Review Article

Pachychoroid diseases of the macula: an update

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ABSTRACT

Background: The pachychoroid disease spectrum comprises a group of chorioretinal disorders characterized by structural and hemodynamic alterations of the choroid that may ultimately lead to dysfunction of the retinal pigment epithelium, choroidal neovascularization, and vision loss. This narrative review aims to summarize the recent advances in the understanding of pachychoroid spectrum diseases, with particular emphasis on pathophysiology, multimodal imaging, and current therapeutic approaches.

Methods: Relevant English-language literature on pachychoroid spectrum disorders published up to 31 May 2026 was reviewed through PubMed/MEDLINE, supplemented by Google Scholar to identify additional relevant studies; relevant conference abstracts presented by that date and published subsequently were also included. Focus was on recent developments in disease mechanisms, imaging characteristics, clinical phenotypes, and management strategies. Search terms included "pachychoroid" and individual pachychoroid spectrum entities in combination with terms related to imaging, pathophysiology, diagnosis, and treatment. Relevant Medical Subject Headings (MeSH) terms were also used where applicable. Particular emphasis was placed on recently published studies reflecting current concepts and advances in pachychoroid disease. Earlier landmark studies with substantial scientific and historical relevance were additionally included to provide the original descriptions and foundational evidence underlying the pachychoroid spectrum.

Results: The pachychoroid spectrum is increasingly recognized as a continuum of disorders associated with choroidal vascular remodeling, venous congestion, and choriocapillaris attenuation. Characteristic multimodal imaging findings include pachyvessels, choroidal hyperpermeability, intervortex venous anastomoses, and variable inner choroidal thinning, while increased choroidal thickness alone may not reliably define the pachychoroid phenotype. Pachychoroid pigment epitheliopathy may occur as an isolated manifestation or coexist with other pachychoroid entities. Central serous chorioretinopathy represents a pivotal entity within the pachychoroid spectrum and may progress toward neovascular complications, including pachychoroid neovasculopathy and polypoidal choroidal vasculopathy. Advances in multimodal imaging, particularly optical coherence tomography angiography and ultra-widefield indocyanine green angiography, have substantially improved the detection of subclinical vascular alterations and disease progression. Although anti-vascular endothelial growth factor therapy and photodynamic therapy remain central treatment approaches, emerging modalities, including no-dose photodynamic therapy and photobiomodulation, are being investigated as potential therapeutic options, but current evidence does not support their routine clinical use.

Conclusions: Pachychoroid spectrum disorders share common choroidal vascular and hemodynamic abnormalities despite considerable phenotypic variability. Ongoing advances in multimodal imaging and evolving therapeutic strategies continue to refine the understanding and management of these disorders.

KEYWORDS

eylea, VEGF-Trap, central serous retinopathy, faricimab-svoa, indocyanine green angiography, pachychoroid, pachychoroid neovasculopathy, pachychoroid pigment epitheliopathy, pachychoroid spectrum, pachydrusen, drusen, retinal, drusen of bruch membrane, photodynamic therapy, idiopathic polypoidal choroidal vasculopathy, polypoidal choroidal neovascularizations, polypoidal CNV

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INTRODUCTION

The term pachychoroid describes a structural choroidal phenotype marked by increased choroidal thickness, dilation of the outer choroidal vessels (pachyvessels), and attenuation of the Sattler layer and choriocapillaris [1]. The diagnosis of pachychoroid spectrum disease is primarily based on multimodal imaging findings that reflect both structural and functional alterations of the choroid: choroidal hyperpermeability or hyperperfusion on indocyanine green angiography (ICGA), dilated outer choroidal vessels on en face optical coherence tomography (OCT) or OCT angiography (OCTA), and varying degrees of choriocapillaris attenuation [2]. These structural alterations may ultimately lead to progressive retinal pigment epithelium (RPE) dysfunction [3, 4]. Inner choroidal ischemia is still considered a significant consequence of pachychoroid disease, potentially leading to neovascular complications and the development of macular atrophy [3].

The pachychoroid spectrum encompasses several core entities, including pachychoroid pigment epitheliopathy (PPE), central serous chorioretinopathy (CSC), pachychoroid neovasculopathy (PNV), polypoidal choroidal vasculopathy (PCV), and pachychoroid geographic atrophy (PGA), that are considered to represent a biological continuum. PPE is regarded as the earliest manifestation, characterized by RPE abnormalities in the absence of serous retinal detachment, whereas PCV and PGA represent more advanced stages, associated with neovascular and aneurysmal complications and with outer retinal and RPE atrophy, respectively (Table 1) [4–6].

Certain conditions, including peripapillary pachychoroid syndrome, dome-shaped macula, focal choroidal excavation, pachyvitelliform maculopathy, and peripheral exudative hemorrhagic chorioretinopathy, have been deemed part of an expanded pachychoroid spectrum [7–13]. However, these entities often lack the defining features of true pachychoroid disease, with the observed vascular alterations more likely reflecting secondary rather than primary processes [1]. Therefore, they will not be discussed in detail in this review. Uncomplicated pachychoroid, characterized by pachychoroid features in the absence of retinal abnormalities, has also been described within the pachychoroid spectrum [14]. As uncomplicated pachychoroid lacks associated retinal pathology, it is likewise excluded from the scope of this review.

Accordingly, the present narrative review focuses on the established pachychoroid spectrum disorders and comprehensively discusses their clinical features, multimodal imaging findings, pathophysiology, and current therapeutic approaches.

Table 1. Clinical, imaging, and management characteristics across the pachychoroid disease spectrum [4–6]

Feature	PPE	CSC	PNV	PCV	PGA
Age (y)	27–89	39–51	52–73	50–65	Predominantly older individuals
Symptoms	Usually asymptomatic	Blurred vision, metamorphopsia, hyperopic shift	Visual distortion, decreased vision	Decreased vision, occasionally acute vision loss	Progressive visual decline
Choroidal thickness	Increased	Increased	Increased or normal	Increased or normal	Variable
RPE abnormalities	Mildly focal abnormalities	Diffuse or focal abnormalities	Present	Prominent	Extensive atrophy
Choriocapillaris attenuation	Mild	Moderate	Moderate–severe	Moderate–severe	Severe
Polypoidal lesions	Absent	Absent	May develop during progression	Characteristic feature	Absent
Type 1 neovascularization	Absent	Possible in chronic disease	Present	Present	Usually absent
Subretinal fluid	Absent	Present as serous retinal detachment	Present in association with neovascularization	Frequently present	Usually absent
Main treatment	Observation	Observation / Laser / PDT	Anti-VEGF ± PDT	Anti-VEGF ± PDT	Observation

Abbreviations: y, years; PPE, pachychoroid pigment epitheliopathy; CSC, central serous chorioretinopathy; PNV, pachychoroid neovasculopathy; PCV, polypoidal choroidal vasculopathy; PGA, pachychoroid geographic atrophy; RPE, retinal pigment epithelium; PDT, photodynamic therapy; VEGF, vascular endothelial growth factor.

METHODS

A literature search was primarily conducted using the PubMed/MEDLINE database, with Google Scholar searched as a supplementary source to identify additional relevant studies not indexed in PubMed, for English-language articles published up to 31 May 2026. Relevant conference abstracts presented by that date and published subsequently were also included. Search terms included "pachychoroid" and individual pachychoroid spectrum entities in combination with terms related to imaging, pathophysiology, diagnosis, and treatment. Relevant Medical Subject Headings (MeSH) terms were also used where applicable. Particular emphasis was placed on recently published studies reflecting current concepts and advances in pachychoroid disease. Earlier landmark studies with substantial scientific and historical relevance were additionally included to provide the original descriptions and foundational evidence underlying the pachychoroid spectrum.

RESULTS and DISCUSSION

Anatomy and Pathophysiology of the Pachychoroid

Normal choroidal anatomy

The choroid is the vascular layer of the uveal tract situated between the retina and sclera, providing the main blood supply to the outer retina [4]. Beyond its well-established vascular function, the choroid also plays important roles in thermoregulation, modulation of intraocular pressure, emmetropization, positional support of the retina, secretion of growth factors, and aqueous humor drainage through the uveoscleral pathway [15]. It is composed of blood vessels and connective tissue elements, including fibroblasts, melanocytes, and collagen. Anatomically, avascular Bruch's membrane forms the innermost boundary of the choroid adjacent to the RPE [4]. According to their anatomical relationship with Bruch's membrane, choroidal vessels are arranged into three layers: choriocapillaris, Sattler's layer with medium-sized vessels, and Haller's layer, which contains the largest vessels [16, 17]. The choriocapillaris is a thin, single-layered network of fenestrated capillaries situated immediately beneath Bruch's membrane, with a thickness range of 10–30 μm [15]. Vascular endothelial growth factor (VEGF) expression by the RPE is critical for sustaining normal choriocapillaris viability [14].

Choroidal venous drainage is classically described as a segmental system organized into four quadrants, with no anastomotic connections between individual vortex veins in healthy eyes [3]. However, subsequent studies have shown that venous outflow frequently exhibits a preferential pattern, most commonly via the superotemporal or inferotemporal routes. Substantial inter-individual variability has also been documented, with up to eight vortex vein ampullae reported in some normal eyes [18, 19].

Anatomically, choroidal circulation is configured to support efficient venous drainage through four to six vortex veins. These vessels drain all choroidal layers, including the choriocapillaris, Sattler's layer, and Haller's layer. At the posterior pole, the vasculature is more densely packed and predominantly vertically oriented, whereas in the mid-peripheral and peripheral regions vessels adopt a radial, sectoral configuration, converging toward the vortex vein ampullae [17, 20, 21].

Pachychoroid features and pathophysiological mechanisms

The pachychoroid phenotype refers to a distinctive choroidal configuration characterized by dilated outer choroidal vessels (pachyvessels) within Haller's layer, together with thinning of the Sattler layer and choriocapillaris. Increased choroidal thickness and hyperpermeability are commonly observed and contribute to its definition [22].

Although a standardized threshold has not been established, pachychoroid is commonly defined by a subfoveal choroidal thickness > 300 μm, with some studies suggesting a higher cutoff > 350 μm depending on the population or imaging modality [1, 23, 24]. Increased choroidal thickness alone should not be considered diagnostic of pachychoroid disease, as eyes without associated retinal or choroidal abnormalities may simply represent uncomplicated pachychoroid [25]. Rather, the defining hallmark of the pachychoroid phenotype is the presence of dilated outer choroidal vessels (pachyvessels), which can be identified clinically or with multimodal imaging [26, 27]. In addition, choroidal thickness and pachyvessel distribution may show regional variation beyond the subfoveal and macular regions [28].

Vascular alterations within Haller's layer may compress the overlying inner choroidal layers, including Sattler's layer and the choriocapillaris [4, 29]. However, mechanical compression alone may not fully explain the choriocapillaris attenuation. Primary RPE dysfunction and subsequent alterations in VEGF regulation have also been proposed as contributors to choroidal hyperpermeability and pachychoroid disease progression [30]. In addition, disruption of RPE

barrier integrity and fluid transport mechanisms may further promote subretinal fluid accumulation and outer retinal dysfunction [31]. Progressive inner choroidal attenuation and choriocapillaris ischemia may further enhance VEGF-mediated angiogenic signaling [32].

Unlike normal choroidal vessels, which gradually taper toward the posterior pole, pachyvessels maintain their enlarged caliber and often terminate abruptly. On en face choroidal imaging, these vessels typically appear as hyporeflective round, oval, or elongated structures [31]. Pachyvessels may be distributed either diffusely or in a localized manner (e.g., confined to one or two quadrants) [33]. A progressive cycle involving choriocapillaris ischemia, RPE injury, and outer retinal atrophy may subsequently develop, as persistent ischemia can perpetuate tissue damage even after partial resolution of venous congestion [34].

Pachyvessels are more distinct compared to dilated or prominent choroidal vessels observed in other chorioretinal disorders, which are typically associated with venous congestion and increased vascular permeability [1]. This distinction is clinically relevant, as congestion is primarily linked to hyperpermeability and exudation, whereas pachyvessels reflect chronic structural alterations capable of inducing sustained mechanical compression, independent of acute vascular leakage [35].

The association between choriocapillaris ischemia and dilated choroidal vessels remains a matter of debate. Some authors suggest that ischemic changes in the choriocapillaris arise secondary to pachyvessels [36]. Consistent with this hypothesis, Gal-Or et al. [37] found that pachyvessels accounted for approximately 60% of the reduction in choriocapillaris flow, while their distribution closely corresponded to areas of choriocapillaris flow voids in pachychoroid eyes [37].

Recent multimodal imaging studies have identified several vascular abnormalities associated with pachychoroid disease, including asymmetric vortex vein drainage, vortex vein ampullary abnormalities, intervortex venous anastomoses, choroidal hyperpermeability on ICGA, and increased choroidal blood flow on OCTA. These findings emphasize the role of choroidal vascular dysregulation in the pachychoroid spectrum [22, 38]. In addition, ultra-widefield ICGA has demonstrated engorgement of the vortex vein ampullae in eyes with CSC, further supporting the concept that impaired venous outflow contributes to pachychoroid pathogenesis [19, 39].

The concept of venous overload choroidopathy has recently been proposed to explain the role of impaired choroidal venous drainage in pachychoroid disease [3, 38]. Arterial blood supplied by the short posterior ciliary arteries perfuses the choriocapillaris and is subsequently drained through the vortex vein system across the sclera. Although venous drainage within each choroidal quadrant is functionally independent, extensive intervortex venous anastomoses may develop. In the setting of vortex vein congestion, venous blood can redistribute through these collateral pathways into adjacent quadrants via retrograde flow, resulting in increased venous pressure, vascular dilation, and choroidal hyperpermeability [6, 40].

