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Management of polypoidal choroidal vasculopathy: Malaysian Consensus Guideline 2023

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Abstract

• The aim for this study was to develop consensus terminology, diagnostic criteria of multimodal imaging and develop a guideline for management of polypoidal choroidal vasculopathy (PCV). A systematic consensus process was conducted to develop updated clinical recommendations for the management of PCV. In order to develop the guidelines, a panel of ten PCV experts nationwide reviewed current evidence, focusing on key randomized controlled trials (EVEREST-II and PLANET), and conducted a systematic literature search to inform the guidelines. Several draft recommendations were evaluated and improved to determine the strength and quality of evidence. Consensus was defined as ≥90% agreement achieved, with multiple voting rounds if needed. The finalized guidelines incorporate the most recent evidence available up to November 30, 2023. The panelists reached an agreement on several aspects of PCV management, including the need for diagnostic criteria, classification, various treatment options and the development of a treatment algorithm. Recommendations are made for the clinical management of PCV based on a professional assessment of current evidence.

• **KEYWORDS:** polypoidal choroidal vasculopathy; anti-vascular endothelial growth factor; photodynamic therapy; surgery

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INTRODUCTION

Polypoidal choroidal vasculopathy (PCV) is a subtype of neovascular age-related macular degeneration (nAMD). It is caused by inner choroidal vessel abnormalities, *i.e.*, multiple, small, polyp-shaped aneurysms that in turn, are caused by defective vascular lining. PCV causes chronic and progressive degenerative changes in the central retina that can lead to blindness or vision loss[1].

PCV is more common in Asian populations, ranging up to 24.5%–54.7% of all nAMD cases, compared with 10%–20% in Caucasian populations[2-3]. A study in 2021 estimated that, by 2050 about 1.5 billion people aged 65 or above will be at risk of developing nAMD and PCV[4]. Risk factors include smoking, alcohol consumption, cardiovascular and metabolic disorders, including hypertension, diabetes, hyperlipidemia,

and elevated C-reactive protein[5]. Smoking is found to increase risk of PCV and nAMD by four-fold while diabetes showed a higher prevalence in nAMD than PCV[6].

nAMD is well described in the Caucasian population. nAMD epidemiology, pathogenesis, clinical presentation, and treatment in Asians, however, has been suggested to differ from the Western terminology of this disease. Western populations were more likely to have choroidal neovascularization secondary to age-related macular degeneration (CNV-AMD) than Asian populations, where PCV appears to be the most common subtype of exudative nAMD[1]. Genetic studies have also revealed differences in genetic determinants of each subtype[1].

The primary goal in the treatment of PCV is to achieve the best visual outcome and to minimise treatment burden[7-10]. Current treatment options for PCV include intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections, combination treatment with photodynamic therapy (PDT), laser photocoagulation and surgery for breakthrough vitreous hemorrhage (VH). Determining the optimal timing and best treatment choices remains challenging due to the significant heterogeneity in clinical presentation. Few evidence-based clinical practices guidelines for PCV patients have focused on comprehensive treatment strategies however, the Malaysia Guideline Consensus attempt to determine the latest treatment modalities which are more relevant to Malaysian population. Therefore, the aim of this paper is to develop consensus terminology of PCV, diagnostic criteria of PCV and develop guideline for management of PCV in Malaysia population.

MATERIALS AND METHODS

In early 2023, a committee consisted of ten Malaysian retina physicians with one external reviewer convened together to discuss current findings and developed a consensus guideline for PCV treatment in relation to international standard of practice. The members were selected from all over Malaysia and selections were based on their experiences in managing nAMD and PCV.

Contextualization of Recommendations in the Absence of Local Data Given the limited availability of comprehensive Malaysian epidemiological, genomic, and real-world outcome data for PCV, a structured contextualization framework was applied to ensure that recommendations were both evidence-informed and feasible within the Malaysian healthcare setting.

Evidence Appraisal and Hierarchical Prioritization Evidence synthesis prioritized high-quality randomized controlled trials (RCTs) and Meta-analyses, followed by multicentre prospective cohort studies and regional Asian subgroup analyses. In absence of Malaysian data, the external validity of international studies was critically assessed before extrapolation with consideration given to population characteristics, baseline lesion profiles, treatment protocols, and outcome measures.

Regional Adaptation Based on Asian Cohort Data Recognizing the higher prevalence and distinct phenotypic characteristics of PCV in Asian populations, evidence from East and Southeast Asian cohorts was preferentially considered when available. This approach aimed to improve translatability by minimizing population-level biological heterogeneity.

Panel deliberations explicitly evaluated differences in polyp morphology, branching vascular network (BVN) patterns, treatment responses to anti-VEGF monotherapy versus combination therapy and recurrence patterns reported in Asian datasets.

Healthcare System Feasibility Assessment Recommendations were further refined through structured assessment of Malaysian healthcare context including the availability of indocyanine green angiography (ICGA), access to optical coherence tomography (OCT) angiography and capacity for PDT, variations between public and private sector pathways, and the feasibility of treatment regimens within resource-limited constrained settings. This process ensure that the proposed diagnostic and management algorithms are applicable across diverse clinical environments.

Drug Accessibility and Regulatory Considerations Therapeutic recommendations were limited to agents approved by the Malaysian regulatory authority and reasonably accessible within the national healthcare system. Considerations regarding drug availability, cost, and reimbursement mechanisms were incorporated during the consensus process to ensure that recommended therapies remain practical for clinical use.

Consensus Integration and Transparency In areas where high-level evidence was lacking, structured expert consensus was employed through iterative panel discussions to reconcile available evidence with local clinical realities. The strength of each recommendation reflects both quality of evidence and its feasibility for implementation. This transparent contextualization process clarifies how international evidence was adopted to the Malaysian setting while acknowledging areas where further local validation is required.

