Updated review of the pachychoroid spectrum and central serous chorioretinopathy

Revisão atualizada do espectro paquicoroide e da coriorretinopatia serosa central

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ABSTRACT

The pachychoroid disease spectrum (PDS) encompasses a range of chorioretinal disorders characterized by increased choroidal thickness, dilated Haller's layer vessels (pachyvessels), and choroidal hyperpermeability, often associated with retinal pigment epithelium (RPE) alterations. This review synthesizes current evidence on pachychoroid pigment epitheliopathy (PPE), central serous chorioretinopathy (CSC), pachychoroid neovasculopathy (PNV), and polypoidal choroidal vasculopathy (PCV), emphasizing their shared pathophysiological mechanisms, multimodal imaging features, and clinical implications. Enhanced depth imaging optical coherence tomography (EDI-OCT) and widefield indocyanine green angiography (ICGA) have been crucial in identifying vortex vein congestion and segmental choroidal drainage anomalies as central pathogenic drivers. Clinically, this framework supports a phenotype-based approach, where anti-VEGF therapy is prioritized for neovascular phenotypes (PNV, PCV) and photodynamic therapy (PDT) is effective for chronic, hyperpermeable non-neovascular CSC. Despite advances, challenges remain regarding standardized diagnostic thresholds, early phenotype detection, and the influence of systemic factors. The integration of hemodynamic concepts, vascular anatomy, and advanced imaging is key to developing personalized management strategies across the pachychoroid spectrum.

RESUMO

O espectro das doenças paquicoroides (PDS) abrange um conjunto de distúrbios coriorretinianos caracterizados por aumento da espessura coroidal, dilatação dos vasos da camada de Haller (paquivasos) e hiperpermeabilidade coroideana, frequentemente associados a alterações do epitélio pigmentar da retina (EPR). Esta revisão sintetiza as evidências atuais sobre a paquicoroidopatia epitelial pigmentar (PPE), a coriorretinopatia serosa central (CSC), a neovasculopatia paquicoroide (PNV) e a vasculopatia coroideana polipoidal (PCV), destacando seus mecanismos fisiopatológicos comuns, achados de imagem multimodal e implicações clínicas. A tomografia de coerência óptica com profundidade aumentada (EDI-OCT) e a angiografia com indocianina verde de campo amplo (ICGA) têm sido fundamentais para identificar a congestão das veias vorticosas e as anomalias segmentares de drenagem coroideana como principais fatores patogênicos. Do ponto de vista clínico, este modelo apoia uma abordagem baseada no fenótipo, em que a terapia anti-VEGF é priorizada para fenótipos neovasculares (PNV, PCV) e a terapia fotodinâmica (PDT) é eficaz para CSC crônica não neovascular com hiperpermeabilidade coroideana. Apesar dos avanços, persistem desafios quanto à padronização de critérios diagnósticos, à detecção precoce de fenótipos iniciais e à compreensão da influência de fatores sistêmicos. A integração de conceitos hemodinâmicos, anatomia vascular e imagem avançada é fundamental para o desenvolvimento de estratégias de manejo personalizadas em todo o espectro paquicoroide.

INTRODUCTION

Choroid is a primarily vascular layer found between the sclera and the retina, responsible for blood supply to the outer retina.[1] Anatomically, the choroid is divided into the avascular Bruch's membrane and the vascular choriocapillaris, Sattler's and Haller's layers.[2] Since 2012, when it became possible to visualize the choroid on optical coherence tomography (OCT), researchers recognized that there is a common disease spectrum of choroidal thickening, including dilated choroidal vessels in Haller's layer, thinning of the choriocapillaris and Sattler's layer, and abnormalities of the retinal pigment epithelium (RPE) over the pachyvessels.[3-5] These choroidal changes are believed to play an important pathogenic role in the development of the following clinical manifestations that occur in the pachychoroid disease spectrum: central serous chorioretinopathy (CSC), pachychoroid pigment epitheliopathy (PPE), pachychoroid neovasculopathy (PNV), polypoidal choroidal vasculopathy (PCV), focal choroidal excavation (FCE) and peripapillary pachychoroid syndrome (PPS).[3-8]