Vortex vein outflow dysfunction, potentially related to increased scleral thickness, shorter axial length, congenital vascular variations, or impaired collateral formation, has been deemed a major contributor to choroidal venous congestion. The subsequent elevation in venous pressure may perpetuate dilation of Haller's layer vessels and increased choroidal thickness, ultimately leading to ischemic and inflammatory injury involving the choriocapillaris, RPE, and neurosensory retina, particularly within the macular region [1, 25]. Inadequate intervortex venous anastomoses may further aggravate venous stasis, contributing to preferential macular involvement despite more diffuse choroidal abnormalities [25].

Based on these observations, a two-hit mechanism has recently been proposed to explain the development and progression of pachychoroid disease. According to this model, anatomical susceptibility factors, including increased scleral thickness, shorter axial length, and asymmetric vortex vein drainage, constitute the first hit, creating a predisposed choroidal environment [31, 41, 42]. The second hit involves additional triggering factors, such as corticosteroid exposure, psychological stress, hormonal alterations, autonomic dysregulation, sleep disturbances, or metabolic abnormalities, which may precipitate clinical disease in susceptible eyes. This concept may explain why pachychoroid features can remain subclinical in some individuals while manifesting episodically or progressively in others [31].

A recently described finding in pachychoroid disease is choroidal meridian breakdown, defined as the extension of dilated choroidal vessels across the choroidal watershed zones on ICGA. Choroidal meridian breakdown appears to localize predominantly to the central macular region, where pachyvessels traverse the watershed zones vertically. The

presence of these abnormal vascular crossings has been associated with choroidal vasodilation, vascular leakage, and increased subfoveal choroidal thickness, suggesting that altered choroidal venous drainage and vascular remodeling may contribute to pachychoroid pathophysiology [43].

Multimodal imaging in pachychoroid spectrum

The choroid-scleral interface is identifiable in most eyes with enhanced depth imaging OCT or swept-source OCT, allowing for quantitative evaluation of choroidal thickness [44]. In addition to increased subfoveal choroidal thickness, CSC frequently shows diffuse enlargement of outer choroidal vessels extending into extrafoveal regions. Compared with conventional cross-sectional OCT, en face swept-source OCT enables more detailed visualization of pachyvessel distribution and associated choroidal structural alterations [22].

Absolute thresholds for choroidal thickness remain controversial because these measurements are affected by numerous physiological and pathological factors. Therefore, choroidal vascular index has been proposed as a more stable and repeatable biomarker for monitoring pachychoroid-related disease progression [25, 45]. Importantly, pachychoroid features may still be present in eyes with normal or even reduced choroidal thickness, particularly when attenuation of the inner choroid coexists with persistent dilation of Haller's layer vessels [22]. Recent studies demonstrating higher choroidal vascularity index values in steroid-associated CSC further support the role of choroidal vascular dysregulation in pachychoroid pathophysiology [46, 47].

Advances in widefield en face swept-source OCT imaging have enabled improved assessment of diffuse RPE alterations within the pachychoroid spectrum. En face imaging aligned to Bruch's membrane plane enables rapid visualization of diffuse or multifocal RPE abnormalities, which may appear as hyporeflective regions against the normally uniform hyperreflective background of the RPE-Bruch's membrane complex [33, 48]. A recent study shows high sensitivity of widefield en face swept source OCT for detecting RPE alterations in CSC, with diagnostic performance approaching that of fundus autofluorescence while providing a rapid and noninvasive assessment of disease extent. Moreover, bilateral en face imaging may reveal subclinical RPE abnormalities in fellow eyes, supporting the concept that pachychoroid disease frequently represents a bilateral chorioretinal disorder despite asymmetric clinical manifestations [48].

Pachyvessels can be identified on en face OCT and ICGA as clusters of relatively straight, enlarged choroidal vessels, with associated findings such as choroidal filling defects, early arterial filling delay, and focal or punctate hyperfluorescence in CSC and PCV, suggesting underlying ischemic alterations within the choroid [25, 49]. Similar diffuse and punctate hyperfluorescent changes are also frequently observed in fellow eyes without clinically overt pathology and may persist even after subretinal fluid resolution in CSC [25].

The mechanism underlying this choroidal hyperpermeability is thought to involve increased diffusion of fluid and protein-bound indocyanine green dye from the choriocapillaris and larger choroidal vessels into the surrounding stroma [25]. More recently, ultra-widefield ICGA has enabled broader *in vivo* visualization of choroidal circulation extending from the posterior pole to the peripheral vortex vein ampullae, thereby improving assessment of peripheral choroidal vascular alterations and venous drainage patterns [22]. Furthermore, a recent ultra-widefield ICGA study has demonstrated that areas of choroidal vascular hyperpermeability frequently colocalize with characteristic patterns of choroidal venous remodeling, including fusiform dilatation, bulbosity, sausaging, venous confluence, and intervortex venous anastomoses [50].

These abnormalities are observed predominantly within dominant choroidal venous drainage systems, further supporting the concept that venous congestion and impaired vortex vein outflow contribute substantially to pachychoroid pathophysiology [50]. Choroidal hyperpermeability is commonly associated with increased choroidal thickness, although not all thickened choroids exhibit hyperpermeability [25, 51]. These observations support the view that pachychoroid disease reflects not only increased choroidal thickness but also a spectrum of disorders driven by choroidal vascular remodeling and hemodynamic dysregulation.

When focal degeneration of the choriocapillaris occurs, the characteristic ICGA pattern of choroidal hyperpermeability may diminish, allowing dilated Haller's layer vessels to become more conspicuous against a hypofluorescent background [3]. Leakage during the mid and late phases of ICGA has also been reported in both affected eyes and fellow eyes of patients with unilateral CSC, and is considered a characteristic feature of the pachychoroid spectrum [38].

An important OCT finding within the pachychoroid spectrum is the double-layer sign, which reflects separation between the RPE and Bruch's membrane. More extensive double-layer sign configurations observed in PNV and PCV are thought to represent more extensive neovascular tissue and progressive impairment of the RPE-Bruch's membrane complex compared with chronic CSC. This observation further supports the concept that chronic CSC, PNV, and PCV may represent sequential stages within the pachychoroid disease spectrum [52].

The double-layer sign is not specific to pachychoroid disease and may also be observed in age-related macular degeneration (AMD), particularly in association with type 1 macular neovascularization. In CSC, a similar structural appearance is frequently described as flat irregular pigment epithelial detachment, which typically refers to a shallow and irregular RPE elevation without the dome-shaped configuration of serous pigment epithelial detachments. Although double-layer sign, flat irregular pigment epithelial detachment, and shallow irregular RPE elevation share overlapping OCT characteristics, these terms arise from different conceptual frameworks based on structural reflectivity, anatomical morphology, and dimensional criteria, respectively [53].

OCTA studies have shown that shallow irregular pigment epithelial detachments associated with the double-layer sign frequently contain type 1 neovascular networks, even in the absence of definitive leakage on conventional angiography. These findings suggest that OCTA may improve the detection of quiescent PNV and enhance differentiation from chronic CSC without neovascularization [54]. Accordingly, OCTA has emerged as an important adjunctive modality for detecting subclinical neovascularization within the pachychoroid spectrum. OCTA may also reveal uncommon neovascular complications in advanced chronic CSC, including retinal neovascularization arising in areas of retinochoroidal atrophy [55].

Collectively, multimodal imaging has substantially improved the understanding of pachychoroid spectrum disorders by enabling comprehensive evaluation of choroidal morphology, vascular remodeling, RPE alterations, and neovascular complications. The complementary integration of these imaging modalities facilitates more accurate diagnoses, longitudinal disease monitoring, and clinical management across the pachychoroid spectrum (Table 2) [31, 56–58].

Pachydrusen

Pachydrusen are observed beneath the RPE in the posterior pole, and are characterized by solitary or scattered yellow-white deposits with distinct margins [59]. Typically exceeding 125 μm in size, they exhibit irregular yet relatively well-demarcated outer contours and are commonly associated with thick choroids showing reduced fundus tessellation in the macular region, though they may also occur in eyes with normal choroidal thickness [31].

Table 2. Multimodal imaging characteristics across the pachychoroid disease spectrum [31, 56–58]

Imaging Modality	Main Findings
Color fundus photography	Reduced fundus tessellation corresponding to areas of choroidal thickening; RPE mottling; serous detachment in CSC; orange nodules, subretinal hemorrhage and SRF/IRF in PCV
Fundus autofluorescence	Gravitational fluid tracts in chronic CSC; mixed hypo/hyperautofluorescence in PPE, hypoautofluorescence in PGA
Fluorescein angiography	Ink-blot or smoke-stack leakage patterns in CSC; occult leakage associated with type 1 neovascularization in PNV
Indocyanine green angiography	Choroidal hyperpermeability; focal punctate hyperfluorescence suggestive of choroidal ischemia; pachyvessels; intervortex anastomoses; pachydrusen; polypoidal lesions; peripheral venous remodeling; branching vascular networks in PCV
OCT	PED; BALAD; flat irregular PED; double-layer sign in PCV; well-defined serous retinal detachment in CSC; type 1 neovascularization in CSC, PNV, and PCV; pachyvessels
Enhanced-depth imaging OCT	Increased choroidal thickness; pachyvessels; attenuation of Sattler layer/choriocapillaris
OCT angiography	Choriocapillaris flow deficits; type 1 neovascularization in CSC, PNV and PCV; branching vascular network in PCV

Abbreviations: RPE, retinal pigment epithelium; CSC, central serous chorioretinopathy; SRF, subretinal fluid; IRF, intraretinal fluid; PCV, polypoidal choroidal vasculopathy; PPE, pachychoroid pigment epitheliopathy; PGA, pachychoroid geographic atrophy; PNV, pachychoroid neovasculopathy; OCT, optical coherence tomography; PED, pigment epithelium detachment; BALAD, bacillary layer detachment.

Their distribution pattern also differs from that of conventional soft drusen [32]. A hallmark feature of pachydrusen is their preferential distribution outside the foveal center. Unlike soft drusen, which typically display centripetal clustering and a gradient of decreasing size toward the retinal periphery, pachydrusen are commonly located near the vascular arcades and peripapillary regions. They often appear as scattered, nonconfluent lesions in the midperipheral fundus, and solitary lesions are common without accompanying smaller surrounding drusen. Pachydrusen are frequently observed in eyes with PPE, CSC, and PCV [60]. Notably, pachydrusen frequently colocalize with pachyvessels and areas of choriocapillaris thinning/attenuation [61].

Compared with soft drusen, pachydrusen generally exhibit minimal overlying hyperpigmentation, providing an additional clinical clue for differentiation. Although pigmentary abnormalities may be present elsewhere in the macula in pachychoroid spectrum disease, these alterations likely reflect chronic RPE dysfunction rather than a defining feature of pachydrusen themselves [60].

On ICGA, pachydrusen often show late-phase hypercyanescence, whereas soft drusen generally remain persistently hypocyanescent throughout the angiographic sequence [56]. These imaging characteristics suggest that pachydrusen may represent pachychoroid-associated sub-RPE deposits related to chronic choriocapillaris insufficiency and inner choroidal ischemia [62].

A significantly higher proportion of eyes with pachydrusen has been reported in Asian populations compared with Caucasian populations [63]. Pachydrusen are present in more than 40% of patients with CSC; prevalence increases with age. They have been identified in 14.1–56% of eyes with PCV [63–66]. Although exudative changes associated with pachydrusen appear to occur more frequently in PCV, their overall prognostic significance remains controversial. Early studies suggested that pachydrusen might represent a risk factor or early clinical marker for progression toward polypoidal disease [56, 67], yet subsequent investigations indicate that pachydrusen may not substantially increase the overall risk of exudative transformation compared with other drusen subtypes [32, 68]. In patients with unilateral neovascular AMD (nAMD), fellow eyes with soft drusen, pseudodrusen, or both presented a higher risk of nAMD development, whereas pachydrusen did not significantly increase the risk of exudative changes compared with eyes lacking drusen [69].

There is limited evidence on optimal monitoring strategies for eyes with pachydrusen alone. Nonetheless, periodic OCT follow-up may be considered, particularly in older patients or in the presence of associated macular pigmentary abnormalities that could indicate an increased risk of neovascular progression [70].

Pachychoroid Spectrum Disorders

Pachychoroid pigment epitheliopathy

PPE is typically asymptomatic and is characterized by RPE mottling, irregular RPE elevations resembling drusenoid lesions, and the absence of soft drusen typically observed in AMD [33]. In contrast to CSC, patients with PPE do not exhibit serous neurosensory detachment or a history of subretinal fluid accumulation [4]. Consistent with this observation, none of the affected eyes in the original description of PPE exhibited clinically detectable subretinal fluid, therefore choroidal vascular hyperpermeability and/or choroidal thickening alone were thought to account for the development of pigment epitheliopathy [49].

Sympathetic α-adrenoceptor activation in younger individuals may cause choriocapillaris ischemia or obliteration, subsequently resulting in RPE injury and the development of PPE [71]. Hormonal dysregulation has also been proposed as a potential contributing factor in pachychoroid spectrum disorders. Consistent with this concept, PPE-like pachychoroid changes have been reported in patients receiving tamoxifen therapy, possibly related to alterations in androgen, cortisol, and estrogen pathways affecting choroidal vascular regulation [72]. Four distinct morphological patterns have been described in PPE, including RPE thickening, hyperreflective RPE spikes, RPE elevations associated with inter-RPE fissures, and pigment epithelial detachment [73].

PPE has traditionally been regarded as a forme fruste of CSC, owing to the absence of neurosensory detachment. Nevertheless, PPE may progress to type 1 neovascularization, with or without polypoidal features, without preceding CSC development [39, 54]. Furthermore, PPE may coexist with CSC in the same eye or occur in the fellow eye. Ersoz et al. [74] showed PPE-related changes in 61% of contralateral eyes among patients with unilateral CSC. Longitudinal studies further support the concept that PPE may represent an early stage within the pachychoroid spectrum rather than a completely static or benign entity [75].

