INVITED COMMENTARY

A new large animal model in venous thromboembolism

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Venous thromboembolism (VTE) is an important venous pathology with high morbidity and mortality.[1,2] The Centers for Disease Control and Prevention report that as many as 900,000 people in the United States could be affected by deep venous thrombosis (DVT) and pulmonary embolism (PE) each year, with 60,000 to 100,000 Americans estimated to die as the result of the diagnosis. Animal models are essential both to establish disease mechanisms and to test new therapies.

Some excellent swine models of VTE have been described[3]; however, many are limited in their diagnostic and therapeutic applicability in human disease. For example, methods that disrupt anatomic integrity (vein ligation) or leave behind materials such as clips and coils are at a disadvantage compared with the minimally invasive approaches to thrombus induction. Additionally, many available models do not account for other anatomically related systemic effects implicated in human disease involving both acute and chronic venous changes due to proximal conditions, such as right heart strain. In this study,[1] Kassab et al propose an updated large animal model of VTE that utilizes the combination of femoral DVT and induced central venous hypertension. Femoral DVT was established in six pigs by repeatedly traumatizing the vein with an overinflated balloon, mimicking both direct endothelial injury and stasis, followed by thrombin injection immediately after occlusion. The novelty of this model is in adding the element of venous hypertension via tricuspid valve insufficiency accomplished by disrupting the tricuspid valve chordae tendineae. Tricuspid regurgitation was confirmed with color flow Doppler, and thrombosis was assessed via histological analysis 7 weeks post-procedure. Although the model has some limitations in terms of mechanical and histological depth of analysis, it nevertheless accomplishes a successful and unique model for studying VTE, especially in the setting of right ventricular dysfunction. This is timely, as there is evidence that in patients with acute PE, right ventricular dysfunction is a predictor of adverse short-term clinical outcomes, and persistent right ventricular dysfunction at hospital discharge after an acute PE is associated with recurrent VTE. This model could be valueable to investigators studying systemic venous hypertension or pulsatile venous insufficiency due to right heart disfunction.

The authors' work is relevant and sets a platform for further research into the utility of central venous hypertension in models of VTE, evaluation of therapeutic devices, and possible subsequent translation in human disease management. Endovascular therapies, such as thrombectomy devices, recanalization tools, balloons, and stents are available to treat VTE; however, these are underrepresented when compared with the tools and devices available for arterial treatment. There is an unmet need for development and testing of these therapies in both acute and chronic VTE, and specifically in more complex cases where staged treatment may be necessary in the face of proximal obstruction. Additionally, it is important to understand the histological and biomechanical properties of the venous wall that occur over time and how they compare with human wall changes, which may be accomplished in a central venous hypertension model.

Many animal models in rats, mice, and rabbit have been published; however, large in vivo animal models are of particular benefit, as they allow for testing of human-sized devices. Although small animal models provide a comparatively low cost and accessibility for genetic modification, they have the disadvantage of small body mass and relatively short life span. Additionally, the porcine coagulation cascade and hind limb vascular anatomy are similar and translationally relevant to humans, making pigs suitable for wide use in vascular research. The authors describe a clinically relevant experimental large animal model of VTE that incorporates acute lower extremity DVT in a setting of tricuspid regurgitation in vivo. Additional studies are needed to fully understand the molecular impact of these results; however, this work serves as a stepping-stone in both future research and translational application.

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DISCLOSURES

None.

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