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EDITORIAL COMMENT

# Transcatheter Aortic Valve Thrombosis

## New Problem, New Insights*

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The spectrum of transcatheter heart valve (THV) thrombosis includes an imaging finding with normal gradients, elevated gradients without symptoms, and elevated gradients with clinical manifestations, including heart failure, thromboembolism, or valve degeneration (**Figure 1**). As the indications for transcatheter aortic valve replacement (TAVR) expand into lower risk populations, there has been considerable interest in understanding THV thrombosis, as this offers an opportunity to further improve TAVR outcomes. This is reflected by the U.S. Food and Drug Administration–mandated imaging substudies incorporated in the ongoing randomized clinical trials of TAVR. THV thrombosis presenting as reduced leaflet motion on computed tomographic imaging without clinical manifestations occurs in up to 10% to 15% of patients after TAVR. Clinically or hemodynamically overt THV thrombosis presenting as elevated gradients or heart failure symptoms has been reported in up to 0.6% of patients within the first 2 years after TAVR (1); however, these rates are likely underestimated because of lack of systematic follow-up obtained in consecutive patients undergoing TAVR in this series as well as possible reporting bias in the absence of prospective follow-up.

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In this issue of *JACC: Cardiovascular Interventions*, Jose et al. (2) report the incidence, clinical characteristics, and impact of anticoagulation on clinically and/or hemodynamically overt THV thrombosis. The study included 642 consecutive patients undergoing TAVR at a single medical center, including 305 self-expanding valves, 281 balloon-expandable valves, and 56 Lotus valves. All patients experiencing worsening of their symptoms or elevated aortic valve gradients underwent transesophageal echocardiography to confirm the diagnosis of THV thrombosis. THV thrombosis was defined as mean aortic valve gradient >20 mm Hg, new-onset more than mild aortic regurgitation, or aortic valve area <1.2 $cm^2$, secondary to thrombosis diagnosed on the basis of response to anticoagulation, or typical findings on computed tomography or transesophageal echocardiography, and/or the presence of thrombotic mass on the aortic valve.

In this study, hemodynamically or clinically overt THV thrombosis was present in 18 of 642 patients (2.8%) after TAVR. Computed tomographic confirmation of thrombus was obtained in 50% of patients (9 of 18); all computed tomograms demonstrated hypoattenuating opacities on the aortic valve leaflets. This finding was more common with balloon-expandable SAPIEN valves compared with self-expanding bioprostheses. THV thrombosis was not present in patients on oral anticoagulation; initiation of oral anticoagulation with warfarin resulted in resolution of THV thrombosis. Balloon-expandable valves, valve-in-valve procedures, and lack of anticoagulation were predictors of valve thrombosis.

The main strength of this study is that it represents prospective follow-up of all patients undergoing TAVR at a single reputable medical center, allowing an accurate assessment of the prevalence of THV thrombosis. On the basis of the results of this study, the prevalence of THV thrombosis presenting with increased transvalvular gradients with or without symptoms was 2.8% overall. Because this finding was not present in patients on anticoagulation and 40% of

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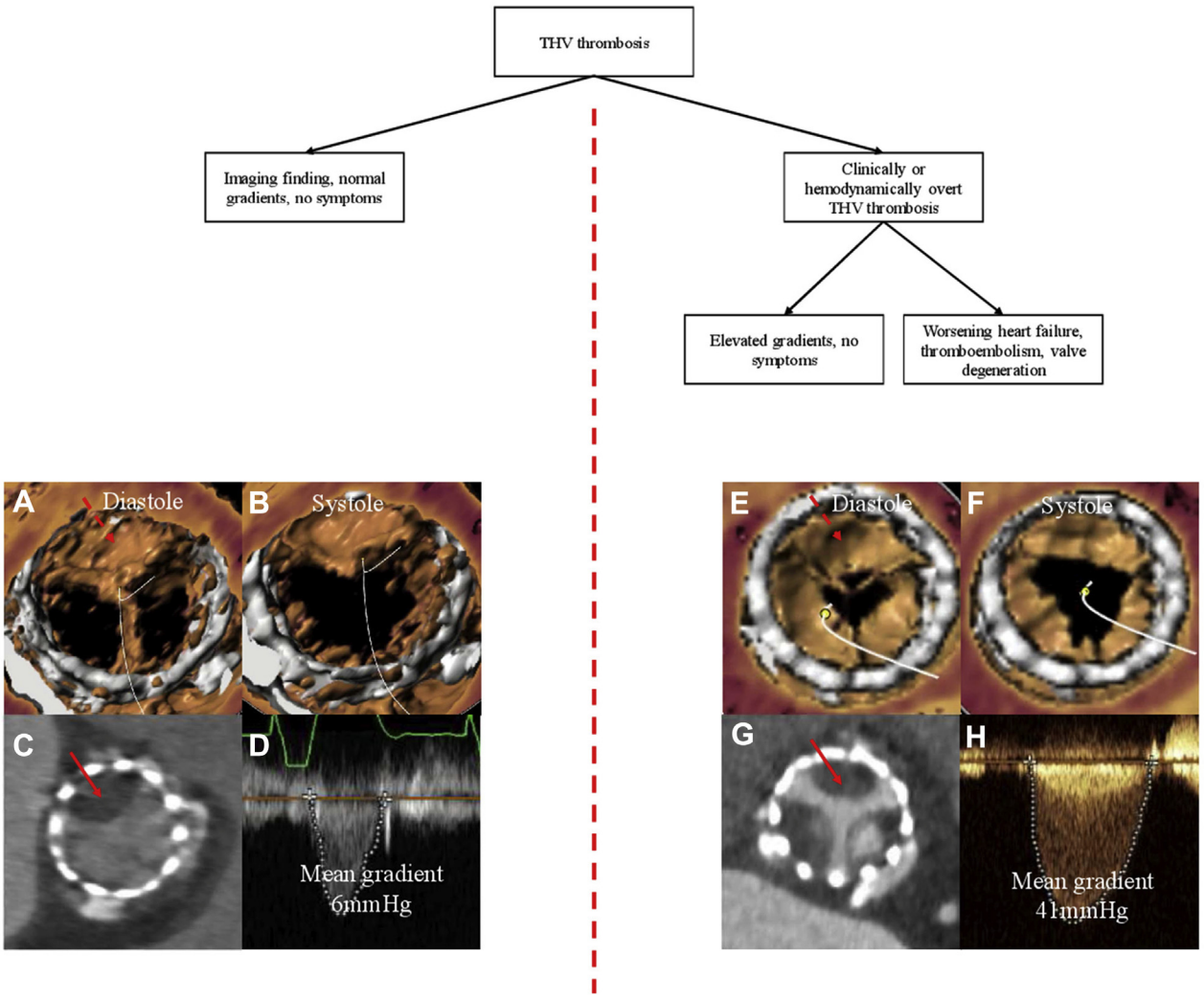
**FIGURE 1** Spectrum of Presentation of Transcatheter Heart Valve Thrombosis




