SB³C2021
Summer Biomechanics, Bioengineering and Biotransport Conference
June 14-18, Virtual

WALL SHEAR STRESS TOPOLOGICAL SKELETON VARIABILITY PREDICTS MYOCARDIAL INFARCTION

Maurizio Lodi Rizzini (1), Alessandro Candreva (2), Claudio Chiastra (1), Takuya Mizukami (2), Diego Gallo (1), Jean-Paul Aben (3), Olivier Muller (4), Bernard De Bruyne (2,4), Carlos Collet (2), Umberto Morbiducci (1)

(1) Polito[BIO]Med Lab, Department of Mechanical and Aerospace Engineering
Politecnico di Torino
Turin, Italy

(2) Cardiovascular Center Aalst
OLV-Clinic
Aalst, Belgium

(3) Pie Medical Imaging BV
Maastricht, The Netherlands

(4) Department of Cardiology
Lausanne University Hospital
Lausanne, Switzerland

INTRODUCTION

Myocardial infarction (MI) is the deadliest complication of coronary artery disease (CAD), with approximately 1 million of cases per year in the United States alone [1]. Coronary atherosclerotic plaques experience a variety of hemodynamic stimuli, such as wall shear stress (WSS) and pressure gradients, linked to plaque progression and destabilization, increasing the risk of an abrupt occlusion [2]. In particular, WSS is purported to play a major role in translating hemodynamic signals to vascular biological phenomena. In this regard, peculiar WSS features obtained from patient-specific computational fluid dynamics (CFD) simulations have been associated with coronary plaque rupture [3]. Therefore, WSS-based quantities may prove to have predictive capability for MI, allowing the identification of lesions prone to rupture improving the medical management of CAD patients.

Accordingly, the present study aims to explore the capability of a comprehensive hemodynamic assessment of coronary lesions to predict MI. To do that, quantitative coronary angiography (QCA), fractional flow reserve derived from angiography (vFFR) and WSS derived from patient-specific CFD simulations were retrospectively tested on a population of patients (N=188 vessels) with future culprit (FC) and non-future culprit (NFC) lesions.

METHODS

Patient population. Patients presenting with acute MI admitted for invasive coronary angiography were retrospectively screened to identify those who had (1) a previous coronary angiography performed between 1 month and 5 years before the event (baseline angiography), (2) a visually identifiable FC mildly stenosed lesion (i.e., $\leq$ 50% diameter stenosis) at the baseline angiography, and (3) at least one additional NFC lesion in the other two major epicardial vessels. This selection resulted in 80 patients and a total of 188 vessels, with 80 FC lesions and 108 NFC lesions.

Computational hemodynamics. The workflow of the study is presented in Figure 1. Three-dimensional QCA vessel reconstructions were performed using two angiographic projections with at least 30 degrees apart, extracting anatomical (percentage area stenosis, %AS) and functional (vFFR) data, using the CAAS Workstation vFFR software (Pie Medical Imaging, Maastricht, the Netherlands). 3D reconstructions were then discretized and transient CFD simulations were performed using a finite element-based code (CAAS Workstation WSS software, Pie Medical Imaging) to obtain the WSS distribution along the luminal surface. Patient-specific mean flow rates were prescribed as inflow boundary conditions scaling a generic Doppler velocity curve, distinctive for the right, left anterior descending, and left circumflex coronary arteries with a diameter-based scaling law [4].

