Does a Relationship Exist Between Posterior Vitreous Detachment, Macular Thickness and Foveal Avascular Zone Dimensions in Myopic Eyes?

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Does a Relationship Exist Between Posterior Vitreous Detachment, Macular Thickness and Foveal Avascular Zone Dimensions in Myopic Eyes?

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Abstract

Background: The posterior vitreous detachment (PVD) is a separation of the posterior vitreous cortex from the internal limiting membrane of the retina. The PVD induces several potentially serious pathologic events at the vitreoretinal interface. The aim of the study is to determine if relationships exist between PVD, macular thickness (MT) and the foveal avascular zone (FAZ) in myopic eyes.

Methods: This is a retrospective case study of 63 myopic subjects who underwent comprehensive eye examination including the optical coherence tomography angiography (OCTA) between January 1 and Jun 30, 2019. The spherical equivalent (SE) was calculated using the manifest refraction. The myopia grouping was based on a severity scale, namely mild, moderate, high and very high using standard refractive error classifications. The PVD classification was based on optical coherence tomography (OCT) images. The status of the PVD and MT were evaluated with Macular Cube 200 × 200 images and the FAZ was imaged with an OCTA, Angioplex. The MT and FAZ dimensions were calculated using a custom algorithm.

Results: A total of 114 myopic eyes subjects had median (range) age of 26.00 (22.00 - 28.00) years. Of this cohort, females comprised 62.3 % of the dataset, and the right eyes were 50.00 %. In this population, 10 eyes had no PVD in any quadrant, and 73 eyes had incomplete PVD in all four quadrants. The inferior quadrant had the maximum number of PVD cases and the nasal quadrant had the least number of cases. High myopic eyes exhibited significantly increased low foveal volume ($p = 0.000$). The inferior part of para- and perimacular area showed a significant thinning in very high myopic eyes ($p = <0.05$). A statistically significant alteration of FAZ circularity index found in very high myopic eyes ($p = 0.002$).

Conclusion: In high and very high myopic eyes, an increasing trend of partial PVD is seen. The most commonly involved location was the inferior quadrant. A significant alteration in foveal volume and circularity index of the FAZ is seen in high and very high myopic eyes.

Keywords: Myopia, Posterior vitreous detachment, Foveal avascular zone, OCT, Macular thickness

Background

Liquefaction of the vitreous gel which is attached to the internal limiting membrane of the retina [1-3] or spontaneous posterior vitreous detachment (PVD) from the retina is considered to be a part of normal aging process [1,4]. The onset of PVD is usually reported around the fifth decade of life or later in normal [4]. The shallow PVD not only helps to predict the prognosis and also determines the indication for vitreoretinal surgery in many vitreoretinal conditions [5]. The usual slit lamp examination with a +90D lens fails to detect shallow PVDs [5] Currently, the spectral-domain optical coherence tomography (SD-OCT) is commonly used [2] to image the structural relationship of the vitreomacular interface [3,6]. The SD-OCT method not only helps to qualitatively diagnose different stages of disease but can also be used to quantify the PVD stages.

The increasing prevalence of myopia worldwide [7,8] can lead to potentially blinding ocular complications especially in the posterior part of the eyes in pathological myopes [7]. Usually the pathological myopic complications are bilateral [9]. Myopes are reported to have long axial length especially in cases of high myopia (>26.5 mm) due to scleral ectasia [7,8,10]. Rhegmatogenous retinal detachment has a higher incidence in axial myopic subjects [4,11]. Foveal retinoschisis and posterior staphyloma are also reported in high myopia [4]. Bond-

Taylor et al. [12] reported the PVD prevalence in normal individuals was 24 % among subjects aged between 50-59 and increases to 89 % in the 9th decade of life.

However, in high myopes, the onset of PVD has been reported to occur much earlier than non-myopic or low-moderate myopic eyes [4,13]. For example, Akiba [11] using a slit-lamp method reported that the onset of PVD in high myopes was in the third decade of life. Similarly, Itakura et al. [4] also reported that in high myopes (worse than -8.00D) PVD could occur as early as the third decade of life.

Many authors have hypothesized that retinal changes occur as a result of mechanical stretching due to axial elongation in myopia [7,8,14]. During axial stretching the traction of the vitreous on the fovea in myopic eyes causes structural changes [7]. Chung et al. [15] reported no significant foveal thickness changes with the axial length up to an axial length of 25.5 mm - 26.00 mm. In high myopic eyes (SE worse than -8.00 D or AXL $\geq$26.00 mm), a significantly thicker fovea was found with a steep foveal slope. [7,16]

Gomaa and Abouhussein [17] reported that retinal morphological changes are common in high myopic eyes and recommended that OCT based investigation should be made routinely. Ito et al. [18] reported close correlations between the degree of PVD and the stages of idiopathic macular hole. Xu et al. [19] classified the vitreomacular interface diseases and its sub-classifications based on vitreomacular adhesion and vitreomacular traction. Hence foveal morphological changes are expected in high myopia, especially in the superficial retinal layers [20] and blood vessels.

To the best of our knowledge there are no reports investigating the relationship between PVD, central macular thickness (CRT) and foveal microvascular zone (FAZ) dimensions in myopic eyes. This is the subject of this study.

Methods

Subject

The electronic medical records (which included OCTA) of all myopic subjects who visited a tertiary eye care hospital's refractive surgery clinic, in Chennai, India between January 1 and Jun 30, 2019 were reviewed. A total of sixty-three subjects (114 eyes) were included in the study. Myopia was classified into four groups based on spherical equivalent (SE) [21], namely low myopia (SE between -0.12 and -3.00 D), moderate myopia (SE between -3.12 and -5.00 D), high myopia (SE between -5.12 and -10.00 D) and very high myopia (SE worse than - 10.00 D). The SE was calculated using the manifest refraction during the ophthalmic examination. The exclusion criteria were any prior history or clinical evidence of retinal or systemic disease.

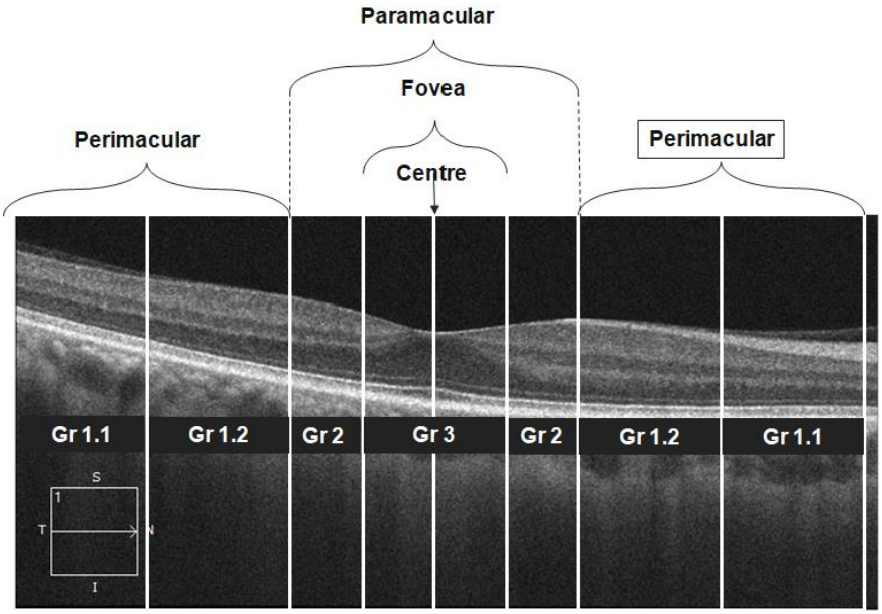

Figure 1: An example and a schematic diagram of a SD-OCT horizontal radial scan image. The PVD classification based on the PVD location. The above picture shows the PVD extended till parimacular area with grade 1.2.

