INTERPRETATION OF CFD DERIVED SHEAR STRESS AND ITS RELATION WITH ATHEROSCLEROSIS IN HUMAN CORONARY ARTERIES

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INTRODUCTION

Average low shear stress is known to play a role in the pathophysiology of atherosclerotic disease[1]. Indeed, previous studies described an inverse relationship between wall thickness and shear stress in atherosclerotic coronary arteries derived from autopsy studies[2], obviously being measured at one moment in time. Nowadays, combination of *in vivo* 3D reconstruction techniques of lumen and wall of atherosclerotic human coronary arteries and computational fluid dynamics allow patient specific determination of the relationship between atherosclerotic wall thickness and shear stress. Preliminary study of patient specific data sets showed that patients have various stadia of atherosclerosis. Although it is known that even during atherosclerosis shear stress acts as a regulatory factor in striving to maintain normal lumen dimensions in a negative feedback loop, in some of these arteries lumen narrowing is observed because of plaque encroachment into the lumen. Obviously, alterations in lumen shape and lumen narrowing change the original shear stress distribution. Given the lumen control system and the observed lumen narrowing, the study of arterial atherosclerotic wall thickening and it relation to shear stress at one moment in time is not straightforward. Appropriate techniques need to be adopted to summarize patient specific data measured at one moment in time in order to enable the understanding of the influence of shear stress in the generation of atherosclerosis.

METHODS

In 12 atherosclerotic patients, angiographically normal coronary arteries (lumen diameter stenosis <50%) were investigated with a combined ANGiographic and ivUS technique (ANGUS) to provide reconstruction of the true 3D lumen and vessel wall geometry [3] Segments (n=24) in between side branches were selected for this study. The 3D lumen reconstruction served to calculate shear stress by computational fluid dynamics. Inflow for the segments was selected to deliver an average shear stress of 1.5 Pa in normal reference (ref) cross sections (maximal plaque free vessel wall). Lumen area (LA) stenosis (AS) was defined as (LAref –LA) / LAref *100%. Shear stress (SS) and wall thickness (Th) data were measured at 16 different circumferential locations. Two methods to summarize the data were analyzed 1) For each segment data were averaged in the axial direction (ax, Figure 1). This method is most sensitive to detect *global effects* of a long time persisting SS pattern in a curved segment. 2) For each segment, data were averaged in circumferential direction (circ, Figure 1). This method is most sensitive to *local effects* by axial (longitudinal) variations of lumen size. Linear regression analysis was used to relate Th to SS for the raw data and both types of averaged data (Th_{ax}, SS_{ax} and Th_{circ}, SS_{circ} (Th=a+b*SS)). Two groups of segments were compared based on the presence or absence of lumen narrowing (AS>10% and AS<10%).

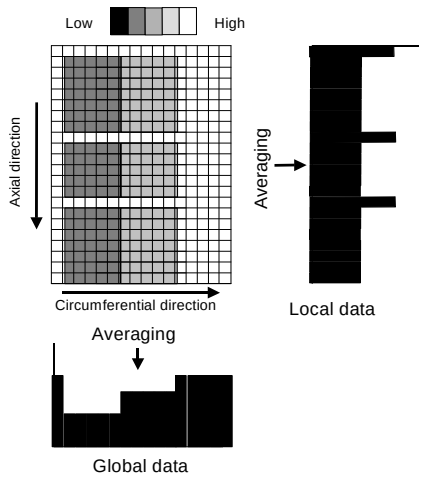

Figure 1: Wall shear stress or wall thickness data (grey scale coded) of a segment displayed in matrix format. Axial and circumferential averaging delivers respectively global and local data. Axial resolution equals 1 mm.

