Taylor & Francis
Taylor & Francis Group

Structural Heart
The Journal of the Heart Team

ISSN: 2474-8706 (Print) 2474-8714 (Online) Journal homepage: https://www.tandfonline.com/loi/ushj20

TAVR Thrombosis: A Blurry Snapshot

James M. McCabe & Mark Reisman

To cite this article: James M. McCabe & Mark Reisman (2017) TAVR Thrombosis: A Blurry Snapshot, Structural Heart, 1:5-6, 265-266, DOI: 10.1080/24748706.2017.1373878

To link to this article: https://doi.org/10.1080/24748706.2017.1373878

Accepted author version posted online: 30 Aug 2017.
Published online: 11 Sep 2017.

STRUCTURAL HEART
2017, VOL. 1, NOS. 5–6, 265–266
https://doi.org/10.1080/24748706.2017.1373878

EDITORIAL

TAVR Thrombosis: A Blurry Snapshot

James M. McCabe, MD and Mark Reisman, MD

Division of Cardiology, University of Washington Medical Center, Seattle, Washington, USA

Subclinical thrombosis of transcatheter aortic valve (TAVR) prostheses has garnered significant attention following serial publications from the Assessment of Transcatheter and Surgical Aortic Bioprosthetic Valve Thrombosis and Its Treatment with Anticoagulation [RESOLVE] and the Subclinical Aortic Valve Bioprosthesis Thrombosis Assessed with Four-Dimensional Computed Tomography [SAVORY] registries, which both used 4D computed tomography to explore the prevalence of subclinical thrombosis and its implications.[1,2]

In the larger of these two analyses,[2] the authors found evidence of restricted leaflet motion and leaflet hypoattenuation on computed tomography (CT) in 13% of patients who underwent TAVR and 4% of patients who underwent surgical valve replacement (SAVR). Rates of non-procedural stroke and transient ischemic attack (TIA) were ~3-fold higher among those with subclinical thrombosis as compared to those without. Yet only 14% of those with subclinical leaflet thrombosis on CT had elevated valve gradients on echocardiogram. Thus, questions remain regarding the implications and natural history of subclinical valve thrombosis: do all subclinical leaflet thrombosis scenarios eventually lead to elevated prosthetic valve gradients? Or are the clinical implications restricted to thromboembolic concerns? Might the valves also be more likely to fail leading to recurrent stenosis, insufficiency, and/or overt heart failure? If anticoagulation is the solution, does starting it earlier rather than later make a difference and for how long should it be prescribed? Given the risks to anticoagulation, are there ways to predict selective populations that might particularly benefit from prophylactic use?

In this issue of *Structural Heart*, Drs. Hafiz and Kalra and colleagues build off the prior data regarding subclinical thrombosis from RESOLVE and SAVORY to explore the implications of clinically manifest transcatheter valve leaflet thrombosis in the United States. To examine this they use the Manufacturer and User Facility Device Experience (MAUDE) database of self-reported adverse events housed and run by the Food and Drug Administration (FDA).

Over a 3-year period from 2012 to 2015, the authors found 156 clinically manifested adverse events listed as transcatheter structural valve dysfunction, of which 30 cases were directly attributed to leaflet thrombosis. There was no obvious pattern of temporal distribution with 40% of reported cases occurring more than 12 months following implantation. Most cases were diagnosed at least 3 months following implantation and one case was recorded at 60 months post implant. In this clinically driven registry, these cases were diagnosed by echocardiography, during surgical explantation, or during autopsy.