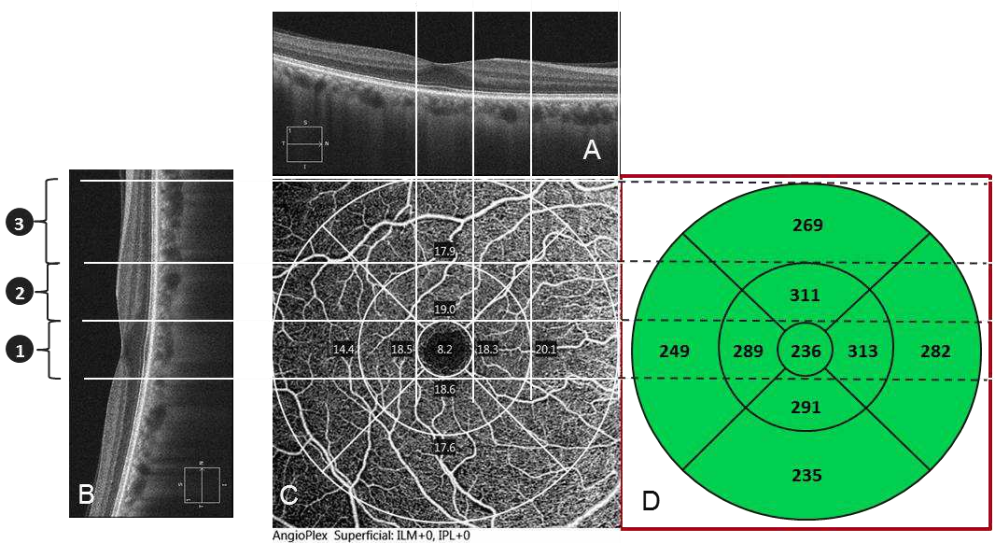

Figure 2: A relationship between PVD location and the corresponding location macular thickness and angioplex image using the ETDRS method. A & B) a radial scan of a horizontal and vertical scan. The numbers 1, 2 & 3 indicating the macular anatomical structures 1) fovea, 2) paramacular and 3) perimacular area. C) An en-face image of macular and FAZ with ETDRS segmentation D) the ETDRS macular thickness (in microns) to the corresponding area of the fovea, para, and peri macular regions.

Central macular thickness and Foveal microvascular dimensions

Both central macular thickness (Macular cube 200 X 200) and foveal microvascular dimensions (Angioplex) were imaged using optical coherence tomography angiography (OCTA; Cirrus 5000 Angioplex; Carl Zeiss Meditec Inc., Dublin, CA). The CMT was calculated by an algorithm inbuilt in the device. The foveal microvascular dimensions were calculated using a custom-developed MATLAB program [22] and this algorithm has been used to study the FAZ dimensions in normal, diabetic and myopic eyes [23]. The macular cube utilized a 6 mm x 6 mm (vertical x horizontal) window axial scans in the macular region. The macular region was divided into 9 quadrants with 3 concentric rings [7] (The central 1.0 mm diameter ring represents the fovea. the second 2.0 mm diameter ring represents the para-macular region and the outer most 3.0 mm ring represents the peri-macula; Figure 2). The macular thicknesses of every sector were defined by the ETDRS map [24] and were averaged for analysis.

PVD Classification

A single clinical expert (RRN) classified the PVD based on the OCT radial images of both vertical and horizontal. Since most of the cases had very early PVD, the method for PVD classification given by Itakura et al [4] was modified. Figure 1 shows the stages of PVDs and its classification. If no PVD was seen within the 6 mm scan it was graded as Grade 0. The Grade 1 PVD is a perimacular area attached PVD, the Grade 2 is the PVD attached to the paramacular area. Grade 3 is the foveally attached PVD. Grade 1 covers a larger area and hence it was further sub-classified to 1.1 and 1.2 based on the PDV location (Figure 1). The PVD was graded for all four quadrants (superior, nasal, inferior and temporal).

Statistical analysis

All statistical analyses were performed using the SPSS version 20 (SPSS Inc, Chicago, Illinois, USA). The normal distribution of quantitative variables was checked using the Kolmogorov-Smirnov test. A one-way analysis of variance (ANOVA) and Kruskal Wallis analysis was performed for comparison between PVD groups. A two-sided unpaired student t-test was used to compare the various parameters of the sub-group myopic groups. The p-value <0.05 was considered significant for all the statistical tests.

Results

Out of the total of 114 eyes, 43 were male (37.72 %) and 71 were female (62.28 %). The median ± interquartile range (IQR) of age, best corrected visual acuity (BCVA) and SE of this population were 26.00 (22.00 – 28.00) years, 0.00 (0.00 – 0.00) logMAR and -5.56 D (-3.09 D - -8.06 D) respectively. The median (IQR) of CMT, FAZ area and macular cube volume (MCV) were 248.00 (235.00 – 260.00) µm, 0.27 (0.20 – 0.34) mm^2 and 9.80 (9.60 – 10.10) for the full sample. Table 1 shows the study sample demographic and clinical characteristics and their sub-groups based on PVD stages.

Table 1: The demographic details of the study population.

	Age (years)	SE (D)	BCVA (LogMAR)
Low myopia	23.0 (21.0 – 27.0)	-2.25 (-1.37 to -2.50)	0.0 (0.0 – 0.0)
Moderate myopia	26.0 (23.0 – 31.0)	-4.25 (-3.50 to -4.50)	0.0 (0.0 – 0.0)
High myopia	26.0 (23.0 – 28.0)	-6.44 (-6.25 to -7.75)	0.0 (0.0 – 0.0)
Very High myopia	27.0 (22.5 – 30.0)	-14.25 (-11.25 to -18.06)	0.0 (0.0 – 0.1)
Overall myopia	26.0 (22.0 – 28.0)	-5.56 (-3.09 to -8.06)	0.0 (0.0 – 0.0)
p-Value	0.568*	0.000**	0.000**

*One-Way ANOVA, **Kruskal Wallis, SE: Mean spherical equivalent, BCVA: Best corrected visual acuity

