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Assessment of Hemodynamic Forces Using *in Vivo* Imaging

Jihoon Kweon
University of Ulsan, Korea

Endothelial shear stress (ESS) plays a key role in early atheroma formation and the evolution of vulnerable plaque rupture as main components of the mechanism underlying acute coronary syndrome. A computational fluid dynamics (CFD) study using three-dimensional (3D) reconstruction of coronary trees facilitates the in vivo evaluation of intra-luminal ESS patterns in order to predict the risk of plaque rupture and future events. Although modelling of high-fidelity coronary geometry is a prerequisite for the precise assessment of fluid dynamics, the intravascular imaging modalities used in daily practice rarely support an appropriate 3D model for ESS analysis.

At present, the novel fusion model that combined 3D reconstructed quantitative coronary angiography (QCA) with cross-sectional imaging [optical coherent tomography (OCT) or intravascular ultrasound (IVUS)-based structural and compositional information] provides more reliable regional mapping of the ESS, which may enable better linkage between the baseline hemodynamic features and the natural history of coronary atherosclerosis. When combining 3D QCA and intravascular imaging, the 3D fusion model demonstrated the local flow patterns, including oscillating or circumferentially varying ESS, which were not captured by the 3D QCA model. Meanwhile, although the 3D QCA model was useful for assessing the ESS profile of normal-looking vessels, it may lead to significant errors in the quantitative assessment of ESS metrics in the stenotic lesions. Combining imprecise lumen boundaries for 3D QCA model might exclude the longitudinal changes in the flow area and therefore hinder more accurate ESS estimation.

In the technical and practical points of view, constructing 3D fusion models may suffer from several limitations. The longitudinal positioning of intravascular imaging planes could be equivocal without appropriate landmarks. For vessels with multiple bifurcations, the incorrect identification of side branches led to the disorientation of imaging planes in the ROI. Also, 3D fusion model may be affected by the motion artifact and geometric errors inherited from 3D QCA. In particular, oblique imaging, which imposed unrealistic roughness at the vessel wall, created locally low and oscillating ESS, unless it was systemically removed. Nonetheless, the introduction of the novel technique and use of dedicated software enabled the reconstruction of coronary models and estimation of ESS with a high reproducibility within a feasible time on a desktop PC. In addition, recent advancements in machine learning allow labor-intensive image segmentation to significantly reduce the required time and cost, even without ECG-gating.

The application of 3D reconstruction of coronary arteries to CFD analyses has helped elucidate the pathophysiologic mechanism underlying the dynamic changes over time. The regional ESS patterns and circumferential ESS distribution were influenced by vascular remodeling and plaque eccentricity. Moreover, serial intravascular imaging studies demonstrated that low oscillatory ESS played a role in the development and progression of coronary atherosclerosis in line with histological analysis of animal models. Furthermore, low ESS led to plaque development and progression, as well as the formation of a rupture-prone thin-cap fibroatheroma. In the Prediction of Progression of Coronary Artery Disease and Clinical Outcome Using Vascular Profiling of Shear Stress and Wall Morphology (PREDICTION) trial, low local ESS was an independent predictor of plaque enlargement and clinically relevant luminal obstruction. Along with introduction of novel methods for ESS assessment, hemodynamic analysis using elaborated fusion techniques will provide a better insight into the detection of high-risk plaques and event-prone lesions.