Target Audience and Scope The purpose of this guideline is to offer evidence-based recommendations for the clinical management of PCV. It is intended for use by all healthcare professionals involved in the care of patients with PCV within the Malaysian population.

Consensus Meetings A standardized framework for the consensus process was established by the committee, including a comprehensive review of current literature and a systematic evaluation of the available evidence pertaining to the management of PCV. A consensus meeting was convened in Kuala Lumpur on February 26, 2023. During this session,

clinical recommendations were deliberated and finalized based on consensus or the best achievable majority opinion, facilitated through anonymous voting.

Prior to the main meeting, a pre-panel consisting of four experts was assembled to formulate draft recommendations. These were informed by the findings of two large multicentre RCTs EVEREST-II[11] and PLANET[11] study and were subsequently refined for group discussion.

A systematic search from electronic databases namely PubMed and Cochrane Library was performed for the period between June and August 2023 to identify relevant literature using a predefined set of search terms: “polypoidal choroidal vasculopathy”, “diagnosis”, “classification”, “laser”, “verteporfin”, “photodynamic”, “PCV”, “bevacizumab”, “ranibizumab”, and “anti-VEGF”. Articles published in English and accompanied by an abstract were included. Full-text articles were retrieved and manually screened to exclude duplicates, review articles, case reports, and studies deemed insufficiently relevant. Ultimately, a total of 34 primary studies were selected to inform the evidence for guideline development.

Three preliminary recommendation statements and one treatment algorithm were developed prior to the meeting, guided by contemporary clinical guidelines and emerging therapeutic trends. The Grading of Recommendations Assessment, Development and Evaluation Working Group methodology was adapted to assess both the strength (strong or weak) and the quality (high, moderate, or low) of each recommendation. These evaluations considered study design, sample size, methodological quality, consistency of findings, and magnitude of treatment effects. In general, a strong recommendation means the panel believes the benefits clearly outweigh any risks or burdens, and most doctors and patients would likely follow it. A weak recommendation means the benefits still outweigh the risks, but the difference is smaller or the evidence is not as strong. Whether to follow a weak recommendation may depend on the patient’s condition or preferences. To rate the quality of the evidence, the panel observed a few criteria such as the type and number of studies, their size, how strong the results were, and whether the findings were consistent.

Consensus was defined as agreement by ≥90% of participating panel members. In instances where consensus was not initially achieved, iterative discussions were conducted, and recommendations were modified accordingly, followed by subsequent voting rounds. Each statement was thoroughly discussed and finalized through verbal consensus. The final set of recommendations reflects the integration of updated evidence, with literature searches conducted through November 30, 2023.

RESULTS

A total of 8987 titles and abstracts were screened for inclusion. Of these, 8875 reports were excluded. We retrieved a total of 112 full texts for inclusion. We further excluded 78 full texts based on our criteria, of which 34 primary studies were included.

The consensus recommendations for the diagnostic criteria, classification, treatment options, and a treatment algorithm of PCV are summarized below.

Criteria for Diagnosis Diagnosis of PCV is primarily based on clinical features, fundus examination, and OCT findings. However, ICGA, which remains the gold standard imaging modality, provides additional multimodal imaging features that support and confirm the diagnosis through comparison of characteristic angiographic findings. ICGA enables direct visualization of the characteristic polypoidal lesions and BVN within the choroidal circulation. In contrast, OCT provides structural features that may suggest the presence of PCV and can support the diagnosis when ICGA is unavailable, but these findings are not considered definitive without angiographic confirmation.

Figure 1 illustrates the fundus features[2-3,11-13], while Figures 2 and 3 present the OCT features[2] and Figure 4 demonstrates the ICGA features[3,11,14]. OCT is an emerging methodology for diagnosis of PCV. Major OCT features include a sharply peaked pigment epithelial detachment (PED), sub-retinal pigment epithelium (sub-RPE) ring-like lesions corresponding to polypoidal structures, and en face OCT detected complex RPE elevation. Minor features include complex or multilobular PED (hyper reflective ring within the PED), the double layer sign [separation between the RPE and Bruch’s membrane indicating a BVN, subretinal fluid (SRF), and intraretinal fluid (IRF)]. While ICGA remains the reference standard, these OCT characteristics provide valuable diagnostic guidance, particularly in settings where ICGA is unavailable. Further studies using OCT are needed to develop standardized diagnostic algorithms for PCV[2].

Interrater agreement, sensitivity, specificity, positive predictive value, and negative predictive value for individual and combined features based on the study by Cheung *et al*[2] are depicted in Tables 1, 2, and 3. These findings were discussed during a meeting to reach consensus on diagnosis criteria.

Individual imaging features demonstrated variable sensitivity and specificity, whereas diagnostic accuracy improved substantially when features were combined, as reflected by area under the receiver operating characteristic curve (AUROC) analysis. Among individual features, diagnostic performance varied considerably, with some features demonstrating limited specificity. In contrast, when combining the three major OCT features namely sharply peaked PED, sub-RPE ring-like