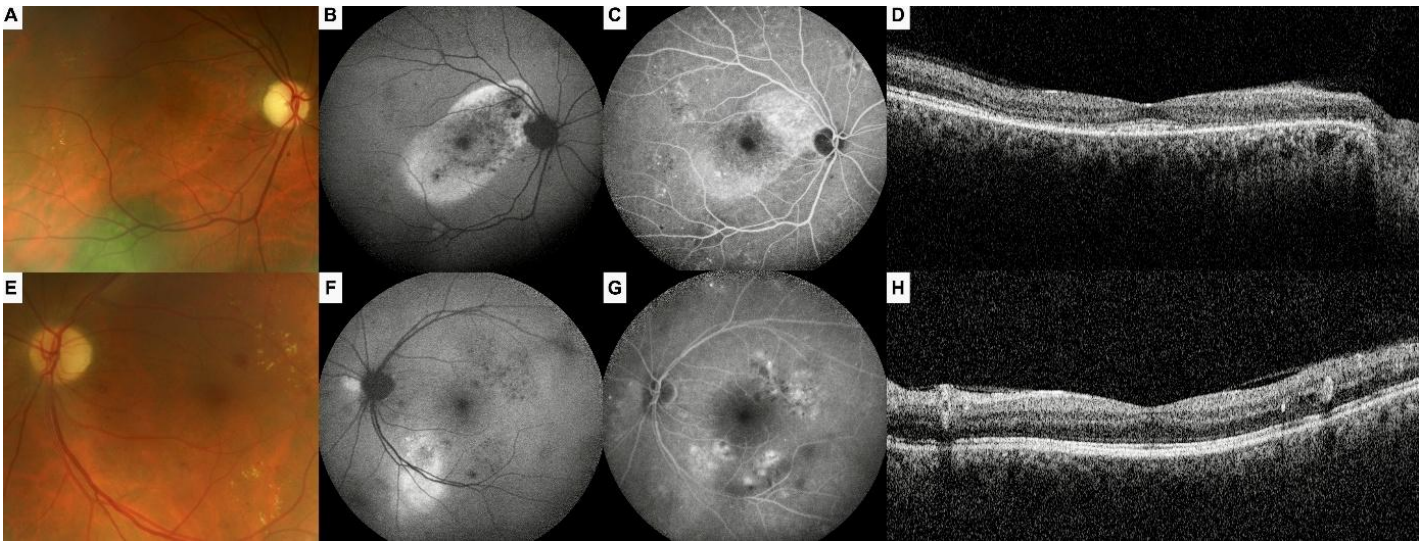

Figure 1. Multimodal imaging findings of a 60-year-old male patient with bilateral nonproliferative diabetic retinopathy and pachychoroid spectrum changes. Color fundus photographs (VISUCAM 500®, Carl Zeiss Meditec, Jena, Germany) of the right (A) and left (E) eyes showing scattered microaneurysms, hard exudates, and mottled retinal pigment epithelium (RPE) alterations involving the posterior pole. Fundus autofluorescence images (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (B, F) revealing extensive areas of mixed hypoautofluorescence and hyperautofluorescence corresponding to chronic RPE alterations. Fluorescein angiography images (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (C, G) show multifocal RPE window defects, granular hyperfluorescence, and scattered microaneurysms associated with diabetic retinopathy in both eyes. Spectral-domain optical coherence tomography scans (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) through the fovea (D, H), revealing pachychoroid features with increased choroidal thickness plus irregularities of the RPE and outer retinal layers, without significant intraretinal or subretinal fluid.

The diagnosis of PPE relies heavily on multimodal imaging. Fundus autofluorescence frequently reveals patchy hypoautofluorescence intermixed with focal hyperautofluorescent changes. Structural OCT typically evidences irregularities of the RPE/Bruch's membrane complex, with occasional shallow pigment epithelial detachments and focal RPE thickening. Alterations involving the ellipsoid zone, interdigitation zone, and outer nuclear layer may also be present, reflecting early photoreceptor injury (Figure 1) [76]. In addition to these outer retinal alterations, PPE is characteristically associated with localized choroidal thickening beneath the affected RPE region [77]. Prominent pachyvessels within Haller's layer, together with attenuation of the overlying choriocapillaris and Sattler's layer, are frequently observed [33]. Multiple scattered RPE elevations corresponding to RPE hyperplasia and sub-RPE drusenoid deposits may also be identified [4].

PPE has been proposed as a precursor to outer retinal atrophy. In a previous study, thinning of the outer nuclear layer and outer plexiform layer was more commonly detected in eyes with PPE compared with uncomplicated pachychoroid eyes and control subjects, supporting the hypothesis that degenerative changes may originate from RPE dysfunction before the onset of fluid accumulation [78]. In addition, PPE may be complicated by quiescent pachychoroid-associated neovascularization [32].

Central serous chorioretinopathy

CSC is characterized by pathological alterations involving the choriocapillaris, Bruch membrane, and RPE, together described as the Ruysch complex [4]. The pathological findings in CSC generally display a focal or segmental pattern, although multifocal involvement can also be observed [25]. CSC commonly presents with symptoms such as reduced or distorted vision, relative scotoma, and micropsia, along with a mild hyperopic shift. Younger patients tend to have unilateral disease, while bilateral involvement is more frequently observed in older individuals [25].

The precise mechanisms underlying CSC remain unclear; however, hormonal and autonomic dysregulation are thought to contribute to disease pathogenesis. Testosterone may contribute to choroidal vasodilation and vascular hyperpermeability through mechanisms similar to those described in other systemic vascular beds [79].

Systemic corticosteroids and sympathomimetic agents are consistently recognized as major risk factors, likely through impairment of choroidal vascular autoregulation [14, 25, 80]. Increasing evidence suggests that the effects of

corticosteroids in CSC may be mediated, at least in part, through overactivation of the mineralocorticoid receptor pathway, which can promote choroidal vasodilation, vascular hyperpermeability, and subsequent subretinal fluid accumulation [81]. Although topical, periocular, and intravitreal corticosteroids are widely used in ophthalmology, CSC associated with ocular steroid administration has been less frequently reported than CSC associated with systemic corticosteroid exposure. New-onset or worsening CSC has been reported following intravitreal and periocular steroid administration, and observational evidence also supports an association between recent topical ophthalmic corticosteroid use and CSC [82, 83]. Interestingly, corticosteroid-associated CSC frequently shows bilateral and atypical clinical features, supporting the hypothesis of an idiosyncratic response in susceptible individuals rather than a purely dose-dependent effect [84]. In addition, patients with Cushing Syndrome display an increased prevalence of pachychoroid spectrum disorders [85].

Abnormal sleep patterns and obstructive sleep apnea have also been identified as significant risk factors for CSC [3]. Beyond systemic and hormonal influences, psychological factors are thought to contribute importantly to CSC susceptibility. Patients with CSC commonly exhibit higher levels of emotional distress, somatization, depressive symptoms, and hostility compared with unaffected individuals [31, 86].

Multiple systemic and vascular associations have been implicated in CSC, particularly hypertension and other cardiovascular disorders. CSC is thought to arise from choroidal vascular hyperpermeability and dysregulation of the mineralocorticoid receptor pathway, both of which share pathogenic mechanisms with cardiovascular disease [87]. CSC has also been associated with an increased incidence of coronary heart disease and ischemic stroke in subsequent years [88, 89]. These findings further support the concept that CSC may reflect broader systemic vascular dysregulation [31].

Eyes with CSC are commonly characterized by shorter axial length and a more hyperopic refractive profile compared with healthy eyes, whereas the condition is uncommon in highly myopic eyes. This association suggests that ocular dimensions may influence choroidal hemodynamics and susceptibility to disease. The oblique transscleral course of the vortex veins, extending approximately 4 mm within the sclera, may predispose to increased venous resistance in the presence of scleral alterations, ultimately resulting in impaired choroidal drainage [90].

Acute CSC tends to resolve spontaneously within 3–6 months and is usually observed during this period. Nevertheless, recurrence is common, affecting nearly 50% of patients, and persistent disease beyond six months occurs in approximately 15% of cases [25].

In recognition of the heterogeneous clinical spectrum of CSC, a revised classification system proposed by an international expert panel in 2020 categorized the disease according to the extent of RPE abnormalities (simple versus complex), disease status (primary, recurrent, or resolved), persistence beyond six months, presence of outer retinal atrophy, foveal involvement, and associated macular neovascularization [91].

The acute form is the most common subtype of CSC and is usually characterized by a focal neurosensory retinal detachment with associated serous pigment epithelial detachments [92]. On fluorescein angiography, focal RPE leakage typically displays either an inkblot or a smokestack pattern [25]. With persistent subretinal fluid, additional features such as elongated photoreceptor outer segments, subretinal fibrin, intraretinal lipid accumulation, and yellowish subretinal deposits may develop [93]. Subretinal fibrin deposition has been associated with progressive fibrotic scarring and unfavorable visual outcomes, occasionally resulting in RPE tears or secondary neovascular complications (Figure 2) [94].

A recently described OCT feature in CSC, termed the “scolex” sign, appears as a focal hyperreflective dot along the wall of a serous pigment epithelial detachment and may represent a resolving or reparative stage of the disease associated with pigment epithelial detachment flattening and subretinal fluid resolution [95]. Retinal fingerprint pattern has also recently been described on en face OCT in CSC, and appears to be associated with greater subretinal fluid accumulation and favorable anatomical resolution [96].

In contrast, chronic CSC, generally defined by the presence of significant RPE damage, is characterized by diffuse RPE alterations and shallow, widespread serous retinal detachments (Figures 3 and 4) [93, 97]. Flat irregular pigment epithelial detachments are also commonly encountered and appear as shallow, broad RPE elevations with an irregular contour distinct from that of serous pigment epithelial detachments [53]. These abnormalities may extend inferiorly as descending tracts, which are most clearly identified on fundus autofluorescence imaging as granular or confluent hypoautofluorescent areas surrounded by hyperautofluorescent borders [93]. Flat irregular pigment epithelial detachments in CSC have been associated with an increased risk of macular neovascularization, particularly when corresponding flow signals are detected on OCTA between the RPE and Bruch’s membrane [98].

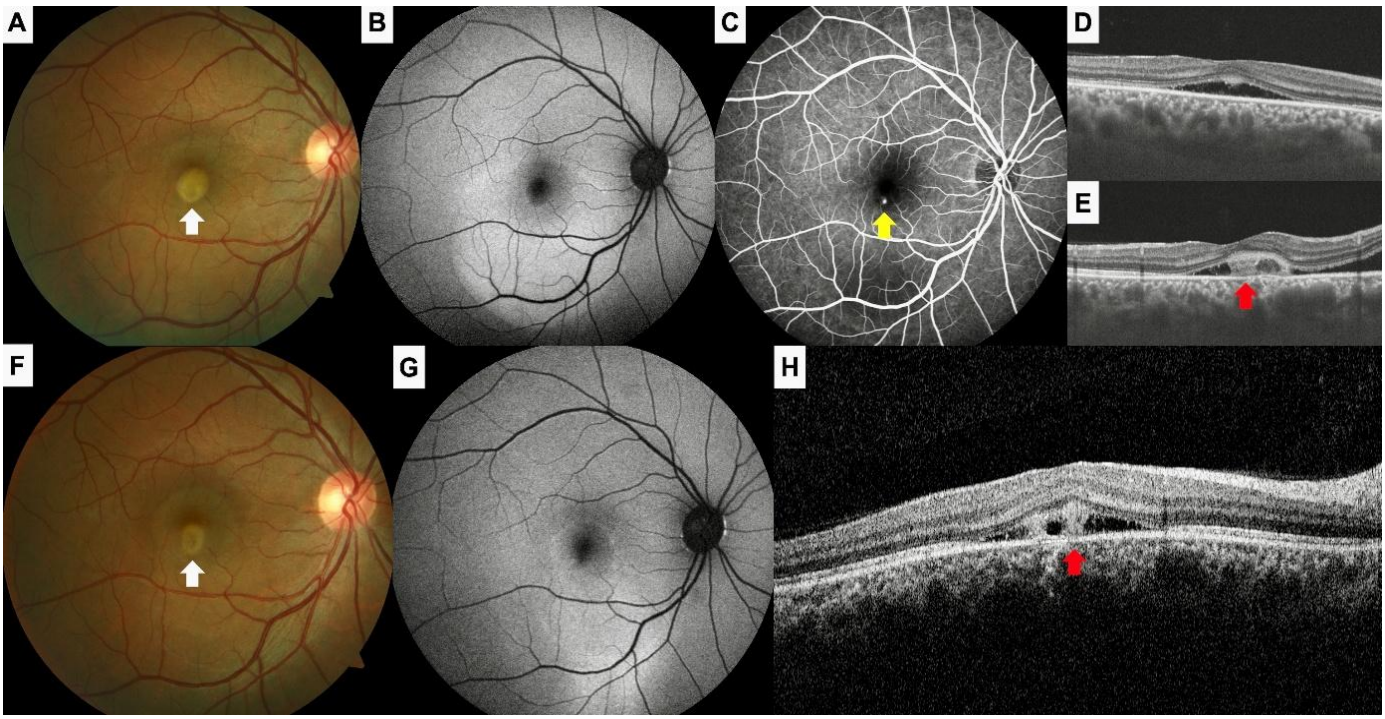

Figure 2. Multimodal imaging findings of a 41-year-old male patient with unilateral fibrinous central serous chorioretinopathy involving the right eye. Color fundus photograph (VISUCAM 500®, Carl Zeiss Meditec, Jena, Germany) obtained at the initial presentation (A) showing a juxtafoveal yellowish subretinal fibrinous deposit (white arrow). Fundus autofluorescence image (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (B) revealing foveal hypoautofluorescence corresponding to the fibrinous deposit alongside gravitational fluid tracking changes. Fluorescein angiography image (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (C) showing focal foveal leakage (yellow arrow). Spectral-domain optical coherence tomography (SD-OCT) scans (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (D, E) revealing increased choroidal thickness and serous neurosensory retinal detachment associated with hyperreflective subfoveal fibrinous material (red arrows). Color fundus photograph (F) and fundus autofluorescence image (G), obtained 10 weeks later without treatment, showing partial spontaneous resolution of the fibrinous subfoveal material. Follow-up SD-OCT scan (H) reveals decreased subretinal fibrinous deposition and reduced subretinal fluid, with residual outer retinal and retinal pigment epithelium irregularities (red arrow).