Table: overview of slopes of the relationship between Th and SS for segments with lumen preservation and lumen narrowing

			Raw data				Average axial direction				Average circumferential direction			
AS	n	AS	b	neg	~	pos	b	neg	~	pos	b	neg	~	pos
<10%	11	1.7±5.6%	0.10±0.17	9%	18%	73%	-0.46±0.55^{0}	64%	18%	18%	0.12±0.11^{0}	0%	54%	46%
>10%	13	18±6%^{0,*}	0.14±0.08^{0}	0%	0%	100%	0.19±0.52*	15%	54%	31%	0.14±0.07^{0}	0%	8%	92%

***: p<0.05 for <10% vs >10%, o: p<0.05 vs 0, AS: area stenosis, b : average slope (mm/Pa), neg: significant negative slope, pos: significant positive slope, ~: no significant relationship**

RESULTS

The observed lumen area stenosis in both groups (AS<10% and AS>10%) was very small (Table), because arterial segments were selected having no significant stenosis. Nevertheless, the variation in AS was quite significant allowing the study of differences in SS related parameters in both groups (p<0.05).

Lumen preservation

Of the segments with preserved lumen, the raw data set showed that 73% of the segments had a significant positive relationship between wall thickness and shear stress (Example Figure 2A, Table), while only 9% (n=1) had an inverse relationship. Figure 2B shows a typical example of the relationship between wall thickness and shear stress after averaging in axial direction. Of all segments (n=11), averaging the data in the axial direction delivered in 64% a significant inverse relation between wall thickness and shear stress, resulting in an average *negative* slope (-0.46±0.55, p<0.05). Axial averaging of the shear stress in this group gives an impression of the long term persisting shear stress distribution. For example because of vessel curvature the low shear stress areas in the inner curve remain low relative to the high shear stress regions in the outer curve even during mild lumen narrowing. Existence of lumen variations in this group of segments, caused by encroachment of atherosclerosic plaque in the lumen is apparent from the significant positive relationship between wall thickness and shear stress after averaging in circumferential direction (Figure 2C, Table). This significant positive relationship was existent in 46% of the segments. The latter might be explained by the control system operable to keep normal lumen dimensions, which remain to show an input residual shear stress increase at diseased cross sections.

Lumen narrowing

In this group (n=13), the frequency of a significant positive relationship between wall thickness and shear stress for respectively the raw data, the data averaged in circumferential direction and the data averaged in axial direction was: 100%, 92% and 31% (Table). Data averaged in the axial direction delivered for only 15% of the segments a significant negative slope. In general no relationship was obtained. These data likely indicate that already for insignificant lumen narrowing (AS=18%) the distribution of shear stress is so much changed compared to the natural distribution that no conclusions regarding the role of shear stress in the generation of atherosclerosis is allowed. Whether other factors than shear stress, including plaque fissuring and healing disturb the wall thickness - shear stress relation warrants further study.

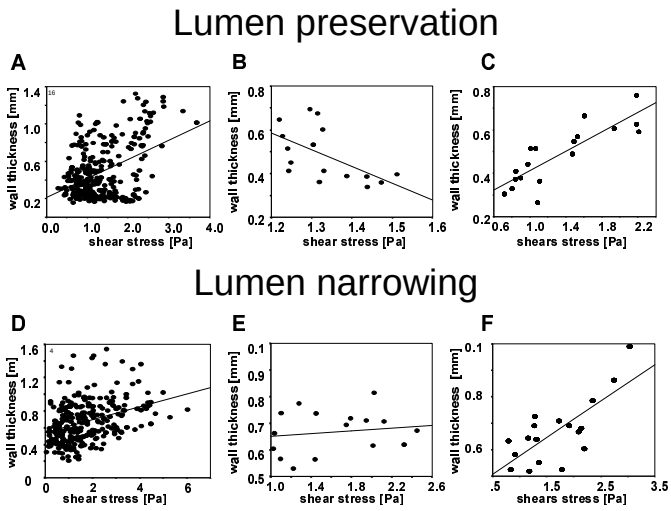

Figure 2: relationships between wall thickness and shear stress for a segment with lumen preservation (A,B,C) and for segment with lumen narrowing (D,E,F); raw data (A,D); data averaged in axial direction (B,E) and data averaged in circumferential direction (C,F)

CONCLUSION

Interpretation of patient specific data measured at one moment in time regarding the influence of shear stress in the generation of atherosclerosis is not straightforward. The influence of persisting shear stress patterns can be demonstrated by averaging the data in the axial direction, showing an inverse relationship between wall thickness and shear stress in the segments with preserved lumen only. Loss of this relationship in segments with lumen narrowing may point to other factors influencing the progression of atherosclerotic disease, like plaque fissuring.

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