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Original Research Article

SENSITIVITY AND SPECIFICITY OF OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN IDENTIFYING POLYPOIDAL CHOROIDAL VASCULOPATHY

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ABSTRACT

Background: To correlate the imaging features on optical coherence tomography angiography (OCT-A) in indocyanine green angiography (ICGA) proven polypoidal choroidal vasculopathy (PCV) and hence estimating its sensitivity and specificity.

Materials and Methods: An observational cross-sectional study was conducted where ICGA was used for definitive diagnosis of PCV and OCT-A was done in same patients, so as to comparatively evaluate sensitivity and specificity in PCV diagnosis.

Results: The mean age was 69.38±8.39 years. The 43 eyes of 36 patients were included. Bilaterality was seen in 7 patients. The vascular abnormalities identified with ICGA were visualized on SD-OCT as areas of moderate reflectivity between RPE & Bruch's membrane in 81%. Pigment epithelial detachment (PED) noticed in all 43eyes; haemorrhagic PED in 77% &serous PED in 23%. On ICGA, polyps were seen in 37 eyes (86%), mainly at macular area& BVN in 22 eyes (51.2%) whereas OCT-A showed polyps in 20 eyes (47%) and BVN in 23 eyes (53%). The cross-sectional OCTA showed clear defined polyp & provided the flow signals showing BVN which were also comparable to ICGA. The leakage was not detected on OCT-A.

Conclusion: Sensitivity of OCT-A in diagnosing PCV was inferior to ICGA. However specificity of OCT-A was more.SD-OCT clearly showed Bruch's membrane beneath the areas of abnormal RPE in same locations where the PCV lesions were evident on ICGA & cross-sectional OCT-A images provides anatomical information of PCV which is comparable to ICGA but OCT-A is a complementary imaging evaluation for follow up.

Keywords: Optical coherence tomography angiography, indocyanine green angiography, pigment epithelial detachment, branching vascular network.

INTRODUCTION

Polypoidal choroidal vasculopathy (PCV) named for its network of branching, choroidal vessels with aneurysmal like dilations. It was first described by Yanuzzi et al[1] in 1990 as a distinct clinical entity characterized by polypoidal, subretinal, vascular lesions associated with persistent, recurrent serous leakage and hemorrhagic detachments of the retinal pigment epithelium (RPE) in the macula which was seen in the elderly population. Initially it was designated as recurrent retinal pigment epithelial detachments (PED) and posterior uveal bleeding syndrome. [2,3,4,5]

The primary abnormality involves the choroidal circulation in which an inner choroidal vascular network ends in an aneurysmal bulge or outward projection, forming a characteristic polyp like structure which is clinically seen as a reddish orange spheroidal structure and as described by Yanuzzi et al.[1,2,6]

PCV which appears clinically as orange-red subretinal nodule shows corresponding indocyanine green hyperfluorescence which is pathognomonic of PCV. It is defined angiographically as the focal nodular appearance of hyperfluorescence arising from the choroidal circulation within the first 6 minutes after injection of indocyanine green and with or without an associated choroidal interconnecting vascular network. The definition of PCV relies on ICGA as it permits choroidal vasculature visualization with enhanced specificity and sensitivity.[7]

OCT-A is a potential substitute for ICGA as it is safe, noninvasive, and has the potential to resolve vascular networks along the z-axis. Thus provide greater information concerning spatial relationships between pathological vascular tissue and the surrounding retinal and choroidal layers.

OCT-A is an imaging technique that employs motion contrast imaging to high-resolution volumetric blood flow information generating angiographic images in a matter of seconds. It compares the signal between sequential OCT b-scans taken at the same cross-section. These signals have been described as decorrelation signal. It is the differences in the backscattered OCT signal intensity or amplitude.[8,9,10] The intensity of the flow signal throughout the BVN is uniform on OCT-A. The pachychoroid with the loss of the choriocapillaries are observed beneath the origin of the BVN.

The aim of this study to correlate the imaging features on optical coherence tomography angiography(OCT-A) in indocyanine green angiography(ICGA) proven polypoidal choroidal vasculopathy(PCV) and hence estimating its sensitivity and specificity.

MATERIAL AND METHODS

We reviewed clinical and imaging data of the patients who were examined and recruited from out-patient department of Vitreo-Retina Services, Narayana Nethralaya, Rajajinagar, Bangalore. This study was conducted after approval from research and ethical committee and Declaration of Helinski was maintained. It was a cross-sectional and observational study.