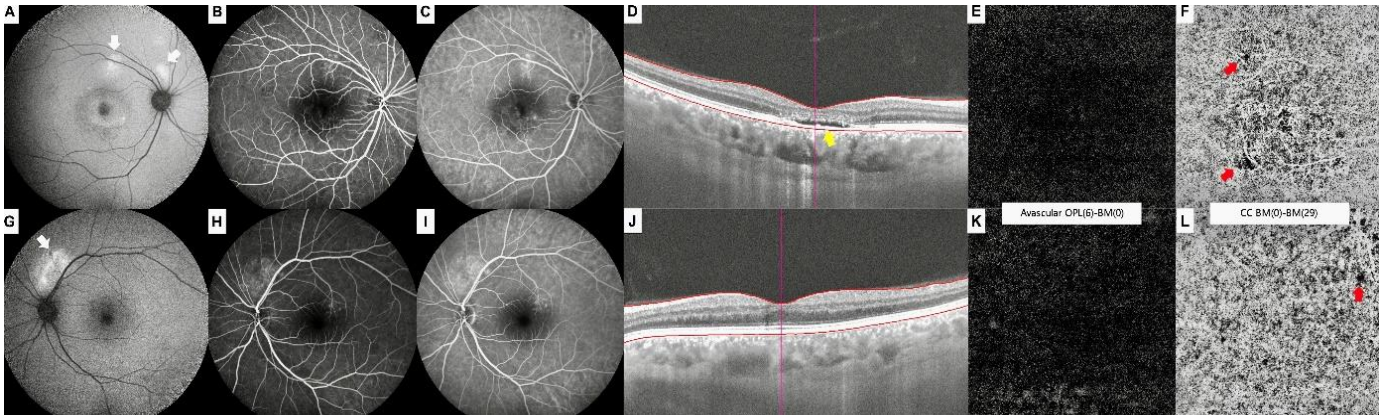

Figure 3. Multimodal imaging findings of a 49-year-old male patient with bilateral chronic central serous chorioretinopathy. Fundus autofluorescence images (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) of the right (A) and left (G) eyes reveal hyperautofluorescent areas along the superotemporal vascular arcade and superior to the optic disc (white arrows), together with perifoveal retinal pigment epithelium (RPE) alterations. Early-phase (B, H) and late-phase (C, I) fluorescein angiography images (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) showing multifocal areas of granular hyperfluorescence, focal leakage, and RPE window defects in both eyes. Swept-source optical coherence tomography scans (BMizar®, TowardPi Medical Technology Ltd., Beijing, China) through the fovea (D, J), revealing increased choroidal thickness in both eyes and irregularities of the RPE and outer retinal layers, and a shallow pocket of subretinal fluid in the right eye (yellow arrow). Swept-source optical coherence tomography angiography images (BMizar®, TowardPi Medical Technology Ltd., Beijing, China) of the outer retina (E, K) showing no evidence of macular neovascularization in either eye, whereas choriocapillaris slabs (F, L) show focal flow deficits (red arrows).

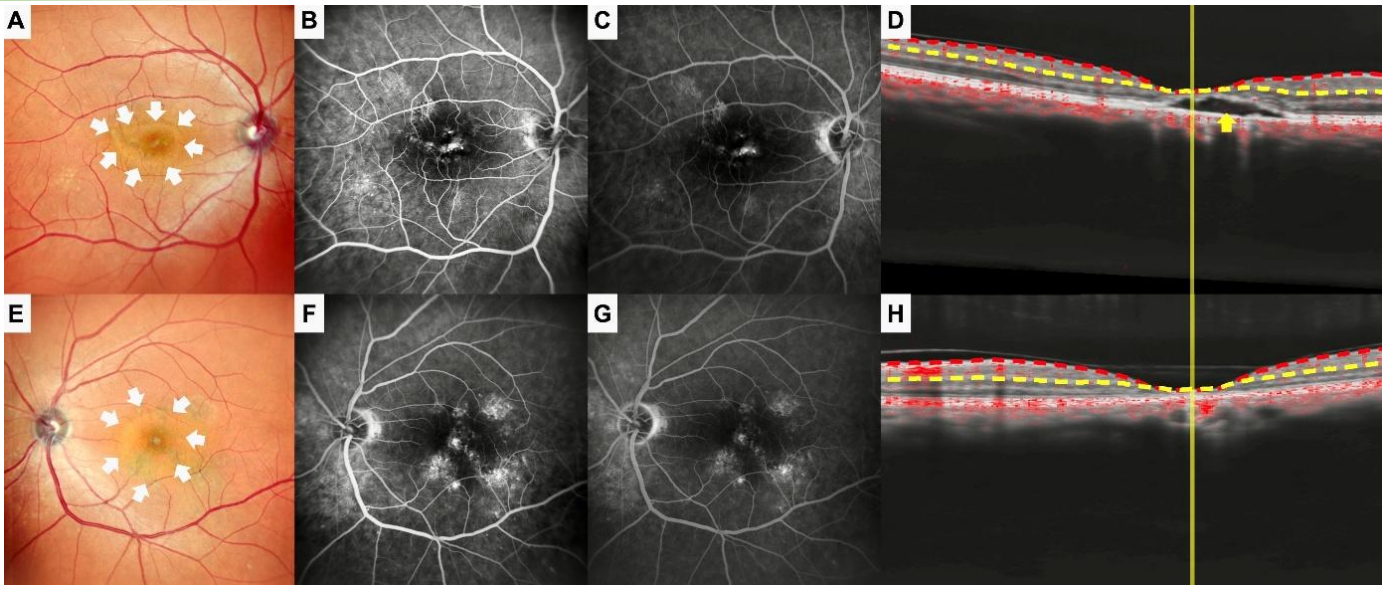

Figure 4. Multimodal imaging findings of a 45-year-old male patient with bilateral chronic central serous chorioretinopathy. Color fundus photographs (Mirante®, Nidek Co., Ltd., Gamagori, Japan) of the right (A) and left (E) eyes showing retinal pigment epithelium (RPE) mottling and parafoveal depigmentary alterations involving the macula (white arrows). Early-phase (B, F) and late-phase (C, G) fluorescein angiography (Mirante®, Nidek Co., Ltd., Gamagori, Japan) images revealing multifocal areas of granular hyperfluorescence, focal leakage, and RPE window defects in both eyes. Spectral-domain optical coherence tomography (Mirante®, Nidek Co., Ltd., Gamagori, Japan) scans through the fovea (D, H) showing irregularities of the RPE and outer retinal layers in both eyes with a shallow pocket of subretinal fluid in the right eye (yellow arrow).

Bacillary layer detachment (BALAD) has recently emerged as an OCT finding in chronic CSC [99, 100]. Histologically, BALAD is thought to result from an intraphotoreceptor split within the myoid zone of the photoreceptor inner segments, just posterior to the external limiting membrane. Fernández-Vigo et al. [100] observed BALAD in 46% of chronic CSC eyes treated with photodynamic therapy (PDT) and established a significantly greater association with subretinal fibrin deposition. BALAD has also been linked to several systemic conditions, particularly psychiatric disorders and corticosteroid exposure, both recognized risk factors for CSC. These observations suggest that BALAD may represent a more severe or biologically distinct phenotype of chronic CSC, potentially associated with heightened choroidal hyperpermeability, inflammatory dysregulation, or steroid-associated vascular alterations [101].

Fibrinous changes may also occur bilaterally in CSC and may coexist with chronic RPE alterations, pigment epithelial detachment, and serous neurosensory retinal detachment (Figure 5) [94]. Bullous CSC represents a rare but severe form of the disease characterized by extensive inferior serous retinal detachment [102]. These eyes commonly exhibit RPE tears and large pigment epithelial detachments containing hyperreflective fibrinous material. Multifocal leakage is frequently observed on fluorescein angiography, and the clinical presentation may mimic acute Vogt-Koyanagi-Harada disease [94, 103]. Furthermore, eyes with bullous CSC have been reported to display increased peripheral retinal nonperfusion, along with hyperreflective alterations involving the choriocapillaris and the walls of large choroidal vessels [94].

In CSC, which is characterized by choroidal vascular congestion and hyperpermeability, PDT has demonstrated substantial efficacy, particularly in chronic disease. The PLACE trial evidenced superior outcomes with half-dose PDT compared with subthreshold micropulse laser therapy for chronic CSC [104].

In selected cases of CSC, conventional focal thermal laser photocoagulation can be directed toward extrafoveal leakage points identified on fluorescein angiography (Figure 6). However, the use of small spot sizes (<100 μm) has been associated with an increased risk of treatment-related choroidal neovascularization [25]. Subthreshold micropulse/yellow subthreshold laser photocoagulation has been used in CSC with persistent subretinal fluid while minimizing thermal injury to the RPE and neurosensory retina [105]. Because it does not create a visible laser burn, it may be used for leakage sites closer to the fovea than those amenable to conventional thermal laser [106].

Photobiomodulation has recently gained attention in retinal diseases because of its potential to enhance mitochondrial activity, modulate oxidative stress, and promote RPE repair. Early studies in chronic CSC show promising anatomical and visual outcomes, suggesting that photobiomodulation may represent a safe and noninvasive therapeutic option in selected cases [107]. Despite corticosteroids being recognized as a risk factor for CSC, a retrospective study reported anatomical improvement after topical prednisolone acetate in eyes with chronic CSC, without significant improvement in visual acuity; however, this approach remains investigational and carries a risk of steroid-induced ocular hypertension [108].

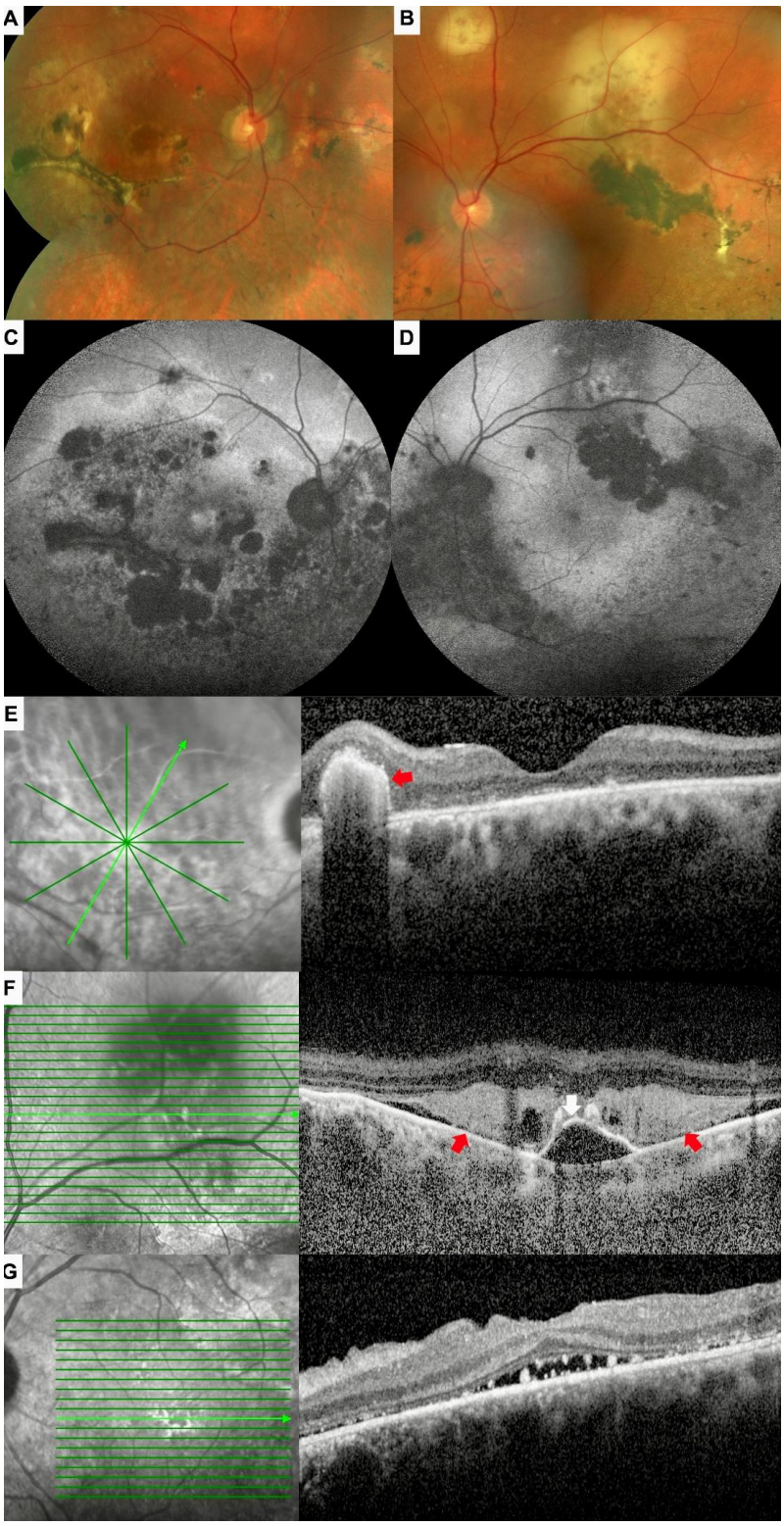

Figure 5. Multimodal imaging findings of a 44-year-old patient with bilateral fibrinous central serous chorioretinopathy. Color fundus photographs (VISUCAM 500®, Carl Zeiss Meditec, Jena, Germany) (A, B) showing widespread hyperpigmented and hypopigmented retinal pigment epithelium (RPE) alterations and multifocal areas of subretinal fibrinous deposition involving both eyes. Fundus autofluorescence images (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (C, D) revealing extensive mixed hypoautofluorescent and hyperautofluorescent changes corresponding to chronic RPE disturbance and fibrinous material accumulation. Enhanced depth imaging spectral-domain optical coherence tomography scan (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) of the right eye (E) displaying pachychoroid features, including increased choroidal thickness, irregular RPE elevations, disruption of the outer retinal layers, and parafoveal subretinal fibrinous deposit (red arrow). Corresponding scans of the left eye (F, G) revealing RPE detachment (white arrow), subretinal hyperreflective fibrinous material (red arrows), irregular RPE alterations, and subfoveal serous neurosensory detachment. Dye-based angiographic imaging was not performed because of underlying chronic renal failure.

