atherosclerosis

Atherosclerosis newsletter

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Volume 341, Issue January 2022

Volume 342, Issue February 2022

These two issues contain several reports of observational studies investigating the prognostic value of vascular or endothelial function tests.

Association of inter-arm systolic blood pressure differences with arteriosclerosis and atherosclerosis: A cohort study of 117,407 people

Several studies have reported that the difference in bilateral blood pressure (also called inter-arm blood pressure difference, IAD) is related to cardiovascular events beyond the conventional diagnosis of hypertension by single-arm blood pressure measurements and cardiovascular risk evaluation. IAD is related to coronary disease, cerebral vascular disease, peripheral vascular disease, and cardiovascular and all-cause mortality. However, the mechanism by which IAD increases the risk of cardiovascular disease (CVD) is not yet known. Lee et al. evaluated the distribution of IADs in a large cohort of apparently healthy people and the association of IADs with brachial-ankle pulse wave velocity (baPWV) and coronary artery calcium (CAC).

Blood pressure was measured in both arms of 117,407 people who participated in the Kangbuk Samsung Health Study (a Korean cohort study consisting of individuals aged ≥18 years who underwent annual or biennial comprehensive health examinations at the Total Healthcare Centers of the Kangbuk Samsung Hospital in Seoul and Suwon). IAD was defined as the absolute difference in systolic blood pressure in both arms and was confirmed by measuring baPWV with an automatic oscillometric device. Arterial stiffness was measured by baPWV, and CAC was assessed with multi-detector computed tomography.

More than 97% of the total population had an IAD ≤10 mmHg. IAD was significantly associated with arterial stiffness, reflecting arteriosclerosis, but not with the presence of CAC, reflecting atherosclerosis.

In primary care, IAD may be a useful tool to identify people with subclinical arterial diseases with normal values for traditional risk factors.

Retinal microvascular function predicts chronic kidney disease in patients with cardiovascular risk factors

Cardiovascular disease (CVD) remains the greatest contributor to increased morbidity and mortality among patients with advanced chronic kidney disease (CKD). Vascular endothelial dysfunction, a sentinel event in the development of focal and systemic vascular disease, is a precursor to atherosclerosis and is implicated in the coexistence between CVD and CKD. Retinal microvascular endothelial vasodilatation, a nitric oxide-dependent phenomenon, provides a direct measure of vascular reactivity in the retinal microcirculation. Theuerle et al. aimed to assess whether flicker light-induced retinal microvascular endothelial function is attenuated in subjects with renal impairment, and whether diminished retinal microvascular function is predictive of long-term CKD progression.

In a single centre prospective observational study, 253 subjects with coronary artery disease and CVD risk factors underwent dynamic retinal vessel analysis. Retinal microvascular dysfunction was quantified by measuring retinal arteriolar and venular dilatation in response to flicker light stimulation. Serial renal function assessment was performed over a median period of 9.3 years using estimated GFR (eGFR).

Flicker light-induced retinal arteriolar dilatation (FI-RAD) was attenuated in patients with baseline eGFR compared to those with normal renal function. In patients with normal renal function, subjects with the lowest FI-RAD responses exhibited the greatest annual decline in eGFR. In uni- and multivariable analysis, among subjects with normal renal function, a 1% decrease in FI-RAD was associated with an accelerated decline in eGFR. FI-RAD was not predictive of CKD progression in subjects with baseline eGFR.

Retinal arteriolar endothelial dysfunction is present in patients with CVD who have early-stage CKD, and serves as an indicator of long-term CKD progression in those with normal renal function.

These study findings are highlighted in an editorial by Bellasi et al.

Sex-related differences in plaque characteristics and endothelial shear stress related plaque-progression in human coronary arteries

Atherosclerosis manifests differently in women compared to men in terms of atherosclerotic plaque size, composition and rupture risk. In general, coronary plaques in women are smaller in size and display fewer features of plaque vulnerability. Furthermore, women more often exhibit non-obstructive coronary disease, which is associated with coronary microvasculature abnormalities. Since endothelial shear stress (ESS), the frictional force of blood flowing along endothelial cells, is known to play a critical role in coronary atherosclerosis development, Wentzel et al. investigated the differences in anatomical characteristics and ESS–related plaque growth in human coronary arteries in men compared to women.

