HSR (LONDON),
HOUGHTON STREET REVIEW JOURNAL
ISSN: 2058-5519|Impact factor-15.9
http://houghtonstreetreview.com/index.php/hsr

MORPHOLOGICAL CHARACTERISTICS AND CLINICAL SIGNIFICANCE OF CORONARY ATHEROSCLEROTIC PLAQUE

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Doi: https://doi.org/10.5281/zenodo.23600356

Abstract. Atherosclerosis, which underlies most cases of coronary artery disease (CAD), is a chronic cardiovascular condition characterized by lipid deposition and persistent inflammation within the walls of large arteries. Over time, these pathological changes may lead to serious clinical outcomes, including myocardial infarction (MI) and stroke. Although atherosclerosis develops gradually over many years and is more commonly associated with older age, it remains a major cause of death worldwide, despite reductions in its incidence in certain regions. The development of atherosclerotic plaques involves the progressive accumulation of lipids, inflammatory cells, vascular smooth muscle cells, and cellular debris within the arterial intima beneath the endothelial lining. As these lesions enlarge, they may narrow the arterial lumen by more than 50%, restricting blood flow and producing symptoms such as angina, particularly during physical exertion or emotional stress. In some cases, plaques with a high lipid content and substantial inflammatory activity become vulnerable to rupture. Plaque disruption in a coronary artery can trigger thrombus formation, potentially leading to complete vessel occlusion and acute myocardial infarction. If thrombotic material travels through the circulation to the cerebral vessels, it may obstruct blood flow to the brain and cause an ischemic stroke.

Key words: Atherosclerosis, lipids, stroke, inflammatory cells, plaque.

Aim. This article summarizes the natural history of aortic and coronary atherosclerosis among adolescents from the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Study, which was a multi-institutional study of atherosclerosis in 15- to 34-year-old, The PDAY Study focused on 25- to 45-year-old subjects because fatty streaks are prevalent and fibrous plaques begin to appear in this age group.

Methods. Study subjects were persons aged 25 through 45 years who had died due to external causes Of the 3210 cases collected, 334 were excluded because they did not meet the study criteria. Of the 2876 cases included in this report, thoracic aortas were obtained from 2856, abdominal aortas from 2823, and right coronary arteries from 2788 Blood, liver, kidney tissue, and standardized arterial wall samples, including samples from the perfusion-fixed left anterior descending coronary artery, were also collected in this study. These samples were used to investigate the associations of atherosclerosis with the risk factors for adult CHD, which are reported elsewhere, and for studies of the microscopic features of aortic and coronary lesions including cellular, fibrous, and lipid-containing components.

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Results. Autopsy studies have demonstrated that atherosclerotic changes can develop early in life, with intimal lesions detected in the aortas of all individuals and in more than half of the right coronary arteries among the youngest examined age group (25 35 years). The prevalence and severity of these lesions increase with advancing age. Although fatty streaks were more extensive in Black individuals than in White individuals, the extent of raised atherosclerotic lesions was comparable between the groups. Raised lesions in the aorta were similar in women and men, whereas women exhibited a lower burden of raised lesions in the right coronary artery than men. Overall, the aorta showed a higher prevalence of total lesions than the right coronary artery, although raised lesions constituted a greater proportion of the total lesion burden in the coronary artery.

Atherosclerosis progresses through the gradual accumulation of lipids and the proliferation of vascular smooth muscle cells and connective tissue, resulting in the enlargement of fatty streaks and the formation of fibrous plaques. Some plaques subsequently undergo structural changes that increase their vulnerability to rupture. Plaque rupture exposes circulating blood to thrombogenic, lipid-rich material, promoting thrombus formation and potentially causing acute myocardial infarction or sudden cardiac death. The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study investigated the progression from early fatty streaks to advanced atherosclerotic lesions and examined the factors associated with this transition. Previous analyses demonstrated that established cardiovascular risk factors, including abnormal serum lipoprotein levels, smoking, hypertension, elevated glycohemoglobin, obesity, age, and sex, are associated with the extent and severity of atherosclerosis in young individuals.In the PDAY study, arterial specimens obtained during autopsy were examined using Sudan IV staining and radiographic imaging. Three pathologists independently assessed the extent of fatty streaks, fibrous plaques, complicated lesions, and calcification in the aorta and right coronary artery. Fibrous plaques, complicated lesions, and calcified lesions were collectively classified as raised lesions. This standardized assessment enabled investigators to evaluate both the distribution and severity of atherosclerotic changes in different arterial regions.The anatomical distribution of atherosclerosis varied considerably across the aorta. In the thoracic aorta, fatty streaks were most prevalent on the dorsal surface, particularly between adjacent pairs of intercostal artery openings, whereas the ventral surface was relatively spared. Advanced raised lesions were uncommon in this region, even among the oldest participants. In the abdominal aorta, fatty streaks were also more frequent on the dorsal than on the ventral surface, although the distribution of susceptible and relatively resistant regions was less clearly defined. Lesions were frequently observed between lumbar artery openings and along blood-flow pathways leading to major visceral arteries, while areas downstream of flow dividers were comparatively less affected. The left dorsal region of the abdominal aorta, extending from the inferior mesenteric artery opening toward the aortic bifurcation, demonstrated particularly high susceptibility to raised lesions. These findings highlight the importance of age, cardiovascular risk factors, and local vascular anatomy in the initiation and progression of atherosclerosis.In the thoracic aorta, the highest prevalence of fatty streaks occurred in the dorsal surface (>50%) while the ventral surface had few fatty streaks (<10%). The region of highest prevalence for fatty streaks was midway between successive pairs of intercostal ostia. The thoracic aorta was virtually spared of raised lesions even in the oldest age group (30-34 years: <4% raised lesions). In the abdominal aorta, the frequency of fatty streaks was greater in the dorsal than in the ventral area, but lesion-prone and lesion-resistant regions were not as sharply defined as in the thoracic aorta. Regions of high prevalence occurred between pairs of lumbar ostia and in flow tracts to

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the celiac, superior mesenteric, renal, and inferior mesenteric arteries, while regions distal to the flow dividers of these ostia were spared. A region on the left dorsal surface of the abdominal aorta, originating at the level of the inferior mesenteric ostium and extending distally to the bifurcation, was the most prone to raised lesions.

Conclusion. In the right coronary artery, fatty streaks are most frequently observed in the proximal segment, while raised atherosclerotic lesions show the highest prevalence within the first 2 cm of the vessel. These findings indicate that coronary arteries contain specific regions that are more susceptible to atherosclerotic changes, alongside areas that demonstrate relative resistance to lesion development. Although coronary catheterization is considered an important diagnostic approach for assessing coronary artery disease, its invasive nature, potential complications, and high cost highlight the need for reliable noninvasive diagnostic alternatives. Biomarkers such as C-reactive protein (CRP), together with imaging techniques including intravascular or extravascular ultrasound and ultrafast computed tomography, may contribute to disease detection and assessment, although each method has certain limitations. Advances in understanding the genetic mechanisms underlying atherosclerosis are also expected to improve diagnostic strategies. Emerging genomic technologies may enable comprehensive genetic screening as well as the identification of specific disease-associated variants in individual patients. Such approaches could help distinguish different atherosclerotic phenotypes and support more personalized pharmacological treatment. Given the heterogeneous nature of atherosclerosis, identifying distinct disease subtypes may improve risk stratification and therapeutic decision-making. While current clinical classification primarily relies on established cardiovascular risk factors, incorporating genetic information may allow more precise disease characterization and individualized management

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