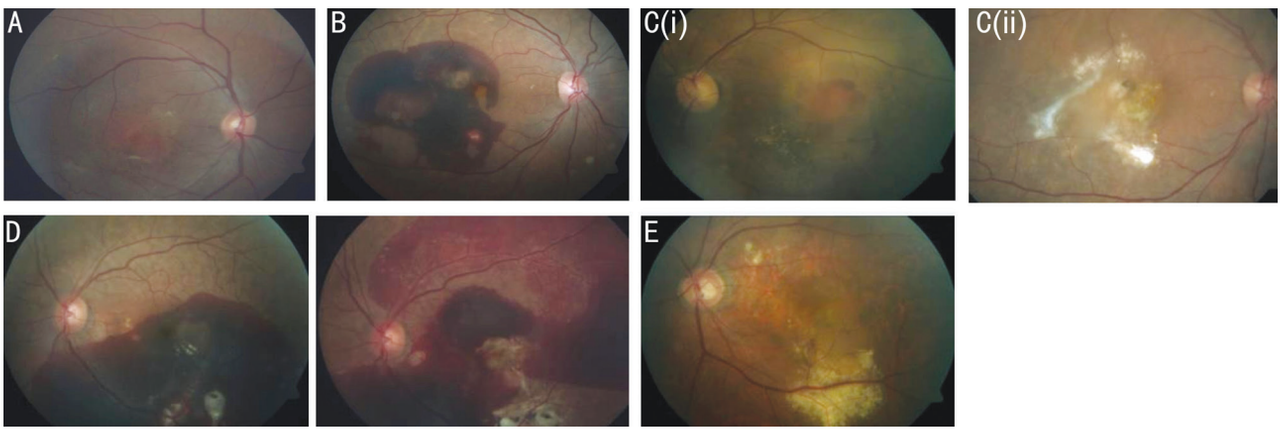

Figure 1 Fundus features A: Reddish orange sub retinal nodules; B: Hemorrhagic pigment epithelial detachment (PED); C: Serosanguinous PED (i) and serous PED (ii); D: Extensive spontaneous submacular hemorrhage (SMH); E: Exudation disproportionate to size of lesion.

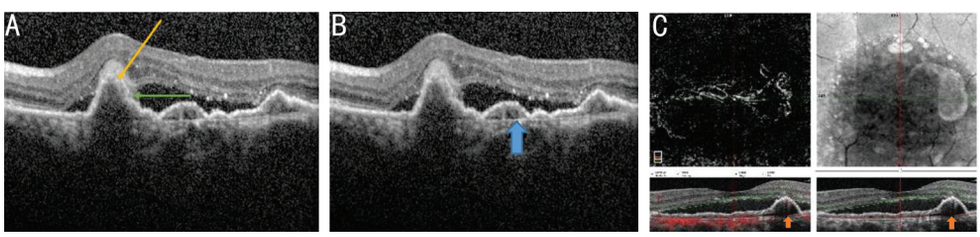

Figure 2 Optical coherence tomography (OCT) features (major criteria) A: Sharp peaked pigment epithelial detachment (PED), tall, right angled PED (orange arrow), Notch (green arrow); B: Sub retinal pigment epithelium (RPE) ring-like lesion (corresponding to polyp; blue arrow); C: En face OCT complex RPE elevation (orange arrow).

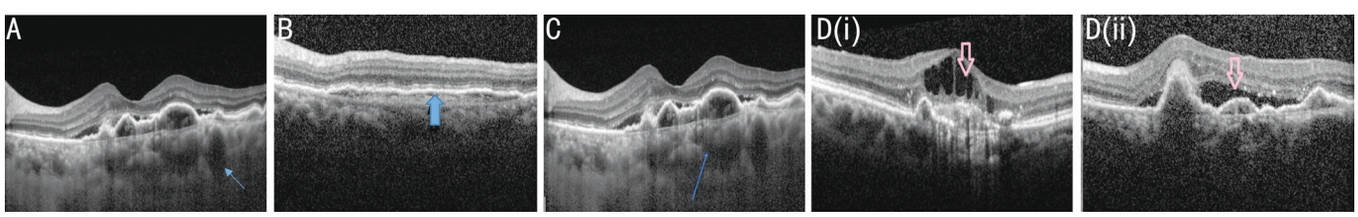

Figure 3 Optical coherence tomography features (minor criteria) A: Complex or multilobular pigment epithelial detachment (PED), hyper reflective ring within the PED (blue arrow); B: Double layer sign (blue arrow); C: Thick choroid with dilated Haller's layer vessels (blue arrow); D: Fluid compartment; D (i): Intraretinal fluid (IRF; pink arrow); D (ii): Subretinal fluid (SRF; pink arrow).

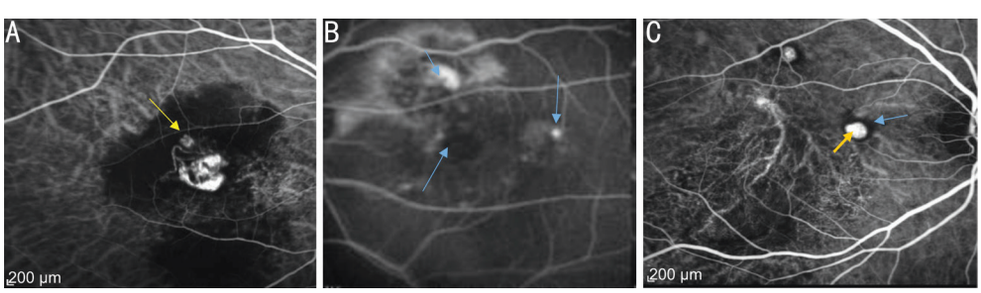

Figure 4 ICGA features (gold standard) A: BVN (yellow arrow); B: Pulsatile filling of polyp, cluster of polyps on ICGA (blue arrow); C: Hypo-fluorescence halo surrounding the focal hyper-fluorescence, hypo-fluorescence halo (blue arrow) around early nodular hyper-fluorescence (yellow arrow) on stereo-ICGA. In cases where initial ICGA features are not conclusive, the ICGA test should be repeated. For clarity, fundus findings such as orange-red sub retinal nodules or SMH are clinical features suggestive of PCV and may prompt further evaluation; however, they are not ICGA-derived features. Definitive ICGA features include focal early hyper-fluorescence polypoidal lesions, BVNs, and characteristic nodular hyper-fluorescence with late-phase washout. ICGA: Indocyanine green angiography; BVN: Branching vascular network; SMH: Submacular hemorrhage; PCV: Polypoidal choroidal vasculopathy.

lesion, and en face OCT complex RPE elevation the diagnostic accuracy improved substantially, achieving an AUROC of 0.90.

