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High myopic eyes, where the basic abnormality is excessive axial elongation, are associated with more chances of having degenerative changes in the sclera, choroids, retinal pigment epithelium and retina. There is also increased risk of choroidal neovascularization (CNV) with high myopia.

The greater the degree of myopia, the higher the chances of developing complications that can threaten vision [88].

The axial elongation has a familial tendency and is present commonly with refractive errors greater than -6.0.D. The stretching of ocular tissues in myopia affects the hemodynamics of the choroids. Diffuse choroidal thinning is resulted and choroidal neovascularisation (CNV) is more likely to develop which are leaky and can easily bleed. [88].

It is assumed that a disturbance of visual stimulation early in life can disrupt emmetropization and thus induce the eye to become either myopic or hyperopic, in combination with a high incidence of astigmatism. This disturbance of visual stimulation may be due to clouding of the dioptric media, though equally to congenital or hereditary defects in the retina or the visual pathways of visual cortex. Myopia was seen in cases of coloboma, both of the optic nerve head as well as of the macular region, and in cases of macular aplasia and hyperplasia [89].

Grossniklaus HE, Green WR [90] noted histopathologic findings and percentage of eyes affected, in decreasing order of frequency, were myopic configuration of the optic nerve head, 37.7%; posterior staphyloma, 35.4%; degenerative changes of the vitreous, 35.1%; cobblestone degeneration, 14.3%; myopic degeneration of the retina, 11.4%; retinal detachment, 11.4%; retinal pits, holes, or tears, 8.1%; subretinal neovascularization, 5.2%; lattice degeneration, 4.9%; Fuchs spot, 3.2%; and lacquer cracks, 0.6%.

Liang Xu, Yibin Li, Shuang Wang, Yun Wang, Yaxin Wang and Jost B. Jonas [91] concluded that in the adult Chinese population, high myopia is associated with a lower number, smaller size and less advanced type of macular drusen, a larger optic nerve head, and decreased best-corrected visual acuity. The risk of early and late macular degeneration was lower for highly myopic participants than for non highly myopic participants.

Jost B. Jonas [92] noted that the optic disk size depends on the refractive error with an increase in highly myopic eyes beyond a -8 diopters and a decrease in highly hyperopic eyes beyond +4 diopters.

Wang TH, Lin SY, Shih YF, Huang JK, Lin LL, Hung PT [93] observed that the optic disc area in highly myopic eyes was similar to that in mildly myopic eyes. However, regression analysis revealed that the optic disc area increased with axial length in subjects with severe myopia. The cup/disc ratio, the disc depth, the neuroretinal rim area, and the tilting of the disc were not significantly different between the severe and mild myopia groups. They concluded that these findings may be useful in further

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investigations of myopic progression and of the mechanisms responsible for the development of myopic complications.

Y Wang, L. Xu, L. Zhang, H. Yang, Y. Ma and JB Jonas [94] observed that optic disc area was significantly correlated with myopic refractive error. With a steep decrease in optic disc area from high myopia to the mid-range of refractive error, a slightly horizontal course in the refractive error range between -8 dioptres and +4 dioptres, and a further decrease in optic disc area towards higher hyperopia. Optic disk area was not related to age or sex. They concluded that mean optic disc size is larger in Chinese people than in white people. In Chinese people highly hyperopic eyes have significantly smaller optic discs, and highly myopic eyes have significantly larger optic discs than emmetropic eyes.

L Xu, Y Wang et al., [95] compared with data from studies in western countries, found that a larger optic disc size in adult Chinese than in adult white population.

Albert Dichtl, Jost B. Jonas, Gottfried O. H. Naumann [96] observed that in the highly myopic eyes, mean optic disc diameter was significantly larger, optic cup was significantly shallower and the peripapillary scleral ring was significantly broader in comparison with the non-highly myopic eyes.

J.B. Jonas, R. Thomas, R. George, E. Berensthein and J. Muliyie [97] observed that optic disc area was statistically independent of age and refractive error, its shape was slightly vertically oval and neuroretinal rim area was significantly and positively correlated with optic disc size and optic cup size. It was independent of age, sex, refractive error and axial length.

Jonas JB, Gusek GC, Naumann GO [210] noted that the optic discs were significantly larger and ovaly configurated in highly myopic eyes i.e more than -8.0 D. Refraction, size of the disk, and area of the parapapillary region with chorioretinal atrophy were significantly correlated with each other. Highly myopic disks can be regarded as secondary acquired macrodisks, the size of which is correlated with refraction and possibly age.

Eugene Tay et al., [98] correlated greater optic disk ovality (tilt) with greater myopia. They concluded that increased optic disk tilt was associated with higher myopia and reduced sensitivity on field testing. These factors are important in the assessment of glaucoma in patients with myopia.

Jonas JB, Papastathopoulos KI [99] observed that for a myopic refractive error of less than -8 D, the normal eyes and the glaucoma eyes did not differ significantly in their slightly vertically oval optic disc shape. In the highly myopic group, the optic disc was significantly more ovaly configurated, more obliquely oriented, and larger than in any other group.

Jonas JB, Budde WM [100] in their study with stereo optic color photographs, concluded that in chronic open-angle glaucoma, optic nerve damage may be more pronounced in highly myopic eyes (equal or higher than -8D) with large optic discs than in non-highly myopic eyes. This may suggest a higher susceptibility for

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glaucomatous optic nerve fiber loss in highly myopic eyes than in non-highly myopic eyes.

Jonas JB, Dichtl A [101] noted significant difference of the optic disc morphology in primary open-angle glaucoma between highly myopic eyes (higher than -8D) and eyes with hyperopia or low to moderate myopia. The highly myopic eyes are characterized by secondary macro-discs with elongated shape; the loss of neuroretinal rim was more concentric, shallow disc cupping, large parapapillary atrophy, and low frequency of localized retinal nerve fiber layer defects. Glaucomatous optic nerve damage in highly myopic eyes, compared to eyes with a normal refractive error, is more diffuse than localized.

