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Commentary: Structural abnormalities after Freestyle full aortic root replacement: Time to accept the facts

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The Medtronic Freestyle stentless porcine aortic root bioprosthesis (Medtronic, Inc, Minneapolis, Minn) has been approved by the US Food and Drug Administration since 1997, with studies demonstrating excellent hemodynamic properties as well as low rates of late structural valve deterioration.¹ Despite this, reports of structural abnormalities after Freestyle implantation, most commonly pseudoaneurysm formation, began to surface as early as 2005,² with the first report dedicated entirely to this topic being that of Ozaki and colleagues from Japan,³ who described the unique failure mode of degeneration of the porcine aortic root sinus of Valsalva wall, leading to perforation and pseudoaneurysm formation.

Subsequent to that initial report, additional case reports and small series began to emerge over the next several years,⁴⁻⁷ and in 2014 our group published the largest study to date at the time examining the issue of Freestyle pseudoaneurysm by aggregating multiple data sets including our institutional series, literature review, and review of the US Food and Drug Administration's Manufacturer and User Facility Device Experience (MAUDE) database, which collects voluntary provider and industry adverse event reports related to medical devices.⁸ Our study suggested a rate of pseudoaneurysm formation as high as nearly 5% after Freestyle implantation as a full root, with pseudoaneurysms continuing to be observed in late follow-up out to more than 10 years postoperatively. Importantly, in 15% of cases, the aneurysmal

Pseudoaneurysm (arrow) of left coronary sinus of Freestyle root requiring late reoperation.

CENTRAL MESSAGE

Structural abnormalities, including pseudoaneurysm formation, are common after Freestyle full aortic root replacement and mandate lifelong imaging follow-up with CTA or MRA.

deterioration of the porcine root resulted in patient death. Further, most patients with the complication had minimal or no symptoms. Finally, as the pseudoaneurysms could not be visualized on routine transthoracic echocardiography (TTE), we recommended lifelong surveillance follow-up imaging of these patients with contrast-enhanced computed tomography angiography or magnetic resonance angiography.^{8,9}

Following publication of our report, the device manufacturer wrote a letter to the editor¹⁰ of the journal suggesting that the pseudoaneurysm formation in Freestyle valve full root implants was "extremely rare and does not appear to have a root cause in the manufacturing process." Further, the company representatives went on to insinuate that pseudoaneurysm formation following Freestyle implantation was a technical failure of the implanting surgeons, a response we found quite disappointing and disturbing, given the safety signal our paper suggested based upon collation of multiple data sources, as well as the potentially fatal consequences of the complication.¹¹

In the current issue of the *Journal*, Dagnegård and colleagues¹² present the largest systematic investigation to date of postoperative structural abnormalities after Freestyle stentless porcine full aortic root implantation. Two hundred fifty-three consecutive patients operated on at Rigshospitalet, Copenhagen University Hospital, and Montreal Heart Institute between 1999 and 2016 underwent postoperative electrocardiogram-gated 4-dimensional cardiac computed tomography (4DCT) of the aortic root late

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FIGURE 1. A, Intraoperative photographs of a patient requiring reoperation for a pseudoaneurysm of the left coronary sinus of Valsalva of a Freestyle stentless xenograft. Note the large amount of chronic thrombus (arrow) present within the pseudoaneurysm sac. B, Photograph of the sac thrombus. We have observed cerebral embolic events in several patients with Freestyle pseudoaneurysms, including one who presented with a disabling embolic stroke.

postoperatively (3.3-year median interval between surgery and 4DCT). Amazingly, the authors found moderate-to-severe structural abnormalities in 46% of patients, with 7% of patients having >1 abnormality. The structural abnormalities included pseudoaneurysms in 13% of patients (nearly 3-fold greater than suggested by our previous work), significant coronary ostial stenosis in 21% of patients, and leaflet thickening or reduced leaflet motion, a finding that has previously been described both in transcatheter and other surgical bioprosthetic valves,¹³ in 20%.

With regards to pseudoaneurysms specifically, similar to our data, the authors found that the incidence increased steadily over time late after surgery. Further, these patients had the greatest late need for reintervention as well as late stroke (Figure 1). Similar to the findings of our previous study,⁸ TTE was found to be an inadequate screening tool for Freestyle roots, as only a small proportion of the structural abnormalities observed on 4DCT were detected by TTE. Importantly, the structural abnormalities observed were associated with a greater incidence of death, stroke, or myocardial infarction as compared with the group without structural abnormalities.

In summary, the evidence is now undeniable that pseudoaneurysm formation is a serious issue after Medtronic Freestyle implantation as a full root, and the time has come for the manufacturer to stop blaming the issue on the implanting surgeon¹⁰ and to add to the device instructions for use that surveillance imaging with TTE is inadequate, and that these patients require lifelong imaging follow-up with computed tomography angiography or magnetic resonance angiography.^{8,9} Further, since previous work has suggested an immunologic etiology for these structural failures,¹⁴ the manufacturer should consider using their many resources to fund research into the

apparent origins (immunologic, inadequate fixation, other) of the problem rather than just denying a problem exists.

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