Patients presented clinically with recurrent subretinal bleed, subretinal nodule or neuro-sensory detachment in vitreo-retina services were taken and then ICGA was used as a definitive diagnosis of PCV in each patient, based on the presence of polypoidal lesions and branching vascular networks in ICGA which are the characteristic of PCV lesion.

Simultaneous FA and ICGA was performed with the Heidelberg Spectralis HRA + OCT (Heidelberg Engineering, Heidelberg, Germany).The patients included were based on early sub retinal ICGA hypercyanescence (appearing within the first 5 min of ICG dye injection) and at least one of the following diagnostic criteria:-Nodular appearance of the polyp, hypofluorescent halo around the nodule, abnormal vascular channel(s) supplying the polyp, orange subretinal nodules corresponding to the hyper fluorescent area on ICGA and massive submacular haemorrhage.

Patients demonstrating polypoidal changes and neovascular tissue on ICGA were further taken for SD-OCT and OCT-A imaging. The patients with any other macular pathologies or comorbid ocular diseases like pathologic myopia, hazy media (e.g. dense cataract) because of the difficulty in acquisition of clear image, who were allergic to iodine, seafood and with liver disease, asthmatics, cardiac disease and pregnancy were excluded from the study.

Optical coherence tomography angiography scans were performed using the RTVue-XR Avanti (Optovue, Inc., Fremont, CA, USA), a 70 kHz spectral-domain OCT system with a center wavelength of 840 nm. Each angiography scan consisted of one horizontal priority (x-fast) and one vertical priority (y-fast) raster scan. For each volumetric raster scan, there were 304 A-scans per B-scan, and two consecutive B-scans at 304 locations. Flow was detected using the SSADA algorithm.[8,13]

Forty patients with 54 eyes were selected clinically and out of which 43 eyes were included in the study after ICGA. Rest of the eyes were not included in the study as they had scarred CNVM (17 eyes), Dry ARMD (3 eyes), RPE atrophic changes (4 eyes), CSCR (2 eyes) and fellow normal eyes (11 eyes), which did not meet the scope of our study.

The pre-operative data of the patients who satisfied the inclusion criteria after ICGA were recorded which were baseline visual acuity on snellen's chart, anterior segment findings on slit lamp microscope (cornea, anterior chamber , lens status and pupillary reaction), posterior segment findings on indirect ophthalmoscope (vitreous, optic disc, macula and peripheral retina with 90 D and IDO) and ICGA findings were noted. Special Investigation-SD-OCT with HRA+OCT Spectralis (Heidelberg Engineering (V.6.0) GmBH) was taken and OCT-A with RTVueXR Avanti (Optovue, Inc., CA) was taken and findings were noted.

Statistical Analysis

Chi-square/ Fisher Exact test and McNemar test were used to find the significance of study parameters on categorical scale between two or more groups.

RESULTS

Forty patients with 54 eyes were suspected clinically for PCV in which 14 patients presented with bilateral involvement. Thirty-six patients were proven as PCV on ICGA. After ICGA, out of 14 patients with clinically suspected bilateral PCV ,7 patients were diagnosed as bilateral PCV and were

included ,1 patient was diagnosed as bilateral CNVM and was excluded , 6 patients had unilateral PCV which were included in the unilateral group. Hence, out of 54 eyes with clinically suspected PCV, 43 eyes were diagnosed with PCV on ICGA.

Overall mean age incidence was 69.38±8.389 years with maximum over all incidence were found between 52 - 87 years (among 36 patients diagnosed as PCV after ICGA). The best corrected visual acuity of the involved eye ranged from 6/6 to 1/60, Log MAR visual acuity range 1.78-0 and mean Log MAR visual acuity +0.60454. Of the 36 patients 20 (56%) were male and 16(44%) female.

- The bilaterality was seen in 7 cases (18%). The involvement of right eyes were 16(44%) and left eyes were 13(36%).
- Patients with hypertension were 13 (30%),3 with history of diabetes (7%),11 patients were both diabetic and hypertensive (26%),1 patient was having raised cholesterol (2%) and 15 patients (35%) were having no history of any systemic illness.
- On ophthalmoscopic examination,19 eyes (44%) presented with reddish orange choroidal nodules and all these nodules corresponded to the polypoidal lesions seen by ICGA.
- Among 43 eyes on ICGA – 6 eyes showed only BVN (14%) and polyp + BVN (37%) and only polyp in 21 eyes (49%) in ICGA. So overall, polyp seen in 37 eyes (86%) out of 43 eyes and BVN in 22 eyes (51.2%) out of 43 eyes by ICGA.
- Location of PCV lesion: - Out of 43 eyes, 37 eyes presented with polypoidal lesion whose location are as follows – 10 eyes in fovea (26%) and 17 extra fovea (45%), peripapillary in 5 (13%), and extramacular in 6(26 %) .1 eye presented with multiple location of polyp within the macular area. The predominant location for these polypoidal lesions was the macular region.