1183 coronary arteries (male/female: 944/239) from the PREDICTION study were studied for differences in artery/plaque and ESS characteristics, and ESS-related plaque progressionamong men and women and after stratification for age. All characteristics were derived from intravascular ultrasound imaging (IVUS)-based vascular profiling and reported per 3 mm-segments.

Coronary arteries and plaques were significantly smaller in females compared to males; but no important differences were observed in plaque burden, ESS and rate of plaque progression. Change in plaque burden was inversely related to ESSwith no difference between women *versus* men. However, stratification for age demonstrated that ESS-related plaque growth was more marked in young women compared to men, reducing in magnitude over the age-categories up till 75 years.

Coronary artery and plaque size are smaller in women compared to men, but ESS and ESS-related plaque progression were similar. Sex-related differences in ESS-related plaque growth were evident after stratification for age. These observations suggest that although the fundamental processes of atherosclerosis progression are similar in men and women, plaque progression may be influenced by age within gender.

Risk of myocardial infarction based on endothelial shear stress analysis using coronary angiography

The frictional force of the flowing blood acting on the endothelium, i.e. wall shear stress (WSS), is a key mechanism translating hemodynamic signals to vascular biological phenomena. In addition, WSS has been associated with vulnerable transformation of atherosclerotic lesions: low WSS has been linked to atherosclerosis progression, whereas high WSS has been associated with platelet activation and plaque rupture. Candreva et al. assessed the value of WSS analysis derived from conventional coronary angiography to detect lesions culprit for future myocardial infarction (MI).

Three-dimensional quantitative coronary angiography (3DQCA), was used to calculate WSS and pressure drop in 80 patients. WSS descriptors were compared between 80 lesions culprit of future MI and 108 non-culprit lesions (controls). Endothelium-blood flow interaction was assessed by computational fluid dynamics.

Median time between baseline angiography and MI was 25.9 months. Mean patient age was 70.3 ± 12.7. Clinical presentation was STEMI in 35% and NSTEMI in 65%. Culprit lesions showed higher percent area stenosis (%AS), translesional vFFR difference (ΔvFFR), time-averaged WSS (TAWSS) and topological shear variation index (TSVI) compared to non-culprit lesions. TSVI was superior to TAWSS in predicting MI. The addition of TSVI increased predictive and reclassification abilities compared to a model based on %AS and ΔvFFR.

A 3DQCA-based WSS analysis can identify lesions culprit for future MI. The combination of area stenosis, pressure gradients and WSS predicts the occurrence of MI. TSVI, a novel WSS descriptor, shows strong predictive capacity to detect lesions prone to cause MI.

Galectin-3 is linked to peripheral artery disease severity, and urinary excretion is associated with long-term mortality

Galectin-3 (Gal-3), a beta-galactoside-binding lectin, is a biomarker involved in fibrosis and vascular inflammation. Gal-3 has been linked to chronic kidney disease (CKD). Conflicting reports exist about the relevance of Gal-3 in peripheral artery disease (PAD). Ursli et al. aimed to elucidate a possible link between serum and urinary Gal-3 and long-term survival in PAD patients without critical limb ischemia and mild to moderate CKD.

Gal-3 was measured in serum and urine of PAD patients using bead-based multiplex assay. Urinary Gal-3 concentration was normalized to urine creatinine (cr) levels. Mortality data were retrieved from the Austrian central death registry after a median observation period of 9.2 years. Survival analyses were performed with the Kaplan-Meier method and Cox-regression.

Serum Gal-3 was higher in patients with claudication symptoms and correlated inversely with the patients' ankle-brachial index. Serum Gal-3 and urinary Gal-3 were associated with the estimated glomerular filtration rate. Serum Gal-3 was not linked to all-cause mortality over 9.2 years. However, uGal-3/cr was associated with all-cause mortality. This association sustained multivariable adjustment for cardiovascular risk factors and renal function.

This study shows an association of uGal-3/cr with long-term mortality in patients with PAD. Gal-3 is not predictive of long-term mortality but seems to be a marker of PAD severity in patients without critical limb ischemia.