Christopher Kai-shun Leung et al., [107] concluded that while optic disc area generally increased with the axial length and myopic refraction, the HRT (Heidelberg Retina Tomography) measurements demonstrated that optic disc size was largely independent of axial length and refractive error between -8 and +4 D. OCT may overestimate optic disc size in myopic eyes and results in poor agreement between the two instrument.

R R A Bourne, P J Foster et al., [113] found that disc and rim areas vary with sex, greater in men than women. Disc area (but not that of the rim) increases with age. They had also noted that Disc area (DA) was positively associated with AL –axial length and height but was unrelated to corneal thickness. DA remained positively associated with AL, height and age.

Schwartz JT, Reuling FH, Garrison RJ [115] noted that there was no significant association with sex, race, or refractive error in the mid-range. However, there was a significant association between size of the cup/disc ratio and age as well as intraocular pressure. It is not always recognized that the size of the normal physiological cup increases with age. But, allowing for individual variation, some persons could show a recognizable acquired increase in cup/disc ratio with age, even in the absence of glaucoma.

Dichtl A, Jonas JB, Neumann, GO [96] found that in the highly myopic eyes compared with the non-highly myopic eyes, mean optic disc diameter was significantly larger (mean 2.33 (SD 0.55) mm versus 1.77 (0.50) mm; p = 0.01), and the optic cup was significantly shallower (optic cup depth 0.34 (0.29) mm versus 0.63 (0.23) mm; p = 0.03).

Koraszewska-Matuszewska B et al., [102] concluded that Optic nerve disc images in myopic and glaucomatous eyes in children are different. Smaller optic disc cup in myopic than in emmetropic eyes can show, that children myopic eyeballs enlarged without nerve fibers atrophy.

Chameen Samarawickramaa, Xiu Ying Wangab, Son C. Huynha, George Burlutskya, Fiona Stapletonb, Paul Mitchella [106] noted that Optic disk parameters in childhood are influenced by axial length, but not by refractive error itself.

Barr DB et al., [104] noted the disc-macula distance to disc diameter ratio (DM: DD ratio) has been advocated as a method of supporting the diagnosis of optic nerve

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hypoplasia. A DM: DD ratio of 3.00 has been claimed to be a satisfactory threshold value for this purpose. There was a trend of increasing DM: DD ratio towards myopia and decreasing DM: DD ratio towards hypermetropia; the DM: DD ratio may be falsely high in high myopia.

John H. Fingerta et al., [105] concluded that the chromosomal location of a gene (in the chromosome 12q locus) responsible for cavitary optic disk anomalies is a key step in identifying the genetic basis of this condition and ultimately may provide important insight into the pathogenesis of more common optic nerve diseases such as normal-tension glaucoma and primary open-angle glaucoma.

Robert A. Honkanena et al., [103] had done genetic linkage analysis of the family with autosomal dominant inheritance of cavitary ONH (optic nerve head) anomalies and abnormal vasculature. They identified the chromosomal location of a gene responsible for ONH development. This may provide insight into the pathogenesis of glaucomatous ONH damage.

Nilufer Berker, Ufuk Elgin, Pinar Ozdal, Aygen Batman, Emel Soykan, Seyhan S Ozkan [108] found a relationship between the severity of ocular Bachet’s disease and optic disc topography determined by HRT. In eyes with smaller optic discs, uveitis was observed to have a more severe course with more frequent relapses than those with larger discs.

S. Zumbroa et al., [120] observed that macular schisis and detachment can occur in patients with presumed enlarged optic nerve head cups in the absence of obvious congenital anomalies of the disk.

Martine Mauget-Fasse et al., [110] concluded that in tilted disk syndrome and high myopia, polypoidal choroidal vasculopathy is a potential cause of visual loss but the pathogenesis was unclear.

Klara Landau et al., [111] found topless optic disk (superior segmental hypoplasia of optic nerve) in the female sex, short gestation time, low birth weight, and poor maternal diabetes control. Pathogenesis remains obscure but the responsible pathogenic event may occur in the perinatal period.

Tong L, Saw SM et al., [112] noted that in subjects with severe myopia, the upper pole of the disk was rotated away from the fovea but to lesser extent than in those with emmetropia or milder myopia. Apart from PPA (peripapillary atrophy), degenerative features were not commonly found in their study.

Weiss AH, Ross EA [116] noted that six of 14 patients with unilateral optic nerve hypoplasia and 5 of 22 patients with bilateral involvement had at least 4 D of myopia. Nine of the 11 patients with asymmetric bilateral involvement had relative myopia in the eye with the more abnormal optic nerve;

Schmidt D, Meyer JH, Brandi-Dohrn [117] in their study of Color fundus photography, taken by the Zeiss Fundus camera SK50 (30 degrees and 50 degrees picture size) and by the Olympus Fundus camera GRC-W (same picture size) found that myopia only occurred in eyes with wide-spread myelinated nerve fibers located on and around the
optic disc which extended to the midperiphery of the retina but not occurred in eyes with circumscribed myelinated nerve fibers.

Nakamura H, Maeda T, Suzuki Y, Inoue Y [118] observed by HRT that the mean cup depth and maximum cup depth were significantly deeper in myopic subjects. Large discs had large cup area, cup/disc area ratio, rim area, cup volume, mean cup depth, cup shape measure, and maximum cup depth. The Retinal nerve fiber layer thickness was smaller in large discs. Rim volume was unaffected by age, refraction, or disc area. They concluded that the age, refraction, and disc area were related to several optic disc parameters obtained by the Heidelberg Retinal Tomography. Because of these relationships, care should be taken to analyze the appearance of the optic disc on the basis of these parameters in patients with glaucoma or other diseases. Rim volume appears to be a good parameter for evaluating the optic disc without considering age, refraction, or disc area.