Wall shear stress-based descriptors. The most widely adopted cycle-average descriptors of WSS magnitude, multidirectionality and topological skeleton features were tested. Here, we focused on the two descriptors that emerged as the strongest predictors of MI, as reported in the following. In detail, the cycle-average WSS (TAWSS) was selected as a measure of the WSS magnitude acting on the endothelium. Moreover, the contraction/expansion action exerted by hemodynamic shear forces on the endothelium was quantified according to a recently proposed Eulerian-based method for the analysis of the WSS topological skeleton based on the divergence of the WSS unit vector field (DIV_{WSS}) [5]: negative (positive) DIV_{WSS} values at the luminal surface identify WSS contraction (expansion) regions. Very recent findings demonstrated that the WSS topological skeleton is able to capture hemodynamic features linked to vascular dysfunction [6,7,8]. Here the quantity Topological Shear Variation Index (TSVI) was used as a measure of the variability of the local contraction/expansion action

exerted by the WSS along the cardiac cycle. Technically, the TSVI is defined as [7,8]:

$$TSVI = \left\{\frac{1}{T}\int_0^T [DIV_{WSS} - \overline{DIV_{WSS}}]^2 dt\right\}^{1/2} \quad (1)$$

where T is the cardiac cycle duration.

Statistical analysis. WSS-based descriptors were averaged over the lesion, identified using the standard QCA-based approach. The predictive capacity of WSS-based descriptors was quantified in terms of receiver operating characteristic (ROC) curve and area under the curve (AUC).

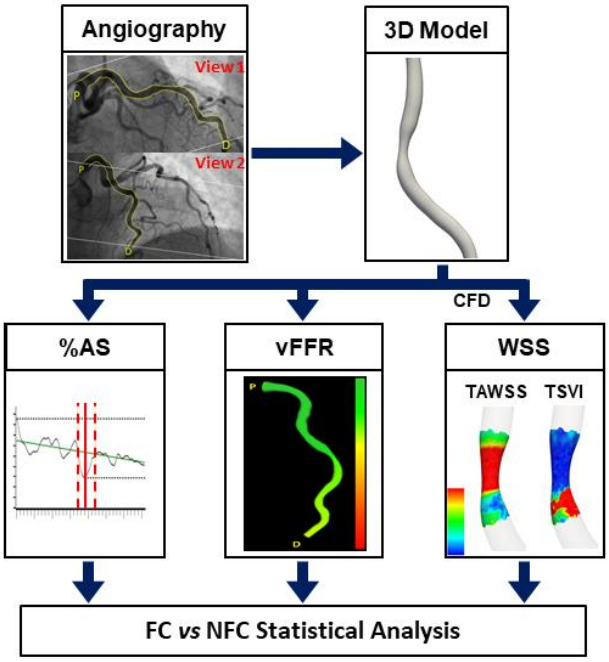

Figure 1: Workflow of the study

RESULTS

The FC and NFC groups were significantly different in terms of both anatomical and functional data ($p<0.001$ and $p=0.009$ for %AS and vFFR, respectively). Significant differences emerged between the FC and NFC distributions of lesion-average values of TAWSS (FC: 3.36 [IQR: 2.51-5.23] Pa; NFC: 2.94 [IQR: 2.36-3.80] Pa, $p=0.011$) and TSVI (FC: 71.08 [IQR: 44.42-116.20] m^{-1}; NFC: 33.21 [IQR: 24.77-60.11] m^{-1}, $p<0.001$), as reported in figure 2. Notably, both TAWSS and TSVI were significantly higher in FC than NFC group, with a more marked statistical significance for TSVI.

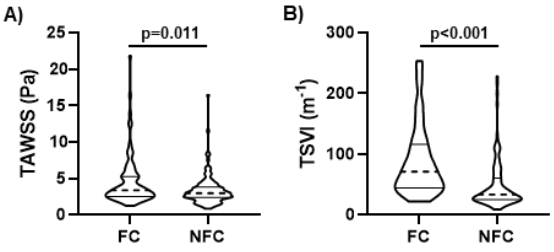

Figure 2: Violin plots of TAWSS (panel A) and TSVI (panel B) averaged over the lesion.