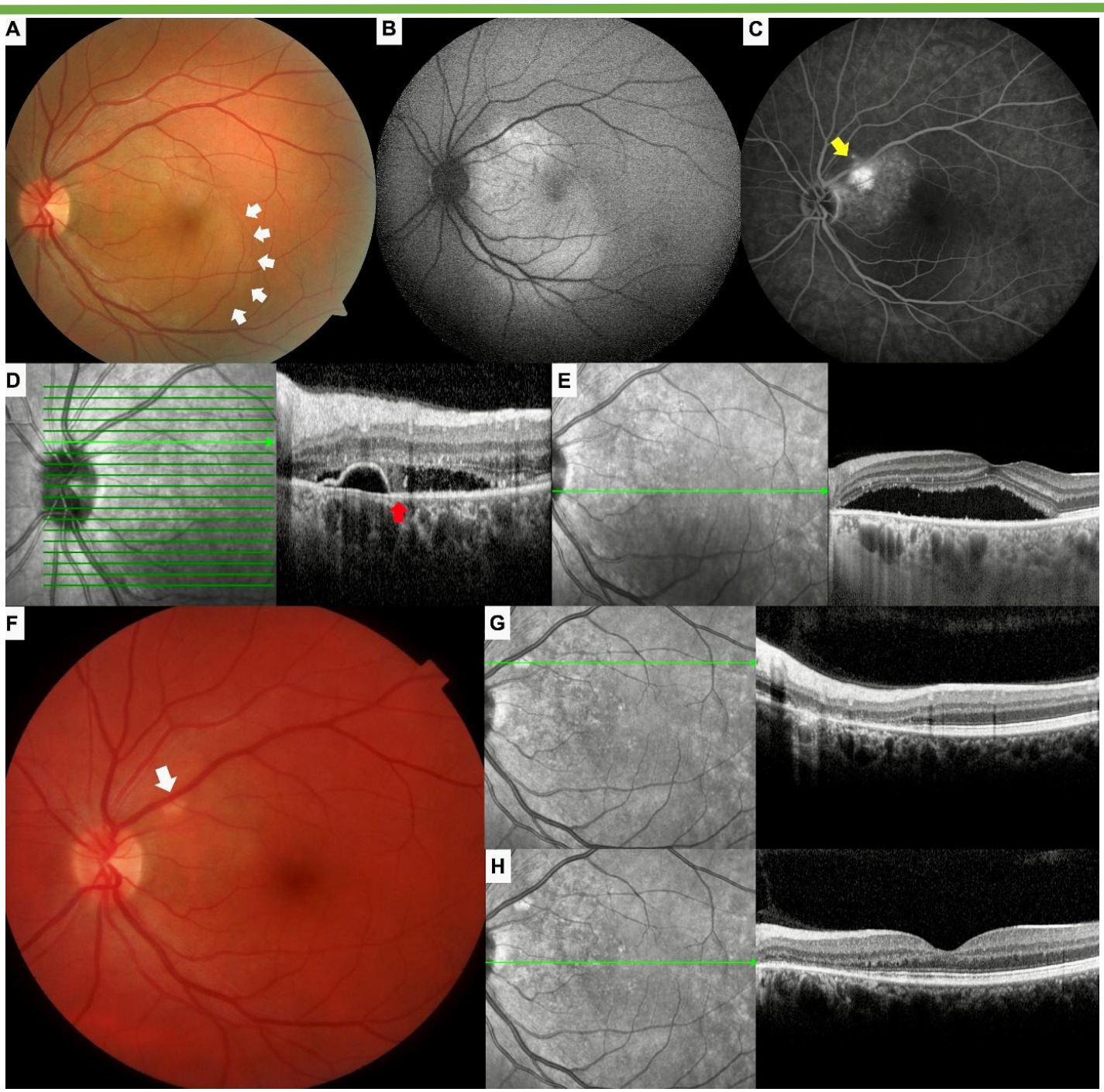

Figure 6. Multimodal imaging findings of a 38-year-old male patient with unilateral fibrinous central serous chorioretinopathy involving the left eye. Color fundus photograph (VISUCAM 500®, Carl Zeiss Meditec, Jena, Germany) obtained at the initial presentation (A) revealing perifoveal retinal pigment epithelium (RPE) alterations and subretinal fluid extending inferior and temporal to the fovea (white arrows). Fundus autofluorescence image (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (B) revealing mixed hyperautofluorescent and hypoautofluorescent alterations corresponding to chronic RPE disturbance and gravitational fluid tracking changes. Fluorescein angiography image (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (C) showing focal leakage superior and temporal to the optic disc (yellow arrow). Enhanced depth imaging spectral-domain optical coherence tomography (EDI SD-OCT) scans (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (D, E) revealing increased choroidal thickness, serous neurosensory retinal detachment, irregular RPE elevations and detachments, and hyperreflective subretinal fibrinous material (red arrow). Color fundus photograph obtained one year after focal laser photocoagulation of the leakage area (100-µm spot size, 100-ms duration, power titrated to produce a light gray burn) (F) showing laser scars superior and temporal to the optic disc (white arrow). Follow-up EDI SD-OCT scans (G, H) revealing complete resolution of subretinal fluid and fibrinous material, with residual RPE irregularities and persistent pachychoroid features.

Key clinical studies investigating therapeutic approaches in CSC are summarized in Table 3 [104, 109–112].

Table 3. Landmark clinical trials evaluating therapeutic interventions for CSC

Author (Year)	Study	n	Follow-up	Treatment Arms	Outcomes Assessed	Principal Findings	Clinical Implications
van Dijk et al. (2018) [104]	PLACE	179	7–8 months	- Half-dose PDT - HSML	- SRF - BCVA - Retinal sensitivity - Treatment burden - Safety	- Complete SRF resolution was achieved in 67.2% vs. 28.8% of eyes. - Mean BCVA gain was +6.78 and +4.48 letters. - Retinal sensitivity improvement was greater with PDT (+3.24 vs. +1.38 dB).	Half-dose PDT was superior to HSML for achieving SRF resolution and functional improvement in chronic CSC, supporting PDT as a preferred treatment strategy within the pachychoroid spectrum.
van Rijssen et al. (2020) [109]	REPLACE	42	12 months	- Crossover to half-dose PDT after failed HSML - Crossover to HSML after failed half-dose PDT	- SRF - BCVA - Retinal sensitivity - Quality of life - Safety	- Complete SRF resolution occurred in 78% vs. 67% of patients. - SRF resolution at first evaluation occurred in 81% of crossover PDT-treated eyes and none of crossover HSML-treated eyes. - Retinal sensitivity improved significantly after crossover PDT only.	Half-dose PDT remained effective in chronic CSC patients with persistent SRF after previous HSML treatment; crossover to HSML after failed PDT yielded limited functional benefit.
Lotery et al. (2020) [110]	VICI	114	12 months	- Oral eplerenone - Placebo	- BCVA - Safety - Hyperkalemia	- Mean BCVA at month 12 was 80.4 and 79.5 letters, with no significant between-group difference. - Adjusted mean BCVA difference was not statistically significant (+1.73 letters). - Hyperkalemia occurred in 14% of both groups.	Eplerenone was not superior to placebo in chronic CSC.
van Rijssen et al. (2022) [111]	SPECTRA	107	3 months	- Half-dose PDT - Oral eplerenone	- SRF - BCVA - Retinal sensitivity - Quality of life - Safety	- Complete SRF resolution occurred in 78% vs. 17% of eyes. - Retinal sensitivity was significantly higher with PDT (25.4 vs 23.9 dB). - Adverse events occurred in 6% vs. 33% of patients.	Half-dose PDT was superior to oral eplerenone for achieving SRF resolution and functional improvement in chronic CSC, while also evidencing a more favorable safety profile.
Feenstra et al. (2026) [112]	SPECTRA Long-term outcomes	80	24 months	- Half-dose PDT - Oral eplerenone	- SRF - BCVA - Retinal and foveal sensitivity - SFCT - Safety	- Complete SRF resolution occurred in 80% of patients primarily treated with half-dose PDT and 87.5% of patients initially treated with eplerenone who mostly crossed over to PDT. - BCVA improved significantly in both groups (+5.9 and +4.1 letters). - Foveal and retinal sensitivity improved significantly in both groups. - Half-dose PDT produced a sustained reduction in SFCT; eplerenone alone showed minimal early choroidal effect. - 90% of eplerenone-treated patients required crossover PDT because of persistent SRF. - No significant long-term differences were observed between groups at 24 months after crossover therapy.	Half-dose PDT provided durable long-term efficacy in chronic CSC, remaining the preferred treatment option.

Abbreviations: n, sample size; PDT, photodynamic therapy; HSML, high-density subthreshold micropulse laser; SRF, subretinal fluid; BCVA, best corrected visual acuity; dB, decibel; CSC, central serous chorioretinopathy; SFCT, subfoveal choroidal thickness. Note: PLACE, Half-Dose Photodynamic Therapy versus High-Density Subthreshold Micropulse Laser Treatment in Patients with Chronic Central Serous Chorioretinopathy; REPLACE, Re-half-dose Photodynamic therapy versus re-high-density subthreshold micropulse LAser treatment in patients with chronic CEntral serous chorioretinopathy; VICI trial, Eplerenone for chronic central serous chorioretinopathy in patients with active, previously untreated disease for more than 4 months; SPECTRA, Half-Dose Photodynamic Therapy Versus Eplerenone in Chronic Central Serous Chorioretinopathy.

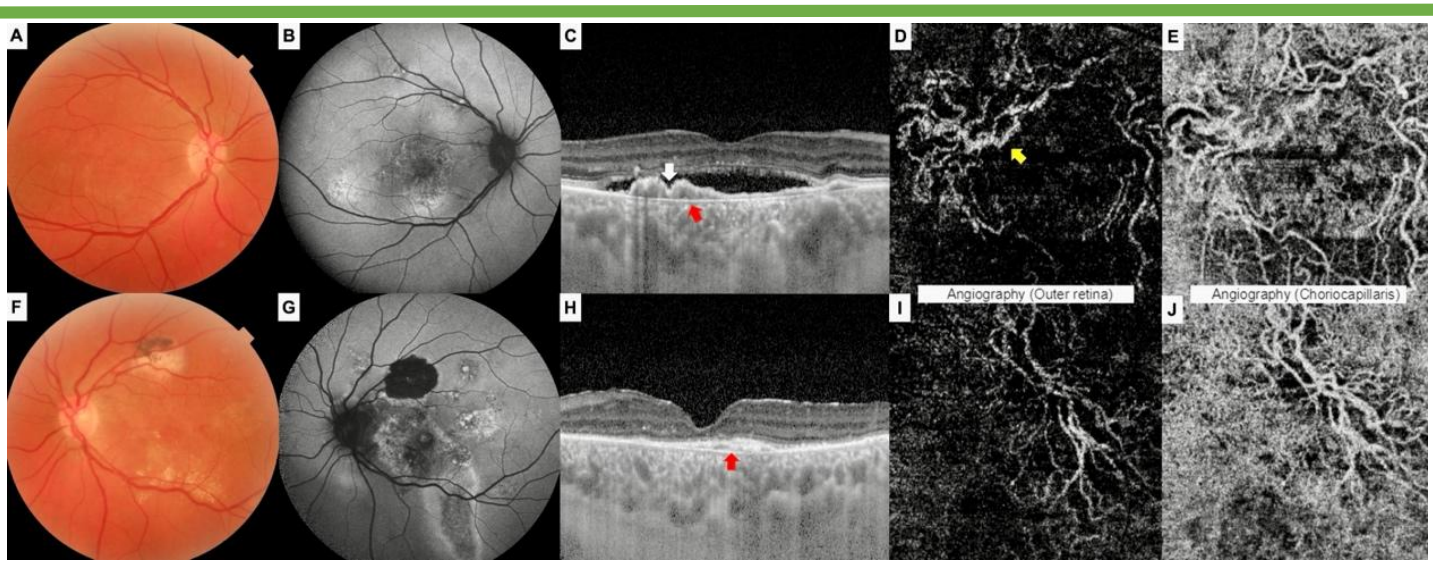

Figure 7. Multimodal imaging findings of a 60-year-old female patient with pachychoroid neovasculopathy secondary to chronic central serous chorioretinopathy. Color fundus photographs (Topcon DRI OCT®, TOPCON Inc, Tokyo, Japan) of the right (A) and left (F) eyes showing retinal pigment epithelium (RPE) alterations involving the macula and the superior and inferior temporal vascular arcades. Fundus autofluorescence images (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (B, G) revealing mixed hypoautofluorescent and hyperautofluorescent changes corresponding to chronic RPE disturbance in both eyes, together with gravitational fluid tracking changes in the left eye. Transfoveal spectral-domain optical coherence tomography scans (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (C, H) exhibiting pachychoroid features, including increased choroidal thickness, irregular RPE elevations, and shallow type 1 neovascular complexes (red arrows). In the right eye (C), the presence of a double layer sign (white arrow) accompanied by subretinal fluid is suggestive of active macular neovascularization (MNV), whereas the left eye (H) displays quiescent type 1 MNV without associated subretinal fluid. Swept-source optical coherence tomography angiography images (Topcon DRI OCT®, TOPCON Inc, Tokyo, Japan) of the outer retina (D, I) and corresponding choriocapillaris slabs (E, J) showing neovascular networks corresponding to type 1 MNV in both eyes (yellow arrow).