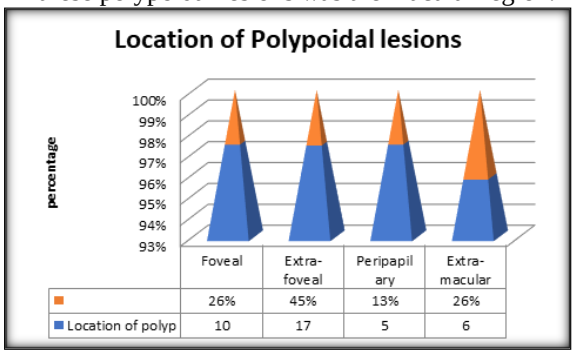

Figure 1: Location of polyp on ICGA

- Out of 43 eyes diagnosed and confirmed by ICGA as PCV, OCT-A showed BVN only in 23 eyes (53%) cases and polyp lesion only in 20 eyes (47%) eyes by OCT-A.
- On comparing OCT-A and ICGA for the confirmation of polyp :- Polyps were revealed in 20 eyes (14 %) by OCT-A and in 37 eyes (86%) by ICGA, which was significant with p value <0.01 (df=2 on Chi square test)

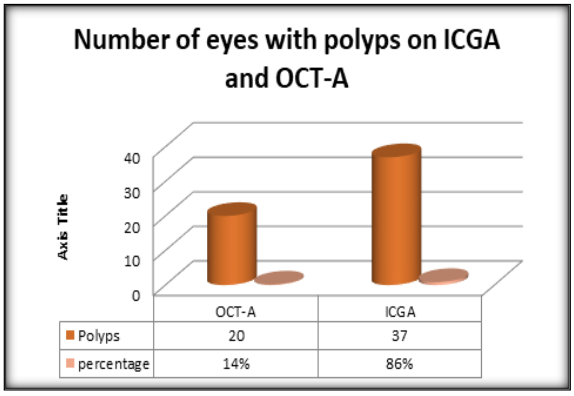

Figure 2: Distribution of polyps in OCT-A and ICGA

- On comparing OCT-A and ICGA for the confirmation of BVN we found on OCT-A BVN is seen and localised in 23 eyes (53.5), not seen in 14 eyes (42.6%) and doubtful seen in 6 eyes (14%) whereas on ICGA the BVN seen in 22 eyes (51.2%) which is found to be significant (p<0.01, on Chi-square test).

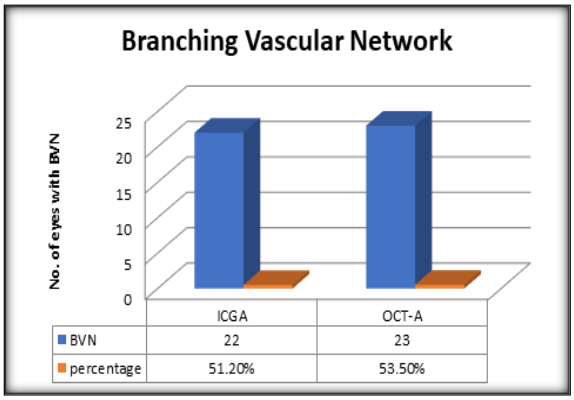

Figure 4: Percentage of BVN detected in ICGA and OCT-A

Of the 54 eyes, 11 eyes (20%) presented without polypoidal lesions most cases the clinical findings were attributed to choroidal neovascular membrane.

Table 1: Characteristics of study population

Characteristics	Value
Minimum age (in years)	52
Maximum age (in years)	87
Mean age (in years)	69.38 ±8.39
BCVA in LogMAR visual acuity range	1.78-0
Mean LOGMAR visual acuity	+0.60454.