Nicolela MT, Drance SM, [119] in their study of optic disc stereo photographs, noted that patients with myopic glaucoma and generalized enlargement of the optic cup discs were significantly younger than patients with focal ischemic and senile sclerotic discs. There were more women in the focal ischemic group. Patients with senile sclerotic discs had a significantly higher prevalence of ischemic heart disease; they also had a higher prevalence of systemic hypertension, which did not reach statistical significance. Intraocular pressure was significantly higher in the generalized enlargement group.

Optic disc drusen are hyaline bodies in the optic nerve head of unknown aetiology, which are present in approximately 2% of the population. Reduced visual acuity associated with optic disc drusen is rare, although visual field defects are common in cases of visible drusen. Although the condition is frequently bilateral, asymmetry is usual. [154]

Rogrio A. Costa et al., [155] found twenty eyes with CRA (choriocapillaris anastomosis) and drusen identified in 11 patients, seven women (63.6%) and four men (36.4%) ranging in age from 69 to 82 years (median, 79 years). Concluded that morphologic features and changes demonstrated by OCT suggest that fibrovascular detachment of the retinal pigment epithelium followed by development of occult CRA are the initial events occurring in eyes with CRA in age-related macular degeneration.

Ronald Klein et al., [156] observed 15-year cumulative incidence in either eye of reticular drusen was 0.7% and 3.0%, respectively. The 15-year incidence of reticular drusen varied with age from 0.4% in those 43 to 54 years of age to 6.6% in those 75 years or older. Risk factors significantly associated with increased risk of incident reticular drusen included: being female, current smoking, less education, B-vitamin complex use, single vitamin B, history of steroid eye drops use, glaucoma and more severe drusen type (e.g., soft indistinct drusen), whereas diabetes at baseline.

I Droz, I Mantel et al., [157] noted that the complement factor H Y402H polymorphism showed a genotype-phenotype association for some drusen features. Additional genetic factors are likely to influence drusen phenotype.

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Arsaell Arnarsson et al., [158] took fundus stereo color photographs and used standard grading system to study the five-year incidence of drusen, pigmentary abnormalities. Found Current alcohol consumption decreased the risk for drusen. Being married rather than divorced or widowed decreased the risk for soft drusen; being single decreased the risk of hypopigmentation as compared with being divorced or married. Both consuming dietary fiber rich vegetables and meat and meat products once a week or less frequently was a risk factor for developing soft drusen and decreased the risk of pigmentary abnormalities. Those who had smoked 20 pack-years or more as compared with nonsmokers had decreased survival rate over the five years.

Dichtl A, Jonas JB, Naumann GO [96] found the peripapillary scleral ring was significantly broader (0.58 (0.65) mm versus 0.08 (0.06) mm; p = 0.001), in highly myopic eye compared with the non highly myopic eyes. The beta zone (0.83 (0.74) mm versus 0.28 (0.25) mm; p = 0.006) of the parapapillary chorioretinal atrophy was significantly larger.

Jonas JB, Dichtl A [101] found that the highly myopic eyes are characterized by secondary macro-discs with elongated shape; the loss of neuroretinal rim was more concentric.

L Xu, Y Wang et al., [95] noted that in adult Chinese, the neuroretinal rim area measures 1.70 (0.30) mm2 on optic disc photographs. It is statistically independent of age and sex. Compared with data from studies in Western countries, the neuroretinal rim is larger in adult Chinese than in adult white populations, corresponding to a larger optic disc size in the Chinese.

R R A Bourne, P J Foster et al., [113] found that like disc, rim area also vary with sex, greater in men than women. Neuroretinal rim area (RA) was also significantly and positively associated with AL and also with height. RA was negatively associated with IOP and was unrelated to blood pressure, history of diabetes, myocardial infarction, stroke or migraine.

J.B. Jonas, R. Thomas, R.George, E. Berensthein and J. Muliyie [97] observed that the neuroretinal rim area was significantly and positively correlated with optic disc size and optic cup size. It was independent of age, sex, refractive error and axial length.

Nakamura H, Maeda T, Suzuki Y, Inoue Y [118] studied by HRT that Rim volume was unaffected by age, refraction, or disc area. Large discs had large cup area, cup/disc area ratio, rim area. Rim volume appears to be a good parameter for evaluating the optic disc without considering age, refraction, or disc area.

Albert Dichtl, Jost B. Jonas, Gottfried O. H. Naumann [96] observed that in the highly myopic eyes, the peripapillary scleral ring was significantly broader in comparison with the non-highly myopic eyes.

Wang TH, Lin SY, Shih YF, Huang JK, Lin LL, Hung PT [93] observed that the neuroretinal rim area and the tilting of the disc were not significantly different between the severe and mild myopia group.

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Peter Martus et al., [121] observed that for patients with elevated intraocular pressure, significantly predictive factors for eventual progression were older age, smaller neuroretinal rim, advanced perimetric damage and larger area of parapapillary atrophy. In contrast, in the normal intraocular pressure group, a significant predictive factor was presence of disk hemorrhages at baseline.

Yaxing Wanga et al., [122] observed that in adult Chinese as in Caucasians, the neuroretinal rim usually follows the ISNT rule i.e. the neurorentinal rim was significantly wider in the inferior disk region followed by the superior disk region the nasal disk region and it was the smallest in the temporal disk region.

K. Yasuzumi, K Ohno-Matsui, T-Yoshida, A. Kojima, N Shimada, S. Futagami, T. Tokoro and M. Mochizuki [123] evaluated peripapillary crescent enlargement in highly myopic eyes by FA & ZA (Fluorescein Angiography and Indocyanine green Angioraphy). They observed two zones of the myopic crescent and concluded that inner zone might develop as a result of mechanical stretching and the outer zone might be the result of a secondary circulatory disturbance and mechanical stretching.

Michael Moore et al., [109] observed a progressive optic nerve cupping and neural rim decrease in a patient with autosomal dominant optic nerve coloboma in both eyes with normal intraocular pressure.