**(A to D)** Transcatheter heart valve thrombosis with reduced leaflet motion **(A, B)** and hypoattenuating opacities on the aortic valve leaflets **(C)** on 4-dimensional volume-rendered computed tomography in the presence of normal transvalvular gradients **(D)**. **(E to H)** Transcatheter heart valve thrombosis with reduced leaflet motion **(A, B)** and hypoattenuating opacities on the aortic valve leaflets **(C)** on 4-dimensional volume-rendered computed tomography in the presence of elevated transvalvular gradients **(D)**. The patient had also been experiencing worsening symptoms of heart failure.

the patients were on oral anticoagulation, the true prevalence of THV thrombosis was 4.8% in the absence of anticoagulation. This number falls between the reported prevalence of 10% to 14% for subclinical leaflet thrombosis on high-resolution computed tomographic imaging (3,4) to 0.6% to 2% of hemodynamically or clinically overt THV thrombosis (1).

The data on anticoagulation are interesting and confirm the previously noted observation of the efficacy of warfarin in the prevention and treatment of THV thrombosis (3-5). The transvalvular gradients increased with THV thrombosis and returned to normal following anticoagulation, average time from initiation of anticoagulation to resolution being 14 days. Several questions remain unanswered regarding anticoagulation in patients undergoing TAVR, including the need for anticoagulation after TAVR in all patients, the optimal duration of anticoagulation following detection of THV thrombosis, the efficacy of novel oral anticoagulant agents compared with warfarin in THV thrombosis,

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the impact of treatment of THV thrombosis on valve durability, and the probability of recurrence of THV thrombosis following discontinuation of anticoagulation.

The investigators report that the incidence of THV thrombosis was lower with self-expanding bioprostheses (0.8%) compared with balloon-expandable SAPIEN valves (4.6%). These are not randomized comparisons; further data in larger registries are needed to confirm this finding. The investigators included multiple valve types in the self-expanding group; however, the predominant valve type in the self-expanding cohort was the CoreValve (296 of 305 patients). There were only 6 cases with the Evolut-R, which is the current-generation self-expanding bioprosthesis. It may be reasonable to state that the incidence of clinically or hemodynamically overt valve thrombosis was less common with the CoreValve compared with the balloon-expandable SAPIEN valve in this study, but additional large datasets are needed to draw definitive conclusions regarding differential rates between balloon and self-expanding valves and if these are attributable to the supra-annular design of CoreValve. Regardless of these findings, clinical decision making and patient treatment, including device selection, should be guided by the outcomes of randomized controlled trials that have established the efficacy of the current-generation SAPIEN 3 valve and CoreValve in patients with aortic stenosis.

This study will likely lead to further research focused on the detection, prevention, and treatment of valve thrombosis. However, the following methodological issues must be noted. All cases of valve thrombosis were identified on the basis of symptoms or transthoracic echocardiographic findings and confirmed with transesophageal echocardiography (computed tomography was used in only 9 patients). The study does not provide information on subclinical leaflet thrombosis that is identified with computed tomographic imaging in patients undergoing bioprosthetic aortic valve replacement. The incidence of this finding was higher in patients undergoing valve-in-valve procedures compared with TAVR in native aortic stenosis in the present study; however, this conclusion is based on a mere 18 valve-in-valve procedures and requires further evaluation. The investigators report new-onset aortic regurgitation in 50% of patients (9 of 18) and more than mild aortic regurgitation in 5.6% of patients (1 of 18). Without core laboratory assessment of echocardiograms, information on the incidence of new-onset aortic regurgitation in patients without THV thrombosis, or the impact of anticoagulation on aortic regurgitation, no meaningful conclusions can be drawn on the impact of THV thrombosis on valve durability or degeneration. Likewise, no conclusions can be drawn on the impact of THV thrombosis on thromboembolic complications. The investigators report an embolic stroke in a patient with THV thrombosis, but clinical outcomes in patients without THV thrombosis are not reported.

In conclusion, the prevalence of THV thrombosis appears significant enough to warrant routine follow-up transthoracic echocardiographic imaging after TAVR. The treating physicians should be vigilant for new elevations in transvalvular gradients or changes in symptoms concerning for THV thrombosis. Confirmatory diagnosis with transesophageal echocardiography or computed tomography, preferably the latter, should precede trial therapy with anticoagulation.

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**KEY WORDS** bioprosthetic aortic valve thrombosis, THV thrombosis, transcatheter aortic valve thrombosis