Oral Anticoagulation Therapy and Progression of Calcific Aortic Valve Stenosis: Factor Xa versus Factor IIa Inhibition?

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Comment referring to: Tastet L, Pibarot P, Shen M, Clisson M, Côté N, Salaun E, Arsenault M, Bédard É, Capoulade R, Puri R, Poirier P, Clavel MA. Oral Anticoagulation Therapy and Progression of Calcific Aortic Valve Stenosis. *J Am Coll Cardiol*. 2019 Apr;73(14):1869–71.

Dear editor,

In the highly interesting study by Tastet et al. [1], the authors were able to demonstrate that warfarin treatment is associated with faster progression of aortic valve stenosis as compared to direct oral anticoagulants (DOACs). The study is of great interest as aortic stenosis is the most frequent valve disease with a substantial socioeconomic impact. Furthermore, atrial fibrillation with indication to permanent oral anticoagulation is common in those patients. However, detailed mechanisms that explain this highly interesting finding remain unclear.

Vascular calcification is increased by vitamin-K anticoagulant (VKA) medication both in patients and in mice [2]. Mechanistically, vitamin K cycle inhibition hinders the gamma-carboxylation of the calcification inhibitor Gla protein and moreover decreases the expression of Gla in plaque material [2]. This leads to calcification of the aortic valve. However, translational studies of human valve material are missing. In patients with chronic kidney disease

(CKD), VKA have been shown to enhance progression of calciphylaxis [3]. Impressively, stopping of VKA treatment even led to healing of calciphylaxis associated lesions that recurred after retreatment with VKA after 1 year [3].

Regarding the recent study by Tastet et al. [1], additional analyses would be intriguing. By now, many patients on VKA were switched to DOACs, as current guidelines recommend DOACs over VKA in patients with atrial fibrillation. In patients with CDK stages 3 and 4, rivaroxaban has already been shown to reduce deposition and progression of cardiac valve calcification compared to VKA medication [4]. Hence, does switching from VKA to DOAC medication have an impact on progression of AS? To date, factor IIa and factor Xa inhibition are available as different types of DOACs. We could show that there are substantial differences between factor IIa- and factor Xa inhibition [5]. In the study by Tastet et al. [1], DOACs were not separated in factor II and factor Xa

inhibitors. This might be interesting to investigate potentially differentiating effects on the progression of AS.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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