Table 2: Characteristics patients with PCV, N= Number of patients

The Characteristics patients with PCV in this study		
Characteristics(Out of total 36 patients presented with PCV in either of eyes)	**N**	**Percentage**
1.Gender		
-Male	20	56%
- Female	16	44%
2.Laterality		
-Bilateral	7	20%
-Right Eye	16	44%
- Left Eye	13	36%

DISCUSSION

Optical coherence tomography angiography is a non-invasive imaging technology for detecting the blood flow in choroidal vasculopathy like PCV.

Our current study compared the angiographic features of PCV detected by ICGA and OCTA. Our results demonstrated that the detection rate of the polypoidal lesions was significantly low in OCTA compared to ICGA, but the BVN was clearly detected by OCTA as well as by ICGA.OCT-A is a newly developed method, which can visualize chorio-retinal circulation without dye injection. There is no clear-cut definition and identification of PCV lesions on OCT-A. Only a handful of published studies gave descriptions on PCV lesions. Many polypoidal lesions are detected as high flow signal spots beside the BVN or as the blood flow signals of polyps under the top of the PED on OCT-A .[11]

The location of PCV in our study showed highest occurrence in macular region (70 %) followed by extramacular area (26%), which is comparable to other studies on Asian populations. Anantharaman et al study,[12] showed PCV lesion in 42.5% in macular region in Indian population and Kwok et al.[13] study showed macula was the predominant location (64%) followed by peripapillary area (32%). Spaide et al,[7] demonstrate single or multiple polyps as vascular aneurysmal dilatations arising from inner choroidal vessels in the early phase as hyperfluorescent spots. Polyps were arranged in clusters in 43 % eyes in our study. Uyama et al1[14] had described clustered grape-like polypoidal lesions on ICGA 25– 67% of cases in Asian populations.

ICGA demonstrated in our study single or multiple polyps as vascular aneurysmal dilatations in 86 % and BVN only in 55.2 % which is similar to Tomiyasu T et al,[15] showing polypoidal lesion in 100% eyes and Uyama et al,[14] showing branching vascular networks with polypoidal dilations at the network terminals beneath the RPE in all patients (100%).

In this study 81% of eyes showed that the vascular lesion was in the sub-RPE space but anterior to Bruch membrane which is contrary to as initial studies suggested by Yannuzzi et al,[1] and Kleiner et al,[4] where PCV lesions were described below bruch's membrane. This is based on the previous studies which showed that the highly reflective thin straight line underlying an abnormally contoured RPE line is seen in abnormal vascular lesions of PCV as well as in the soft drusen, PED, or occult CNVM of PCV which is a common feature representing sub-RPE lesions of many macular diseases. The line most likely represents Bruch's membrane, based on the histopathological observation.[16]

Optical coherence tomography angiography is a new device to visualize chorio-retinal circulation without dye injection and has already been applied to various retinal vascular disease.

In our study, polyp lesions was seen and localised in 46.5% and BVN in 56% by OCT-A which is similar to Inoue et al study who have evaluated the PCV lesions by using OCTA where polyps were visualized in only three of seven cases (42.9%) by OCTA[17].Kim et al[8] mentioned that only 50% polyps were hyper-reflective lesions on the outer retinal reference on OCTA. Doubtful polyps were seen in 13 eyes (30.2%) in OCT-A in this study which was either due to peripheral locations of PCV lesions or due to the submacular haemorrhage and haemorrhagic PED which obscured the site of lesion.

On comparing OCT-A with ICGA for detecting the polyps; they were not found on OCT-A in 10 eyes, out of which ICGA detected in 4 eyes (10.8%); doubtful detected in 13 eyes but all were clearly seen on ICGA and in rest 20 eyes polyps were clearly seen in both ICGA and OCT-A ($p < 0.001$) and were co-localized (46.5%). Hence our study showed ICGA more easily detected the polyps than OCT-A. Whereas Wang et al[11]showed polyps detected in 92.3% cases with the outer
retinal slab on OCT-A. Polypoidal lesions showed variable patterns on OCTA and hence were not always detected.

The BVN was seen on OCT-A clearly in 23 eyes (53.5%) out of which only 16 eyes showed the lesion (BVN) on ICGA. The doubtful localization of BVN on OCT-A was seen in 6 eyes in which 5 eyes showed BVN clearly on ICGA. Rest in 14 eyes OCTA was not able to locate BVN and out of these only 1 eye (2.3%) showed BVN on ICGA. Hence total BVN seen on ICGA were 22 eyes (51.25). Thus our study showed OCT-A was able to detect BVN better than ICGA with p value < 0.001 which is significantly significant. Whereas, Wang et al[37]showed detection of BVN in 100% cases with the on OCT-A. Hence OCT-A better depicts the BVN than ICGA.

