 patients receiving TAVR, the prevalence of CAD was 63\%. Of the patients with significant coronary lesions, only 17\% underwent revascularization before TAVR and there was no difference in mortality between this group and groups that did not undergo revascularization. This once again suggests that TAVR is safe in the presence of CAD.

In the era of TAVR, the question of whether or not to treat significant CAD depends on the answers to 2 key questions: Can TAVR be performed safely in the setting of the patient’s coronary anatomy? And will the extent of CAD impact the patient’s symptoms as well as long-term survival?

The answers to these key questions should guide the decision whether or not to perform PCI. The decisions will need to be patient specific. For example, a patient with preserved left ventricular function and single-vessel disease is unlikely to have significant issues related to CAD during the TAVR procedure. However, a patient with an ejection fraction <30\%, New York Heart Association class IV disease, and triple-vessel disease is more likely to have ischemia-related complications during TAVR. In the latter patient, the series presented by Kapadia et al suggests TAVR should be staged after a BAV and PCI. Besides procedural safety, another consideration is whether the extent of CAD will impact procedural success and long-term durability. The Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery (SYNTAX) trial, which compared PCI and CABG for patients with multivessel disease, demonstrated that in patients with complex CAD, CABG had improved long-term results.\textsuperscript{15} Therefore, patients with AS and a high SYNTAX score may be better suited for CABG/AVR than TAVR/PCI provided they are reasonable surgical candidates.

There are numerous other factors that must be considered before deciding whether or not to perform PCI. First, will the use of antithrombotic agents impact bleeding complications after TAVR, especially via the transapical approach? Second, will this concern of bleeding impact the decision of bare metal versus drug-eluting stents? What is the ideal interval between PCI and TAVR? Also, if TAVR precedes PCI, does PCI become more difficult to perform? There are concerns that the prosthesis will impact the ability to engage the coronaries adequately with a guiding catheter. Yet successful PCI after TAVR with either the Edwards Sapien or Medtronic Core Valve system has, in fact, been performed.\textsuperscript{16,17}

The treatment of concomitant CAD in the setting of AS will continue to evolve. In the current environment in which TAVR is approved only for patients at extreme risk for surgery, the threshold for PCI should be high unless it will affect the safety of the procedure. However, as TAVR is performed in lower-risk patients with better long-term prognosis independent of the AS, the threshold for treating CAD will become lower because the potential impact of the CAD on long-term mortality and quality of life will become greater. Ongoing randomized studies such as Placement of AoRtic TraNscaTheter ErVe Malfunction (PARTNER) and SURgical Replacement And Transcatheter Aortic Valve Implantation (SURTAVI), which include patients with CAD in need of revascularization, will compare AVR with or without CABG to TAVR with or without PCI. Hopefully from these studies and others, the best PCI strategy for different clinical scenarios will emerge. Until then, treatment strategies will be guided by best clinical judgment and our limited data.

Disclosures

Dr Kodali is a case proctor and on the steering committee of the PARTNER trial for Edwards Lifesciences; he has consulted for St. Jude Medical and is on the scientific advisory board for the Thubrikar Aortic Valve. Dr Moses is on the executive committee of the PARTNER trial for Edwards Lifesciences and is a consultant for Abbott Vascular and Boston Scientific.

References


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Coronary Artery Disease and Aortic Stenosis in the Transcatheter Aortic Valve Replacement Era: Old Questions, New Paradigms: The Evolving Role of Percutaneous Coronary Intervention in the Treatment of Patients With Aortic Stenosis

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