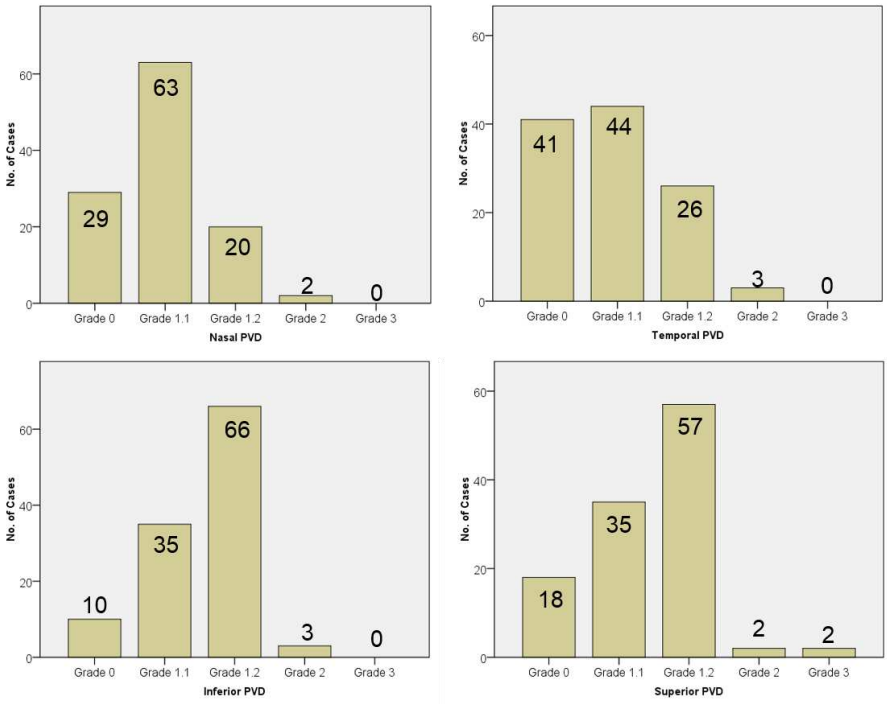

Figure 3: Distribution of PVD in all four quadrants.

The stage of the PVD was classified using the predefined PVD grading scheme (Figure 1). Out of 114 myopic eyes, 10 eyes (8.77 %) had no PVD in any of the quadrants, 31 eyes (27.19 %) had PVD in one or more than one quadrant, and 73 eyes (64.04 %) had PVD in all four quadrants. The figure 3 shows the frequency distribution of PVD in all four quadrants. The inferior quadrant PVD was common and PVD in the nasal quadrant was least common. Figure 4 & 5 show the quadrants wise changes in macular thickness in different degrees of myopia.

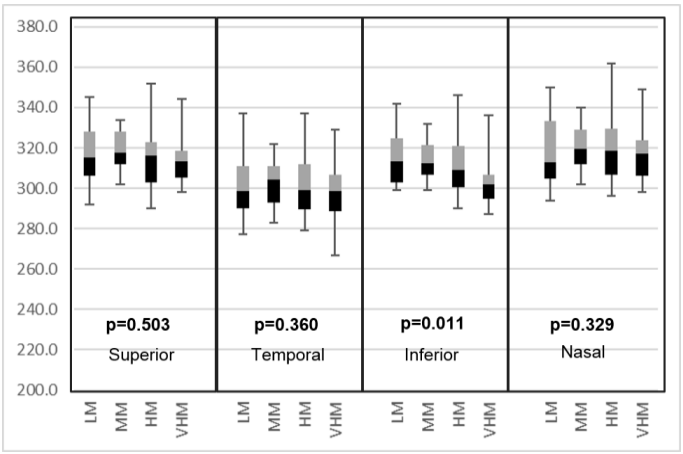

Figure 4: A box-plot between para-macular thickness in four quadrants and degree of myopia

LM: Low myopia, MM: Moderate myopia, HM: High myopia VHM: Very high myopia

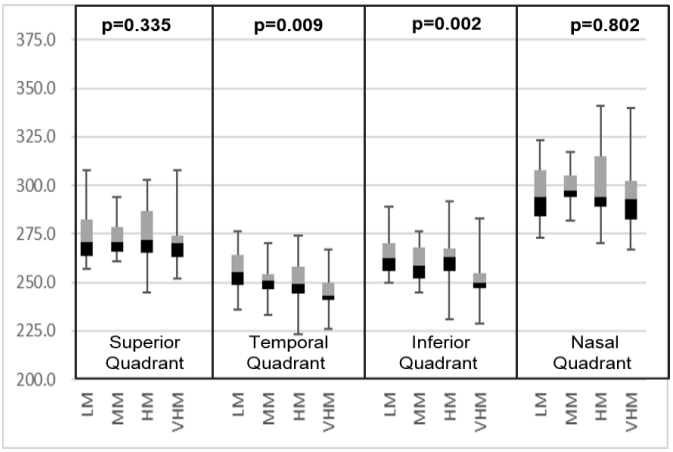

Figure 5: A box-plot of Peri-macular thickness in all the four quadrants and degree of myopia

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Table 2: FAZ and Foveal dimensions for different degrees of myopia

	FAZ dimension			Foveal characteristics		
Myopia	**Area (mm^2)**	**Perimeter (mm)**	**Circularity**	**Thickness (µm)**	**Volume (mm^3)**	**Vessel Density**
Low	0.26 (0.21-0.34)	2.02 (1.85-2.45)	0.79 (0.71-0.81)	245.0 (230.0-254.0)	9.80 (9.60-10.30)	9.50 (6.90-11.40)
Moderate	0.28 (0.20-0.34)	2.17 (1.87-2.30)	0.75 (0.73-0.78)	251.0 (238.0-260.0)	9.90 (9.80-10.00)	9.90 (7.60-10.80)
High	0.29 (0.18-0.37)	2.20 (1.78-2.47)	0.76 (0.67-0.77)	249.0 (235.0-258.0)	9.90 (9.60-10.30)	8.85 (7.00-10.80)
Severe	0.27 (0.21-0.31)	2.16 (1.85-2.47)	0.70 (0.61-0.74)	249.0 (238.0-267.0)	9.50 (9.10-9.80)	7.90 (4.70-10.45)
Total	0.27 (0.20-0.34)	2.16 (1.81-2.43)	0.75 (0.69-0.79)	248.0 (235.0-260.0)	9.80 (9.60-10.10)	9.10 (6.80-11.10)
p-Value	0.731*	0.774*	0.002**	0.131*	0.000*	0.195*

*ANOVA, **Kruskal Wallis

Table 2 shows an alteration in FAZ dimension and foveal characteristics in different degree of myopia. Only the FAZ circularity (p=0.00) and foveal volume (p=<0.00) exhibited significantly alteration as the degree of myopia increases.

Table 3: A cross correlation table between PVD location and degree of myopia

	Myopia				
	Low	Moderate	High	Severe	Average
Superior	78.60	83.30	89.50	83.30	83.68
Temporal	50.00	83.30	63.30	62.50	64.78
Inferior	82.10	95.80	97.40	87.50	90.70
Nasal	64.30	79.30	81.30	70.80	73.93
Average	68.75	85.43	82.88	76.03	

Values are in percentage (%)

Table 3 shows a cross correlation table between PVD location and degree of myopia. We found an asymmetry in the PVD location. The results suggest an increasing trend of PVD as the degree of myopia increases with a location asymmetry. In low myopia the temporal quadrant showed the least PVD (50.0 %) whereas high myopic eyes exhibited the most PVD in the inferior quadrant (97.40 %). Figure 6 & 7 show the relationship between paramacular and peri-macular vessel density changes in various stages of PVD. In the paramacular area, the

inferior and nasal quadrants showed a significantly decreased vessel density (p=<0.05). However, in the peri-macular area, the nasal quadrant alone showed significant loss of vessel density. Table 4 shows the correlation between myopia (SE) verses macular thickness and macular vessel density different ETDRS quadrants. A significant negative correlation was found between myopia and foveal thickness. However, a weak positive correlation was seen with inferior para-macular region and overall peri-macular thickness.