Recently, the following diagnosis criteria were proposed for pachychoroid: reduced fundus tessellation; pachyvessels, defined as dilated choroidal vessels seen on OCT or indocyanine green angiography (ICGA), extending the entire length of the vessel to the vortex vein ampullae, causing choriocapillaris and Sattler layer attenuation; and a lack of soft drusen (an exception is made for pachydrusen, which are irregular, scattered yellow-white deposits across the posterior pole), and the presence of CSCR characteristics, such as RPE abnormalities, choroidal vascular hyperpermeability (CVH) or a prior CSCR diagnosis.[9]

Pang et al. reported ultra-widefield ICGA allowing the entire vortex vein in CSC to be visualized. The affected vortex veins showed dilatation and hyperpermeability, converging to the dilated ampulla. These findings indicate that the dilated choroidal veins of the posterior fundus, as seen on conventional ICGA, are in fact branches of the vortex vein. The dilated ampulla suggests stasis of the vortex vein to be caused by an obstruction to its passage through the sclera.[10]

The dilatation of vortex veins occurs at their distal ends, suggesting that the elevated retrograde venous pressure is transmitted to the beginning of vortex veins. Hence, dilatation is marked at the level of vortex veins and moderate at the Sattler layer, without any dilatation involving the choriocapillaris.[10]

Hayreh described that the venous outflow tract of the choroid is divided into four quadrants on the basis of a horizontal and a vertical watershed zone and noted that one or two vortex veins are independently responsible for the venous drainage in each of these quadrants.[11] In eyes with CSC, venous anastomosis occurs between the superior and inferior vortex veins at the watershed zone. The anastomotic vessels were dilated, and dilatation of Haller vessels was observed on OCT B scans. Comparison of acute CSC and chronic CSC revealed the macular choroid to be significantly thinner in eyes with chronic CSC.[12]

Therefore, venous congestion has been highlighted as a potential mechanism of pachyvessel and pachychoroid formation. Obstruction of vortex veins, especially the dominant vortex vein, which drains the macula, may contribute to the engorgement of Haller vessels and the development of subretinal fluid.[13,14]

In this review, our objective was to perform an update of the pachychoroid spectrum and central serous chorioretinopathy.

LITERATURE REVIEW

This comprehensive literature review was conducted through a systematic search of peer-reviewed articles published in English available in the PubMed database. The search was conducted since the inception of the database until April 2025. The inclusion criteria were original studies, reviews and relevant articles that addressed the pachychoroid spectrum in relation to neuroimaging, clinical manifestations and pathophysiology, or that were related to the topic. The selection of studies was performed independently by two reviewers through analysis of titles and abstracts, followed by full reading of potentially eligible articles. Discrepancies were resolved by consensus or by a third reviewer.

Data extraction was conducted using a standardized form, including information from the authors, year of publication, study focus, and main findings related to pachychoroid spectrum and its association with central serous retinopathy. The methodological quality of the studies was assessed, if applicable, using standard tools, such as the observational study assessment tool, to ensure the validity of the evidence.

The collected data were qualitatively synthesized, highlighting the most recent advances in the understanding of the spectrum, pathophysiological mechanisms, imaging findings and clinical implications associated with central serous retinopathy within the pachychoroid spectrum.

Table 1 shows that subfoveal choroidal thickness (SFCT) was frequently increased, with values between 315 and 625 μm across cases.[4,5,9] However, thickening of

Haller's layer and the presence of dilated outer choroidal vessels were also observed in some eyes with SFCT below 200 µm,[3,4] challenging the notion that only elevated total SFCT is indicative of pachychoroid disease.

