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Mini-Review

Hemodynamics and Wall Content in Cerebral Aneurysm: A Mini-Review

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Cerebral aneurysms are pathological enlargements of the walls of cerebral arteries. Rupture of aneurysms causes 80% of subarachnoid hemorrhages. It is generally accepted that the abnormal hemodynamics within the aneurysm sac can lead to a breakdown in the normal process of collagen renewal and remodeling leaving the aneurysm vulnerable to rupture. However, the link between hemodynamics and wall integrity, as well as the underlying mechanisms governing the aneurysm pathophysiology remain poorly understood. The goal of this paper is to review the current state of knowledge about hemodynamics and wall content of cerebral aneurysms.

Keywords: Cerebral aneurysms, hemodynamics, wall content

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Introduction

Cerebral aneurysms are focal dilatations of the wall of cerebral arteries, existing in 2% to 8% of adult population **Error! Reference source not found.-Error! Reference source not found.**. 80% to 85% of cerebral aneurysms are located in the anterior circulation, most frequently found at the junction of the internal carotid artery and posterior communicating artery, the anterior communicating-artery complex, and the trifurcation of middle cerebral artery, In the posterior circulation, the basilar artery bifurcation is the most common location of aneurysm **Error! Reference source not found.**. Although the rupture rate of incidental aneurysms is very low (estimated at 0.3-3% per year), rupture of aneurysms causes 80% of subarachnoid hemorrhages (SAH), which is a major clinical problem in the United States, with occurrence of approximately 1 in 10000 people each year. The mortality rate of SAH from ruptured aneurysm is ~50%, including 12% pre-hospital deaths, and one-third of survivors suffer morbidity **Error! Reference source not found.-Error! Reference source not found.**.

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Clinical management

The management of unruptured aneurysms is controversial, because the risk associated with treatment options, including surgical clipping and endovascular therapies, can exceed the natural risk of rupture **Error! Reference source not found.-Error! Reference source not found.**. Therefore, treatment or observation is the important decision clinicians and patients often have to make. Aneurysm size, location, aspect ratio, and presence of bleb or blister morphology, as well as patient's age, family history and smoking status are used in assessing the development, enlargement and rupture of intracranial aneurysms **Error! Reference source not found.-Error! Reference source not found.**. Although aneurysm size is widely used as a measure for evaluating rupture risk, a significant number of aneurysms smaller than the critical size (7 mm) were ruptured in previous studies, indicating size is insufficient as a single parameter to assess rupture risk **Error! Reference source not found.**, **Error! Reference source not found.**. Improving the clinical management of aneurysm requires an understanding of the underlying mechanisms governing the development, enlargement and rupture of cerebral aneurysms.

Natural history

It is commonly accepted that the natural history of cerebral aneurysms is driven by flow-induced progressive degradation of the wall **Error! Reference source not found.-Error! Reference source not found.**. Histological analysis of resected human aneurysm tissue suggested that abnormal aneurysmal flow conditions likely cause endothelial dysfunction, which induces accumulation of cytotoxic and pro-inflammatory substances in the wall as well as thrombus formation, that leads to loss of mural cells and wall degeneration **Error! Reference source not found.**. However, the mechanisms and interactions between the various factors involved in the evolution of cerebral aneurysms remain poorly understood **Error! Reference source not found.**.

Rupture risk assessment

A large body of research has been focused on identifying a link between rupture and hemodynamic parameters such as magnitude of wall shear stress (WSS) and oscillatory shear index (OSI) **Error! Reference source not found.-Error! Reference source not found.**. However, to date these results are inconsistent and have not identified a clinically useful hemodynamic marker. An underlying assumption of this past work is the cells necessary to sense and respond to hemodynamic loads exist within the aneurysm sac. However, this has been shown not to be the case. In a large percentage of aneurysms, the endothelium is missing **Error! Reference source not found.**. In many of these aneurysms, the wall is hypo-cellular and hence has lost its capacity for wall maintenance and remodeling. Clearly, there are different stages of aneurysm pathology, with some stages lacking the means to sense and respond to

hemodynamic loading **Error! Reference source not found.**. The interconnection between intra-aneurysmal hemodynamics and wall structure has never been studied. Until we have a more integrated understanding of hemodynamics, wall structure and wall strength, it is unlikely we will be able use patient specific hemodynamics to gauge rupture risk.