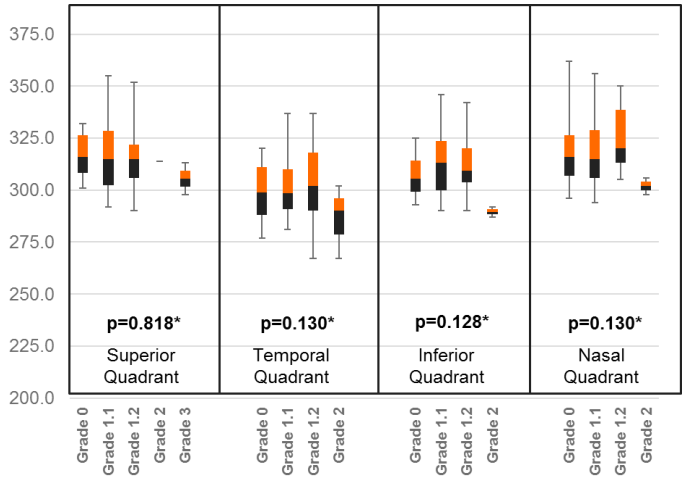

Figure 6: Relationship between paramacular vessel density & PVD stages

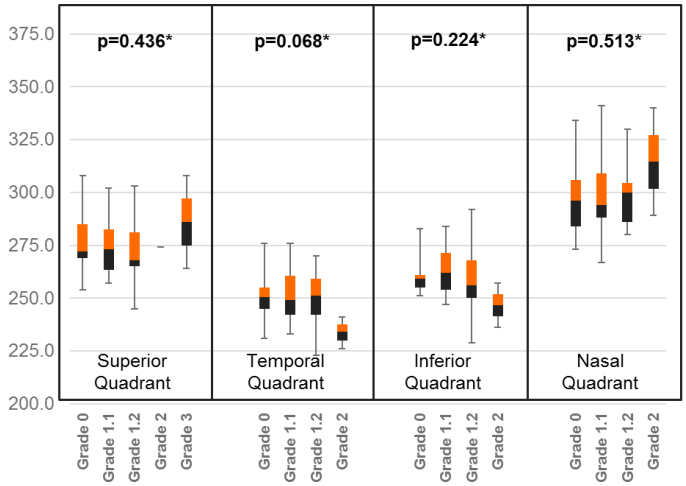

Figure 7: Relationship between peri-macular vessel density & PVD stages

Table 4: Correlation between degree of myopia and macular dimensions.

	Thickness (µm)		Vessel density	
	r*	p Value	r*	p Value
Foveal area	***-0.261***	***0.007***	0.253	0.066
Average para-macular	0.097	0.330	***0.519***	***<0.000***
Superior para -macular	0.065	0.514	***0.500***	***<0.000***
Temporal para-macular	0.094	0.344	***0.448***	***<0.000***
Inferior para-macular	***0.276***	***0.004***	***0.493***	***<0.000***
Nasal para-macular	-0.051	0.608	***0.524***	***<0.000***
Average peri- macular	***0.251***	***0.011***	***0.516***	***<0.000***
Superior peri -macular	0.110	0.269	***0.415***	***<0.000***
Temporal peri -macular	***0.356***	***0.000***	***0.442***	***<0.000***
Inferior peri -macular	***0.397***	***0.000***	***0.488***	***<0.000***
Nasal peri-macular	0.054	0.588	***0.527***	***<0.000***
Overall	***0.503***	***<0.000***	***0.503***	***<0.000***

*Pearson's Correlation Coefficient

Discussion

The current study reports the onset of PVD was in the third decade of life but it did not show any difference in the degree of myopia. However, previous publications [4, 25] report the onset of PVD in high myopia (worse than -8.00 D SE) was in the third decade of life. This difference could be due to the methodology. We report the changes in foveal morphology and microvasculature in myopia and its correlation with various stages of PVD. In those with no PVD, high myopia patients had increased foveal thickness and macular cube volume as compared to low and moderate myopia. We also found that in those with no PVD, the FAZ area became smaller as the degree of myopia increased. Previous studies have shown conflicting results regarding foveal thickness and severity of myopia [26]. Samuel et al. [7] reported results similar to ours, namely higher foveal thickness in high myopia. They also reported a correlation with the axial length, namely, longer axial lengths had higher foveal thickness. Similarly, Xie et al. [27] showed that the minimum and average foveal thickness were similar in emmetropia and low myopia groups but increased in high myopia groups. However, Lim et al. [28] showed that the average macular retinal thickness did not significantly vary between various degrees of myopia. The possible reason for discrepancies in the association of myopia severity and foveal thickness could be due to the fact that these

studies did not take into account the influence of PVD. We found that there was a reduction in macular volume with degree of myopia. This result is similar to that of Hwang et al. [29] who found that macular volume was lower in very-high myopia. This could be due to progressive thinning of the para- and peri- foveal thickness with increasing myopia. Zhao et al. [16] reported that the para- and peri-foveal thickness were negatively correlated with the axial length and positively associated with the SE.

Gołębiewska et al. [30] studied the foveal microvasculature and found that the FAZ area was larger in myopic eyes than in the control group. However, studies by Leng et al. [31] and Ucaket al. [32] showed no difference in FAZ area in both high and low myopic eyes. The custom developed automated algorithm [22] used in this study could detect boundaries with an error of 1.99% compared to the manufacturer's inbuilt algorithm with 6.42% error excluding orientation. This thresholding method dilates the irrelevant part of the image without distorting the actual FAZ boundary and reduces the number of false positives. In this study we found a smaller FAZ area in high myopia in subjects with IPVD attached at the macula.

Kumagai et al. [33] described the changes in OCT characteristics after an asymptomatic PVD and showed a thinning of the central foveal thickness, deepening of the pit, and widening of the foveal floor after PVD. The mechanism by which the PVD alters the foveal shape and regional macular thickness is not understood. Possible mechanisms may include the release of the tractional force on the fovea by the peri-foveal IPVD. An anterior centrifugal traction could cause a thickening of the fovea, and the release of this traction would then presumably reduce the foveal thickness. Likewise, mechanical forces might explain the smaller FAZ in high myopia with IPVD attached at macula. These results come from a relatively small sample size and hence should be considered as preliminary results. The clinical significance of these results, namely that there is an increasing trend of partial PVD has definite clinical implications and need to be further explored.

Since the current study was retrospective, we had very few cases with axial length data. The best way to classify myopia should be based on the corneal-axial ratio or at least by axial length. Sampson et al. [20] reported that the FAZ area is affected by its axial magnification during the image acquisition. This can be rectified by correcting for image magnification induced by the axial length variation [34]. In cases of high myopia (SE -6.00 to -10.00D) or very high myopia (SE >-10.00 D) of our sample, none of the cases had a corneal curvature >44.00D. Likewise, no eyes had cataractous changes and all the subjects had axial myopia. The second shortcoming was the low sample size of the various myopic sub-groups. We hope to further expand on the datasets as well as pathological conditions in future research.

Conclusions

In summary, we report characteristic retinal changes in high and very high myopic eyes. An increasing trend of partial PVD is seen in eyes classified as having high and very high myopia. An asymmetric PVD in location was observed and the most commonly involved quadrant was the inferior quadrant. A statistically significant alteration was observed in foveal volume and the FAZ circularity index. However, our data did not show any relationship between PVD and macular thickness and foveal microvascular parameters in high myopic eyes.