Treatment strategies varied between observation, intravitreal anti-VEGF therapy and photodynamic therapy (PDT).[13,14] Functional outcomes were generally favorable, with final visual acuities ranging from 20/25 to 20/40, even in cases presenting with chronic structural abnormalities.[3,9,13]

Comparisons between eyes with SFCT greater or less than 200 µm revealed significant structural differences. Eyes with thicker choroids tended to show greater contribution from Haller's layer and a reduced relative thickness of the choriocapillaris/Sattler's layer.[3,6] Despite these differences, central retinal thickness and final visual acuity were largely similar between groups.[4]

Table 1. Clinical characteristics and subfoveal choroidal thickness in pachychoroid spectrum diseases

Study	Entity	Age (mean)	Sex	Risk factors	SFCT (µm)
Warrow et al.[3]	PPE	54	Female predominance	Corticosteroids, stress	315-460
Pang et al.[4]	PNV	56	Male predominance	CSC history	> 300
Lee et al.[5]	PCV	65	Mixed	Hypertension	386-625

SFCT: subfoveal choroidal thickness; PPE: pachychoroid pigment epitheliopathy; PNV: pachychoroid neovasculopathy; CSC: central serous chorioretinopathy; PCV: polypoidal choroidal vasculopathy.

Table 2 shows that OCT revealed serous pigment epithelial detachments (PEDs), outer retinal changes and prominent dilation of outer choroidal vessels.[3,7] Autofluorescence imaging showed mottled hyperautofluorescence, occasionally with gravitational tracts.[6] Indocyanine green angiography demonstrated dilated vortex veins and focal areas of hyperpermeability, often corresponding to zones of RPE disturbance.[3,5,6] Indocyanine green angiography frequently showed delayed choroidal arterial filling and lobular hyperperfusion, reinforcing the concept of venous outflow impairment.[3,10]

These findings overlapped with zones of PED and RPE damage, which strengthens the hypothesis of choroidal congestion as a driving mechanism.[3,4,10] Pachychoroid pigment epitheliopathy was identified by RPE mottling over choroidal thickening without fluid.[3,4,7] Acute CSC was characterized by subretinal fluid with relatively rapid resolution.[4,13] Chronic CSC featured RPE degeneration and risk of type 1 neovascularization.[4,9] PCV was categorized into an AMD-like thin choroid variant and a pachychoroid variant with choroidal hyperpermeability.[5,6]

Table 2. Imaging findings in pachychoroid spectrum diseases

Study	Modality	Findings
Pang et al.[7]	EDI-OCT	Pachyvessels, outer retinal changes
Margolis et al.[8]	EDI-OCT	Thick choroid, dilated Haller's layer vessels
Kishi et al. [12]	ICGA, EDI-OCT	Vortex vein asymmetry with delayed choriocapillaris filling, suggesting venous outflow impairment.
Spaide et al.[14]	ICGA	Dilated vortex veins, delayed filling, hyperpermeability

EDI: Enhanced Depth Imaging Optical Coherence Tomography; OCT: optical coherence tomography; ICGA: indocyanine green angiography; OCT-A: optical coherence tomography angiography.

The literature reviewed supports the hypothesis of choroidal venous overload as a unifying mechanism. Impaired vortex vein outflow results in increased hydrostatic pressure, choroidal hyperpermeability and subsequent outer retinal injury.[3,4,10] Segmental variations in vascular anatomy likely explain lesion topography.[3,11]

Table 3 shows that most cases had favorable outcomes with appropriate therapy. PDT was especially effective for chronic CSC and pachychoroid PCV,[9,10] while anti-VEGF therapy was preferred in neovascular cases.[4,5] PPE generally remained stable under observation.[1,7]

Table 3. Treatment strategies and visual outcomes

Study	Entity	Treatment	Response	Final VA
Lee et al.[5]	PCV	Anti-VEGF	Variable by phenotype	Improved or stabilized
Prünte et al. [13]	CSC	Half-dose PDT	Effective and safe	20/30 average
Spaide et al. [14]	Chronic CSC	PDT	Fluid resolution	20/25–20/40

VA: visual acuity; CSC: central serous chorioretinopathy; PDT: photodynamic therapy; PCV: polypoidal choroidal vasculopathy; VEGF: Vascular Endothelial Growth Factor; PPE: pachychoroid pigment epitheliopathy.

