JACC: CARDIOVASCULAR IMAGING
VOL. 9, NO. 8, 2016

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcmg.2016.06.007

iVIEW

EDITOR'S PAGE

When Is an Image Telling the Truth? Discordant Lessons From Imaging TAVR

James K. Min, MD,[a] Y. Chandrashekhar, MD,[b] Jagat Narula, MD, PhD[c]

Since the first randomized control trial of aortic valve replacement by a transcatheter approach by Leon et al. in 2010 (1), the field of interventional cardiology has witnessed a revolution in minimally invasive cardiovascular care. Rigorous studies have substantiated its use in an increasingly wider array of patients, and the U.S. Food and Drug Administration recently approved the first large prospective randomized trial of transcatheter aortic valve replacement (TAVR) in low-risk patients. It is becoming more and more important to predict, a priori, which patients will benefit with which TAVR strategies, and imaging is best positioned to make this possible.

Two-dimensional and 3-dimensional echocardiography and cardiovascular computed tomography angiography (CTA) have become essential diagnostic components in the evaluation of patients who may be candidates for TAVR, during the TAVR procedure itself, and for follow-up after TAVR. CTA is visually superior in imaging complex anatomy, while echocardiography is superior in temporal resolution and ease of imaging; however, they remain complementary, with some unique niche roles (2). CTA has essentially displaced echocardiography for sizing the aortic valve. In addition, many relatively novel observations have led investigators to evaluate other parameters on CTA that would predict TAVR complications, including peri- or post-procedural paravalvular regurgitation, aortic rupture, and stroke. Computed tomography investigators have consistently emphasized the noncircular nature of an aortic annulus that is expected to accommodate an intrinsically circular stent valve. However, the clarity of CTA, the nearly unlimited multiplanar reconstruction planes, and the wide-angle nature of the dataset, while allowing unprecedented access to newer formulations, have also tempted conclusions that, although logical, may be of uncertain import in clinical practice. For example, some studies did not find long-term outcome differences between pre-operative aortic valve area calculated by echocardiographically assumed versus computed tomographically visualized left ventricular outflow tract anatomy (3). Many studies involving CTA have been relatively small in size and retrospective in nature and hence might have offered conclusions that would not be important or would be disproved in subsequent studies or in larger trials.

An example of such a logical hypothesis with uncertain clinical import can be found in this issue of *iJACC*, in which 2 papers report the diagnostic evaluation post-TAVR of a new metric using CTA, namely, the aortoventricular angle. Abramowitz et al. (4) examined 582 patients from a single high-volume TAVR center and identified a direct relation of aortoventricular angle to procedural success. Specifically, a 27% reduction in procedural success was noted for patients with larger aortoventricular angles, defined as greater than 48° (the group mean), with greater risk for needing a second valve, increased radiation exposure, valve embolization, and paravalvular regurgitation. This seems to specifically affect the self-expanding valve. There were, however, no differences in 30-day outcomes on the basis of aortoventricular angle. Popma et al. (5) evaluated the same parameter in a much larger prospective registry of 3,578 patients undergoing self-expandable TAVR and found no relation of aortoventricular angle to procedural success, post-TAVR paravalvular regurgitation,

From the [a]Dalio Institute of Cardiovascular Imaging, Weill Cornell Medical College and New York Presbyterian Hospital, New York, New York; [b]University of Minnesota & VA Medical Center, Minneapolis, Minnesota; and the [c]Icahn School of Medicine at Mount Sinai, New York, New York.
The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

or 30-day outcomes. These studies, very relevant to all physicians and patients involved with TAVR, also emphasize a not uncommon challenge to the practicing community of what to do with seemingly discordant data pervasive in other types of imaging studies as well. As an example, early reports of diagnostic performance of nearly all imaging methods for coronary artery disease evaluation reported exceptionally high accuracy that decremented over time.

How should clinicians (and journal editors) digest these discordant messages? Should one be concerned about the safety of the self-expanding prosthesis based on the substantial data of Abramowitz et al. (4) or be reassured by the manifold larger dataset of Popma et al. (5)? Rather than jumping to a conclusion that this finding is unvaryingly true or not true, the studies themselves should be examined for important details that could have produced discordant results from similar image analytic approaches.

For one, the methods of image interpretation were similar but not identical between the studies. Specifically, the aortoventricular angle was measured from a coronal view and defined as the angle between the aortic annular plane and the horizontal plane. This approach, although precise, nevertheless suffers from limitations of accuracy. A host of factors will result in imprecision of measurements. Slight deviations in between-patient positions of the ventricle, aortic annulus, and aorta will result in significant differences in aortoventricular angle measurements. These between-patient differences are common and can relate to simple biometric factors such as age, anteroposterior chest diameter, height, and others. To obtain a true aortoventricular angle, the angle between the annular plane and horizontal plane in an oblique view should be maximized, and this view is not necessarily in the coronal plane. Furthermore, Popma et al. (5) evaluated the aortoventricular angle in the end-systolic phase, while Abramowitz et al. (4) did not specify the point within the cardiac cycle at which they measured angulation. Their illustrative frames do not appear to be in an end-systolic phase. Given the 3-dimensional actuation of the ventricle during systole, which includes torsion, it is expected that aortoventricular angle measurements may be dependent on the time within the cardiac cycle.