List of abbreviations

PVD: Posterior vitreous detachment, SD-OCT: Spectral-domain optical coherence tomography, SE: Spherical equivalent, CRT: Central macular thickness, FAZ: Foveal microvascular zone dimensions, OCTA: Optical coherence tomography angiography, OCT: Optical coherence tomography, MT: macular thickness, BCVA: Best corrected visual acuity, MCV: Macular cube volume, D: Diopter, LM: Low myopia, MM: Moderate myopia, HM: High myopia, VHM: Very high myopia.

Declarations

Ethics approval and consent to participate

This retrospectives study was approved by the Institutional Review Board of the Vision Research Foundation, Chennai, India. The study conformed to the tenets of the Declaration of Helsinki, and signed informed consent was obtained from all subjects.

Consent for publication

Not applicable

Availability of data and materials

All the clinical data and materials supporting the manuscript are maintained in our Hospital.

Competing interests

The authors declare that they have no competing interests.

Funding

None

Authors' Contribution

Concept and design: JJB, RR and VL; Software Development and validation: AA and VL; Data acquisition: JJB; Data analysis / interpretation: JJB and VL; Draft the manuscript: JJB; Critical revision of the manuscript: VL and RR; Supervision: VL and RR. All authors read and approved the final manuscript.

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Figures

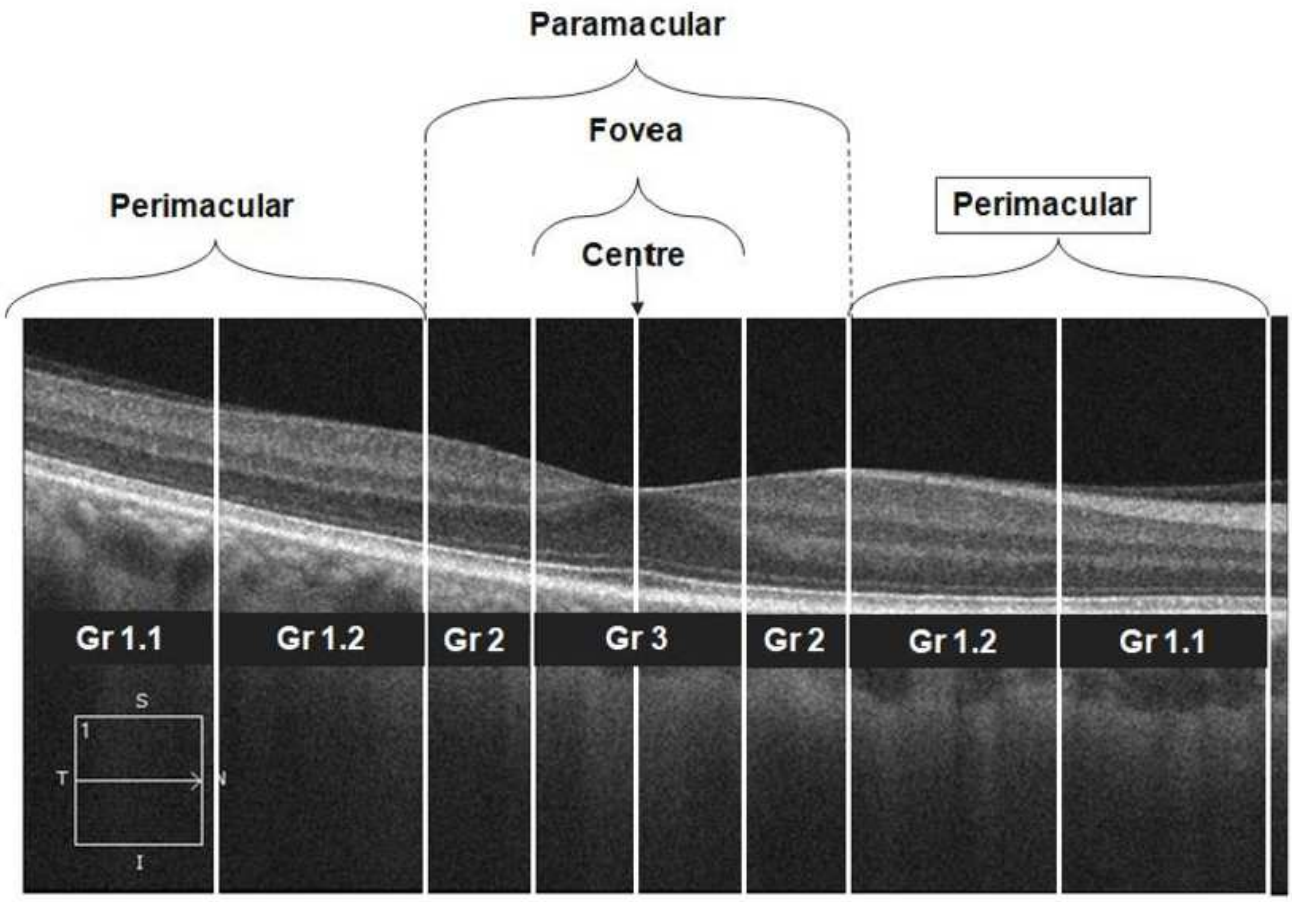

Figure 1

An example and a schematic diagram of a SD-OCT horizontal radial scan image. The PVD classification based on the PVD location. The above picture shows the PVD extended till parimacular area with grade 1.2.