Classification PCV can been classified by its location on ICGA, the subtype as well as clinical features[3] namely by location such as 1) macular which can be present at subfovea

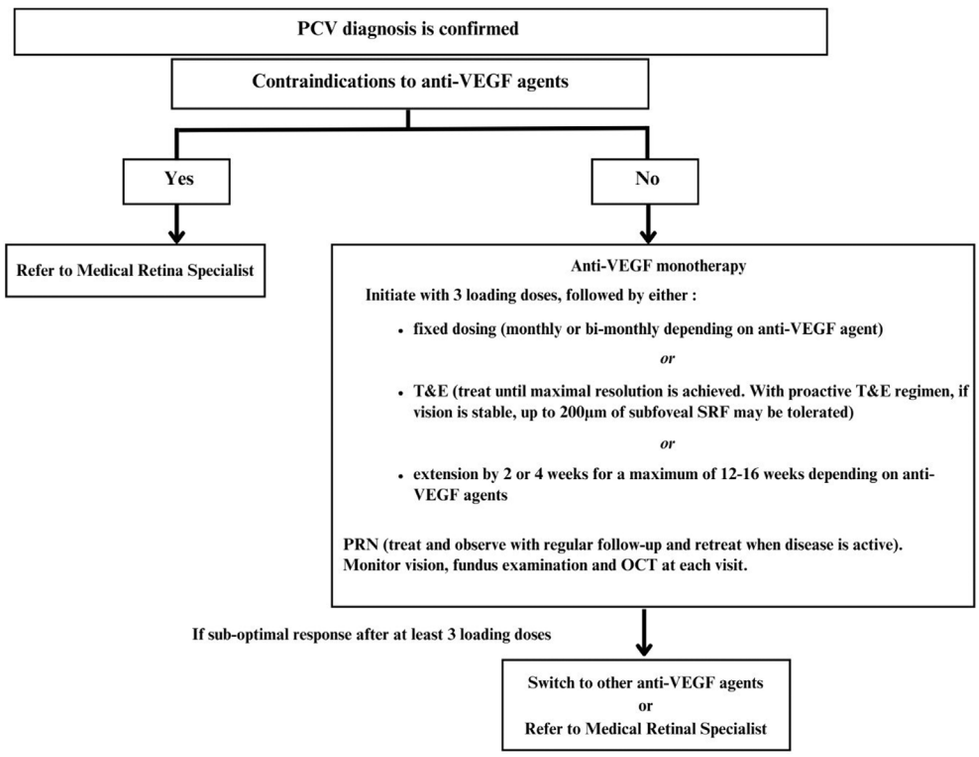

Figure 5 Treatment algorithm for PCV Anti-VEGF: Anti-vascular endothelial growth factor; PCV: Polypoidal choroidal vasculopathy; T&E: Treat-and-extend; SRF: Subretinal fluid; PRN: *Pro re nata*; OCT: Optical coherence tomography.

Table 1 Diagnostic performance of individual imaging features %

Features	Sensitivity	Specificity	PPV	NPV
Sharply peaked PED	78	85	82	81
Sub-RPE ring-like lesion	72	88	84	77
Double-layer sign	80	70	75	76
Multilobular PED	65	82	79	69
SRF	85	50	68	72
IRF	60	55	58	57

PPV: Positive predictive value; NPV: Negative predictive value; PED: Pigment epithelial detachment; RPE: Retinal pigment epithelium; SRF: Subretinal fluid; IRF: Intraretinal fluid.

Table 2 Diagnostic performance of individual fundus and OCT features

Features	Sensitivity	Specificity	PPV	NPV
Sub-RPE ring-like lesion	0.81	0.87	0.88	0.79
En face OCT complex RPE elevation	0.80	0.84	0.85	0.79
Sharply peaked PED	0.79	0.79	0.79	0.79
Orange nodule	0.69	0.84	0.88	0.61
Thick choroid with dilated Haller's layer	0.63	0.74	0.81	0.54
Complex or multilobular PED	0.76	0.68	0.61	0.81
Double-layer sign	0.78	0.60	0.42	0.88
Extensive subretinal haemorrhage	0.62	0.58	0.64	0.72
Fluid compartment	0.57	0.52	0.42	0.65

OCT: Optical coherence tomography; RPE: Retinal pigment epithelium; PED: Pigment epithelial detachment; PPV: Positive predictive value; NPV: Negative predictive value.

(below fovea), juxtafovea (located within 1-199 μm), and extrafovea (located 200 μm or more from the centre of fovea); 2) peripapillary where it is located within 1 disc diameter (DD) from the margin of the disc; 3) peripheral which is located outside the arcade.

Management of Treatment

Considerations in treatment of PCV For patients with active subfoveal or juxtafoveal PCV, treatment should be given. Active disease is defined based on the following criteria: a) IRF/SRF OR, b) Sub-RPE or sub retinal hemorrhage OR, c) Increasing height of PED with visual symptoms OR, d) Vision loss [5 early treatment diabetic retinopathy study (ETDRS) letters or 1 Snellen line attributed to disease]; for patients with inactive PCV (no features of active disease or increasing height of PED with no visual symptoms), patients may be observed. These patients should be monitored as there is risk of progression.

Risks versus benefits of treatment should be discussed with patients prior to initiation.