DISCUSSION

The pachychoroid spectrum encompasses a group of macular disorders united by structural and hemodynamic alterations in the choroid, particularly involving thickening and vascular congestion.[1,2,4] Conditions such as PPE, CSC, PNV and PCV are now seen as stages or variations of a broader phenotype driven by chronic choroidal stress.[4,5,9]

Spaide et al. proposed the concept of "venous overload choroidopathy," highlighting the central role of impaired vortex vein drainage.[14] Anatomical studies confirmed that the choroid is organized into non-overlapping drainage territories, meaning any obstruction or inefficiency in venous outflow causes localized venous hypertension.[3,11] This leads to dilation of pachyvessels, increased permeability and ultimately RPE dysfunction and serous detachment.[3,4,6]

This venous-centric model explains why lesions often cluster in specific areas, especially where drainage territories overlap or where collateral formation is insufficient.[3,11] The spatial distribution of leakage on ICGA correlates with this anatomical framework.[3,6] Furthermore, this helps reinterpret the traditional separation between PPE, CSC and PNV: rather than distinct diseases, they represent

stages of compensation and decompensation in choroidal outflow.[3,4,9]

Advanced imaging has been instrumental in characterizing these stages. EDI-OCT and SS-OCT can detect subtle Haller's layer dilation and early neovascularization, while OCT-A aids in identifying subclinical type 1 neovascular networks.[4,6,7] Widefield ICGA further delineates venous drainage territories and supports this sectoral model of congestion.[3,6]

From a therapeutic standpoint, this paradigm has practical implications. PDT has been shown to reduce choroidal hyperpermeability and vascular dilation, making it effective in CSC and some PCV cases.[9,10] Anti-VEGF therapy remains first-line for neovascular phenotypes but may be insufficient alone in pachychoroid-driven PCV.[4-6] The choice of therapy must consider phenotype, imaging biomarkers and individual disease trajectory.[4,5,9]

Despite these advances, several challenges remain. No universal definition of "pachychoroid" exists, and quantitative thresholds for SFCT or pachyvessel dilation vary across studies.[2,4] Furthermore, systemic contributors such as cortisol, stress or autonomic imbalance may modulate disease activity but remain underexplored.[7-9]

Pachychoroid disease spectrum has redefined the understanding of several chorioretinal disorders, uniting them under a common pathophysiological framework centered on chronic choroidal venous overload and impaired vortex vein drainage. Multimodal imaging techniques, particularly enhanced-depth imaging OCT and widefield ICGA, have played a pivotal role in uncovering the structural vascular features underlying these entities, facilitating more precise phenotypic classification and disease staging.[3-7] The model of venous overload choroidopathy proposed by Spaide et al. emphasizes the segmental nature of choroidal outflow and its link to localized hyperpermeability and remodeling, thus shifting diagnostic emphasis from purely morphological patterns to vascular and hemodynamic alterations.[3,11,14]

This framework has also influenced therapeutic paradigms, promoting a phenotype-guided approach. Anti-VEGF therapy remains essential for neovascular manifestations such as PNV and PCV,[4,5] whereas PDT has demonstrated significant efficacy in non-neovascular yet hyperpermeable forms such as CSC, improving anatomical and visual outcomes when guided by imaging features.[7,9,10,13]

Recognition of early phenotypes such as PPE remains limited in clinical practice despite their potential role as precursors in the disease continuum.[3,4,6,7] Nevertheless, substantial challenges persist. There is a lack of consensus on diagnostic thresholds for choroidal thickness and vascular morphology, and the systemic, genetic and anatomical factors influencing phenotypic expression and progression are not fully elucidated.[4-6,8,9]

Longitudinal studies are required to clarify transitions between phenotypes and to identify reliable prognostic markers for chronicity and treatment response. Future research should focus on standardizing diagnostic criteria, integrating systemic risk profiling and validating staging systems to enable more personalized and effective management strategies across the pachychoroid spectrum.[3,5,6,9,14]

The pachychoroid disease spectrum reframes chorioretinal disorders as manifestations of chronic choroidal venous overload, supported by multimodal imaging, particularly EDI-OCT and widefield ICGA, which elucidate the role of vortex vein congestion in disease pathophysiology. This understanding reinforces a phenotype-guided therapeutic approach. Anti-VEGF agents for neovascular variants and PDT for chronic non-neovascular CSC have demonstrated improved outcomes when tailored to imaging findings. Despite these advances, consistent diagnostic criteria and recognition of early disease expression remain limited, and some associated systemic and anatomical factors are still unknown.

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