The FFA showed BVN in total 27 eyes (62.8%), whereas OCT-A detected in 23 eyes (53.5%) as described above. BVN was not seen in 14 eyes with OCT-A, out of which,11 eyes showed BVN with FFA. Among 23 eyes with BVN seen on OCT-A,16 eyes showed BVN on FFA. All doubtful 6 eyes with BVN on OCT-A were clearly seen on FFA. Hence proving FFA detected the BVN more than OCT-A ($p < 0.001$). No study showed any kind of relation between FFA and OCT-A.

CONCLUSION

PCV is characterized by age of onset around seventh decade with male predominance, unilateral and macular involvement. PCV is more predominant either with hypertensive or with normal systemic status.

The orange sub-retinal nodule and sub-retinal hemorrhage on ophthalmoscopic evaluation (44%) suggest the presence of PCV. All above features with hemorrhagic or serous pigment epithelial detachment strongly advocates the use of ICGA in these patients. The ICGA characteristics are single or multiple polyps as vascular aneurysmal dilatations arising from branching vascular network, where the polypoidal lesions are located primarily in the macula and are arranged in clusters.

PCV is indistinguishable from occult CNVM using FFA. So, ICGA should be considered in patients with occult CNVM. Although the branching vascular network can be seen on FFA more easily but clusters of polypoidal lesions are difficult to detect. Thus a careful interpretation of FFA images in patients with PCV is required in hospital set-ups with FFA imaging modality only.

The hemorrhagic PEDs and multiple PEDs with or without subretinal fluid are more suspicious of PCV on OCT. The incidence of PCV is high in patients presenting with hemorrhagic pigment epithelial detachment in Indian population.

The locations of PCV lesions on SD-OCT and OCT-A is same as on ICGA. The polyps were not visualized in some cases (23.3%) on OCT-A, possibly due to the poor blood flow in the polyp as OCTA can detect the blood flow but not the blood vessels themselves. Branching vascular networks are more clearly seen on OCTA than ICGA. Among FFA and OCT-A, FFA detects BVN more precisely.

Polypoidal lesions had variable patterns on OCTA and were not always detected and hence inferior to both FFA and ICGA. Overall polypoidal lesion is clearly detected on ICGA among all imaging modalities. Additionally, it's not possible to generate informative OCT-A images with automated or manual segmentation techniques in cases with the presence of extensive edema, exudation, hemorrhage, and large pigment epithelial detachment (PED). The leakage from active neovascular tissue is clearly identified on ICGA but the distinguishing features on OCT-A cannot be defined in eyes where leakage is present.

On comparing the imaging modalities, the OCT-A is superior to ICGA for visualizing the branching vascular network. But for the polypoidal lesion detection, ICGA found superior to all.

OCT-A is helpful in understanding the pathology of PCV lesion but it can be used as a supplementary to ICGA because of few limitations of OCT-A as described below.

Although ICGA is a gold standard imaging modality for PCV lesions, OCT-A can be considered in detecting the PCV lesions with branching vascular networks.SD-OCT detects and confirms the haemorrhagic and serous PED better than all other imaging modalities. OCT-A is a new, non-invasive emerging imaging modality which can be used in detecting polypoidal lesions better than FFA. It demonstrate the branching vascular networks far better than polypoidal lesion. OCT-A can be considered in follow- up cases as it is a non-invasive imaging modality as compared to dye angio-graphy and also in cases where dye is contra-indicated in allergic patients and patients with liver and/ or renal failure.

There are few limitations of OCT-A which makes it supplementary to ICGA imaging modality.

Limitations

- Our study included both treatment and treatment naïve patients with PCV lesions and many were recurrent cases.
- Our study dealt with patients with hemorrhagic or serous pigment epithelial detachment only, thus increased the number of doubtful cases on OCT-A.
- OCT-A imaging confined to the posterior pole, predominantly the macula. Thus decreasing the efficacy of OCT-A in peripherally located PCV lesion.
- OCT-A imaging requires steady fixation, which is difficult to acquire in cases with severe vision loss or with massive sub-macular haemorrhage.
- OCT-A imaging is susceptible to a range of artifacts.
- Limited information about leakage and activity of neovascular tissue by OCT-A.

Hence the specificity of OCT-A for diagnosing PCV is more than ICGA but sensitivity is inferior to ICGA.

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