The aim of treatment of PCV Retinal fluid in PCV is associated with poor visual outcomes. Based on current clinical data, outcomes are best if all fluid is treated vigorously. Multiple studies have shown inter retina fluid to be a poor prognostic factor for visual function and needs to be treated until maximum resolution is achieved. Therefore, the treatment for PCV is aimed to improve the visual outcomes.

The treatment options are depicted in Table 4[11-12,15-43] and Figure 5. The objectives of the treatments are divided into two categories where the primary objectives include to improve

Table 3 Diagnostic performance of combined OCT features for PCV

Feature combination	AUROC (95%CI)	Sensitivity	Specificity	PPV	NPV
Any two major criteria					
Sub-RPE ring-like lesion+en face OCT complex RPE elevation	0.89 (0.83–0.93)	0.74	0.91	0.93	0.68
Sub-RPE ring-like lesion+sharply peaked PED	0.82 (0.75–0.88)	0.80	0.84	0.85	0.79
En face OCT complex RPE elevation+sharply peaked PED	0.84 (0.79–0.89)	0.73	0.86	0.89	0.68
All 3 major criteria	0.90 (0.85–0.95)	0.75	0.91	0.93	0.68
3 major criteria+any minor criterion	0.91 (0.86–0.95)	0.78	0.91	0.94	0.68

OCT: Optical coherence tomography; PCV: Polypoidal choroidal vasculopathy; AUROC: Area under the receiver operating characteristic curve; CI: Confidence interval; PPV: Positive predictive value; NPV: Negative predictive value; RPE: Retinal pigment epithelium; PED: Pigment epithelial detachment.

visual acuity (VA) and to ensure fluid resolution and/or appropriate fluid control whereas the secondary objective is to achieve polyp regression.

Special Considerations There are many potential complications for anti-VEGF agents which include systemic complications such as cardiovascular aortic thromboembolism and cerebrovascular; ocular complications of the intravitreal injection such as endophthalmitis, retinal detachment, lens touch and suprachoroidal hemorrhage and ocular complications of anti-VEGF treatment such as intraocular inflammation (IOI)[44]. Anti-VEGF must be used with precautions especially it cannot be prescribed anti-VEGF agents in patients who experienced a cerebrovascular accident or myocardial infarction within the previous 3mo. However, special considerations may apply based on physician discretion following a discussion of the benefit-risk profile.

Long-Term Follow-up and Management of PCV Long-term management of PCV requires a structured and individualized follow-up strategy guided by disease activity, treatment response, and risk of recurrence are shown in Table 5. Given the chronic, relapsing nature of PCV, sustained monitoring is essential to preserve visual function and to detect early signs of disease reactivation. Current evidence from major clinical trials and consensus statements supports a dynamic approach to follow-up that balances treatment burden with the need for close surveillance[2,11-12].

For active PCV, patients should be monitored at intervals of 4–8wk, particularly during the initial treatment phase or when there is evidence of ongoing disease activity. Each visit should include an assessment of the best corrected visual acuity (BCVA) and OCT to evaluate for SRF, IRF, and PED. These imaging biomarkers are well-established indicators of disease activity and treatment response[2]. ICGA may be performed when clinically indicated, especially in cases of incomplete response to anti-VEGF therapy, suspicion of persistent or recurrent polypoidal lesions, or prior to considering combination therapy with PDT[11-12].

For inactive PCV, defined by the absence of exudative changes on OCT and stable VA, follow-up intervals may be extended to 3–6mo. During this maintenance phase, regular monitoring remains important, as recurrence can occur even after prolonged quiescence. OCT remains the primary imaging modality for surveillance due to its non-invasive nature and high sensitivity in detecting early fluid recurrence, while ICGA may be reserved for cases where structural changes are ambiguous or when reactivation of polypoidal lesions is suspected[2].

Treatment discontinuation may be considered in selected patients who demonstrate sustained disease remission. Suggested criteria include complete resolution of SRF and IRF on OCT, along with the absence of active polypoidal lesions on ICGA for a minimum duration of 12mo. These criteria are consistent with long-term outcomes observed in clinical studies, where durable remission is associated with improved visual stability and reduced treatment burden[11-12]. However, discontinuation decisions should be individualized, considering baseline lesion characteristics, prior recurrence patterns, and patient-specific risk factors.

Despite apparent remission, long-term surveillance remains essential, as PCV is associated with a significant risk of recurrence. Recurrence should be suspected in the presence of new or increasing SRF or IRF, new-onset sub retinal hemorrhage, or changes in PED morphology on OCT. Reactivation of polypoidal lesions may also be confirmed on ICGA when necessary. In such cases, prompt re-initiation of therapy is recommended to prevent irreversible visual loss. Treatment strategies may include resumption of anti-VEGF therapy, with consideration of combination therapy with PDT in cases of recurrent or treatment-resistant disease, as supported by evidence from the EVEREST-II and PLANET studies[11-12].

In addition, a treat-and-extend (T&E) approach may be considered during long-term management to optimize treatment intervals while maintaining disease control. This strategy allows gradual extension of treatment intervals in patients with stable disease, thereby reducing treatment burden without compromising efficacy[11].