Second, the methods of TAVR themselves were different between the 2 studies. In the study by Popma et al. (5), an aortoventricular angle of 70° or less was a requisite for a transfemoral or left subclavian approach, while a right subclavian approach was deemed necessary for aortoventricular angles <30°. In contrast, in the single-center experience of Abramowitz et al. (4), it appears that these access protocols were not mandatory and may represent a more "real-world" experience.

Third, and of equal importance, the units of analysis were markedly different between the 2 studies. In the case of Popma et al. (5), aortoventricular angles were judged in an ordinal fashion in 10° increments, while in the case of Abramowitz et al. (4), a dichotomous approach was used to cut below or above the mean 48° angle. Given the seemingly normal distribution of aortoventricular angles, this seems to be appropriate. Importantly, the largest number of patients in the study of Popma et al. (5) was in the category of aortoventricular angles of 41° to 50°, which obscures the differences between patients above and below 48°.

So why did we publish discordant findings? Is it not the editors' role to provide the truth, and should such discordant studies not muddy the waters? First, we strongly believe that our role is to showcase controversial findings (both positive and negative) with a balanced perspective and let the ferment of science address the truth. Small studies are often hypothesis generating and lead to larger definitive studies. Second, it is usually difficult to conclude about the truth with 1 study, given the nature of experimental conditions (patient cohort, physician expertise), and experiences from different centers possibly bring us closer to the truth. The larger dataset was from meticulously curated centers and had great support from the vendor as well as greater scrutiny as it was a pivotal trial. It also had core laboratory-interpreted data as opposed to site-interpreted data. Such data are, as in all clinical trials, far removed from general clinical practice, and some real-world data give us a feel for what can happen when the same methods are allowed a freer rein.

Is this story closed? If smaller studies are considered hypothesis generating and ensuing larger ones definitive, then fortunately we have both at the same time, and should it not be reasonable to go with the findings of the larger study? The answer may be still uncertain in this case and should generate more thinking about groups, with both types of valves, in which outcomes can still be different. For example, while clinical outcomes of acute procedural success were lower in patients with >48° aortoventricular angles in the study of Abramowitz et al. (4), albeit with very wide confidence intervals (odds ratio: 0.15; 95% confidence interval: 0.03 to 0.78), there also was a trend toward increased 30-day outcomes in the analysis of Popma et al. (5) for measures of major stroke ($p = 0.07$), minor stroke ($p = 0.018$), major vascular complication ($p = 0.08$), and permanent pacemaker implantation ($p = 0.062$). There may logically yet be a situation in which aortic angle might influence device outcomes. In the interest of good patient care, our work is never done, and constant evaluation and analysis are the only way to improve outcomes.

One lesson learned from these 2 studies is that the details matter. Seemingly minor differences in methodology can generate major controversies. Differences in study design, procedural methodology, and statistical analyses can engender marked differences in study findings. As imagers, we can take a lesson from the playbook of our colleagues in interventional cardiology, who at a very early stage had standardized definitions for clinical outcomes and procedural success. In contrast, we as imagers have not generally taken this approach. This deficiency is highlighted in the 2 studies in this issue of *iJACC* wherein a systematic approach with a start point in the coronal view will inevitably result in confusing findings that can be statistically analyzed but not practically implemented. Given the slew of new transcatheter structural heart disease technologies that are emerging, including transcatheter mitral valve replacement (which will be much more complex in 3-dimensional anatomy) and others, it would be wise for multimodality imagers to rigorously implement standardized image evaluation and reporting protocols so that the results can be generalized to the whole of the field.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Jagat Narula, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, New York, New York 10029. E-mail: narula@mountsinai.org.

REFERENCES

1. Leon MB, Smith CR, Mack M, et al. PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363:1597–607.

2. Bloomfield GS, Gillam LD, Hahn RT, et al. A practical guide to multimodality imaging of transcatheter aortic valve replacement. J Am Coll Cardiol Img 2012;5:441–55.

3. Clavel M-A, Malouf J, Messika-Zeitoun D, et al. Aortic valve area calculation in aortic stenosis by CT and Doppler echocardiography. J Am Coll Cardiol Img 2015;8:248–57.

4. Abramowitz Y, Maeno Y, Chakravarty T, et al. Aortic angulation attenuates procedural success following self-expandable but not balloon-expandable TAVR. J Am Coll Cardiol Img 2016;9:964–72.

5. Popma JJ, Reardon MJ, Yakubov SJ, et al., for the CoreValve US Clinical Investigators. Safety and efficacy of self-expanding TAVR in patients with aortoventricular angulation. J Am Coll Cardiol Img 2016;9:973–81.