Myung-Kyoo Ko, Dong-Seob Kim and Yoon-Koo Ahn [124] observed cases with the circle of zinn-Haller which appeared as concentric or zigzag – shaped vascular fillings within the temporal crescent region in pathological myopia with peripaillary atrophy and tilted disc.

Tekiele BC and Semes L [125] found that the fundus findings in moderately to highly myopic eyes were more prevalent in the posterior pole (44.7%) lesion is optic nerve head crescent.

Shimada N et al., [126] identified peripapillary detachment in pathologic myopia in 31 of 632 highly myopic eyes (4.9%). The optical coherence tomographic scan across the PDPM lesion revealed a localized detachment of retinal pigment epithelium adjacent to the optic nerve. Although PDPM was always situated adjacent to the inferior edge of the optic disc, in some patients it surrounded almost the entire optic disc. Study indicates that PDPM is not uncommon among highly myopic eyes.

Age-related macular degeneration (AMD) leads to visual dysfunction in a significant fraction of the elderly population worldwide. AMD primarily affects the macular region of the retina; early signs include the appearance of soft drusen and regions of altered pigmentation in the retina, whereas advanced stages exhibit choroidal neovascularisation or atrophy of photoreceptors and the retinal pigment epithelium (RPE). Diverse cellular processes have been implicated in AMD pathogenesis, including inflammation, oxidative stress, altered cholesterol metabolism and/or impaired function of the RPE. It is widely believed that manifestation of distinct characteristics in AMD is the result of a complex interplay among genetic and environmental factors. Although the casual pathways underlying AMD are not fully understood. [127]
Asbjorg Geirsdottir et al., \cite{128} observed 54\% (469 of 863) of all those 75 years and older had advanced AMD, 64\% (258 of 406) of all those 85 years and older, 74\% (37 of 50) of all those 95 years and older, and all (eight of eight) 100 years and older had advanced AMD. They concluded that with increasing age, a gradually larger proportion of participants had advanced AMD.

Ning Cheung et al., \cite{129} studied middle aged population from their fundus photographs, found no association between Carotid artery stiffness with signs of early AMD, which provide no evidence of a link between age-related elastoid changes and early atherosclerotic processes in the carotid arteries and early AMD.

Hem K Tewari, Vijay B. Wagh et al., \cite{130} observed that the macular thickness and volume parameters have a significant correlation with age but not with gender, axial length and refraction.

Sandra C. Tomany, Jie Jim wang et al., \cite{209} observed that smoking was related to an increased risk of incident AMD. Current smokers were at higher risk of incident AMD than both past smokers and those who never smoked.

Jay C. Eriea et al., \cite{131} observed that a higher urinary Cadmium (Cd) Level, which reflects the total body burden of Cd, was associated with AMD in smokers. Accumulated Cd exposure may be important in the development of smoking related AMD.

Michael D. Knudtson et al., \cite{132} observed that alcohol Consumption is unlikely to strongly increase (or decrease) the risk of AMD.

Elaine W.-T. Chong et al., \cite{133} found, heavy alcohol consumption (more than three standard drinks per day) is associated with an increased risk of early AMD. Although this association seems to be independent of smoking, residual confounding effects from smoking cannot be excluded completely.

Morsal Mehryar et al., \cite{142} concluded that altered uric acid metabolism could play a role in ARMD damage and pathogenesis.

Elena Rochtchina et al., \cite{144} found that homocysteine >15 µmol/l was associated with an increased likelihood of AMD in participants aged <75 years. A similar association was found for vitamin B12 <125 pmol/l. Increased homocysteine and low vitamin B12 were independently associated with an increased risk of AMD.

Samantha Fraser-Bell et al., \cite{143} observed, higher Diastolic B.P and uncontrolled diastolic hypertension were associated with exudative AMD. Suggest that in Latinos cardiovascular risk factors may play a role in advanced AMD. Latinos have a high prevalence of cardiovascular risk factors, reducing these risk factors may also have a beneficial impact on the risk of having early and advanced AMD.

Robert B. Nussenblatt and Frederick Ferris \cite{141} concluded that the loss of the downregulatory immune environment is central to the development of AMD, permitting activation of the immune system. If so, immunotherapy could positively alter the course of the disease.

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Hirvela H. et al., [134] observed, the prevalence of ARMD increased steadily with age without overall significant difference between men and women. The condition was, however, related to high body mass index in men. The ARM appeared to be also associated with the presence of cataract.

Milam A. Brantley et al., [136] observed that the Y 402 H CFH Variant Carried a significantly increased risk for developing AMD.

S V Goverdhan et al., [137] concluded, the pro-inflammatory homozygous Interleukin8 -251AA genotype is an important risk factor for AMD. This may have implications for future therapy with biological agents that could target this cytokine.

Sarah Ennis et al., [138] noted that the findings are consistent with evidence that, in addition to the widely described Y402H variant, there is at least one and, most probably, several other mutations in the complement factor H gene which determine disease manifestation in AMD. A genetic model in which multiple mutations contribute to a varying degree to disease aetiology has been previously well described in ophthalmic genetics, and is typified by the COL2A1 and ABCA4 genes.

Jane-Ming Lina et al., [139] concluded, vascular endothelial growth factor (VEGF) +936 C/T and complement factor H (CFH) Y402H polymorphisms are dependently associated with wet AMD in the Taiwan Chinese population [139-ii]. They also found that the pigment epithelium derived factor (PEDF) Met72Thr T allele may be a risk factor for wet AMD in the Taiwan Chinese population. PEDF may play a role in the pathogenesis of wet AMD [139-ii].

R. Keith Shuler jr. et al., [140] found that the LOC387715 variant appears to be an independent risk factor for grade 5 (neovascular) AMD. This variant may also be associated with an earlier onset of AMD. Phenotypes that suggest a high-risk genotype may prove valuable for diagnostic, therapeutic, and research purposes.