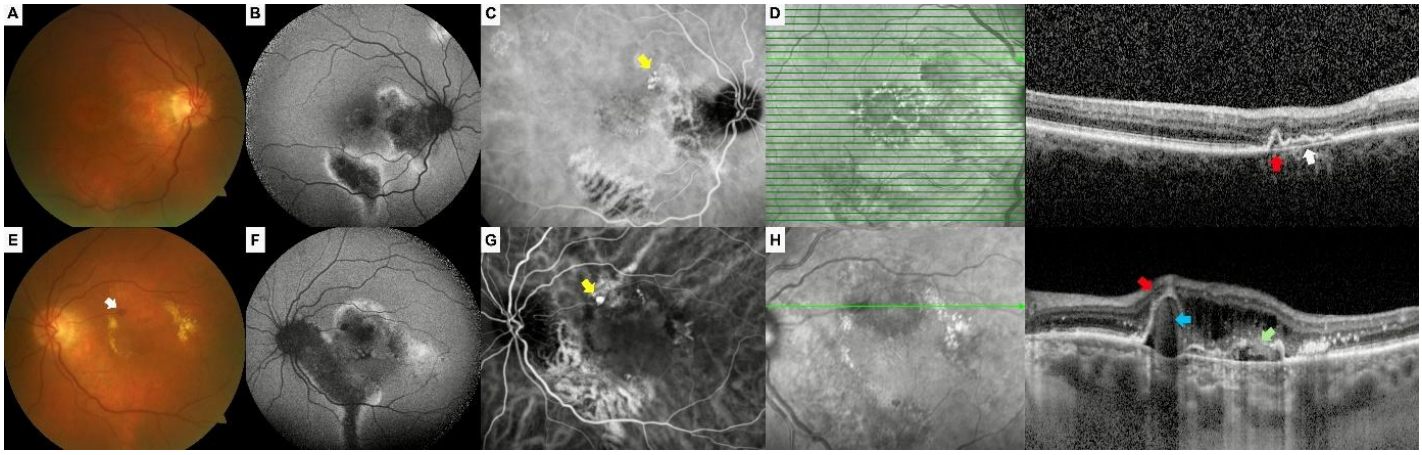

Figure 8: Multimodal imaging findings of a 70-year-old male patient with bilateral polypoidal choroidal vasculopathy developing on the background of chronic central serous chorioretinopathy. Color fundus photographs (VISUCAM 500®, Carl Zeiss Meditec, Jena, Germany) of the right (A) and left (E) eyes revealing extensive retinal pigment epithelium (RPE) alterations in both eyes, with scattered exudative changes and subretinal hemorrhage in the left eye (white arrow). Fundus autofluorescence images (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (B, F) revealing widespread mixed hypoautofluorescent and hyperautofluorescent changes corresponding to chronic RPE disturbance together with gravitational fluid tracking changes. Indocyanine green angiography images (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) (C, G) showing focal hypercyanescent polypoidal lesions (yellow arrows). Enhanced depth imaging spectral-domain optical coherence tomography scans (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) passing through the polypoidal lesions (D, H) revealing pachychoroid features, including increased choroidal thickness, RPE alterations, and thumb-like polypoidal lesions in both eyes (red arrows). Additional findings include a double layer sign in the right eye (white arrow) and a sub-RPE ring-like lesion (blue arrow), RPE microrip (green arrow), and associated intraretinal and subretinal fluid in the left eye.

Pachychoroid neovasculopathy

Chronic alterations involving the outer retinal layers, RPE, and choriocapillaris in pachychoroid disease have been proposed as a factor contributing to the development of type 1 neovascularization in susceptible individuals [113]. Eyes with longstanding or previously documented CSC developed type 1 neovascularization, likely due to progressive choroidal abnormalities (Figure 7). Subsequently, the term PNV was introduced to describe type 1 neovascularization occurring within the pachychoroid disease spectrum rather than exclusively secondary to CSC [32].

The exact relationship between pachychoroid and neovascularization remains uncertain. The choriocapillaris plays a critical role in supplying oxygen and nutrients to Bruch's membrane and the RPE. In pachychoroid disease, impaired choroidal circulation may reduce oxygen delivery to the outer retina, resulting in increased VEGF-A production and subsequent choroidal neovascularization formation, as seen in PNV [4].

PNV represents a distinct form of macular neovascularization within the pachychoroid disease spectrum [39]. Affected eyes typically display characteristic pachychoroid features, including reduced fundus tessellation and the absence of soft drusen, reflecting increased choroidal thickness surrounding the type 1 neovascular lesion [25].

Neovascularization is typically confirmed by leakage on fluorescein angiography, often presenting as late leakage of uncertain origin, with corresponding late plaque-like staining on ICGA [114]. While similar angiographic patterns may occur in chronic CSC due to widespread RPE dysfunction and choroidal hyperpermeability, PNV eyes do not show the classic serous macular detachment or fundus autofluorescence features such as descending tracts [39]. Reflecting this heterogeneity, PNV has been subclassified into forms with or without neurosensory detachment [115].

These observations further support the notion that PNV may differ from chronic CSC in several structural and hemodynamic aspects [29]. Consistent with these observations, Demirel et al. [116] showed significant differences in central choroidal thickness and choroidal vascularity index among PNV, PCV, and CSC; however, PPE showed values similar to both PNV and CSC. These findings raised questions about PNV and PCV simply representing progressive stages of CSC, as both entities exhibited relatively lower choroidal vascularity index values [29, 116].

Recent multimodal imaging studies have further highlighted several non-invasive features that may help distinguish PNV from nAMD, including increased choroidal thickness and choroidal vascularity index, absence of soft drusen, intervortex venous anastomoses, and immature neovascular networks lacking a prominent vascular trunk on OCTA [117].

PNV may also display progressive morphological evolution during the course of disease. Non-exudative PNV may evolve into an exudative form characterized by subretinal fluid accumulation. On OCTA, exudative PNV generally exhibits dense lacy-wheel or sea fan-shaped neovascular networks with numerous microvascular branches, whereas non-exudative lesions tend to show indistinct vascular networks or long filamentous linear vessels [118]. In addition, aneurysmal lesions may develop over time, sometimes accompanied by large RPE detachments located at the terminal end of the neovascular network [119]. In a study of fellow eyes in unilateral typical nAMD and PCV, branching neovascular networks were observed in 18.8% of eyes and were identified as a significant risk factor for subsequent PCV or macular neovascularization development. These branching neovascular networks may represent underlying PNV and, in some eyes, may eventually progress to polypoidal dilatation [120]. Supporting this hypothesis, branching neovascular networks and even polypoidal lesions have been identified in fellow eyes of unilateral PCV prior to the development of exudative changes [121]. In addition, subretinal hyperreflective material and intraretinal fluid in PNV have been associated with subsequent retinal atrophy, suggesting that structural degeneration may contribute to disease progression beyond exudative activity alone [122].

In a single case of PNV treated with half-fluence PDT combined with intravitreal aflibercept, ICGA demonstrated downstream pulsation at a vortex vein that became occluded after treatment; the general significance of this isolated observation remains uncertain [123]. Additional evidence of venous dysregulation in PNV was provided by Matsumoto et al. [124], who identified dilated choroidal veins and intervortex venous anastomoses as characteristic findings in PNV, further supporting the role of impaired venous drainage in disease pathogenesis. Compared with typical nAMD, PNV typically requires fewer anti-VEGF injections [125]. In addition, aqueous VEGF levels have been reported to be lower in PNV than in nAMD [126].

Several treatment approaches have been proposed for PNV. While PDT alone may effectively address the choroidal vascular hyperpermeability component, anti-VEGF therapy is usually still necessary to control the associated neovascularization. Combined PDT and anti-VEGF therapy has generally shown favorable tolerability and may decrease injection frequency and retreatment requirements [127].

Polypoidal choroidal vasculopathy (aneurysmal type 1 neovascularization)

Since its initial description in 1982, the term PCV has expanded to encompass aneurysmal (polypoidal) lesions occurring in diverse clinical settings, leading to ongoing uncertainty regarding its terminology and classification [128]. Hence several authors, including Lawrence A. Yannuzzi, have proposed the term aneurysmal type 1 neovascularization to better emphasize the predominantly vascular rather than epithelial nature of these lesions [4, 128].

PCV may develop via different pathogenic mechanisms, including chronic choroidal congestion and vascular remodeling resulting in aneurysmal dilations in pachychoroid-dominant eyes, or as terminal outgrowths of neovascular complexes in the setting of nAMD or PNV [1]. In PCV, aneurysmal lesions are consistently located beneath the RPE between its basal lamina and the inner collagenous layer of Bruch's membrane, consistent with type 1 (sub-RPE) neovascularization [129].

In step with this concept, advances in high-resolution OCT and OCTA have demonstrated that the branching neovascular network in PCV is localized within the sub-RPE compartment rather than the inner choroid [130, 131]. These vascular complexes typically give rise to terminal aneurysmal dilatations corresponding to the clinically observed polypoidal lesions [132].

Although PCV may occur across a wide age range, from 20 to 80 years, it is most frequently observed in patients aged 50–65 [4, 132]. The classification of PCV as a subtype of AMD remains controversial [59]. Traditional and Asian concepts of nAMD reveal both overlap and important differences. Conventionally, nAMD has been defined by the presence of AMD-related changes such as drusen and pigmentary abnormalities. However, in Asian countries angiographic findings play a more central diagnostic role, and drusen are not invariably present. Consequently, Asian nAMD may present with a wider range of phenotypes, including typical nAMD, PCV, and type 3 choroidal neovascularization (retinal angiomatous proliferation) [133].

Chronic inflammation induced by drusen is considered a central mechanism underlying the pathogenesis of nAMD. In Asian populations, however, macular neovascularization may also develop through pachychoroid-associated pathways distinct from the conventional drusen-dependent model [134]. AMD and PCV appear to share common genetic risk factors, particularly involving complement factor H (CFH) and HtrA serine peptidase 1 (HTRA1) polymorphisms. This genetic overlap has contributed to the hypothesis that PCV may represent a distinct variant of AMD [135].

Studies from Japan have reported that PCV may account for up to 54.7% of nAMD cases, whereas its prevalence among Caucasian populations is considerably lower, representing approximately 10% of cases [4, 136]. Anatomical distribution of PCV lesions also appears to vary between ethnic groups, with Asian (Japanese) and Caucasian patients more commonly showing macular involvement, whereas Afro-Caribbean patients frequently exhibit lesions arising from the peripapillary choroidal circulation [137, 138].

Several classification systems for PCV have been proposed [139]. Anatomically, lesions may be described as subfoveal, juxtafoveal, extrafoveal, peripapillary, or peripheral; clinically, the disease may be classified into quiescent, exudative, or hemorrhagic subtypes [140].

PCV can also be categorized into thin- and thick-choroid variants [14, 141]. Historically, PCV has also been subdivided into type 1 and type 2 forms. Type 1 PCV was described as an nAMD-related phenotype characterized by polypoidal lesions arising from sub-RPE neovascular complexes; type 2 PCV was considered more closely related to the pachychoroid spectrum and is characterized by increased choroidal thickness and distinct genetic features [141]. Similarly, Chang et al. [142] classified PCV into pachychoroid and non-pachychoroid groups and showed that the pachychoroid subtype was associated with younger age at presentation, fewer AMD-like features, more CSC-like findings, and poorer response to anti-VEGF therapy, with PDT appearing to be a more effective treatment strategy. Additional evidence suggests that younger pachychoroid-associated PCV eyes more commonly have hemorrhagic presentation, increased choroidal thickness, and characteristic OCT features, including sharp-peaked pigment epithelial detachments [143].

Multimodal imaging modalities, particularly ICGA and OCT-based techniques, play an important role in the diagnosis of PCV. The EVEREST Study Group further established widely adopted diagnostic criteria for PCV based on the presence of early subretinal hyperfluorescence on ICGA together with characteristic angiographic or funduscopic features, including branching neovascular networks, pulsatile polyp filling, hypofluorescent halos, large submacular hemorrhage, or orange-red subretinal nodules [144, 145]. Where ICGA is unavailable, a combination of three OCT-based major criteria, including a sub-RPE ring-like lesion, en face OCT complex RPE elevation, and sharp-peaked pigment epithelial detachment, may support the diagnosis of PCV [146].

Typical manifestations of PCV include serous or hemorrhagic pigment epithelial detachments surrounding the polypoidal lesions and associated subretinal or intraretinal exudation [29, 147]. Polypoidal lesions are commonly located at

the margins of pigment epithelial detachments and appear as focal RPE elevations, while en face OCT may display ring-shaped hyperreflective RPE lesions in eyes without pigment epithelial detachments [147, 148]. Massive hemorrhage, including submacular and breakthrough vitreous hemorrhage, represents a vision-threatening complication of PCV [148].

Additional spectral-domain OCT findings suggestive of PCV are polypoidal lesions located within the sub-RPE space and adherent to the posterior RPE surface, along with irregular bumpy or M-shaped pigment epithelial detachment configurations, which are considered highly characteristic of the disease [149]. The double-layer sign is also commonly observed in PCV, particularly in eyes with associated serous retinal detachment and exudative activity [53]. Enhanced depth imaging OCT may further reveal peaked pigment epithelial detachments with thumbprint signs or ring-like hyperreflective structures containing hyporeflective lumens. In some cases, a double hump sign can be observed when leakage from one pigment epithelial detachment extends toward an adjacent pigment epithelial detachment. Saccular dilations may also appear as hyperreflective lesions at the RPE level on en face OCT [150].

