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Fluid-structure interaction models based on patient-specific IVUS at baseline and follow-up for prediction of coronary plaque progression by morphological and biomechanical factors: A preliminary study

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ABSTRACT

Plaque morphology and biomechanics are believed to be closely associated with plaque progression. In this paper, we test the hypothesis that integrating morphological and biomechanical risk factors would result in better predictive power for plaque progression prediction. A sample size of 374 intravascular ultrasound (IVUS) slices was obtained from 9 patients with IVUS follow-up data. 3D fluid-structure interaction models were constructed to obtain both structural stress/strain and fluid biomechanical conditions. Data for eight morphological and biomechanical risk factors were extracted for each slice. Plaque area increase (PAI) and wall thickness increase (WTI) were chosen as two measures for plaque progression. Progression measure and risk factors were fed to generalized linear mixed models and linear mixed-effect models to perform prediction and correlation analysis, respectively. All combinations of eight risk factors were exhausted to identify the optimal predictor(s) with highest prediction accuracy defined as sum of sensitivity and specificity. When using a single risk factor, plaque wall stress (PWS) at baseline was the best predictor for plaque progression (PAI and WTI). The optimal predictor among all possible combinations for PAI was PWS + PWSn + Lipid percent + Min cap thickness + Plaque Area (PA) + Plaque Burden (PB) (prediction accuracy = 1.5928) while Wall Thickness (WT) + Plaque Wall Strain (PWSn) + Plaque Area (PA) was the best for WTI (1.2589). This indicated that PAI was a more predictable measure than WTI. The combination including both morphological and biomechanical parameters had improved prediction accuracy, compared to predictions using only morphological features.

1. Introduction

Atherosclerotic plaque progression and rupture involve complex biological, biochemical, biomechanical and pathological processes, etc. (Stary et al., 1995; Virmani et al., 2000; Ku et al., 1985; Tang et al., 2009). The pioneering works of Fry, Caro, Ku, Giddens, Friedman and Malek, among others, showed that initiation of atherosclerosis process correlates positively with low and oscillating flow shear stress (Fry, 1968; Caro et al., 1971, Ku et al., 1985; Giddens et al., 1993; Friedman et al., 1987; Malek et al., 1999). However, the mechanism governing advanced plaque progression has not been fully understood (Tang et al., 2014). Loree et al. Ohayon et al. and Gijsen et al., our group and other groups have conducted studies on assessing plaque vulnerability from both biomechanical and morphological perspectives for coronary and carotid arteries (Loree et al., 1992; Ohayon et al., 2008; Wang et al. 2015a; Gijsen et al., 2015). Glagov et al. investigated coronary vessel enlargement and lumen narrowing processes occurring in coronaries during plaque growth using histological human coronary sections from 136 hearts (Glagov et al., 1987). It should be noted that most of the earlier studies were based on one-time plaque data, while plaque progression needs to be quantified using patient follow-up data (at least two observations).

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Several groups have made great effort to find the potential indicator to predict the plaque development over time. Results from the PROSPECT study (n = 697) showed that nonculprit lesions associated with recurrent events were more likely to have plaque burden of 70% or greater than those not associated with recurrent events ($p < .001$) (Stone et at., 2011). From the PREDICTION study, Stone PH et al. concluded that progressive plaque enlargement and lumen narrowing could be predicted independently by baseline large plaque burden and low endothelial shear stress (Stone et at., 2011). In an IVUS-based follow-up study with 20 patients recruited, Samady et al. divided IVUS slices into low, intermediate and high wall shear stress (WSS) groups. They reported that the low-WSS group developed significant progression in plaque area and necrotic core, whereas the high-WSS group had progression of necrotic core but regression of fibrous and fibro-fatty tissue (Samady et al., 2011). Following a similar method, Corban et al. found that the group with baseline plaque burden >40% and WSS <10 dyn/cm^2 had significantly greater change in plaque area at follow-up (0.68 ± 1.05 mm^2), compared to the group with plaque burden >40% and WSS >10dyn/cm^2 (Corban et al., 2014). Using a multi-level modeling approach, Sakellarios et al. claimed endothelial shear stress and low-density lipoprotein had a significant correlation with the changes in plaque area, therefore these factors had the potential to predict the regions that are prone to plaque progression (Sakellarios et al., 2017). Most of the studies in the literature (with a few exceptions) focused on flow shear stress and did not take the effect of structural mechanical conditions on plaque development into consideration (Maurice et al., 2004). For this reason, our group has published preliminary results on plaque progression using wall thickness and the mechanical conditions from the fluid–structure interaction (FSI) models (Wang et al., 2015b). Even though most existing studies focus on the relationship between plaque progression and morphological features, we conjecture that integrating all possible risk factors including morphological and biomechanical factors from plaque structure and blood flow would result in better predictive power for plaque progression prediction.

