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Commentary: On the basis of stasis: Mechanistic insight into transcatheter aortic valve replacement thrombosis

Manuel K. Rausch, PhD,^a and Tom C. Nguyen, MD^b

Transcatheter aortic valve replacement (TAVR) is becoming the interventionalist's weapon of choice in the battle against aortic valve stenosis. This is especially true as its indications are being expanded to also include low-risk patients.¹ As early challenges of TAVR have been largely mitigated through operator experience, better imaging, and continuous valve improvements, another challenge has taken the center stage: thrombus formation in the so-called "neosinuses" that are created between the TAVR and the perivalvular host tissue.^{2,3} Although some observational and early studies have suggested that blood flow dynamics in the neosinuses may have a causative role in thrombosis, no direct experimental evidence has been reported.

In this issue of the *Journal*, Trusty and colleagues⁴ set out to fill this knowledge gap and test whether thrombus volume in the neosinuses of TAVR patients is related to stasis within the same.⁴ To this end, they made use of their extensive experience in in vitro modeling of heart valves and designed an elegant yet simple experiment. They first identified patients who had undergone TAVR with available computed tomography (CT) data and echocardiography-based data on cardiac output, both collected within 12 months of the intervention. Valve-in-valve recipients were excluded. Based on CT data, they 3D-printed patient-specific aortic root geometries and implanted either SAPIEN 3s (size 26 or 29) or Core Valve Evolut Rs (size 26) into the root geometries, ensuring that

Manuel K. Rausch, PhD (left), and Tom C. Nguyen, MD (right)

CENTRAL MESSAGE

Thrombosis of transcatheter aortic valve replacements may be at least partially explained by hemodynamic stasis in the neosinuses between the implant and its host tissue.

in vitro implantation parameters, such as valve type, size, height, and tilt, matched the parameters from patients. They next tuned valvular flow in their well-established left heart simulator to match patient-specific cardiac output. They also included coronary flow, but those values were based on literature reports and thus were not patient-specific.

To quantify the degree of stasis within the neosinus regions of their in vitro models, they injected dye and quantified its washout time. In short, they found a convincing correlation between washout time and thrombus volume measurements from CT images.

This is an outstanding contribution to our understanding of neosinus thrombosis in TAVR recipients. Its significance stems from its clear and strong evidence that explains, at least in part, why thrombi form within the neosinuses. That is, it convincingly suggests flow stagnation, one of Virchow's 3 fundamental prothrombotic factors leading to this clinically important presentation. Its impact is broadened by further suggesting the use of CT-based washout time estimation for intraprocedural guidance and as a decision metric for prophylactic anticoagulation therapy. It also provides direct device placement and design recommendations, highlighting SAPIEN 3 stent height and cusp angle as correlates to washout time and thus thrombus volume.

If we had to identify a potential shortcoming of this work, we suggest that a detailed flow visualization could have provided further mechanistic insight into the geometric or fluid dynamic causes of stasis, and that a comparison with stasis

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in the neosinuses of surgical valves could have expanded our understanding of TAVR as their replacements.

Naturally, this work is also subject to some limitations. Among them, we highlight their use of a rigid substrate as opposed to a flexible one; use of a blood analog, which likely altered local hemodynamics; and use of non-subject-specific coronary flow. Finally, this work provides yet another gentle reminder that we are still learning about TAVR and should consider this uncertainty when choosing TAVR over surgical options, especially in lower-risk patients.

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Commentary: Just go with the flow: Transcatheter aortic valve thrombosis

Alvise Guariento, MD,^a and Nicholas Oh, MD^b

As summarized by what became known as Virchow's triad, there are 3 factors that contribute to thrombosis: stasis, endothelial injury, and hypercoagulability. The first of these concepts has recently gained some attention in the world of flow dynamics, especially when applied to prosthetic valve implantation and function.¹

As the indications for transcatheter aortic valve implantation (TAVI) broaden and technology improves, understanding the role of flow in aortic valves is extremely relevant, particularly how it relates to the risk of thrombosis (Figure 1). Several studies have examined thrombosis formation after TAVI through the use of retrospective clinical data and in vitro reconstruction.^{2,3} The main findings of these investigations correlate thrombosis with the geometry of the valve after deployment and therefore to its correct symmetrical expansion. Some data suggested that a reduced

Fluid dynamics of the aortic root after transcatheter aortic valve implantation.

CENTRAL MESSAGE

More studies are needed to investigate the pathophysiologic factors that influence transcatheter aortic valve thrombosis.

flow is significantly present in the neosinus (the area between the TAVI leaflets and the stent), and this can potentially lead to thrombus formation.³

In the current issue of the *Journal*, Trusty and colleagues⁴ present an elegant study demonstrating a direct association between flow stasis in the neosinus and thrombus volume. Using in vitro simulations of reconstructed TAVI from real patients, the authors support the association of flow stagnation via washout times and neosinus thrombosis.

There are many previously investigated factors that are known to contribute to TAVI configuration, such as a patient's cardiac output, proximal aortic anatomy, implantation depth, overexpansion, or oversizing of the valve. Only some of these factors were examined in the current study, but others should be explored in follow-up studies. Nevertheless,

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