Fundus autofluorescence imaging in PCV commonly reveals two distinct patterns: confluent hypoautofluorescence surrounded by a hyperautofluorescent ring, corresponding to polypoidal lesions, and granular hypoautofluorescence associated with the branching vascular network [151].

Anti-VEGF therapy currently represents the mainstay of treatment for PCV. Recent evidence from systematic reviews suggests that faricimab may represent a promising addition to therapeutic options for PCV, owing to its dual inhibition of VEGF-A and angiopoietin-2. Faricimab has been associated with favorable anatomical outcomes, including high rates of retinal fluid resolution, meaningful reductions in retinal and choroidal thickness, and polyp regression rates around 50%. Nevertheless, the current evidence base remains largely derived from small retrospective cohorts and short-term studies, underscoring the need for larger prospective trials and long-term comparative data to better define its role relative to established treatment strategies [152, 153]. Given the relatively limited rates of complete polyp regression achieved with anti-VEGF monotherapy, combination strategies incorporating PDT have been investigated and may provide improved anatomical outcomes in selected cases [140, 145, 154]. Recent 6-year follow-up data from the Aflibercept in PCV (PLANET) study emphasized the chronic and relapsing nature of PCV, highlighting the need for long-term retreatment and surveillance despite favorable early anatomical and visual responses [155].

Surgical intervention is rarely required in PCV but may be considered in severe hemorrhagic complications such as breakthrough vitreous hemorrhage or large submacular hemorrhage. Pars plana vitrectomy has been reported to provide visual improvement in selected eyes with vitreous hemorrhage, although induction of posterior vitreous detachment may carry an increased risk of retinal breaks. Various approaches, including intravitreal or subretinal tissue plasminogen activator combined with gas tamponade and anti-VEGF therapy, have also been used to manage large submacular hemorrhage [156, 157].

Focal thermal laser photocoagulation may also be considered in carefully selected eyes with extrafoveal or extramacular polypoidal lesions located away from the foveal center, although scar enlargement, late RPE atrophy, and recurrence remain important limitations of this approach (Figure 8) [158–160].

Key clinical studies investigating therapeutic approaches in PCV are summarized in Table 4 [145, 154, 155, 161–166].

Pachychoroid geographic atrophy

PGA is a recently identified late-stage form within the pachychoroid spectrum, characterized by focal outer retinal and RPE atrophy over pachyvessels in the absence of drusen or typical features of AMD [167].

Choroidal ischemic changes caused by choriocapillaris obliteration and pachyvessel compression may represent an important mechanism underlying retinal and choroidal dysfunction. In this context, PGA has been associated with significant choriocapillaris loss [5].

PGA differs from conventional drusen-related geographic atrophy in several respects. It tends to develop in younger, predominantly male patients, is associated with better visual function, and exhibits characteristic morphologic findings, such as smaller and frequently unifocal atrophic lesions with slower progression [167].

Differential Diagnosis

Pachychoroid spectrum disorders should be differentiated from several chorioretinal conditions with overlapping clinical and imaging features. Differentiating PNV from nAMD is clinically important, as PNV may benefit from combined PDT and anti-VEGF therapy and generally shows longer retreatment-free intervals (Table 5) [168–173].

Table 4. Landmark clinical studies evaluating therapeutic strategies for PCV

Author (Year)	Study	n	Follow-up	Treatment Arms	Outcomes	Main Findings	Clinical Implications
Koh et al. (2012) [145]	EVEREST	61	6 months	-PDT + ranibizumab (3+PRN) -PDT monotherapy -Ranibizumab monotherapy(3+PRN)	-Polyp regression -BCVA -CST -Leakage on FA -Safety	-Complete polyp regression was higher with combination therapy (77.8%) and PDT alone (71.4%) than with ranibizumab alone (28.6%). -Mean BCVA gain was +10.9, +7.5, and +9.2 letters. -Mean CST reduction was −145.6 μm, −98.1 μm, and −65.7 μm.	PDT-containing regimens achieved superior anatomical outcomes in PCV.
Koh et al. (2017) [154]	EVEREST-II	322	12 months	-PDT + ranibizumab (3+PRN) -Ranibizumab monotherapy (3+PRN)	-Polyp regression -BCVA -CST -Treatment burden -Safety	-Mean BCVA gain was significantly greater with combination therapy (+8.3 vs +5.1 letters). -Complete polyp regression was significantly higher with combination therapy (69.3% vs. 34.7%). -Median ranibizumab injections were lower with combination therapy (4 vs. 7).	Combination therapy improved visual and anatomical outcomes with lower treatment burden.
Lee et al. (2018) [161]	PLANET	318	52 weeks	-Aflibercept 2 mg monotherapy (3+Q8) -Aflibercept 2 mg + rescue PDT	-BCVA -CST -Polyp regression -Rescue treatment -Safety	-Mean BCVA gain at week 52 was +10.7 and +10.8 letters. -Complete polyp regression occurred in 38.9% and 44.8% of eyes. -Rescue PDT was required in 12.1% and 14.3%	Aflibercept monotherapy yielded favorable outcomes in most PCV patients without routine PDT.
Lim et al. (2020) [162]	EVEREST-II	322	24 months	-PDT + ranibizumab (3+PRN) -Ranibizumab monotherapy (3+PRN)	-BCVA -Polyp regression -CST -Leakage on FA -Treatment burden -Safety	-Mean BCVA gain at month 24 was +9.6 vs. +5.5 letters. -Complete polyp regression occurred in 56.6% vs. 26.7% of eyes. -Median number of ranibizumab injections was 6 vs. 12.	Combination therapy with ranibizumab and PDT provided greater visual gain, higher polyp regression, and fewer injections than ranibizumab monotherapy.
Yanagi et al. (2025) [163]	EVEREST II Japanese subgroup analysis	20	6 years	-PDT + ranibizumab (3+PRN) -Ranibizumab monotherapy (3+PRN)	-BCVA -CST -Treatment burden -Treatment pattern -PDT exposure -Safety	-BCVA remained stable through year 6 (67.2 letters). -Mean CST decreased to 255 μm at year 6. -Proactive anti-VEGF regimens were more common in Japanese patients.	Long-term proactive anti-VEGF treatment, particularly fixed or T&E regimens, was associated with sustained visual and anatomical outcomes over 6 years in PCV.
Lee et al.† (2025) [164]	SALWEEN	135	16 weeks	-Faricimab 6 mg monotherapy (4+T&E)	-BCVA -CST -IRF/SRF resolution -Polyp regression -Safety	-Mean BCVA gain at week 16 was +7.8 letters. -Mean CST reduction was −144.6 μm. -IRF/SRF absence was achieved in 80.3% of eyes. -Complete polyp regression occurred in 51.0% of eyes. -No new safety concerns were identified.	Faricimab was associated with rapid visual and anatomical improvements during the loading phase, early regression of polypoidal lesions, and no new safety concerns through week 16 in this single-arm study.
Teo et al. (2026) [155]	PLANET Long-term outcomes	72	6 years	-Aflibercept 2 mg monotherapy (3+Q8) -Aflibercept 2 mg + rescue PDT	-BCVA -CST -Polyp persistence -Treatment burden	-BCVA improved by +14.6 letters at year 2 but declined to baseline by year 6. -Mean CST measured 261.2 μm at year 6. - 10.2 mean injections during years 2–6.	Long-term disease control remained challenging despite initial favorable outcomes.
Lee et al. (2026) [165]	PULSAR PCV subgroup analysis	139	48 weeks	-Aflibercept 8 mg monotherapy (3+Q12W) -Aflibercept 8 mg monotherapy (3+Q16W) -Aflibercept 2 mg monotherapy (3+Q8W)	-BCVA -CST -Polyp regression -Polyp inactivity -Treatment durability -Safety	-Mean BCVA gain at week 48 was +9.5 letters (8 mg Q12W), +8.4 letters (8 mg Q16W), and +9.1 letters (2 mg Q8W). -Mean CST reductions were −159, −152, & −161 μm. -Complete polyp regression occurred in 37%, 47%, and 38% of eyes. -Inactive polypoidal lesions occurred in 69–71% of eyes across treatment groups. -87% maintained ≥12-week intervals through week 48 with aflibercept 8 mg. -Mean injection numbers were 6.1, 5.1, and 7.0.	High-dose aflibercept (8 mg) achieved visual and anatomical outcomes comparable to standard-dose aflibercept while substantially extending treatment intervals, supporting its use as a durable monotherapy option for PCV.
Lai et al.* (2026) [166]	SALWEEN	135	48 weeks	-Faricimab 6 mg monotherapy (4+T&E)	-BCVA -CST -IRF/SRF resolution -Polyp regression -Polyp inactivity -Durability -Safety	-Mean BCVA gain over weeks 40–48 was +8.9 letters. -Mean CST reduction over weeks 40–48 was −126.5 μm. -Absence of IRF/SRF was achieved in 76.4% of eyes at week 48. -Complete polyp regression occurred in 61% of eyes, and inactive polypoidal lesions were observed in 86%. -At week 48, 53.2% of patients were assigned to Q20W dosing. -Median injections through week 48 were 6.	Faricimab monotherapy was associated with substantial visual and anatomical improvements, high rates of polyp inactivation and regression, and assignment to extended dosing intervals through week 48 in this single-arm study; controlled comparative data are required to establish its relative effectiveness in PCV.

Abbreviations: PCV, polypoidal choroidal vasculopathy; PDT, photodynamic therapy; PRN, pro re nata; BCVA, best corrected visual acuity; CST, central subfield thickness; FA, fluorescein angiography; T&E, treat and extend; VEGF, vascular endothelial growth factor; IRF, intraretinal fluid; SRF, subretinal fluid. Note: Treatment regimen abbreviations: 3+PRN, three initial monthly loading injections followed by pro re nata treatment; 3+Q8W, three initial monthly loading injections followed by fixed dosing every 8 weeks; 3+Q12W, three initial monthly loading injections followed by fixed dosing every 12 weeks; 3+Q16W, three initial monthly loading injections followed by fixed dosing every 16 weeks; 4+T&E, four initial monthly loading injections followed by a treat-and-extend regimen. EVEREST, Efficacy and Safety of Verteporfin Photodynamic Therapy in Combination with Ranibizumab or Alone Versus Ranibizumab Monotherapy in Patients with Symptomatic Macular Polypoidal Choroidal Vasculopathy; PLANET, Study of Intravitreal Aflibercept Injection in Patients With Polypoidal Choroidal Vasculopathy; SALWEEN, Study Assessing the Efficacy, Durability, and Safety of Faricimab in Patients With Polypoidal Choroidal Vasculopathy; PULSAR, Intravitreal Aflibercept 8 mg in Patients With Neovascular Age-Related Macular Degeneration. †Conference abstract presented at the Association for Research in Vision and Ophthalmology Annual Meeting, Salt Lake City, Utah, May 4 to 8, 2025, and published in *Investigative Ophthalmology & Visual Science*. *Conference abstract presented at the Association for Research in Vision and Ophthalmology Annual Meeting, Denver, Colorado, May 3 to 7, 2026, and published in *Investigative Ophthalmology & Visual Science*.

While both PNV and type 1 nAMD share sub-RPE neovascularization, they differ in their underlying pathogenesis and structural context. PNV is typically observed in the absence of significant drusen and is associated with pachychoroid-related changes identifiable on multimodal imaging. Several structural OCT features may further support the diagnosis of pachychoroid-associated neovascularization, including sharp-peaked and inhomogeneous pigment epithelial detachments, reduced choroidal shadowing, and the presence of a hyporeflective halo on infrared en face imaging [173]. In contrast, type 1 nAMD develops in a drusen-rich degenerative environment, where RPE dysfunction and complement-mediated pathways play a central role [54]. Despite advances in multimodal imaging, pachychoroid-associated neovascularization may still be misclassified as nAMD, particularly in older individuals with exudative macular neovascularization [174]. These pathophysiological differences may also influence the origin of exudation. Consequently, unlike AMD, subretinal fluid in PNV may result from exudation related not only to the neovascular complex itself but also to the underlying pachyvessels [115].

The pigmentary changes associated with PPE may create a clinical appearance similar to that of age-related maculopathy, pattern dystrophy, or non-neovascular AMD. In contrast to non-neovascular AMD, however, PPE usually affects younger patients and tends to remain relatively asymptomatic [4, 175].

Certain drug-induced retinopathies may closely simulate CSC. Fibroblast growth factor receptor inhibitor-associated retinopathy, particularly with erdafitinib therapy, has been reported to produce bilateral multifocal serous retinal detachments with a pseudo-CSC phenotype, highlighting the importance of careful medication history in atypical cases (Figure 9) [176].

Bullous or atypical CSC may also mimic inflammatory chorioretinal disorders, particularly Vogt-Koyanagi-Harada disease and posterior scleritis, owing to the presence of extensive exudative retinal detachment and multifocal leakage on angiography [94].

Uveal effusion syndrome should also be considered in the differential diagnosis, particularly in cases presenting with extensive exudative retinal detachment or atypical pachychoroid features. Although classically associated with scleral thickening and impaired vortex vein outflow, type III uveal effusion syndrome may exhibit overlapping pachychoroid features, including choroidal thickening and dilated outer choroidal vessels [177].

Rare vascular anomalies should also be considered in atypical cases. Choroidal macrovessel may produce focal choroidal thickening, attenuation of the choriocapillaris, and secondary RPE alterations that resemble pachychoroid disease on multimodal imaging [178].