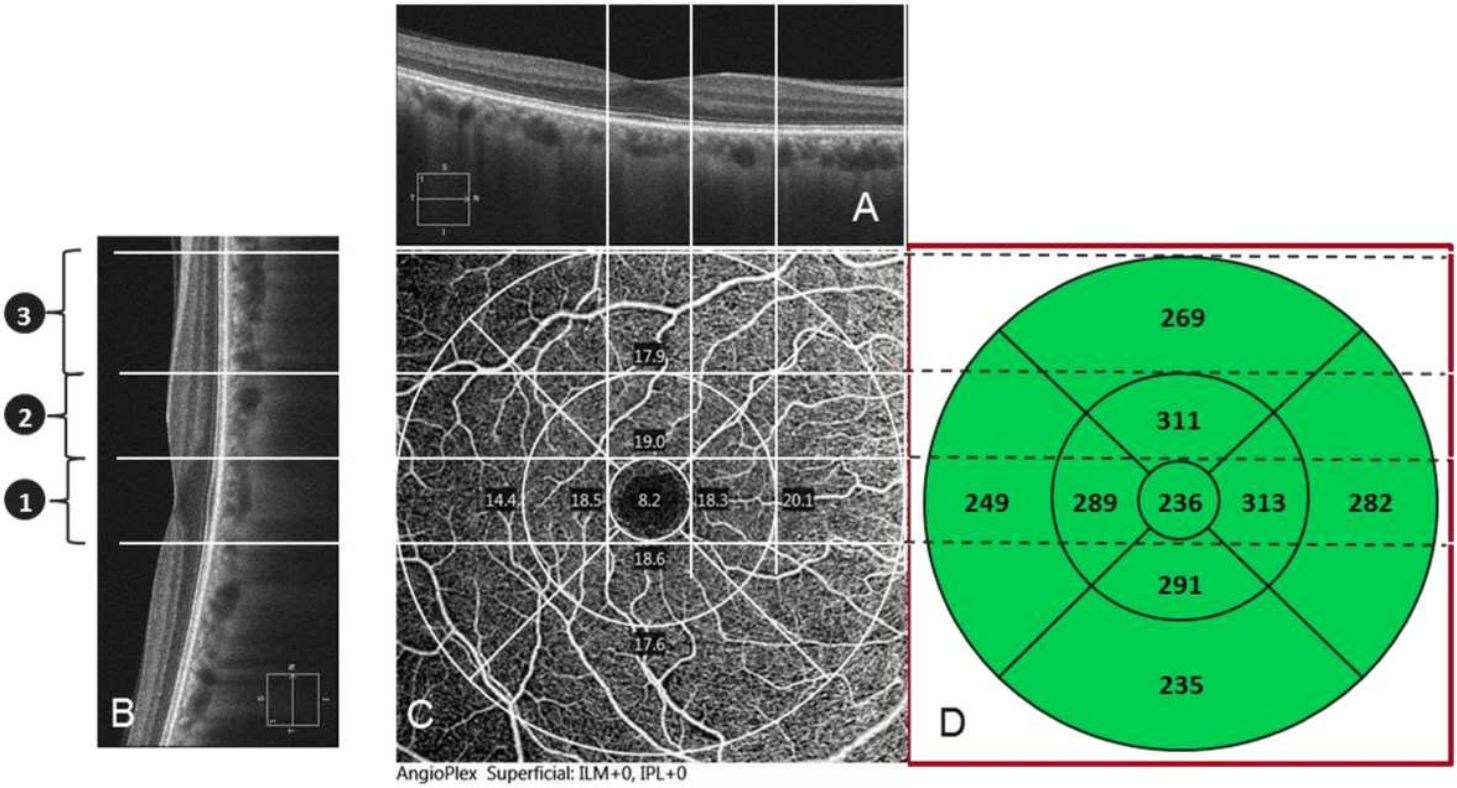

Figure 2

A relationship between PVD location and the corresponding location macular thickness and angioplex image using the ETDRS method. A & B) a radial scan of a horizontal and vertical scan. The numbers 1, 2 & 3 indicating the macular anatomical structures 1) fovea, 2) paramacular and 3) perimacular area. C) An en-face image of macular and FAZ with ETDRS segmentation D) the ETDRS macular thickness (in microns) to the corresponding area of the fovea, para, and peri macular regions.

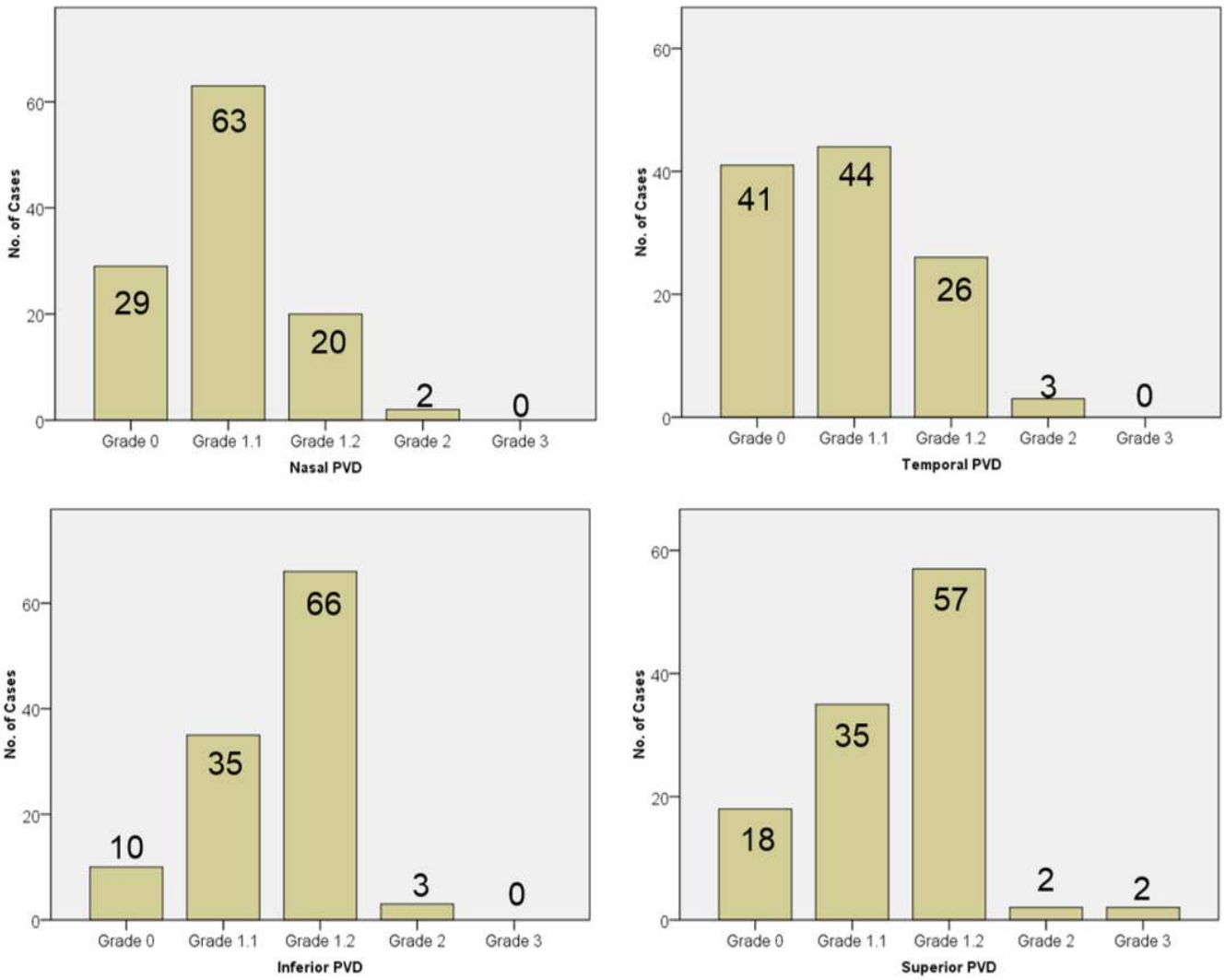

Figure 3

Distribution of PVD in all four quadrants.