Ilse Krebs et al., [135] found that persistent attachment of the posterior vitreous cortex to the macula may be another risk factor for the development of exudative AMD via vitreo-retinal traction inducing chronic low-grade inflammation, by maintaining macular exposure to cytokines or free radicals in the vitreous gel, or by interfering in transvitreous oxygenation and nutrition of the macula. Inducing PVD may provide prophylactic benefit against exudative AMD.

Rogrio A. Costa et al., [155] concluded, morphologic features and changes demonstrated by OCT suggest that fibrovascular detachment of the retinal pigment epithelium followed by development of occult CRA (chorioretinal anastomosis) are the initial events occurring in eyes with CRA in age-related macular degeneration.

Peripapillary choroidal neovascularisation (PPCNV) comprises about 10% of all cases of choroidal neovascularisation. Starting at the nasal margin of the disc the condition does not become symptomatic until fluid, exudate, blood, or the membrane itself have extended from the disc toward the macula, threatening central vision. Very large PPCNVs are defined as more than 3.5 disc areas or greater in size and involve 180° or
more of the disc circumference. Although less common than smaller PPCNVs, the very large ones may lead to severe visual loss. PPCNVs can be idiopathic or secondary to various conditions.\textsuperscript{[145]}

Grossniklaus HE and Green WR\textsuperscript{[90]} noted subretinal neovascularisation 5.2\% by histopatologic findings.

Florence Coscas et al.,\textsuperscript{[146]} detected 62.7\% occult CNV (choroidal neovascularisation) in AMD (age related macular degeneration) by OCT (optical coherence tomography) examination. They observed polymorphic nature of occult CNV in AMD. 98\% PED (pigment epithelium detachment) was observed.

Toshiko Matsuo et al.,\textsuperscript{[147]} concluded that both genetic and environmental factors underlie the development of choroidal neovascularization in myopic eyes (myopia-6.75 (Rt) and – 7.75 (Lt)).

Milam A. Brantley et al.,\textsuperscript{[136]} observed Genotype and phenotype correlations regarding choroidal neovascular lesion.

Noriaki Shimada et al.,\textsuperscript{[148]} noted that eyes at the atrophic stage of myopic CNV have a higher risk of developing a macular hole, so they recommend periodic OCT examinations for macular holes or macular retinoschisis, even in asymptomatic, highly myopic eyes, after the CNV has progressed to the atrophic stage.

C Calvo-González et al.,\textsuperscript{[149]} concluded that predominantly classic juxtafoveal CNVs are highly aggressive lesions that demonstrate poor response despite combined therapy using PDT (photodynamic therapy) and Mucagen.

Izumi Yamamoto et al.,\textsuperscript{[150]} and H Sakaguchi et al.,\textsuperscript{[153]} found that intravitreal bevacizumab seems to be safe and potentially efficacious in eyes with subfoveal CNV secondary to pathological myopia.

Gianni Virgili et al.,\textsuperscript{[151]} found that visual and anatomic outcomes of PDT, in large group of patients (97 patients) with nonsubfoveal myopic CNV and good visual acuity, suggest that it may halt the progression of the disease in most cases.

Alfredo Pece et al.,\textsuperscript{[152]} found, Verteporfin PDT is a promising treatment modality resulting in stable or improved vision in 76\% of the myopic eyes with juxtafoveal CNV. Younger patients appear to respond more favorably to treatment.

Arsael Arnarsson et al.,\textsuperscript{[158]} in fundus stereo color photographs found that being single decreased the risk of hypopigmentation as compared with being divorced or married. Both consuming dietary fiber rich vegetables and meat and meat products once a week or less frequently was a risk factor for developing soft drusen and decreased the risk of pigmentary abnormalities.

Samantha Fraser-Bell et al.,\textsuperscript{[143]} found that Obesity was associated with increased retinal pigment in Latino eye study.
Malgorzata Mrugacza et al., [160] found, newborns with Retinopathy of prematurity (ROP) and with retinal hemorrhages, macular pigmentary changes were found in 3 (6%) patients. They found that the presence of the macular pigmentary changes may be related to the hemorrhage and not to the specific therapy or to the disease.

Haemorrhage at the macula causes deterioration of visual acuity within seconds or minutes. Biomicroscopy reveals a dome-shaped acute bleeding in the macular area, but the precise localisation of the blood - that is, subhyaloidal or macular - is mostly unknown. Different primary causes of subhyaloidal or macular haemorrhage are valsalva retinopathy (most common) and terson syndrome. In addition, such haemorrhages may occur secondary to vascular diseases such as arteriosclerosis, hypertension, retinal artery or vein occlusion, diabetic retinopathy, retinal macroaneurysm, chorioretinitis, blood disorders as well as shaken baby syndrome, age-related macular degeneration, and can also occur spontaneously. [159]

Malgorzata Mrugacza et al., [160] found, newborns with Retinopathy of prematurity (ROP) and with retinal hemorrhages, macular pigmentary changes were found in 3 (6%) patients. Of these 3 patients, the first had prethreshold ROP, the second threshold ROP and had underwent diode laser photocoagulation, and the third patient had stage 2 ROP. In the patients with prethreshold and threshold ROP retinal hemorrhages appeared 6 weeks after birth and macular pigmentary changes were found 6 months after birth. In the patient with stage 2 ROP hemorrhages appeared 7–8 weeks after birth and macular pigmentary changes were detected 12 months after birth. Their results may suggest that the presence of the macular pigmentary changes may be related to the hemorrhage and not to the specific therapy or to the disease.

Karolien De Maeyer et al., [161] observed Sub-ILM (Interlimiting membrane) haemorrhages in five patients (median age 32 years) based on the fundoscopic appearance and clinical setting of Terson’s syndrome (n = 1), valsalva retinopathy (n = 2), blood dyscrasia (n = 1) and blunt facial trauma (n = 1). Vision was severely impaired in all patients (to hand movements in four of five) because of a premacular location of the haemorrhage. Concluded that Sub-ILM haemorrhages often occur in a specific clinical context and can lead to severe visual impairment in young patients. Given the excellent results and low complication rates, timely surgical intervention is justified when spontaneous resorption is insufficient.

