

Transcatheter or Surgical Aortic Valve Replacement in Patients With Chronic Lung Disease? The Answer, My Friend, Is Blowin' in the Wind

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In Bob Dylan's iconic song, *Blowin' in the Wind*, the refrain "The answer, my friend, is blowin' in the wind" has been described as "impenetrably ambiguous: either the answer is so obvious it is right in your face, or the answer is as intangible as the wind."¹ The treatment of patients with chronic lung disease and aortic stenosis (AS) likely belongs in the latter category.

Chronic obstructive pulmonary disease (COPD) affects nearly 5% of the US population and is the third leading cause of death.² The most common classification of COPD severity is the GOLD (Global Initiative for Chronic Obstructive Lung Disease) staging system, with patients with GOLD stage III and IV frequently requiring oxygen and having a high risk of COPD exacerbations and respiratory complications.³ Similarly, AS is the most common valvular disorder in the Western world, with a prevalence of 2% in patients over the age of 65 years.⁴

Both illnesses share several common features. Smoking is the most common cause of COPD and is also an established risk factor for calcific valve disease.⁴ The cardinal symptom of both illnesses is shortness of breath, and frequently, chest pain and cough. Almost diabolically, severe AS can make the diagnosis of COPD challenging.⁵ Functional limitations are frequently present in both, and increased frailty, reduced mobility, and malnutrition are common accompanying conditions. In the Euro Heart Survey, patients with COPD constituted ≈15% of patients referred for aortic valve

replacement.⁶ COPD can affect surgical outcomes in several ways. Firstly, it is an important component of both the European System for Cardiac Operative Risk Evaluation II and Society of Thoracic Surgeons' risk scores for surgical aortic valve replacement (SAVR) and thus elevates the surgical risk for even first-time isolated aortic valve replacements.^{7,8} Secondly, a number of these patients are on long-term glucocorticosteroid therapy, which affects wound healing and increases bleeding. Patients with COPD can develop pulmonary hypertension, which also elevates the surgical risk, independent of the underlying lung disease.⁹ Several postoperative pulmonary complications including ventilator dependence, reintubation, pneumonia, atelectasis, adult respiratory distress syndrome, mediastinitis, and sternal wound infections are higher among patients with COPD compared with those without prior lung disease.¹⁰

COPD is also one of the main reasons for denial of SAVR among patients with aortic valve disease. In the same Euro Heart Survey, COPD alone was the reason for denial in 1 out of every 7 patients.⁶ In fact, in the inoperable cohort of the PARTNER (Placement of Aortic Transcatheter Valve) trial, COPD was noted in close to 50% of enrolled patients, of whom 23% were oxygen dependent.¹¹ Transcatheter aortic valve replacement (TAVR) has thus increasingly become an attractive treatment option in this patient population.¹²

What Does This Study Add?

The appropriate treatment of patients with COPD and AS remains unclear. Against this background, the study by Ando and colleagues in this issue of *Journal of the American Heart Association (JAHA)* provides several important insights.¹³ In this well-done study from the National Inpatient Sample between 2011 and 2014, the authors used propensity matching to compare COPD patients undergoing TAVR versus isolated SAVR for AS. Patients undergoing transapical TAVR were excluded. Of 7548 patients (1595 TAVR, 5953 SAVR) included in this database during this timeframe, the authors were able to match 2418 patients (1210 TAVR; 1208 SAVR). About 12.6% of these patients had oxygen-dependent COPD;

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the rest had an undetermined severity of COPD. As expected, patients undergoing TAVR were older with a higher burden of comorbidities. Furthermore, pulmonary complications including reintubation, pneumonia, and tracheostomy were higher among patients undergoing SAVR. Similar to prior comparative studies, bleeding and acute renal failure were significantly lower with TAVR as well.¹⁴ Interestingly, overall in-hospital mortality and acute myocardial infarction were both also lower among patients undergoing TAVR compared with SAVR, although mechanisms for these findings were unclear. Not surprisingly, resource utilization including hospital length of stay and total costs were also lower among the TAVR patients.¹³ This study is important in the realm of comparative- and cost-effectiveness research. It addresses a patient population that is frequently encountered, yet hard to enroll in meaningful numbers in clinical trials. By using a community-based cohort, the investigators provide effect estimates that may be more generalizable than those reported from clinical trials, which are typically conducted at high-volume and highly experienced sites. This study thus provides important evidence supporting the effectiveness of TAVR among patients with COPD. Notably, even among COPD patients in whom SAVR was selected as the treatment option, in-hospital mortality was acceptable (4.2%).