Table 4 Treatment options for PCV

Options	Evidence
Anti-VEGF[a] monotherapy: 1) Aflibercept; 2) Ranibizumab; 3) Brolucizumab	Anti-VEGF agent monotherapy should be the first line of treatment in eligible patients[b]
	1) Aflibercept monotherapy[12,15-17]: Demonstrated improvement in VA, CST reduction, and polypoidal lesions regression in the PLANET study with 3 monthly loading doses followed by a fixed every 8wk dosing regimen in the first year[12]. Demonstrated improvement in VA, CST reduction in the ALTAIR PCV subgroup analysis with treat-and-extend (T&E) dosing regimen and a maximum interval of extension up to 16wk[15-17]. Addition of rescue PDT was not associated with additional efficacy compared to aflibercept monotherapy in the PLANET study[12]. Hence, rescuing PDT may not be required with aflibercept monotherapy
	2) Ranibizumab monotherapy[18-20]: Demonstrated improvement in VA and rate of polyp regression with 3 monthly loading doses followed by a fixed every 4wk regime up to 1y. However, the addition of PDT to ranibizumab treatment resulted in superior BCVA gain, polypoidal lesion regression, and fewer ranibizumab injections in the EVEREST II study[11,21]. Following 3 monthly injections at baseline, ranibizumab can be prescribed on a *pro re nata* basis, as demonstrated in the LAPTOP study[22], with follow-ups every 3mo
	3) Brolucizumab monotherapy[23]: Limited clinical evidence (only post hoc analysis from HAWK PCV subgroup is available). A higher incidence of IOI events was associated with brolucizumab 6 mg compared with aflibercept 2 mg[24-26]. Of the 1088 study eyes treated with brolucizumab in HAWK and HARRIER study, IOI of any form was detected in 50 eyes (4.6%), of which 36 eyes (3.3%) had concomitant retinal vasculitis and 23 (2.1%) had concomitant retinal vascular occlusion[27]
	Adjunct PDT may be considered any time after the administration of anti-VEGF loading doses if response is sub-optimal (sub-optimal response is defined as failure to achieve fluid resolution and/or appropriate fluid control)
Combination therapy (PDT plus anti-VEGF therapy)	PDT in addition to anti-VEGF injections may provide additional disease control in terms of preventing massive SMH, especially in sub-optimal or aggressive cases[28-29]. PDT and ranibizumab combination therapy improve visual and anatomical outcomes, polyp regression, and prevents massive SMH. A higher rate of polyps' regression was associated with PDT than ranibizumab monotherapy (64.4% *vs* 33.3%, $P<0.001$)[11,20,22]. Combination therapy (ranibizumab plus PDT) is preferred to ranibizumab monotherapy for superior visual outcomes (BCVA), fewer injections, and high proportion of polyp regression. Rescue PDT in addition to aflibercept monotherapy resulted in similar visual and anatomical outcomes improvement compared to aflibercept monotherapy[12].
PDT monotherapy	PDT monotherapy may be considered in those who are contraindicated to anti-VEGF treatment[11,22]
Focal laser	Focal laser may be considered as an adjunctive treatment[c] to anti-VEGF therapy for extra foveal polyps (ICGA-guided). However, lasering feeder vessels is not helpful[30-32].
Surgical	1) SMH: Surgical intervention is recommended for massive SMH[33]. SMH is an accumulation of blood between the neurosensory retina and the RPE from the choroid within the macular region. SMH are classified by their size[34-36]: Small: measures at least 1 DD but smaller than 4 DDs; medium: measures at least 4 DDs, but does not extend beyond the temporal vascular arcades; large: extends beyond the temporal vascular arcades but not pass the equator; massive: extends past the equator in at least two quadrants. SMHs are usually less than 500 μm thick[37]. They are labelled as thick SMHs if greater than 500 μm. Thick subfoveal hemorrhages are defined as blood under the fovea that causes obvious elevation of the retina with obscuration of the RPE on fundus examination. Differentiating between sub retinal and sub-RPE hemorrhages is crucial because hemorrhages beneath the retina can be more detrimental to photoreceptors. Clinically, subretinal hemorrhages typically present as bright red, whereas sub-RPE hemorrhages appear darker. OCT is important to determine the level of SMH or sub-RPE hemorrhage and the thickness of hemorrhage. Subretinal hemorrhage damages tissues through a variety of mechanisms[38]: Iron, hemosiderin, and fibrin in the blood have toxic effects on the overlaying photoreceptors; clot retraction can shear and damage photoreceptors; physical separation of the photoreceptors from the RPE can lead to atrophy and disciform scar formation. Patients with submacular/subfoveal hemorrhages experience progressive visual decline. As the mechanisms of damage are time-dependent, early intervention is generally better. The correct strategy for massive SMH secondary to PCV is under debate. The treatment options currently available for SMH fall into 2 broad categories[36,39-41]: non-vitrectomizing techniques (include intravitreal injections of gas, tPA, anti-VEGF, or a combination thereof); vitrectomizing techniques (include treatment with tPA or anti-VEGF, gas, or a combination of these administered as sub retinal injections, intravitreal injections, or both). Recommendations for SMH treatment: Prompt initiation of intravitreal anti-VEGF is recommended for all SMH secondary to PCV; Anti-VEGF monotherapy may be considered for small SMH[42]; PD is recommended for medium and large SMH[42]; pars plana vitrectomy in combination with subretinal tPA and PD may offer a more effective option than anti-VEGF monotherapy for massive or severe SMH[42]. Remarks: Patients who received intravitreal gas within 14d of their symptoms showed a better final VA than those treated after 14d; Greater liquefaction after injection of subretinal tPA in eyes with sub retinal hemorrhage of 7d duration or less[43].
	2) VH: VH associated with PCV can occur as the initial presentation or during the follow-up period or after treatment/manipulation[43]. Ultrasonography was crucial in the setting of VH obscuring fundus detail and helped to exclude more urgent etiologies. Two characteristic types of ultrasonography findings: 1) Hypoechoic opacities on both sides of a hyper-reflective membrane indicating hemorrhages distributed both in the vitreous cavity and in the subretinal space; 2) A dome-shaped elevation with hypo echoes inside and even a fluid level, representing hemorrhagic PED. Ultrasonography could also help to exclude other possible causes of VH, such as intraocular tumors or PVD. The mainstay of treatment for dense breakthrough VH is vitrectomy to clear the media both to restore vision and to accurately assess the retinal status[41]. The visual prognosis in eyes with PCV-related breakthrough VH is variable after vitrectomy. Initial polyps at the extra foveal area led to better functional outcomes. Early vitrectomy may be beneficial for visual recovery after PCV-related VH. The most common reported surgical complication was iatrogenic retinal break which occurred typically during induction of PVD, cataract, recurrent VH, retinal detachment, and choroidal detachment[39].
	Risks and benefits of surgical intervention need to be addressed. Important remarks for both SMH and VH: Early referral to vitreoretinal surgeon is important for early intervention.