Kokame GT et al., [162] studied in 10 eyes of 9 patients (7 female and 2 male, 8 Asian and 1 white) aged 14 to 79 years. All patients experienced an acute onset of visual symptoms. Eight eyes had mild to severe myopia (-2.50 diopters [D] to -9.50 D), and 8 eyes had a tilted disc. Hemorrhage within the disc and adjacent subretinal hemorrhage were located nasally in 6 eyes, superiorly in 2 eyes, and temporally in 2 eyes. Vitreous hemorrhage was noted in 6 of 10 eyes. Hemorrhage spontaneously resolved within 1 to 7 months, and there were no recurrent hemorrhages with an average follow-up of 13.5 months. They concluded that Intrapapillary hemorrhage with adjacent peripapillary subretinal hemorrhage is more common in myopic eyes and spontaneously resolves without treatment. The unique structural architecture of the elevated nasal edge of the myopic tilted disc and the choroidal blood supply of the prelaminar optic nerve may predispose patients to bleeding from the optic discs, which may be spontaneous or may be precipitated by acute disc edema, valsalva maneuver, or vitreopapillary traction.

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A macular hole is a full-thickness defect of retinal tissue involving the anatomic fovea, thereby affecting central visual acuity. Macular holes have been associated with myriad ocular conditions and originally were described in the setting of trauma. The pathogenesis of idiopathic, age-related macular holes remains unclear despite a litany of theories. Recently, Gass has postulated that tangential vitreous traction may play a role. Cellular components surrounding the rim of macular holes may also contribute tangential traction forces and elevate the rim. Pseudomacular holes may be mistaken for macular hole lesions, despite careful clinical examination. Careful biomicroscopic examinations help to ensure accurate diagnosis. Newer imaging technology, such as optical coherence tomography, helps distinguish true macular holes from pseudoholes and may provide additional insight into the pathogenesis of this condition. Surgical management can improve vision in selected cases [163].

Noriaki Shimada et al., [148] noted higher risk of development of macular hole in atrophic stage of myopic CNV. A macular hole was detected by OCT (optical coherence tomography) in six eyes (14%) had a myopic CNV surrounded by CRA (chorio retinal atrophy) larger than 1 disk area (43 eyes). So periodic OCT examination recommended in highly myopic eyes, after the CNV has progressed to the atrophic stage.

Copp AM et al., [164] detected macular hole by OCT in 24 of 383 (6.26%) myopic eyes. These MHs were defined as asymptomatic (AMHs). The presence of AMHs was more prevalent in myopic patients younger than 50 years and with concomitant myopia of > -20 D.

Raimondo Forte et al., [165] studied high myopia using en face optical coherence tomography (OCT), observed a macular hole present in three eyes (1.5%). They detected posterior retinal detachment in 37 cases (18.5%). In 15 eyes (7.5%) detachment was associated with a macular hole. In the remaining 22 eyes (11%), the detachment was located in the area of the staphyloma, and was associated with vitreoretinal traction in four eyes (18.2%) of 22 eyes. Concluded that En face OCT provides accurate imaging of retinal abnormalities in high myopia and allows width measurement and point-to-point localization of alterations. Thus, it can represent a noninvasive way to detect minimal changes during follow-up.

From an analysis of the changes in the vitreoretinal relationship identified by OCT, Hideyasu Niwa et al., [168] found three (11%) of 27 fellow eyes in patients with unilateral idiopathic macular hole developed a full-thickness macular hole.

Yoshinori Oie and Kazuyuki Emi et al., [167] observed that the probability of the fellow eyes with high myopia developing MHRD (Macular Hole resulted Retinal Detachment) was significantly higher than that of eyes without high myopia, which indicates that the fellow eyes should be examined and followed carefully. The incidence of MHRD among the highly myopic fellow eye was 12.8%. The average interval was 51 months. The Kaplan-Meier estimated probability of the fellow eye developing MHRD was 3.7% at 18 months and 8.0% at five years.

David Gaucher et al., [166] observed in twenty-nine operated and non operated cases of Macular Foveoschisis (29 eyes of 23 patients) with Mean refraction was -14.4

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diopters, and mean axial length was 29.1 mm. by OCT scans, revealed that a lamellar macular hole in six (20.7%) of 29 eyes. During follow-up, foveoschisis and visual acuity worsened in 20 eyes, a macular hole occurred in nine eyes, six of which had previously exhibited foveal detachment. Eleven eyes with foveoschisis underwent surgery, which improved visual acuity significantly but three eyes developed a macular hole.

Arevalo JF et al. [169] found that in 60% of cases, the MH developed < or =6 months after LASIK, and in 30% of cases it developed > or =1 year after LASIK. Eighteen of 19 (94.7%) patients were female. Mean age was 46 years (range, 25-65). All eyes were myopic (range, -0.50 to -19.75 diopters [mean, -8.9]) i.e., MH may infrequently develop after LASIK for the correction of myopia. They studied that vitreoretinal surgery can be successful in restoring vision for most myopic eyes with a MH after LASIK.

Jost Hillenkamp et al. [170] done anatomical closure in 19 of 28 eyes (68%) with a persisting macular hole after vitrectomy, ILM (internal limiting membrane) peel, and gas tamponade. BCVA (best corrected visual acuity) improved in 11 of 19 eyes with anatomical closure, and in one of eight eyes without closure. Macular hole size, type of tamponade, macular hole duration before the first operation, or preoperative BCVA did not significantly correlate with visual or anatomical outcome.

Recent literature on macular hole surgery report very high success rates, but regardless of the specific surgical techniques used, not all macular holes are able to be closed after primary surgery. A meta-analysis on 1654 eyes treated using different techniques reported that 87.5% of eyes achieved anatomic success, with 12.5% failing to close i. Therefore, persistence of a macular hole after vitrectomy is still one of the major complications [171].