What Insights Are Missing?

Despite these strengths, there are a few limitations to consider. Since this is an administrative database, it lacks granularity for important variables such as the severity of COPD and the existence and severity of pulmonary hypertension. Both are important for clinical decision-making. Patients with mild COPD have a very different postoperative risk compared with those who have oxygen-dependent COPD, and it is really the more severe COPD patients in whom clinicians struggle the most in deciding the best approach. Furthermore, data regarding frailty, mobility, malnutrition, etc are not available. This is particularly important since there is likely a significant overlap between COPD, AS, and these impairments, and for clinicians, the complete picture is key to deciding next steps. Another limitation of using an administrative database is that it can be hard to clearly distinguish postoperative complications (eg, stroke) from a preoperative comorbidity. Furthermore, as the study was conducted between 2011 and 2014, it likely includes mostly high-risk and inoperable patients in the TAVR group. Thus, even though sophisticated statistical techniques were used, the analyses may be unable to truly compare similar types of COPD patients (an inoperable patient, by definition, should have no surgical match), and confounding by indication likely still exists. Next, the National Inpatient Sample data set has several strengths,

one of them being that by being publicly and easily accessible, it has truly democratized health services research. However, its design properties require specific analytical considerations. For instance, the data sampling methodology changes from 2012 onwards, which requires different adjustments for stratification and clustering of National Inpatient Sample data for data before 2012 and after.^{15,16} This study spans both timeframes, and it is unclear whether the appropriate adjustments were made by the investigators. Finally, the timeframe of analysis also means that current-generation TAVR valves were not included. This likely underestimates the benefits of TAVR in the contemporary era, especially given that surgical techniques are unlikely to have significantly evolved over this timeframe.

What Are Other Unresolved Issues in This Patient Population?

As TAVR technology advances, efforts are under way to evolve TAVR from a procedure performed among high-risk surgical turn-downs to one done among lower-risk patients, particularly those most likely to improve from it.¹⁷ COPD, particularly when associated with very low forced expiratory volume in 1 s values (<30% predicted), remains an important risk factor for poor outcomes following TAVR.¹⁸ It is now well established that patients with severe chronic lung disease have a significantly higher risk of both in-hospital and 1-year mortality following TAVR, and patients with moderate and severe COPD have fewer days alive and outside the hospital at 12 months following TAVR compared with others.^{19,20} Patients with COPD are also less likely to experience functional improvement post-TAVR,²¹ and in 1 study, TAVR was deemed futile among >40% of patients with COPD.²²

On the other hand, no treatment can have worse outcomes for both mortality and quality of life in this patient population.²³ There is value in treating selected COPD patients with aortic valve replacement (surgical or percutaneous) because this can help alleviate symptoms from 1 of these 2 competing illnesses, and potentially reduce hospital readmissions and improve cardiovascular survival. Thus, one of the biggest challenges for clinicians is deciding the correct approach for these patients—SAVR, TAVR, or palliative.^{12,23} Compounding the issue of symptomatic benefit is that in the setting of severe AS and severe COPD (particularly with concomitant pulmonary hypertension), it may be hard to identify which condition is contributing most to a patient's symptoms. Noninvasive (eg, Brain natriuretic peptide testing) and invasive testing (eg, right heart catheterization) can sometimes be helpful in the differentiation. There may also be a role for balloon aortic valvuloplasty to help with discrimination and

prognostication in such patients with COPD, and this is something that deserves careful study in the future.^{24,25}

Final Thoughts

Patients with COPD and severe AS are frequently encountered in clinical practice and remain a difficult patient population to treat. The current study indicates that appropriately selected patients may have fewer pulmonary complications with TAVR compared with SAVR. Most importantly, it highlights the need for more research to examine patients with various COPD stages and identify factors that impact the differential outcomes between TAVR and other treatment modalities.

Disclosures

Kumbhani reports honoraria from the American College of Cardiology. The remaining authors have no disclosures to report.

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