WALL SHEAR STRESS AND ATHEROSCLEROTIC PLAQUE PHENOTYPES IN FOCAL AND DIFFUSE CORONARY ARTERY DISEASE

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Introduction

Translesional pressure gradient during hyperemia is a fundamental clinical parameter to evaluate the functional severity of coronary artery disease (CAD), being associated with adverse clinical events [1]. Its measurement is performed in the distal part of the coronary artery, thereby reflecting the cumulative pressure losses along the whole vessel [2]. Automatic pullback pressure measurements allow quantifying pressure losses along the vessel, differentiating the CAD functional pattern in focal or diffuse [2]. In addition to pressure gradients, wall shear stress (WSS) profiles are associated with plaque progression and destabilization [3], and with adverse clinical events [4].

In this study, a combination of (1) invasive pressure pullback measurement, (2) angiography-based WSS obtained with computational fluid dynamics (CFD) simulations, and (3) plaque phenotype characterization based on optical coherence tomography (OCT) was adopted to unveil possible relationship between CAD functional patterns, WSS, and plaque phenotype.

Methods

A total of 105 coronary arteries with flow limiting lesions, identified by distal fractional flow reserve (FFR) lower than 0.80, underwent pressure pullback measurement and angiography-based WSS analysis. A subset of 51 vessels was analyzed with OCT pullback.

FFR motorized pullback tracings (Volcano R100, Volcano Corporation) during maximal hyperemia were used to obtain the pressure pullback gradient (PPG), a non-dimensional continuous quantity, ranging from 0 (diffuse CAD) to 1 (focal CAD) [2]:

$$\mathrm{PPG} = \frac{1}{2}\left[\frac{MaxPPG_{20mm}}{\Delta FFR_{vessel}} + \left(1 - \frac{L_{FD}}{L_{TOT}}\right)\right] \qquad (1)$$

where $MaxPPG_{20mm}$ was defined as the maximum PPG over a 20 mm length, ΔFFR_{vessel} as the difference between FFR values obtained at the ostium of the vessel and at the most distal anatomical location, the length of functional disease L_{FD} as the length with FFR drop ≥0.0015 per mm, and the total vessel length L_{TOT} was derived from the motorized pullback pressure tracing.

3D vessel models were reconstructed from two angiographic projections at least 30° apart. Lesions and mid segment (i.e., the segment of the lesion where the severity is maximal) were identified using an automatic approach. The anatomic severity was characterized in terms of percentage area stenosis (%AS). Then, CFD simulations were performed on reconstructed 3D vessel models using a finite element-based code (CAAS Workstation WSS software, Pie Medical Imaging). WSS vector field was characterized in terms of time-average WSS (TAWSS) and topological shear variation index (TSVI) [4], which accounts for variability of WSS contraction/expansion action on the endothelium along the cardiac cycle. TAWSS and TSVI values were averaged over the mid segment of the lesion [4]. Finally, plaque composition analysis [5] was performed acquiring OCT pullbacks of 75 mm length. For the statistical analysis, odd ratios (OR) were obtained from the exponential of the standardized correlation coefficients of generalized linear models.

Results

Focal lesions (PPG above median value of 0.67) presented significantly lower distal FFR, higher %AS, TAWSS and TSVI ($p<0.001$ for all). Focal lesions presented a lower fibrous cap thickness with respect to diffuse ones ($p=0.005$). PPG was associated with the presence of thin-cap fibroatheroma (OR 2.85, $p=0.029$) and plaque rupture (OR 4.94, $p=0.002$). A significant association emerged between TAWSS and the presence of macrophages (OR 1.15, $p=0.018$), TSVI and plaque rupture (OR 1.01, $p=0.024$), TSVI and the presence of cholesterol crystals (OR 1.01, $p=0.041$).

Discussion

The findings of this study, schematized in Fig. 1, support the hypotheses that: (1) the hemodynamic profile is different in patients presenting with focal and diffuse CAD; (2) this different hemodynamic profile is also associated with different plaque phenotype; (3) focal CAD and higher TAWSS and TSVI are associated with high risk plaque phenotypes. These results, combined with previous observations [2,4], make focal lesions the favourite candidates to revascularization interventions.

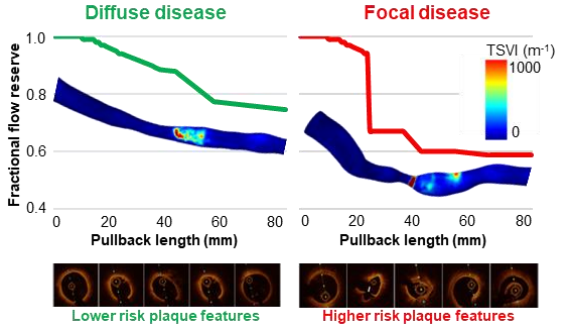

Figure 1: interplay between coronary hemodynamics and plaque composition in diffuse vs. focal lesions.

References

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