Wall structure

There are at least three categories of unruptured aneurysm wall with great variability in intramural structure including cellular content and organization: (A) endothelialized wall with linearly organized SMC, (B) thickened wall with disorganized smooth muscle cells (SMC), and (C) hypocellular wall with either myointimal hyperplasia or organizing luminal thrombosis, as shown in Figure 1 A, B, and C. The extracellular matrix is manufactured by SMCs and fibroblast cells, so we would expect the heterogeneity in collagen architecture and therefore mechanical properties within the unruptured aneurysms due to this variability in mural content.

Hemodynamics

A large variety of flow patterns in unruptured aneurysms was found **Error! Reference source not found.-Error! Reference source not found.**. Four flow types with very difference inflow and vortex characteristics were reported by Cebral et al. in unruptured aneurysms, unchanging direction of inflow jet with one vortex; unchanging direction of inflow jet with multiple associated vortices lasting during the whole cardiac cycle; changing direction of inflow jet with one vortex; changing direction of the inflow jet with creation or destruction of multiple vortices **Error! Reference source not found.**. More recently, Cebral's group has developed a quantitative method for scoring IA flows **Error! Reference source not found.**.

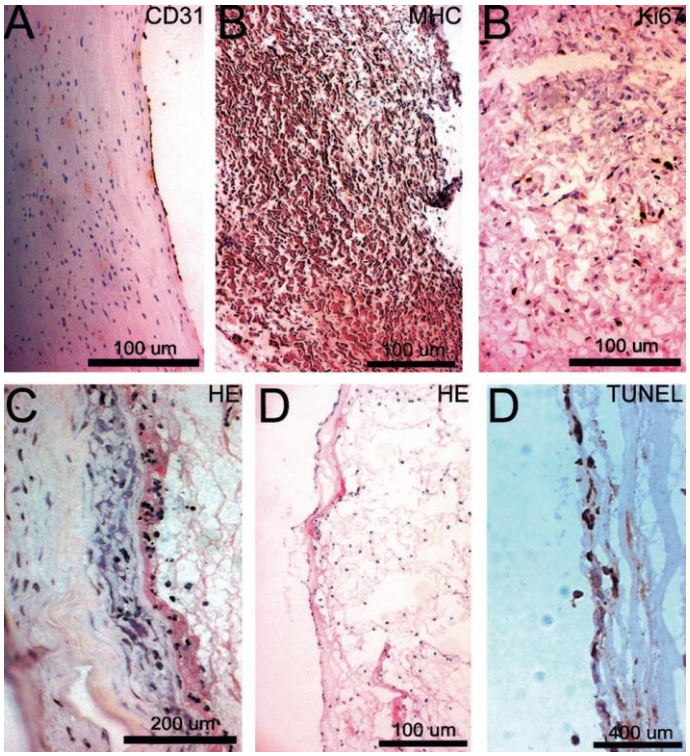

Figure 1. Four aneurysm wall types identified. A, Endothelialized wall with linearly organized SMCs; B, Thickened wall with disorganized SMC; C, Hypocellular wall with either intimal hyperplasia or organizing luminal thrombosis; D. An extremely thin thrombosis-lined hypocellular wall. Only type D is 100% associated with ruptured aneurysms. (Reproduced with permission from **Error! Reference source not found.**, Copyright Wolters Kluwer Health, Inc.)

A comprehensive effort that combines histological analysis and computational fluid dynamics are needed to understand how hemodynamics are tied to wall structure in human cerebral aneurysms [32-34].

Competing interests

The authors declare that they have no competing interests.

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