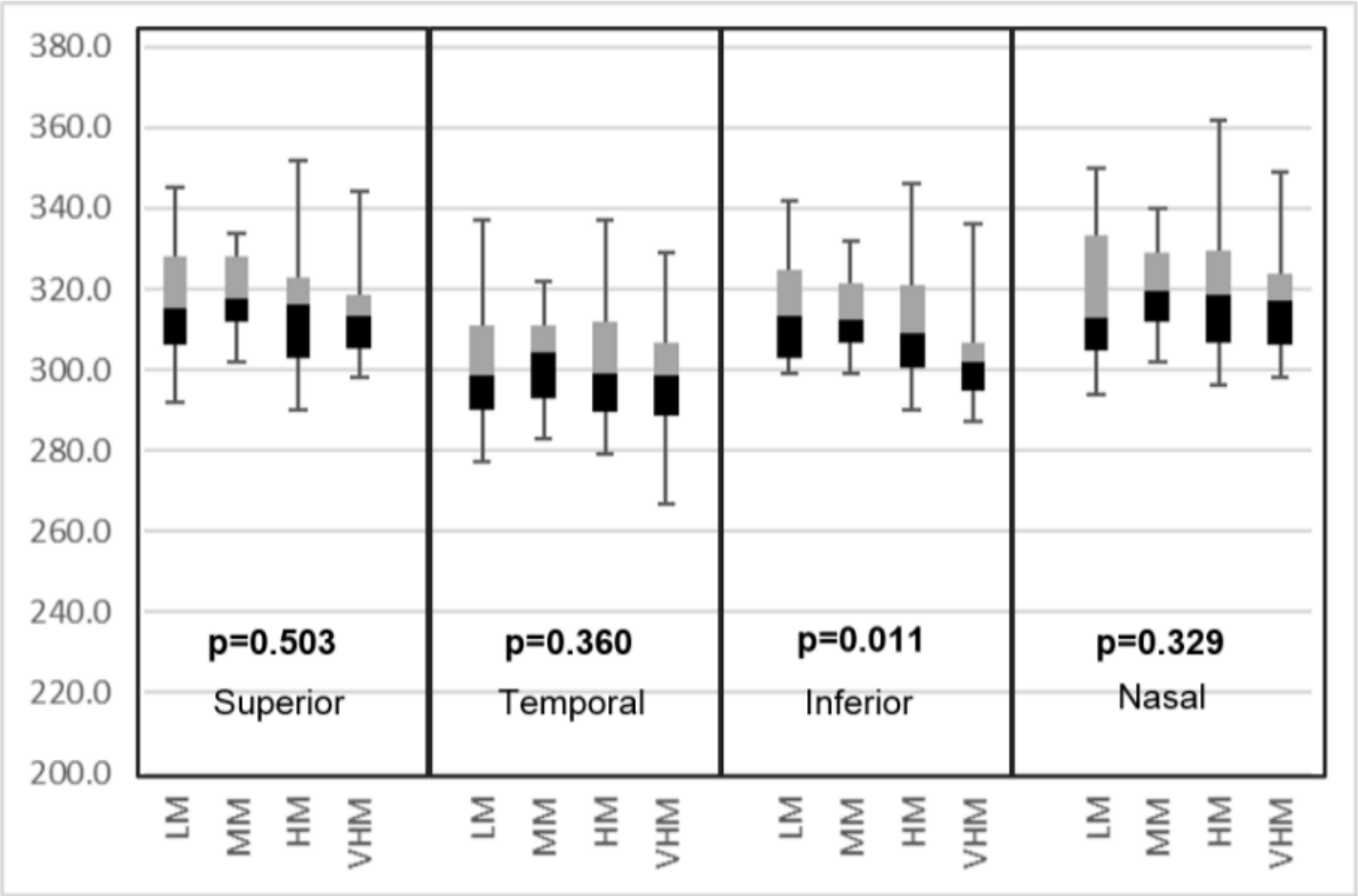

Figure 4

A box-plot between para-macular thickness in four quadrants and degree of myopia LM: Low myopia, MM: Moderate myopia, HM: High myopia VHM: Very high myopia

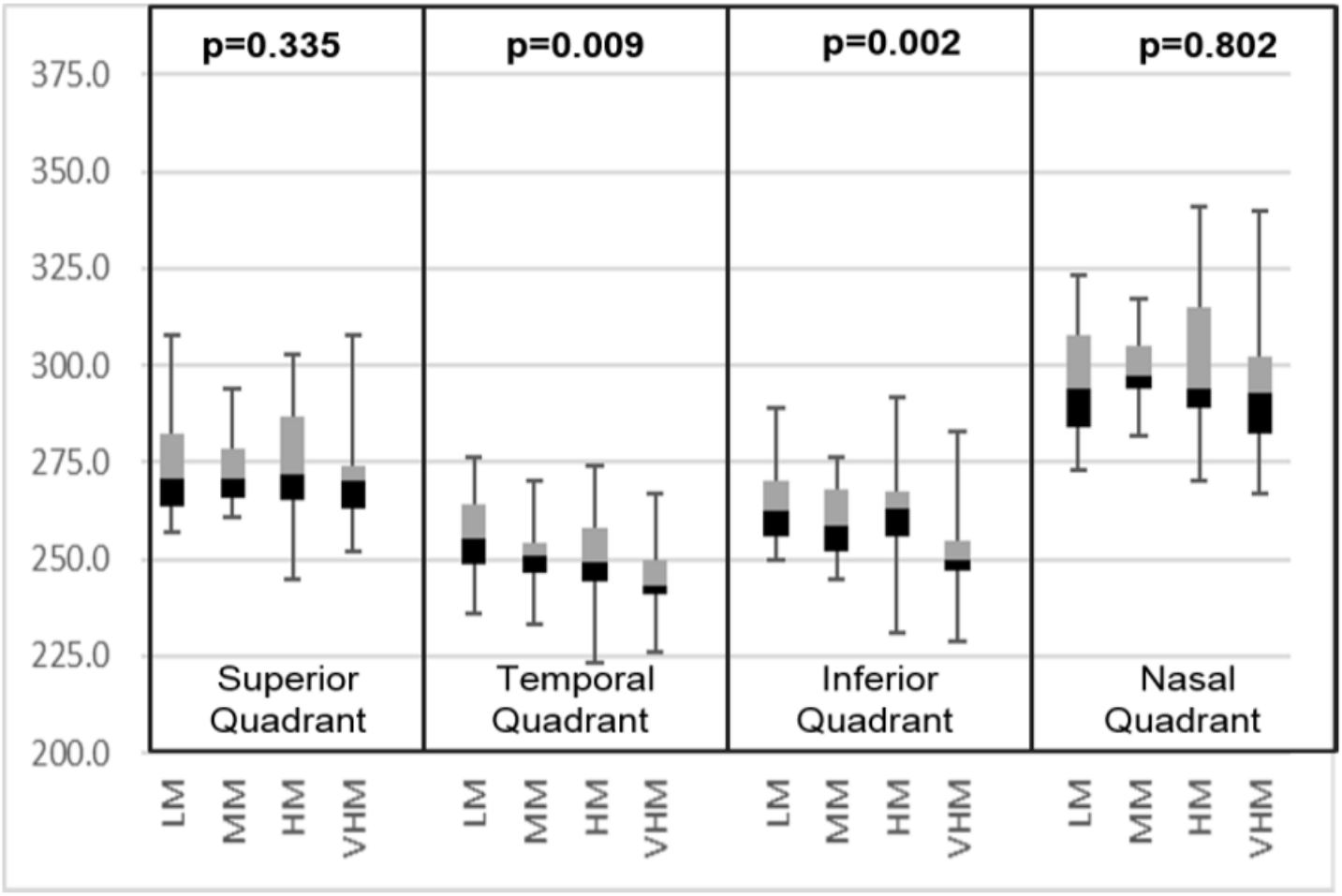

Figure 5

A box-plot of Peri-macular thickness in all the four quadrants and degree of myopia

