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INVITED COMMENTARY

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The impact of local blood residence time in neo-sinus on post transcatheter aortic valve replacement subclinical leaflet thrombosis—a commentary

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Qiu and Azadani [1] studied the impact of three-dimensional blood flow in the neo-sinus on subclinical leaflet thrombosis (SLT) after transcatheter aortic valve replacement (TAVR). This study considered the blood residence time and flow-induced viscous shear stress as 2 predictors of SLT. The authors applied a one-way fluid–structure interaction (FSI) method to computationally visualize the blood flow in a neo-sinus region of a 3rd-generation balloon-expandable prosthesis (26-mm Edwards SAPIEN 3 valve; Edwards Lifesciences, Irvine, CA, USA) [1]. They also set up an *in vitro* experiment and visualized the flow regime using Particle Image Velocimetry. The 3 main conclusions of this article [1] are:

1. Leaflet motion drives the blood flow in the neo-sinus. As a result, re-designing the geometry of the leaflets helps reduce the chance of subclinical leaflet thrombosis.
2. The blood residence time is longer close to the leaflet's fixed boundary edges.
3. Flow in the neo-sinus is three-dimensional and time dependent.

This study [1] focuses on the importance of leaflet motion on BRT. However, there is a necessity to add more patient-specific anatomical details to the model. SLT is a complicated phenomenon that depends on numerous indicators, such as valve and root anatomy [2], haemodynamics [3, 4], age of the patient [5], medication history [5], valve type (bicuspid or tricuspid), and valve size [6]. For instance, we would like to note that according to our most recent dimensional analysis study, we showed that the coronary artery ostia locations, mean jet velocity, area of the neo-sinus opening, cross-sectional area of neo-sinus, ejection time and flow separated area (area between the valve stent and the aortic wall) significantly impact the risk of SLT [2]. We showed that all these parameters can be grouped into 1 nondimensional parameter called normalized circulation. Normalized circulation is a fast predictor of the risk of thrombus formation [2]. The method we have developed can be applied prior to the transcatheter aortic valve replacement and assist in finding the optimum replacement location and expansion degree to minimize the risk of SLT [2]. The volume and geometry of neo-sinus are affected by the pattern of calcium deposition in the native aortic valve tissue. This geometry directly impacts the haemodynamic, flow-induced viscous shear stress and BRT.

Qiu and Azadani [1] nicely discussed that the shear stress magnitude and exposure time are well below the threshold; therefore, flow-induced shear stress does not cause SLT. This conclusion is the direct result of simplifications in the geometry and may be changed by using patient-specific models. A patient-specific model of an aorta will demonstrate that the aortic root and leaflets are not symmetric; hence, nor are the assumptions for symmetry. Although the *in vitro* and *in silico* models are crucial in understanding certain flows through the valve, it may be an over-simplification for BRT.

A two-way FSI is recommended to prevent adding inaccuracies to the model through the input data related to the leaflets' motion. A two-way fluid–structure interaction simulation of flow in an aorta with a TAVR has been developed and validated previously [7]. Setting up a two-way patient-specific FSI model is extremely challenging and computationally

expensive. Even in the case of a successful set-up of such simulations, the computational time for 1 cardiac cycle is orders of magnitude longer than a real cardiac cycle. Reduced-order models, and physics-informed machine-learning methods, should be incorporated into the current haemodynamic computational models to decrease the calculation time. The accuracy of machine-learning predictions is restricted by the volume of the input data required to train the algorithm. This large volume of input data can be provided by running computer models several times and generating data, which, as mentioned earlier, can be time-consuming and might not even be precise enough to be trusted. The second way of collecting input data is using clinical or *in vitro* experimental data. The clinical data are unavailable to many researchers, can be inconsistent in implementation and require time-consuming data preparation procedures. The *in vitro* experimental data are generated under controlled conditions; thus, they are more consistent in comparison to the clinical data. Meanwhile, the *in vitro* models do not contain the unknown details of the phenomena clinically.

Despite the limitations in *in vitro* studies on TAVR, we congratulate the authors for steps in discovering the impact and significance of individual parameters on the chance of thrombus formation on transcatheter aortic valve leaflets.

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