INTIMA-MEDIA ROUGHNESS: A NEW QUANTITATIVE ULTRASOUND PARAMETER DESCRIBING THE ATHEROSCLEROTIC PROCESS

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The measurement of the intima-media thickness (IMT) is an accepted mean for the assessment of the atherosclerotic burden of the arterial vascular system. Several studies have shown an association with the prevalence of atherosclerotic risk factors [1-4]. Moreover, prospective studies gave evidence that the IMT is at least equal or superior to the major atherosclerotic risk factors considering the prognosis for future cardiovascular events such as myocardial infarction or stroke [5-7]. This seems to be logical because the ultrasound examination shows directly the atherosclerotic vascular damage whereas risk factors or their combination indicate more or less the possibility of an ongoing atherosclerotic process.

However, IM thickening happens not only in association with the amount and severity of atherosclerotic risk factors, but is also strongly dependent on aging. Homma et al. [8] showed that the IM layer thickens linearly across the life span from young adults to centenarians. In a previous study [9] we found an age-dependent increase of common carotid IMT of 0.052 mm/10 years in male subjects screened for the absence of cardiovascular risk factors. In population-based studies the increase of IMT was between 0.08 - 0.12 mm/10 years [10,11]. This age-dependent IM thickening clearly weakens the power of the IMT to discriminate between “healthy aging” of the arterial wall and atherosclerotic wall changes predicting future cardiovascular events.

As a consequence more specific markers for the atherosclerotic wall process are needed. According to various studies [12-14] aside IM thickening, the presence of plaques in the carotid tree was independently associated with manifest coronary artery disease (CAD). Thus, the prevalence of plaques may provide additional information to the IMT about the risk for future cardiovascular events. But what is the definition of a plaque in ultrasound studies of the carotid tree? Is every local encroaching of the arterial wall into the lumen or an IM thickness above a certain value or at least a doubling of the IMT compared to the adjacent IM region already a lesion? Since the development of plaques is best reflected by a continuous process from early reversible flat lesions type I-III to raised lesions type IV-VII, the named definitions are principally all different stages of the plaque development [15].

In a prospective study Belcaro et al. [16] observed a graded association of cardiovascular events with different stages of atherosclerotic wall changes in the carotid tree. Granulations representing the least severe changes had the lowest event rate followed by prominent plaques, non-stenotic and stenotic arterial plaques. The lesions were classified in four qualitative categories by the subjective judgment of two experienced sonographers. However, this procedure has not accomplished any diversified usage in the assessment of atherosclerotic alterations but highlights an increase of risk parallel to the severity of atherosclerotic changes.

Looking at the wall of the common carotid artery we noticed that patients with coronary artery disease had stronger irregularities of the IMT than age-matched healthy subjects although the mean and maximum IMT itself was not significantly altered. Furthermore, it was visible as described by Kornet et al. [17] that the IMT thickens from proximal to distal. Both, the IMT and
the irregularities of the IMT seemed to be highest in the wall segment directly before the opening to the carotid bulb.

In a histopathologic study Solberg and Eggen [18] found that the severity of atherosclerotic lesions increased with age in the carotid tree and were most prominent at all ages in the region of the common carotid artery (CCA) directly before the opening to the bulb, in the bulb itself, and in the proximal internal artery, respectively. This was concordant with our ultrasound observations [19]. Since atherosclerotic lesions are not distributed regularly across the arterial wall, the irregularity of the IM thickness visible in ultrasound images might be the equivalent of manifest atherosclerotic lesions. Taking this into consideration we hypothesized that patients with manifest CAD have stronger irregularities of the IMT in the distal segment of the CCA than age-matched healthy controls. Furthermore, aging in subjects with low risk factor burden should be reflected more precisely by an increase of the IMT than by IMT irregularities.

For the measurement of the IMT irregularities (in future called IM roughness) in the CCA we adapted a recently developed automatic detection program of the intimal and adventitial borders [20,21]. The mechanical basis for the variable IM roughness was the ISO standard 4287/1 “surface roughness; terminology, surface and its parameters.” In order to avoid the influence of the increase in the IMT towards the bifurcation on the calculated IM roughness, the regression line of all IMT measurement points in the identified wall segment (standard segment length = 1 cm) was calculated. The IM roughness \((R)\) was then calculated as the arithmetic mean of the sum of the profile deviations from the regression line \((y)\) by the following equation:

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R = \frac{1}{n} \sum_{i=1}^{n} |y_i|
\]

The value of the IM roughness usually was between 0.03 and 0.08 mm and thus around one tenth of the IMT. The intra-observer error \((S)\) ranged between 7% and 10% \((S = \text{standard deviation of the differences between measurements of session one and two}/\sqrt{2})\) [19].

Comparing CAD patients \((62.1 \pm 9.3\) years, \(N = 46)\) with healthy age-matched subjects \((62.9 \pm 3.5\) years, \(N = 22)\), we found that they had only 14% higher mean and 16% higher maximum IMT whereas the IM roughness was 90% higher in CAD patients. On the other hand, the age-associated difference across 4 decades between healthy older subjects and young subjects \((24.9 \pm 2.3\) years, \(N = 15)\) of the mean and maximum IMT was 40% and 34%, respectively, but the IM roughness was only 14% higher in the older subjects [19].

In addition, the AUCs for the mean and maximum IMT and IM roughness predicting patients with CAD were 0.66, 0.71, and 0.80, respectively. This showed the best discriminative power of the IM roughness among the three parameters between subjects with and without coronary artery disease [19].

Based on the present data it is not possible to show any superiority of the IM roughness on the prevalence of plaques or IM thickening in the carotid bifurcation and internal carotid artery with respect to the discrimination between subjects with and without ischemic heart disease. This has to be evaluated in additional studies. However, the better visualization of the CCA wall (> 99%) compared to the carotid bifurcation (80.5%) and inner carotid artery (61.3%) is a reasonable argument to use the CCA as a measurement side [19].

In conclusion, the measurement of the IM roughness offers the opportunity for an improved detection of subjects at increased risk for future cardiovascular events. It may strengthen the value of non-invasive ultrasound as a mean for the quantitative assessment of the
atherosclerotic burden and for monitoring the effect of therapeutic interventions on the atherosclerotic process.

Reference List


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