[a]Only licensed anti-VEGF agents are included in this section. [b]The use of anti-VEGF agents is contraindicated in patients with a recent cerebrovascular accident or myocardial infarction within the last 3mo. Refer to "Special Considerations" section for more information. [c]Focal laser treatment should be carried out using 100–200 μm spots size with duration of 0.1–0.2s with laser power titration to achieve a "greyish white" response[21,30-31]. Anti-VEGF: Anti-vascular endothelial growth factor; VA: Visual acuity; CST: Central subfield thickness; PCV: Polypoidal choroidal vasculopathy; BCVA: Best corrected visual acuity; PDT: Photodynamic therapy; IOI: Intraocular inflammation; SMH: Submacular hemorrhage; ICGA: Indocyanine green angiography; DD: Disk diameter; RPE: Retinal pigment epithelium; tPA: Tissue plasminogen activator; VH: Vitreous hemorrhage; PD: Pneumatic displacement; PED: Pigment epithelial detachment; PVD: Posterior vitreous detachment.

Table 5 Consensus recommendations for diagnosis and management of PCV

Domain	Recommendation	Strength	Quality of evidence
Diagnosis	ICGA should be performed to confirm PCV diagnosis whenever available	Strong	High
Diagnosis	OCT features may be used to support diagnosis when ICGA is unavailable	Strong	Moderate
Diagnosis	Combined OCT features should be used to improve diagnostic accuracy	Strong	Moderate
Classification	Lesions should be classified based on location (subfoveal, juxtafoveal, extrafoveal)	Strong	Moderate
Treatment	Anti-VEGF therapy is recommended as first-line treatment	Strong	High
Treatment	Combination therapy (anti-VEGF+PDT) should be considered in selected cases	Strong	High
Treatment	Treat-and-extend (T&E) regimen may be used for long-term management	Weak	Moderate
Follow-up	Active PCV should be monitored every 4–8wk	Strong	Moderate
Follow-up	Inactive PCV should be monitored every 3–6mo	Strong	Low

ICGA: Indocyanine green angiography; PCV: Polypoidal choroidal vasculopathy; OCT: Optical coherence tomography; Anti-VEGF: Anti-vascular endothelial growth factor; PDT: Photodynamic therapy.

Overall, these recommendations are based on integration of current evidence and expert consensus and are intended to provide a pragmatic framework for long-term management of PCV. The proposed follow-up strategies are adaptable to diverse clinical settings, including resource-limited environments, where access to ICGA or PDT may be variable. Continued research and real-world data from Asian populations will be important to further refine long-term management strategies and improve patient outcomes[2].

DISCUSSION

This paper presents the updated nomenclature and diagnostic considerations for PCV based on the current understanding derived from emerging clinical and imaging evidence. A set of diagnostic criteria and treatment options for PCV can achieve high sensitivity and specificity with ICGA as the gold standard. In routine clinical practice, diagnosis is primarily guided by clinical presentation, fundus examination, and OCT findings. However, multimodal imaging with ICGA, which remains the reference standard for confirming PCV, enables direct visualization of characteristic polypoidal lesions and the associated BVN. Diagnostic criteria for PCV have demonstrated high sensitivity and specificity when evaluated against ICGA as the reference standard.

An AUROC of 0.90 was achieved when three principal OCT features were combined: sub-RPE ring-like structure on cross-sectional OCT, complicated RPE elevation on en face OCT, and sharp-peaked PED on cross-sectional OCT[41]. These criteria may be particularly valuable in clinical environments where ICGA is not readily available. In such settings, OCT-based diagnostic frameworks provide a practical, rapid, and non-invasive approach that can address the needs of most clinical scenarios[45].

The ability to identify PCV using readily accessible OCT criteria may facilitate clinical decision-making in patient management, including consideration of combination therapy, selection of specific anti-VEGF agents, and situations where patient adherence to frequent follow-up visits may be limited[45]. Persistent polypoidal lesions have also been associated with an increased risk of massive submacular hemorrhage (SMH), highlighting the need for continued research into the clinical course and optimal management strategies for PCV[45].

Expanded Efficacy Assessment and Recommended Long-Term Follow-Up While BCVA and anatomical fluid resolution which is defined by OCT-detected SRF or IRF remain central short-term endpoints, these measures alone may not fully capture disease control and long-term prognosis in PCV. Increasing evidence suggests that structural lesion activity, particularly polyp regression detected on ICGA, together with longitudinal measures of recurrence and treatment burden, provides additional insight into durability of response and long-term visual outcomes.

Recent randomized and real-world studies have reported variable rates of polyp inactivation, with complete regression differing according to imaging modality and treatment regimen. Notably, combination therapy with anti-VEGF agents and PDT has frequently demonstrated higher polyp regression rates compared with anti-VEGF monotherapy, accompanied by differences in retreatment frequency and long-term disease control[46-47]. Therefore, a multidimensional efficacy framework for both future clinical trials and real-world evaluations is proposed namely for:

Polyp regression (structural endpoint) ICGA-confirmed polyp regression should be reported whenever feasible. Meta-analyses indicate that combination therapy (PDT plus anti-VEGF) achieves higher rates of polyp regression and may be associated with improved clinical outcomes compared with anti-VEGF monotherapy. When ICGA is unavailable, surrogate structural markers may be considered, although their interpretation should be undertaken with caution.