Retinal detachment remains the most common serious complication of macular surgery. Careful examination of the peripheral retina is a key issue in preventing retinal detachment occurring after macular surgery [172].

Benson T O Cheung et al. [173] concluded that HDSO (High Density Silicon oil) seemed to be an effective tamponade agent for myopic macular hole retinal detachment in 12 eyes of 12 patients. After the removal of HDSO, 10 (83%) eyes had macular hole closure with retinal reattachment without any tamponade. One eye had retinal reattachment after re-operation and the other refused further surgery. The mean age of the patients was 67.8 years and the mean spherical equivalent refractive error was -13.4 diopter.

Jerry Vongphanit et al. [174] observed in persons aged 49 years or older, staphyloma present in 26 participants (0.7%), bilateral in 35%, with a strong concordance of staphyloma location.

Muka Moriyama et al. [175] analyzed 57 highly myopic eyes of 36 patients by Indocyanine green angiograms; a displacement of the entry site of the posterior ciliary arteries into the choroid was observed in 76.6% of the eyes with posterior staphyloma and in 25.3% of the eyes without. These findings indicate that the choroidal...
vasculature can be significantly altered in highly myopic eyes, and this is more prevalent in eyes with posterior staphyloma.

Huang Wei Hsiang et al.,[176] studied two hundred and nine eyes of 108 consecutive patients, younger than 50 years and 50 years and older with high myopia. Ninety percent of 209 eyes had a staphyloma. The prevalence of staphylomas and more advanced grades of staphylomas (≥ grade 2) were significantly higher in the older than in the younger patients. The higher grades of staphylomas were associated with more severe myopic retinal degeneration. The morphologic features of staphylomas worsens as the patient ages. The progression from type II to type IX probably increases the mechanical tension on the macular area of highly myopic eyes, which then leads to myopic fundus lesions.

Akizawa Y and Masahiro I[177] concluded that the posterior part of the eyeball of myopic eyes was displaced superotemporally in the muscle cone. The more the eyeball expanded, the farther it was displaced, the most elongated high myopic eyes would dislocate out of the muscle cone.

David Gauchera et al.,[178] found a dome-shaped macula within a myopic staphyloma, visible on both B-scan ultrasonography and OCT: a characteristic bulge of the macular retina, RPE (retinal pigment epithelium), and choroid within the concavity of the moderate posterior staphyloma. The mean refractive error of the affected eyes was -8.25 diopters.

Baba T et al., [179] concluded, in highly myopic eyes with posterior staphyloma, the prevalence of foveal retinal detachment without macular hole was 9.0%. In eyes with this type of retinal detachment, visual acuity varies and foveal retinal detachment tends to be missed on routine examination. Periodic examination using OCT is recommended for highly myopic eyes with severe myopic degenerative changes and posterior staphyloma.

Grossniklaus HE, Green WR[90] noted posterior staphyloma, 35.4% in pathologic myopia obtained from 202 patients by histopathologic findings.

Myopic retinopathy was defined to include staphyloma, lacquer cracks, Fuchs spot and myopic chorioretinal atrophy. Jerry Vongphanit et al.,[174] found Staphyloma in 26 participants (0.7%), Lacquer cracks in 8 participants (0.2%), Fuchs spot in 3 (0.1%), and chorioretinal atrophy in 7 (0.2%). Forty-six eyes (68.7%) with myopic retinopathy were reexamined after 5 years; 8.7% had new or increased numbers of lacquer cracks and 15.2% had new or expanded areas of chorioretinal atrophy.

Pruett RC et al.,[180] studied the pattern of break formation in 60 eyes with myopic lacquer cracks, angioid streaks, or traumatic tears in Bruch's membrane, using a graphics composition technique and computer analysis of digitized images. Lacquer cracks were found in a reticular distribution within a posterior staphyloma; angioid streaks occurred in a spider-web configuration centered on the optic nerve; traumatic tears were characteristically curved, perineural, and eccentric temporally. The specific break patterns imply the operation of biomechanical forces.
Ohno-Matsui K, Tokoro T \[181\] found Lacquer cracks in the posterior fundus of 4.3% of highly myopic eyes. They represent healed and mechanical breaks of the retinal pigment epithelium, Bruch's membrane, and choriocapillaris complex. The lacquer cracks progressed in 37 eyes (56.1%). Of these 37 eyes, the number of lacquer cracks increased in 14 eyes and turned into other myopic fundus changes in 25 eyes. These changes included patchy atrophy, diffuse atrophy, and choroidal hemorrhage with neovascular membrane (Fuchs' spot). Concluded, A high incidence of lacquer cracks progressed into advanced fundus changes during a mean follow-up period of 6 years. Even faint lacquer cracks may characterize an unfavorable prognostic course, leading to macular pathology in patients with pathologic myopia.

Wen F, Wu D, Wu L \[182\] found lacquer cracks In 9 of 14 eyes, appeared at the sites of macular hemorrhage or around the hemorrhage. They concluded that Subretinal neovascularization and the formation of lacquer cracks result in two forms of high myopia (divided into two forms by causes): macular hemorrhage with and without subretinal neovascularization. ICGA (indocyanine green angiography) combined with FFA (fundus fluoroscien angiography) is more useful in evaluating the two forms of hemorrhage.

Liang Xu et al., \[183\] found that the most frequent cause of low vision/blindness in adult Chinese is cataract (36.7%/38.5%), followed by degenerative myopia (32.7%/7.7%), and glaucomatous optic neuropathy (14.3%/7.7%), with degenerative myopia dominating in younger groups and cataract dominating in elder groups. Optic nerve damage (2.0%/7.7%), Age-related macular degeneration (AMD) (2.0%/7.7%) and diabetic retinopathy (0%/7.7%) were responsible for a minority of cases.

Tekiele BC and Semes L \[125\] found that the fundus findings in moderately to highly myopic eyes were more prevalent in the posterior pole alone (44.7%), the retinal periphery alone (21.4%), those occurring in both the posterior pole and retinal periphery (10.7%). This study also confirms that the most-prevalent posterior pole lesion is optic nerve head crescent and the most-frequent peripheral retinal change is lattice degeneration.