In this paper, follow-up intravascular ultrasound (IVUS) coronary plaque data were acquired from 9 patients and IVUS-based FSI models with cyclic bending were constructed to obtain data for eight selected key plaque morphological and biomechanical parameters including wall thickness (WT), plaque wall stress (PWS), plaque wall strain (PWSn), wall shear stress (WSS), lipid percent, min cap thickness, plaque area (PA) and plaque burden (PB). All possible combinations of these risk factors were fed into generalized linear mixed models (GLMM) to predict plaque progression in two measures: wall thickness increase (WTI), plaque area increase (PAI). All possible combinations were tested to identify the optimal predictor with highest prediction accuracy defined as the sum of prediction sensitivity and specificity for each measure. Correlation analyses were performed between plaque progression and risk factors using linear mixed-effect models (LME).

2. Data, method and model

2.1. Data acquisition and processing

IVUS with virtual histology (IVUS-VH) coronary plaque data were acquired from 9 patients (Mean age: 59, 7 males) with one-time follow-up (follow-up time span 6–12 months, median 9 months) at Cardiovascular Research Foundation (New York, NY) with informed consent obtained (the PROSPECT study, Stone et al., 2011). Patient demographical information are provided by Table 1. Data acquisition procedures were described previously in (Wang et al. 2015a, 2015b). X-ray angiogram (Allura Xper FD10 System, Philips, Bothel, WA) was obtained at both scans to show the location of the coronary artery stenosis, vessel curvature and cyclic bending caused by heart contraction. VH-IVUS data provides maps of lipid, calcification, and fibrotic tissues. Fusion of IVUS data and X-ray angiography to reconstruct 3D blood vessel geometry were performed after the segmentation and co-registration of the one-by-one paired slices at baseline and follow-up using information from angiography, location of myocardium, vessel bifurcation, stenosis and plaque components following established procedures (Wang et al., 2015b). Fig. 1 gives one sample with selected registered IVUS-VH images and segmented contours at baseline and follow-up, angiography, and vessel sagittal view with maximum and minimum curvatures demonstrating cyclic bending.

2.2. The fluid–structure interaction (FSI) model

In vivo IVUS-based 3D FSI models with anisotropic material properties and pre-shrink-stretch process were constructed for each coronary plaque to obtain plaque stress, strain and flow wall shear stress conditions. Blood flow was assumed to be laminar, Newtonian (Yang et al., 2007; Kari et al., 2017), and incompressible. The Navier-Stokes equations with arbitrary Lagrangian-Eulerian (ALE) formulation were used as the governing equations. The structure model included equilibrium equations (equation of motion), the nonlinear Cauchy-Green strain-displacement relation and Mooney-Rivlin material properties. Pulsating pressure conditions were prescribed at the inlet and outlet of the vessel. No-slip boundary conditions were imposed on the fluid-vessel interface. Other boundary conditions were prescribed to the appropriate interfaces to recover the physiological conditions and cyclic bending movement of coronary (Yang et al., 2009).

2.3. The Mooney-Rivlin material model

The vessel tissue was assumed to be hyperelastic, anisotropic, nearly-incompressible and homogeneous. Plaque components (lipid core and calcification) were assumed to be hyperelasic, isotropic, nearly-incompressible. A modified Mooney-Rivlin material model was used to describe the material properties of vessel tissue with the strain energy density function given below (Holzapfel et al., 2000):

$$W = W_{iso} + W_{ansio}. \tag{1}$$

$$W_{iso} = c_1(I_1 - 3) + c_2(I_2 - 3) + D_1[\exp(D_2(I_1 - 3)) - 1] \tag{2}$$

$$W_{aniso} = K_1/2K_2\{\exp[K_2(I_4 - 1)^2 - 1]\}. \tag{3}$$

$$I_1 = \sum C_{ii}, \quad I_2 = 1/2[I_1^2 - C_{ij}C_{ij}], \tag{4}$$

where I_1 and I_2 are the first and second invariants of right Cauchy-Green deformation tensor $\mathbf{C}$ defined as $\boldsymbol{C} = [C_{ij}] = \mathbf{X}^T\mathbf{X}$, $\mathbf{X} = [X_{ij}] = [\partial x_i/\partial a_j]$, (x_i) is current position, (a_i) is original position, $I_4 = C_{ij}(\mathbf{n}_c)_i(\mathbf{n}_c)_j$, $\mathbf{n}_c$ is the unit vector in the circumferential direction of the vessel, c_1, c_2, D_1, D_2, and K_1 and K_2 are material constants determined by fitting the biaxial testing experimental data using a two-step square-least method. The parameters for the vessel (fibrous tissue) used in this paper were: $c_1 = -1312.9$ kPa, $c_2 = 114.7$ kPa, $D_1 = 629.7$ kPa, $D_2 = 2.0$, $K_1 = 35.9$ kPa, $K_2 = 23.5$. The parameters used for lipid and calcification are: Lipid: $c_1 = 0.5$ kPa, $c_2 = 0$ kPa, $D_1 = 0.5$ kPa, $D_2 = 1.5$; Ca: $c_1 = 92$ kPa, $c_2 = 0$ kPa, $D_1 = 36$ kPa, $D_2 = 2.0$. Material parameters were used in our previous publications and are also consistent with data available in the literature (Holzapfel et al., 2000; Kural et al., 2012; Yang et al., 2009; Teng et al., 2014).

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