Chapter 2

Early Stages of Atherosclerosis Documented in Early Embryologic Life

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Additional information is available at the end of the chapter

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Abstract

The composition of arterial bifurcations primarily changes blood flow and has a substantial role in the development of vascular disorders. Hence, it is essential to know the structural physiognomies of the common carotid artery (CCA) and its branches for the early onset of atherosclerosis in newborns. Some studies were conducted to evaluate the characteristics of CCA in newborn cadavers. Correlation between area ratios and atherosclerotic endothelial damage was determined. Investigations demonstrated that carotid bifurcation regions depicted widespread occurrence of intimal lipid accumulations, while carotid bifurcation region structure demonstrated abundant blood cells and disconnected endothelial cells. Fibrin collection on endothelial surface in low area ratios was another essential finding in the examinations of their endothelial surface erosion. The abovementioned morphological findings seemed to be matching to outflow to inflow area ratio statistics, favoring low area and degeneration. The correspondence between area ratios and the histological characteristic of cerebral vessels of newborn cadavers specifies that the early stages of atherosclerosis began in early embryologic life.

Keywords: carotid artery, cerebral blood flow, endothelium, newborn cadaver

1. Introduction

Atherosclerosis is described by a noticeable condensing and solidification of blood vessels [1–4]. Obtained risk factors such as high blood pressure, smoking, diabetes mellitus, and dyslipidemia are main factors in the onset of atherosclerosis [4–10]. Further, anatomical, histological, and hemodynamic features of the arteries and the genetic factors are other dynamics that predispose the onset of atherosclerosis [3–5, 11, 12].

2. Structural physiognomies of the common carotid artery (CCA) and its branches

Blood vessels and their luminal physiognomies have long been questioned as additional risk factors for atherosclerosis referring their stimulus on blood flow [9, 13–15]. Some arteries are more predisposed for the onset of the atherosclerotic plaques on the endothelial surface [2, 4, 10, 15, 16]. Current studies specified that the variations in the luminal diameter of the vessel have a collision on the beginning of atherosclerosis [3, 5, 6, 13].

Carotid artery is one of the two main vessels that stream blood to brain. Obstruction in the carotid artery leads to erosion and causes some brain symptoms. The anatomical elements of the common carotid artery (CCA) and its branches receive attention from researchers and clinicians, referring their scientific and clinical results. Also, another important factor is their involvement in plaque formation [7, 8, 10, 13, 17–21]. Hence, it is essential to distinguish the anatomical topographies of the CCA and its branches. CCA divides into two branches, that is, internal carotid and external carotid arteries. Atherosclerosis progresses mainly at bends and major branches of the arterial network, such as the carotid bifurcation and its subdivisions [2, 3, 15, 17]. Alike other bifurcation of large vessels, carotid bifurcation at the neck region is more prone to the initial growth of atherosclerotic plaques [3, 6, 14–16]. Flow models suggest that vessel anatomy, in particular vessel diameter and area ratios, affects plaque formation at arterial bifurcations. The carotid bifurcation is one of the most common of atherosclerotic plaques [2, 3, 9, 20, 22]. Therefore, assessing the diameters of the CCA, internal, and external carotid arteries (ICA and ECA) is important for evaluating the pathological changes [6, 22–25].

3. The correlation between area ratios and the histological characteristic of cerebral vessels of newborn cadavers

Despite the progression of atherosclerosis with aging being widely studied, there are limited studies in newborns. Many studies evaluated the diameters of peripheral vessels in adults, but only few studies were conducted on CCA and its branches in newborns [3, 6, 12, 19, 22]. Thus, an early beginning of atherosclerosis is suggested to initiate in the early period of life. Then, the purposefulness was to scrutinize the anatomical and histological characteristics of cerebral vessels in newborn cadavers. Consequently, it has been hypothesized that variations in carotid bifurcation lumen geometry would be the self-regulating prognosticators of ICA atherosclerosis, aiming to reveal the early beginning of atherosclerosis in newborn cadavers. The relation between the endothelial destruction and the outflow to inflow area ratio was also been inspected in some studies.

4. Other related predisposing risk factors

Atherosclerosis is a series of complex events that can begin in early fetal life [3, 4, 16, 26]. The onset of atherosclerosis was implied to be connected with several risk factors such as diabetes, genetics, and so on [4, 26]. Such as aorta abdominalis, bifurcation regions have been mentioned as primary locus that is prone to atherosclerosis [6, 20]. In recent studies, it has been suggested that the vessel diameter and area ratios are hypothetically important elements of plaque improvement [9, 20, 23]. With this information in mind, it earlier-published findings have been continued [6, 17], by observing the characteristics of vessel positioned in the bifurcation regions in young cadavers [6, 11, 13, 27].

As specified in the study, a vessel diameter and area ratio (score) are approximately 1.15 [12]. Low ratios could be reflective of increased local stress and endothelial damage. As a predictable result, the endothelial reaction to the damage might be amplified permeability accompanied by monocyte adhesion and migration.

The diameters of the CCA, ECA, and ICA have again been analyzed in the recent studies. The relative vessel dimension was shown to be significant in the progress of the disease [6, 11, 13, 19, 27]. Consequently, ICA/CCA, ECA/CCA, ECA/ICA ratios as well as the outflow to inflow area ratio have been calculated. Furthermore, vessels have been histologically evaluated using histo-staining methods and scanning electron microscopy (SEM) to determine the extent to which atherosclerotic pathology exists, if any [3]. The other central aims were to calculate the mean diameters of CCA, ICA, and relationships between atherosclerosis and ECA and outflow to inflow area ratio in the newborn period group. These records can be of use in intravascular composition and also for understanding the changes in these vessels that occur in fetal life [3].