Table 5. Differential diagnosis of PNV and type 1 nAMD based on findings reported in the literature [168–173]

Feature	PNV	Type 1 nAMD
Age	Typically younger patients	Typically older patients
Prior CSC history	Frequently present	Typically absent
Soft drusen	Typically absent	Common
Pachydrusen	Frequently present	Rare
Pachyvessels	Characteristic finding	Usually absent
Choroidal thickness	Increased	Normal or reduced
Choroidal vascularity index	Generally higher	Generally lower
Choroidal vascular hyperpermeability	Common	Less common
Intervortex anastomoses	Common	Rare
PED morphology	Sharper, steep	Flatter fibrovascular
OCTA morphology	Immature/lacy network	Mature trunk morphology
VEGF levels	Generally lower	Generally higher
Anti-VEGF response	Often requires fewer injections but may show persistent fluid in some cases	Typically demonstrates an initial favorable response, although long-term treatment burden remains substantial
PDT role	Frequently considered as adjunctive therapy	Limited role in routine management

Abbreviations: nAMD, neovascular age-related macular degeneration; PNV, pachychoroid neovasculopathy; CSC, central serous chorioretinopathy; PED, pigment epithelium detachment; OCTA, optical coherence tomography angiography; VEGF, vascular endothelial growth factor; PDT, photodynamic therapy.

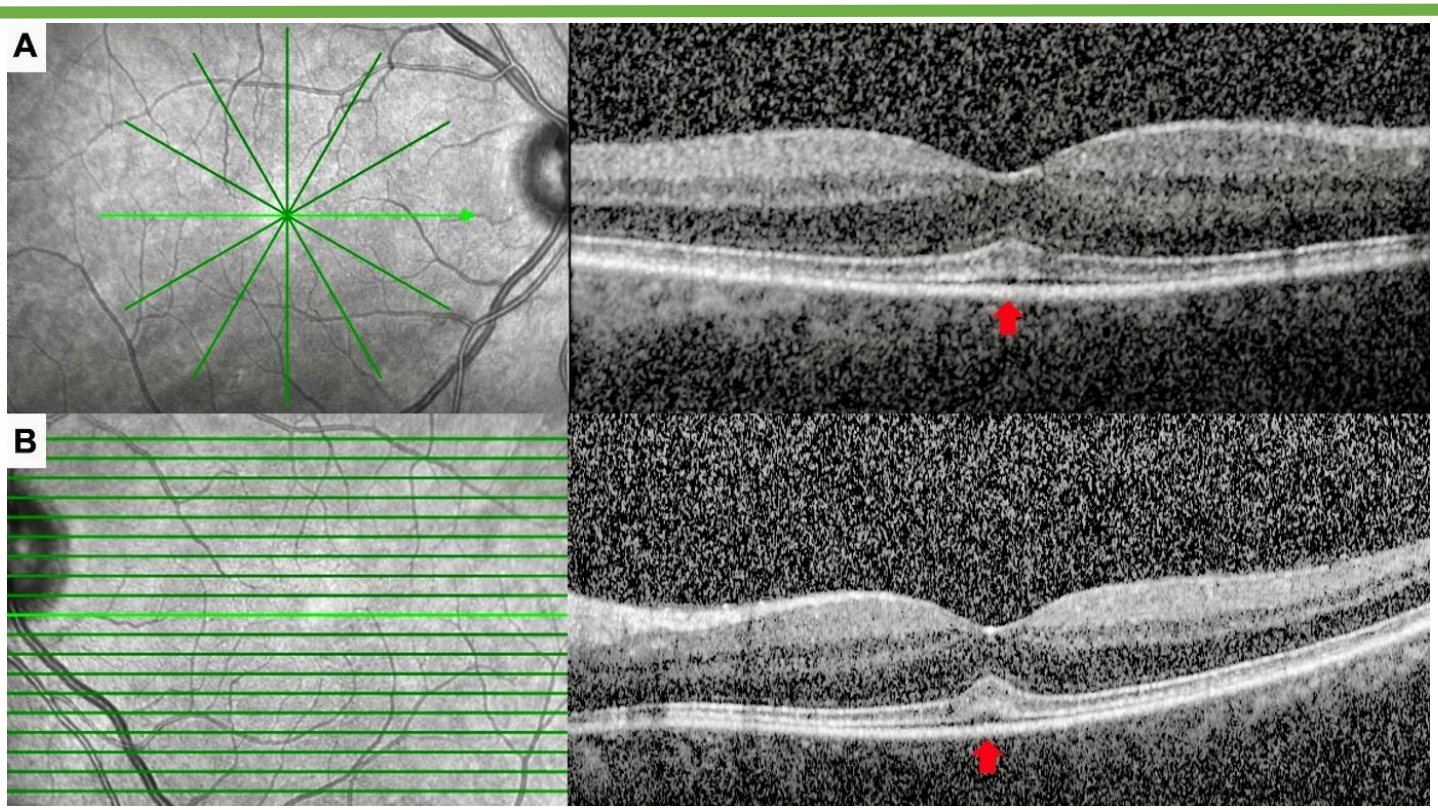

Figure 9. Spectral-domain optical coherence tomography findings (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) in a 65-year-old male patient receiving erdafitinib therapy for the treatment of metastatic urothelial carcinoma. Transfoveal scans of the right (A) and left (B) eyes showing shallow bilateral serous neurosensory retinal detachments associated with subtle retinal pigment epithelium irregularities (red arrows).

Current Role of Photodynamic Therapy in Pachychoroid Spectrum Disorders

Although treatment strategies differ across pachychoroid spectrum disorders (Table 6) [29, 107, 152, 179, 180], PDT has gained a central role in the management of several pachychoroid-associated conditions, particularly chronic CSC and selected cases of PNV and PCV [181].

PDT is a treatment modality that combines light irradiation with a photosensitizing agent. Following systemic administration, the photosensitizer preferentially accumulates within target pathological tissues. Subsequent exposure to light of a specific wavelength activates the agent, leading to the generation of reactive oxygen species and singlet oxygen, which selectively damage abnormal tissues [182].

Verteporfin received initial FDA approval in 2000 for the treatment of predominantly classic subfoveal choroidal neovascularization due to AMD [183]. Its approved US indications subsequently included predominantly classic subfoveal choroidal neovascularization due to pathologic myopia and presumed ocular histoplasmosis [184]. Since then, its off-label use has expanded to include several pachychoroid-related disorders, particularly CSC and PCV, as well as choroidal hemangioma [185]. In PDT, verteporfin serves as the photosensitizing agent and preferentially localizes to abnormal vascular endothelial tissue via low-density lipoprotein receptors. Subsequent irradiation with 689-nm near-infrared light activates verteporfin, leading to photochemical injury, vascular thrombosis, and selective vessel occlusion [186].

Conventional PDT consists of intravenous administration of verteporfin at 6 mg/m² body surface area over 10 minutes, followed 15 minutes later by application of 689-nm near-infrared laser light to the treatment area for 83 seconds at a fluence of 50 J/cm² [187].

Although PDT is generally considered safe and effective, treatment-related complications such as choroidal ischemia, RPE atrophy, and secondary macular neovascularization may occasionally occur [188, 189]. To improve PDT safety and tolerability, modified protocols have been developed, including half-fluence PDT with reduced light energy, half-dose PDT with reduced verteporfin, and half-time PDT with shorter irradiation [181, 187].

Either half-dose or half-fluence PDT is widely regarded as one of the most effective treatment options for chronic CSC [181]. Comparative studies evaluating half-dose and half-fluence PDT have yielded inconsistent results. While some reports suggest more rapid and sustained subretinal fluid resolution with half-dose PDT, others have shown comparable anatomical and functional outcomes between the two protocols [190–192].

Table 6. Current therapeutic approaches in pachychoroid spectrum diseases [29, 107, 152, 179, 180]

Pachychoroid disease subtype	Observation	Anti-VEGF	PDT	Laser	Other
PPE	Main approach	Not routinely indicated	Not routinely indicated	Not routinely indicated	-
Acute CSC	First-line	Limited role	Not routinely indicated	Focal laser photocoagulation for extrafoveal leakage sites	Risk factor modification and corticosteroid avoidance
Chronic CSC	Selected stable cases	Primarily when associated with MNV	Preferred treatment modality	Subthreshold micropulse laser in selected cases	Photobiomodulation (investigational)
PNV	Generally not appropriate	First-line treatment	Adjunctive therapy in selected cases	Limited role	Monitoring with long-term multimodal imaging
PCV	Rarely appropriate	First-line treatment	Adjunctive therapy in selected cases	Occasionally considered for extrafoveal lesions	Surgical displacement strategies for large submacular hemorrhage; vitrectomy for breakthrough vitreous hemorrhage
PGA	Main approach	No established role	No established role	No established role	-

Abbreviations: VEGF, vascular endothelial growth factor; PDT, photodynamic therapy; PPE, pachychoroid pigment epitheliopathy; CSC, central serous chorioretinopathy; MNV, macular neovascularization; PNV, pachychoroid neovasculopathy; PCV, polypoidal choroidal vasculopathy; PGA, pachychoroid geographic atrophy.

PDT appears to be most effective in eyes with pachyvessels associated with increased choroidal thickness and sustained hyperpermeability [181]. In contrast, its efficacy may be limited in eyes with thinner choroid, where it may also increase the risk of choroidal ischemia [181]. Key imaging markers, such as increased choroidal thickness and the presence of subretinal fluid on OCT, as well as leakage identified on ICGA, can guide the selective use of PDT in clinical practice [1].

PDT was previously considered the standard treatment for PCV and was shown to provide short-term visual stabilization and polyp regression [132]. Nevertheless, recurrence remained common because of persistent branching neovascular networks and recurrent lesion activity, while severe complications including subretinal hemorrhage and RPE tears were occasionally observed. With the introduction of anti-VEGF agents, therapeutic approaches increasingly evolved toward anti-VEGF monotherapy and combination therapy with PDT [181, 193].

Major randomized trials, including EVEREST and PLANET, further evaluated the role of PDT in PCV management. While the EVEREST studies demonstrated superior polyp regression and improved outcomes with combination of PDT and ranibizumab therapy compared with anti-VEGF monotherapy, repeat PDT was generally administered at intervals of at least 3 months in the EVEREST II protocol. In contrast, the PLANET study suggested limited additional benefit of rescue PDT when aflibercept was used [145, 154, 160, 161].

Given the dual pathophysiological components of PNV, including choroidal vascular hyperpermeability and type 1 neovascularization, combination therapy with PDT and anti-VEGF agents has been proposed as a rational treatment strategy. Several retrospective studies have yielded favorable anatomical and visual outcomes with combined therapy, along with reduced retreatment requirements [127, 194, 195].

Ongoing global verteporfin shortages have stimulated interest in alternative laser-based strategies that eliminate the need for exogenous photosensitizers. Preliminary studies evaluating 689-nm laser application without verteporfin, described as no-dose PDT or photostatic therapy, have shown promising anatomical and functional outcomes in chronic CSC. These approaches are hypothesized to exert therapeutic effects through photobiomodulatory and subthreshold thermal mechanisms targeting the RPE and choroid, rather than through conventional verteporfin-mediated photochemical reactions [179, 196]. Nevertheless, current evidence remains limited and largely exploratory, warranting further prospective controlled investigations before widespread clinical adoption.

The present review has several strengths. It provides a comprehensive and up-to-date overview of the pachychoroid

disease spectrum by integrating recent advances in pathophysiological mechanisms, multimodal imaging, and evolving treatment strategies into a unified clinical perspective. In addition to summarizing the current evidence, it incorporates landmark studies that established the fundamental concepts of the pachychoroid spectrum, thereby providing historical context alongside recent developments. Furthermore, the inclusion of representative multimodal imaging examples enhances the clinical applicability of the review by facilitating the recognition and interpretation of characteristic imaging findings. This review also has several limitations. First, it is a narrative rather than a systematic review, which may introduce selection bias in the included literature. Second, the literature search was restricted to English-language publications and limited to PubMed/MEDLINE, supplemented by Google Scholar, which may have led to the exclusion of relevant studies indexed in other databases or published in non-English languages. Third, although recent studies were prioritized and selected earlier landmark studies were included, the nonsystematic study-selection process may have resulted in omission of other relevant foundational studies. In addition, heterogeneity in imaging modalities, diagnostic criteria, and disease definitions across studies limits direct comparability of findings. Finally, several aspects of pachychoroid pathophysiology remain based on observational imaging studies rather than experimentally validated mechanisms.

Directions ahead: Future research should focus on establishing standardized diagnostic criteria for pachychoroid spectrum disorders, particularly incorporating quantitative imaging biomarkers such as choroidal vascular index and vortex vein mapping. Longitudinal multimodal imaging studies are needed to clarify disease progression pathways, especially the relationship between CSC, PNV, and PCV. Artificial intelligence-based image analysis may enable earlier detection of subclinical disease and improve risk stratification [197, 198]. Improved understanding of scleral biomechanics and venous outflow resistance may provide novel therapeutic targets [3, 41, 42]. Prospective clinical trials are required to evaluate emerging therapies such as photobiomodulation and verteporfin-free PDT protocols [196, 199].

CONCLUSIONS

Pachychoroid disorders are increasingly recognized as manifestations of a broader syndrome of choroidal vascular dysregulation characterized by venous overload, vascular remodeling, and progressive dysfunction of the choriocapillaris-RPE complex. Advances in multimodal imaging have substantially refined the current understanding of pachychoroid disease by revealing previously unrecognized alterations involving vortex vein remodeling, choroidal hyperpermeability, and subclinical neovascularization. At the same time, modified PDT protocols continue to refine management strategies for selected patients, while emerging noninvasive modalities remain investigational. As knowledge of pachychoroid disease continues to evolve, improved phenotypic characterization and deeper insight into choroidal hemodynamics may ultimately facilitate more individualized diagnostic and therapeutic approaches.

ETHICAL DECLARATIONS

Ethical approval: Ethical approval was not required for this narrative review. All clinical images were obtained from our unit's patient archives, and informed consent for publication of the deidentified images and accompanying clinical information was obtained from all patients.

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