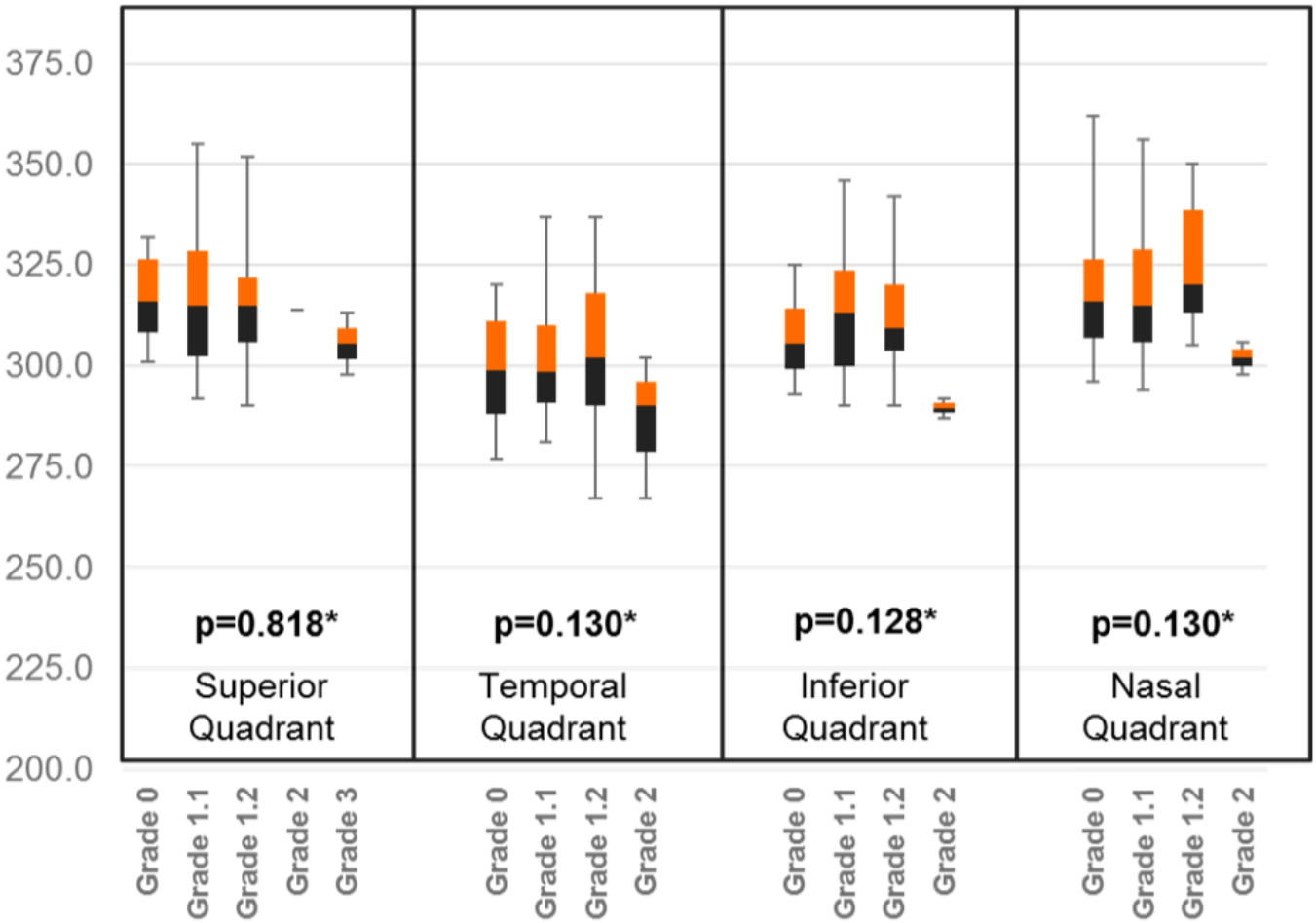

Figure 6

Relationship between paramacular vessel density & PVD stages

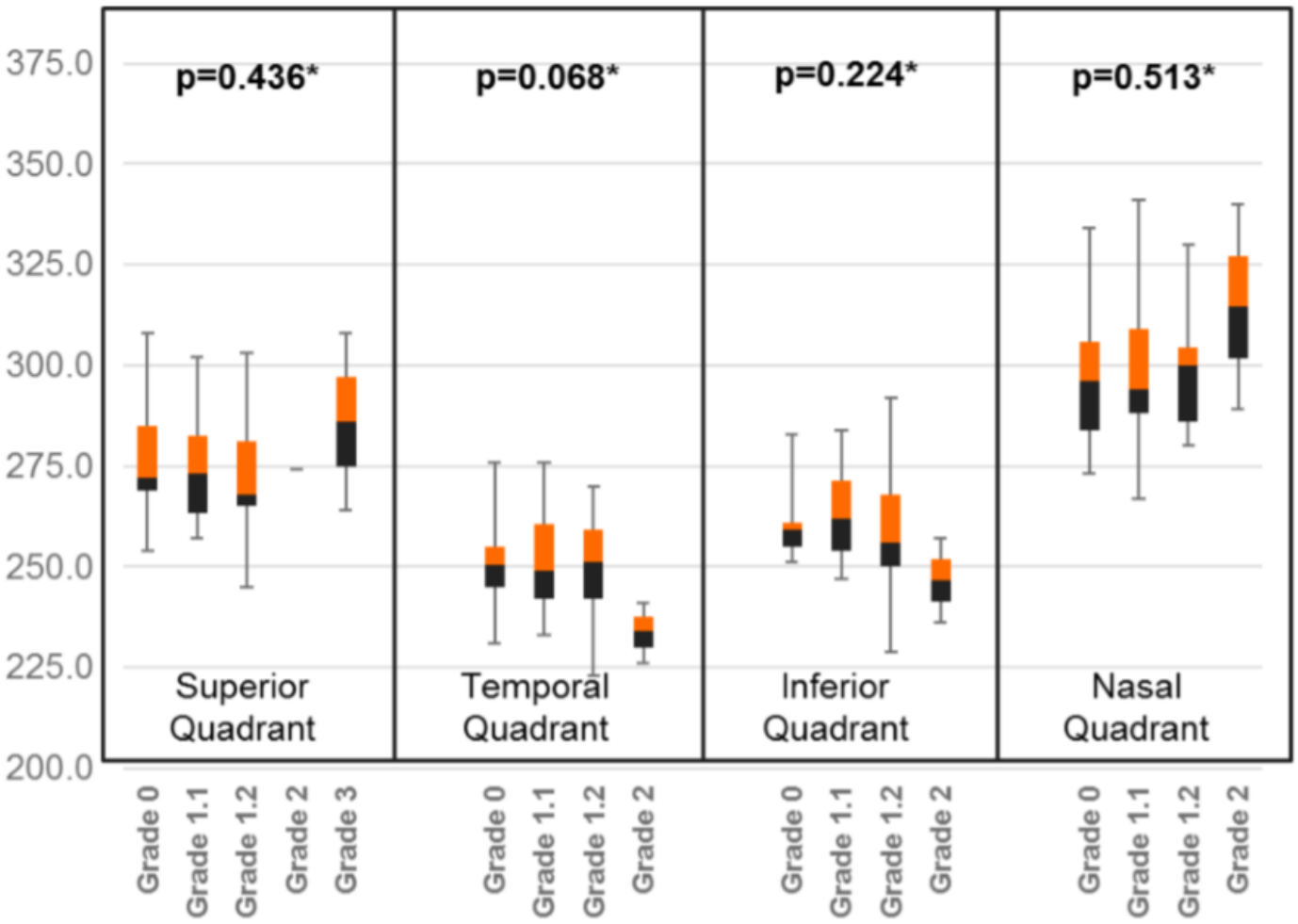

Figure 7

Relationship between peri-macular vessel density & PVD stages