The substantial intra-individual and inter-individual alterations of the carotid artery have previously been publicized in some studies [6, 9, 11, 13, 16, 20, 27]. Recently, it has been tried to discover the answer whether these differences were present in the early period of life [3].

5. Regarding atherosclerotic plaque establishment

Atherosclerotic plaque formation has been suggested to be thoroughly related to a shrinkage in the outflow to inflow area ratio [6]. This information has been sustained in several studies [9, 18, 21, 28–30].

Fisher and Fieman, and Schultz et al., publicized that the bifurcation anatomy stimuli the blood flow that produces the endothelial destruction [9, 20]. Mortensen also declared endothelial impairment and clarified that a quantity of a pulse wave reaching a bifurcation is reflected, and the higher the quantity of reflection, the more the hemodynamic stress might progress locally. The increase in the pressure could lead to endothelial destruction and support atherosclerotic plaque improvement [19]. In terms of endothelial damage, findings presented parallel results to the literature [3].

Initial examinations of this geometric risk theory were assessed in part, owing to relatively small sample sizes. Fisher and Fieman studied the conclusions of bifurcation angle and area ratio asymmetry on the improvement of atherosclerosis [6, 9, 21]. Also, it had limited samples because of the difficulties in obtaining human cadavers [3].

It has been shown that in early lesions of the atherosclerosis, fatty streaks progress very early in fetal period [3, 4]. The creation of fatty streaks also depends on many dynamics such as the susceptibility of the arteries and genetic factors, and the maternal hypercholesterolemia. The locations of a lesion demonstrate variability, and the fatty streaks tend to occur focally in certain predisposed regions while sparing neighboring unaffected sections [3]. Abdominal aorta and common carotid are much more prone to the development of fatty streaks [4]. The intracranial arteries are less prone to laceration enlargement than extra-cranial arteries; hence, the initial lesions develop in extra-cranial arteries rather than in intracranial ones [4].

The purpose why certain arteries are more disposed to atherosclerotic changes is not well understood. The hemodynamic factors and morphologic features of the artery may play a role [9, 12, 14, 20, 21]. It has been concentrated on the carotid bifurcation [3].

Shultz et al. outcomes [16] demonstrated that variation in carotid bifurcation anatomy is not restricted to differences in absolute vessel dimension. In addition, vessel diameter and area ratios diverge between and within individuals [20].

Selected studies, which have studied the relation between bifurcation's luminal geometry and the occurrence of cerebral artery aneurysms on angiographic images, have localized atherosclerotic lesions at the bifurcations of human cerebral arteries on autopsy cases. However, in this study, there were no available data on the endothelial topography in bifurcation geometry of newborn cadavers in the CCA and its major branches. For this motivation, histologic assessment makes last studies more valuable [3, 31].

Gosling et al. analyzed the optimal area ratio of an arterial bifurcation, producing the least reflection of pressure to be 1.15. That proportion can be close to ideal in human infants; however, in the long term, the decrease in outflow to inflow area ratio can lead to atherosclerotic plaque development. Gosling et al. studied 19 cases, with ages ranging from 0 to 10 and the outflow to inflow area ratio was found to be 1.11 ± 0.02 at 0 age group. Uslu's consequences were closer to the optimum ratio [3, 12].

Sitzer attempted to deliver a mechanistic link by proposing that their angle or rotation of ICA origin may be related to the ICA angle of insertion (comparable with the ICA-CCA angle of Lee et al.), which has been linked to flow turbulences [2, 25].

There are several studies on the diameters of CCA, ICA, and ECA in adults, but few studies are on newborns. To our knowledge, there are no earlier documents available on the relationship between the diameter of newborn cadavers and the CCA, ICA, and ECA [6].

Sehirli reported the mean outflow to inflow area ratio as 1.10 ± 0.33 mm in female and 1.18 ± 0.22 mm in male newborn cadavers for the common carotid artery bifurcation [6]. The consequences of Uslu's study on intracranial bifurcations show that the means of the outflow to inflow area ratio in fetal material are close to the optimum value in fetal material for the cerebral vessels.

Consistent with the results, the luminal geometry of arterial bifurcations impacts the blood flow that produces endothelial damage [3, 9, 13, 26].

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6. Potential limitations and implications for these types of diameter calculations

Numerical changes were convincing, but not perfect. Studies were retrospective, comparatively small, and focused on an inadequate number of newborn cadavers. Sample availability was insufficient for both affected groups and controls. It should also be noted that studies were not planned to be an epidemiological study, and therefore, groups did not signify the characteristics of a wide-ranging population. Recognition of blood cells and fibrin on the endothelial surface are interpreted as pathological definitions. Conversely, there might be problems with the poor fixation of specimens, that is, blood could not be washed out from the arterial lumen before fixation procedure. Lastly, scanning electron microscopy (SEM) studies can be associated with various kinds of artifacts. The authors then hope to approve their pathological findings using transmission electron microscopy in upcoming studies. Despite the above possible limitations, the current studies seem to establish a modest upper bound on the influence of local versus known or unknown systemic cardiovascular risk factors on wall setting. Thus, last results are parallel with the earlier ones to support theory that carotid bifurcation geometry (and/or local hemodynamics) is a risk factor for initial carotid wall solidifying.

7. Conclusion

In newborns, the results showed that the outflow to inflow area ratio was very close to optimum. Recent data can be very helpful for understanding the anatomical variations of the CCA, ECA, and ICA. The correlations between area ratios and the histologic assessments of cerebral vessels of newborn cadavers specify that the early stage of atherosclerosis began in early embryologic life. Last results encourage the hypothesis that carotid bifurcation anatomy is among the main risk factors for the early onset of atheroma plaques. Still, supplementary studies are needed to underline the other factors, potentials, and mechanisms.

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