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Major review

Choroidal physiology and primary angle closure disease

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ABSTRACT

Primary angle closure disease (PACD), prevalent in Asian countries, is generally associated with a shallower anterior chamber, a shorter axial length, thicker lens, hyperopia, and female sex. Other physiologic factors, however, may be important, especially with regard to triggering acute primary angle closure. Thickening of the choroid has been demonstrated in untreated and treated, acute and chronic PACD eyes. Recently, there has been growing interest in studying the role of the choroid in the pathophysiology of PACD. The emergence of new imaging technology such as the enhanced depth imaging mode of spectral-domain optical coherence tomography and swept-source optical coherence tomography has contributed to understanding PACD pathologies. We summarize the functions of the choroid and choroidal changes in the pathogenesis of PACD, and discuss potential future developments.

1. Introduction

According to the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) classification, primary angle closure disease (PACD) has been classified into primary angle-closure suspect (PACS), primary angle closure (PAC), and primary angle-closure glaucoma (PACG).[19] PAC was further subdivided into chronic PAC and acute PAC (APAC), with APAC representing an ophthalmic emergency. Based on a recent survey, the global prevalence of PACG was 0.50%.[75] The total number of people aged 40–80 years with PACG in 2013 was estimated to be 20.2 million, and this is predicted to increase to 23.4 million in 2020 and to 32.0 million in 2040. Asians have a higher risk of PACG compared with other

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ethnicities, with a prevalence ranging from 0.12% in Singapore to 1.5% in the south of China.[26] In a population-based study in India, 22% of PACS patients progressed to PAC, and 28.5% of PAC patients developed PACG within 5 years unless treated.[76]

The pathogenesis of PACD is complex. Several biometric studies showed that PACD eyes have a shallower anterior chamber depth, shorter axial length, greater lens thickness, and flatter corneas.[14,24] The smaller ocular dimensions, also described as nanophthalmos or anterior nanophthalmus, were a clear risk factor for the disease; however, they could not explain ethnic differences in the prevalence of the disease.[80] In addition, a recent study suggested that anatomic abnormalities in the anterior segment explained only about one-third of the variance in the prevalence of APAC.[68] Other factors may therefore be important and require further investigation.

The choroid is a highly vascular structure of variable thickness that is regulated by various factors. Choroidal expansion has been demonstrated in untreated and treated eyes with acute PACD or chronic PACD.[22,61,64,71] Quigley and colleagues hypothesized that choroidal expansion may play a role in the pathogenesis of PACD, where choroidal expansion pushes the lens-iris diaphragm forward, initiating or aggravating a closure of the anterior chamber angle.[58–60] Since the publication of the landmark study by Spaide and coworkers on the visualization of the choroid by enhanced depth imaging optical coherence tomography (OCT),[70] the interest in the association between choroidal thickness and PACD has markedly increased.[4–7,12,17,18,23,25,28,39,45,82,84,90,91] We therefore reviewed the current literature to summarize the function of choroid and the role it may play in the pathogenesis of PACD.

2. Structure and function of choroid

The choroid is the posterior portion of the uvea and extends from the margins of the optic nerve head to the ora serrata, from where it is contiguous with the anterior uvea located in the pars plana and pars plicata of the ciliary body. This highly vascularized tissue can histologically be divided into the choriocapillaris, the layer of medium sized vessels (Sattler layer), and the layer of large vessels (Haller layer). These layers are located between Bruch membrane, the outer part of which is formed by the basement membrane of the choriocapillaris and the sclera.[10] The choroid is firmly attached to the sclera at the scleral spur, at the optic nerve head, and at the 4 vortex vein exits. The choroid accounts for approximately 90% of the intraocular blood flow.

The choroid serves several functions, including supplying oxygen and nutrients to the retina and retinal pigment epithelium (RPE). The photoreceptor outer segments in association with the RPE form the metabolically most active tissue in the body, with a high demand of oxygen in an essentially blood-free environment. The choroid has to cool the foveal photoreceptor outer segments or RPE complex by conducting away the heat generated by light focused on the fovea. The choroid influences the ocular pulse by a pulse-synchronous thickening and thinning leading to corresponding changes in the intraocular pressure (IOP). The RPE actively moves water from subretinal space to the choroid with an energy-requiring process, helping the retina in remaining attached. Because of a higher osmotic pressure in the choroid than in the vitreous, an osmotic pressure gradient exits between the intravitreal compartment and the choroidal compartment that leads to a movement of fluid from the intravitreal space and from the subretinal space through the RPE into the choroidal space. From there the fluid is either absorbed into the choroidal vessels or leaks through the water-permeable sclera into the orbit. An even greater osmotic pressure gradient of about 20 mm Hg prevails between the intrachoroidal extravascular space and the intrachoroidal intravascular space. The fluid movement from the intravitreal or subretinal space into the choroidal space can be observed in patients with a rhegmatogenous retinal detachment and subretinal fluid, which is spontaneously drained through the choroid after surgical closure of the retinal break. In eyes with abnormally low IOP, the choroid retains the fluid and the choroid swells. The choroid also plays an important role in draining aqueous humor from the anterior chamber through the uveoscleral pathway. Other functions of the choroid include secretion of growth factors and, potentially, refractive error adjustment.[11,51] A structurally and functionally normal choroid is essential for retinal function.

Subfoveal choroidal thickness (SFCT) has a mean of approximately 250 μm in elderly subjects with a mean age of 65 years and declines by 4 μm per year of age and decreases by 30 μm for every millimeter increase in axial length in myopia.[86] In addition, thicker SFCT is found in men than in women. In multivariate analysis, higher best-corrected visual acuity was significantly associated with thicker subfoveal choroid in general and with a subfoveal choroid thicker than 30 μm in particular.[67] SFCT is also dependent on the time of the day and the body position. In the morning and in the supine position, the choroid is thicker than in the evening and in the standing position.[73,77] A recent study suggested that higher cerebrospinal fluid pressure is associated with a thicker subfoveal choroid.[29] Choroidal thickness is not a static anatomic measurement, but shows dynamic changes. The level of IOP may be a chief determinant of choroidal thickness. Saeedi and colleagues reported that choroidal thickness increased with IOP reduction after trabeculectomy by 3.4 μm per 1 mm Hg decrease in IOP.[62] Some also suggest a relationship between ocular perfusion pressure and choroidal thickness.[33,45] In glaucoma suspects and glaucoma patients, thinner macular choroidal thickness was measured in subjects with lower diastolic ocular perfusion pressure (26 μm/10 mm Hg lower).[33,45] Choroidal thickness was not related to the presence or severity of open-angle glaucoma. Choroidal thickness did not differ between eyes with moderate open-angle glaucoma, fellow normal eyes, or eyes with mild glaucoma.[41,84] Similar results were obtained in another cross-sectional study and in a meta-analysis.[83] In general, one may move away from measuring only SFCT and begin to measure the choroidal dimensions as choroidal volume in a fixed posterior area. A single-point measurement for a 3-dimensional structure is inferior to a volumetric measurement.

Emmetropization is regulated by complex mechanisms. Choroidal thickness increased in response to visual deprivation in chicks.[52] In addition, the choroid affects the