The MAUDE registry, which serves as the basis for this analysis, is an intriguing and clever mechanism by which to study clinical valve failure as it houses all the Medical Device Reports (MDRs) submitted to the FDA. However, it is a very limited registry in regard to many of the specific clinical details of the recorded events. Device reporting has been mandated in various forms in the US through Congressional regulation since 1984. Reports of device-related adverse events are required from device manufacturers and encouraged from the broader medical community. Drs. Hafiz and Kalra and their colleagues note that by its nature the registry is susceptible to both under- and over-reporting. However, the U.S. General Accounting Office investigated the MDR system in 1997 prior to the implementation of MAUDE. They noted that the volume of submitted reports rose significantly in the late 1990s following regulation changes. This growth in turn inundated the capacity of the FDA to process and review these reports in a timely manner and they were forced to prioritize claims involving patient deaths over reports of device malfunction (such as prosthetic valve leaflet immobility) (http://www.gao.gov/assets/230/223583.pdf). Whether or not this process impacts how we interpret the currently presented data is unclear: after all, 20 years is plenty of time to address weaker aspects of the US medical device reporting program. And it was in the face of such findings that the MAUDE electronic database system was developed. It does seem intuitive, however, that such a registry is enriched for the most severe adverse events and indeed, within the presented cohort, 30% of the patients died and 10% had a clinically apparent TIA or stroke.

For context, also in 1997, 18 people in Hong Kong contracted an unusual strain of influenza previously only found in birds.[3] This H5N1 "bird flu" virus killed 6 of the 18 infected patients and, despite infecting a mere 0.000003% of Hong Kong's 6.5 million inhabitants, it quickly captured the attention of the populace and media alike, prompting widespread fear and the mass sacrifice of poultry in the area to ensure containment.

Of course, transcatheter valve thrombosis is neither infectious nor a particularly significant problem in chickens. But there are some potential parallels as to how both conditions have captured our attention. This study by Kalra and colleagues is not one of incidence and cannot speak to rates of clinically apparent valve thrombosis. Nevertheless, a recent TVT report suggested that 42,988 commercial TAVR implants were performed in the US during the time frame in question.[4]

CONTACT James M. McCabe jmmccabe@cardiology.washington.edu University of Washington School of Medicine, University of Washington Medical Center, 1959 NE Pacific Street, Seattle, WA 98195-6171, USA.

Even if MAUDE is capturing only 5% of the total cases of clinically apparent valve thrombosis, that true total would still represent only roughly 1% of the TAVR valves implanted. And thus, the burning question: Is there justification for anticoagulation post TAVR, given its inherent risks, when the incidence of clinically manifest valve thrombosis remains unknown, especially considering that the manifest clinical events may commonly occur 1, 2, or even 5 years after implantation? Certainly long-term echo follow-up of early generation TAVR valves has demonstrated no significant changes in aggregate prosthesis gradients, suggesting, at the least, that clinically apparent valve thrombosis is not a widespread problem.[5]

The current article by Drs. Hafiz and Kalra and colleagues in this issue of *Structural Heart*, helps us understand that there is a clinically manifest form of transcatheter leaflet thrombosis and that it is not simply a matter of thromboembolic complications but can present with valve dysfunction or even cardiogenic shock. Yet, it remains unknown if leaflet thrombosis is the pandemic scourge by which TAVR may run a-fowl.

Disclosure statement

The authors have no conflicts of interest to report.

References

1. Makkar RR, Fontana G, Jilaihawi H, et al. Possible subclinical leaflet thrombosis in bioprosthetic aortic valves. *N Engl J Med*. 2015;373(21):2015–2024. doi:10.1056/NEJMoa1509233.
2. Chakravarty TC, Søndergaard PLSN, Friedman JF, et al. Subclinical leaflet thrombosis in surgical and transcatheter bioprosthetic aortic valves: an observational study. *Lancet*. 2017;389 (10087):2383–2392. doi:10.1016/S0140-6736(17)30757-2.
3. Chan PKS. Outbreak of avian influenza A(H5N1) virus infection in Hong Kong in 1997. *Clin Infect Dis*. 2002;34(S2):S58–S64. doi:10.1086/338820.
4. Carroll JD, Vemulapalli S, Dai D, et al. Procedural experience for transcatheter aortic valve replacement and relation to outcomes: the STS/ACC TVT registry. *J Am Coll Cardiol*. 2017;70(1):29–41. doi:10.1016/j.jacc.2017.04.056.
5. Daubert MA, Weissman NJ, Hahn RT, et al. Long-term valve performance of TAVR and SAVR: a report from the PARTNER I trial. *JACC Cardiovasc Imaging*. 2016;10(1):15–25. doi:10.1016/j.jcmg.2016.11.004.