Anatomical and functional data emerged as moderate predictors for MI (AUC=0.65 and AUC=0.63 for %AS and vFFR, respectively). In figure 3, the ROC curves for lesion-average values of TAWSS and TSVI are presented. From the analysis, it emerged that TAWSS was a moderate (AUC=0.61; 95% CI: 0.53 to 0.69, $p=0.011$) but weaker MI predictor than anatomical and functional data. TSVI (AUC=0.77; 95% CI: 0.70 to 0.84, $p<0.001$) emerged as a stronger MI predictor than anatomical and functional data, as well as TAWSS. The best identified threshold values were: (1) 5.01 Pa for TAWSS, resulting in sensitivity equal to 0.34 and specificity equal to 0.89; (2) 40.52 m^{-1} for TSVI, resulting in sensitivity equal to 0.85 and specificity equal to 0.65.

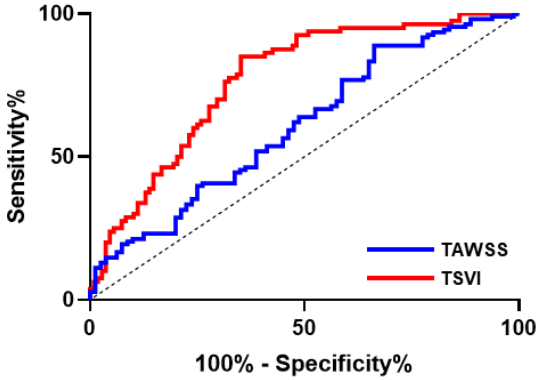

Figure 3: ROC curves based on TAWSS (blue) and TSVI (red) prediction of MI.

DISCUSSION

This study investigated the prediction capability for MI of anatomical, functional, and CFD-derived WSS-based quantities. The main results can be summarized as follows: (1) significantly different anatomical (%AS), functional (vFFR) and hemodynamic quantities (TAWSS and TSVI) characterized FC and NFC groups; (2) vFFR, %AS, and high TAWSS exhibited a moderate MI prediction capability; (3) high TSVI emerged as the strongest MI predictor. The obtained results enforce the hypothesis that (1) endothelial shear stress is a main actor in CAD, and (2) TSVI represents a relevant hemodynamic cue in CAD. The emergent predictive power of TSVI expands its association with long-term restenosis after carotid endarterectomy [7] and ascending aortic aneurysm wall degradation [8]. Physically, TSVI describes the variability of the contraction/expansion action exerted by WSS on the endothelium. Thus, it describes different features of the WSS vector field with respect to TAWSS and it represents a different hemodynamic stimulus to the endothelium. Translating this into mechanistic implications, the variability in the contraction/expansion action exerted by shear forces on endothelial cells reflects on intracellular tension variability that could lead to aggravating biological events [9]. A high temporal variability of WSS contraction/expansion action may result in fibrous cap fragility, accelerated disease progression, plaque fatigue, ending in plaque rupture and subsequent MI. This hypothesis, which needs further investigation, is also supported by the fact that TSVI identifies blood flow stagnation, recirculation and separation regions usually classified as flow disturbances promoting vascular dysfunction.

In conclusion, high TSVI resulted a strong predictor of MI in the analyzed population, encouraging further clinical trials to enforce the presented results and translate this concept into clinical practice.

REFERENCES

[1] Virani SS et al. *Circulation*, 2020.
[2] Lee JM et al., *JACC Cardiovasc Imaging*, 12(6):1032-43, 2019.
[3] Kumar A et al., *J Am Coll Cardiol*, 72(16):1926-35, 2018.
[4] van der Giessen AG et al., *J Biomech*, 44(6):1089-95, 2011.
[5] Mazzi V et al., *Biomech Model Mechanobiol*, 19(5):1403-23, 2020.
[6] Arzani A et al., *J Biomech*, 73:145-152, 2018.
[7] Morbiducci U et al., *Ann Biomed Eng*, 48:2936–49, 2020.
[8] De Nisco G et al., *Med Eng Phys*, 82:119-129, 2020.
[9] Lei M et al., *Med Eng Phys*, 18(4):326-32, 1996.