Recurrence metrics The incidence of recurrence and time-to-first recurrence should be documented. Longitudinal

studies indicate that PCV frequently recurs beyond 12mo, emphasizing the importance of follow-up periods of at least 24mo to adequately assess treatment durability.

Treatment burden and durability Cumulative injection numbers, the need for adjunctive PDT, and clinic visit frequency at 12 and 24mo provide pragmatic indicators of regimen effectiveness and healthcare system impact. Real-world evidence suggests that combination therapy may reduce treatment burden while maintaining visual improvements.

Functional and structural complications Long-term monitoring of BCVA trajectories, development of submacular fibrosis, and haemorrhagic complications contributes to more comprehensive prognostic assessment.

Standardized time points and minimal dataset Standardized outcome reporting at baseline and at 3, 6, 12, and 24mo (minimum) is recommended to facilitate cross-study comparisons and support future Meta-analyses[48].

This expanded evaluation framework aligns with recommendations from recent comprehensive reviews of PCV diagnosis and management that emphasize multimodal outcomes and long-term follow-up as key components of evidence-based clinical practice[46]. Core variables should include BCVA (ETDRS or logMAR conversion), OCT central subfield thickness (CST), ICGA polyp status where available, injection counts, retreatment intervals, and adverse events. Implementation of standardized outcome reporting within prospective registries and institutional audits will enable direct comparison of therapeutic strategies and support cost-effectiveness analyses relevant to the Malaysian healthcare context.

The PLANET and EVEREST II trials have highlighted instances where patients without polypoidal lesions continued to experience persistent disease activity, while others with existing polyps showed no disease activity. The correlation of polyps, disease activity, and visual outcome remains to be elucidated. Some studies have explored variables related to treatment response or disease reactivation[45-49]. Additional research of small-scale with extended follow-up may provide continuing insights into the efficacy and limitation of different treatment combinations. Therefore, physicians should discuss the available evidence with patients to develop individualized management plans, considering treatment response and patients' expectation of functional and anatomical outcomes[45-49]. The panel acknowledged the need for further clinical studies or real-world experiences to refine optimal treatment protocols, beyond anti-VEGF and PDT. Additionally, basic and mechanistic research elucidating the genetic and environmental risk factors and pathomechanisms associated with different clinical features of PCV is crucial. Integration of these research areas will enhance healthcare quality and alleviate the burden of disease and treatment for PCV patients.

Comparison with International PCV Guidelines and Distinctive Contributions of the Malaysian Consensus

The present Malaysian consensus is broadly aligned with established international recommendations for the diagnosis and management of PCV, particularly those developed in Japan and other Asia-Pacific regions. Consistent with these frameworks, ICGA is recognized as the reference standard for confirming PCV, while anti-VEGF therapy remains the cornerstone of treatment, either as monotherapy or in combination with PDT.

Despite this broad concordance, the Malaysian consensus introduces several important conceptual and practical advances. Most notably, it operationalizes diagnostic and therapeutic recommendations within a structured framework that explicitly accounts for variability in healthcare resources. In contrast to several existing guidelines developed in settings where access to ICGA and PDT is assumed, this consensus incorporates a pragmatic diagnostic pathway for environments where ICGA is unavailable. In such scenarios, validated OCT-based diagnostic criteria including sub-RPE ring-like structures, sharp-peaked PED, and characteristic en face OCT features are formally integrated as an operational alternative to guide diagnosis and clinical decision-making.

Second, while previous guidelines have primarily focused on short-term functional outcomes such as BCVA and fluid resolution, the Malaysian consensus advances a broader, multidimensional efficacy framework. This framework integrates structural lesion activity (including polyp regression), recurrence dynamics, treatment burden, and standardized longitudinal follow-up. By proposing harmonized outcome reporting at defined time points (baseline, 3, 6, 12, and 24mo) together with a minimal dataset for registries and institutional audits, the guideline moves beyond therapeutic recommendations toward systematic outcome surveillance and real-world evidence generation.

Third, the consensus explicitly contextualizes treatment recommendations within the Malaysian healthcare landscape, where heterogeneity in drug accessibility, reimbursement structures, and availability of PDT may influence therapeutic choices. Rather than assuming universal access to combination therapy, the guideline emphasizes individualized treatment planning that considers disease phenotype, expected adherence to follow-up, and local resource availability.

Finally, the consensus transparently acknowledges current limitations in national epidemiological, genetic, and real-world treatment outcome data for PCV. In response, it advocates the establishment of multicentre registries and prospective observational cohorts to support continuous evidence generation and iterative refinement of clinical

recommendations. This forward-looking approach distinguishes the Malaysian framework from many existing guidelines derived predominantly from high-resource settings. Taken together, while the Malaysian consensus remains consistent with international principles of PCV diagnosis and management, its principal contribution lies in contextual adaptation, structured diagnostic prioritization, and the establishment of a standardized long-term outcome framework designed to enhance feasibility, comparability, and policy relevance within Malaysia and potentially other resource-variable healthcare systems.

The Malaysia consensus recommendations for the management of PCV were developed based on expert evaluation of current evidence and collective clinical experiences. These recommendations are grounded in robust evidence from two significant multicentre clinical trials, the PLANET study and the EVEREST study, both of which provide level I evidence. A practical algorithm for treatment allocation under initial treatment and re-treatment/rescue treatment clinical setting was proposed. The recommendations are expected to offer sufficient guidance for ophthalmologists in making treatment decisions and to ease communications with the patients.

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