Grossniklaus HE and Green WR \[90\] noted myopic degeneration of the retina, 11.4%; retinal detachment, 11.4%; retinal pits, holes, or tears, 8.1%; subretinal neovascularization, 5.2%; lattice degeneration, 4.9%; Fuchs spot, 3.2%; and lacquer cracks, 0.6%.

Dantas AP et al., \[184\] found that in children who had severe malnutrition during the first six months of life with visual acuity from 0.3 to 0.1 and less than 0.1, the fundoscopic alterations were pale optic nerve (2.2%), increased disc cup (4.4%), increased vascular tortuosity (6.6%), alteration of retina color (13.2%) and retinal pigment epithelium cell atrophy (12.0%). They concluded that early malnutrition interferes in the individual's visual health but further studies are necessary to establish a more precise cause-effect relationship.

Liang Xu et al., \[185\] observed in population-based studies on Chinese, myopia was more prevalent in younger subjects, was associated with urban region, educational background, female gender, decreasing visual acuity, and nuclear cataract. Myopia of
>0.50 D, 1.0 D, >6.0 D, and >8 D, respectively, occurred in 22.9%, 16.9%, 2.6%, and 1.5% of the subjects, respectively.

Prost M \cite{186} performed Eye examinations before and after delivery in 42 patients with high myopia and 4 patients with high myopia and retinal detachment, surgery in one eye. Found no progression of retinal changes and development of retinal tears, but in some patients retinal hemorrhages and macular edema were observed. Concluded that High myopia is not the indication for the cesarean section, but the patients should be examined after the delivery.

Luo HD et al., \cite{187} noted that in children, increasing axial myopia was associated with reduced macular volume and thickness. These findings suggest that early anatomic changes may be present in the retinas of children with axial myopia.

S H Melissa Liew et al., \cite{188} found, Genetic factors appear to play an important role in CRT central retinal thickness. CRT statistically related to refractive error, with increasing myopia associated with a thinner CRT.

Jonas JB, Berenshtein E et al., \cite{189} noted, in highly myopic eyes, the lamina cribrosa is significantly thinner than in non-highly myopic eyes, which decreases the distance between the intraocular space and the cerebrospinal fluid space and steepens the translaminar pressure gradient at a given intraocular pressure, which may explain the increased susceptibility to glaucoma in highly myopic eyes. As in non-highly myopic eyes, thinning of the lamina cribrosa gets more pronounced in highly myopic eyes if glaucoma is also present.

An increase of the thickness of the lens induced by senile cataract, drugs or diabetes mellitus, a forward shift of the lens or the iris-lens-diaphragm will lead to refractive myopia and may provoke an angle closure glaucoma. Pigmentary glaucoma occurs in younger patients in connection with low or medium myopia and more rapidly destroys the optic nerve head due to higher intraocular pressure values in comparison to the primary open-angle glaucoma. Due to the increased risk to develop glaucoma patients especially with high myopia are advised to consult their ophthalmologist on a regular basis \cite{190}.

Xu L et al., \cite{191} noted that marked to high myopia with a myopic refractive error exceeding -6 D may be a risk factor associated with glaucomatous optic neuropathy.

Mamidipudi R. Praveena et al., \cite{192} observed that nuclear cataract was associated strongly with high axial myopia. The density of the cataract was higher in the high myopia group. No association was observed between cortical cataract and high axial myopia.

Dwight Stambolian et al., \cite{193} found that the locus on chromosome 8p23 independently confirms a report by Hammond and associates, mapping a myopia quantitative trait loci (QTL) present to this region.

Gregg FM, Feinberg EB \cite{194} examined a patient with decreased visual acuity and macular changes attributable to pathologic myopia. A pedigree spanning six generations was constructed that demonstrated an X-linked mode of inheritance. This

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finding has important genetic and therapeutic implications for similarly affected patients.

Jorge L Alioa et al., [195] concluded that LASIK For myopia of up to -10 D and over -10 D is a safe procedure with myopic regression that slows down with time and a high rate of Best spectacle-corrected visual acuity (BSCVA) increase in the long-term.

Antonio Leccisotti et al., [196] concluded, Angle-supported IOLs (Intraocular lens) can effectively correct high myopia, although residual refractive errors may require secondary procedures. The main intraoperative and postoperative complications were halos, steroid response, and incorrect IOL sizing.

Andrew Ewen, Kristine E. Lee, B.E.K. Klein; and Ronald Klein [197] observed that measurement of optic disk & cup diameter taken from nonstereoscopic digital images through a dilated pupil were similar to those taken from stereoscopic film images. Lack of stereoscopic effect may lead to small differences in measuring the optic disk and cup diameters. They had noted advantages of digital imaging over film based imaging:

(a) The photographs are provided with nearly immediate feedback.

(b) Low illumination of the fundus can often be immediately observed and illumination readjusted to attempt to improve the image.

(c) Digitally captured images can be sent electronically to clinicians or to reading centers for grading.

(d) Images can be cataloged and tracked more efficiently.

S S Sandhu and S J Talks [199] found that OCT is good at detecting the presence of CNV in patients suspected of having new CNV. However, it is less accurate at identifying the exact components of CNV. OCT cannot at present replace FFA in accurately diagnosing CNV components. However, this imaging method may have a role as a screening tool to help prioritise FFA requests.

Garca-Layana A et al., [200] noted, once the diagnosis of CNV associated with pathological myopia was established, before treatment, OCT had a sensitivity of 96.96% for detecting CNV activity. After treatment, OCT had a good sensitivity (95.23%) and a moderate specificity (69.69%) in determining CNV activity, which resulted in a diagnostic efficiency (proportion of correct results) of 79.62%. OCT appears to be useful for indicating CNV activity. Therefore, it may serve as a complementary technique for deciding the need for PDT and re-treatment in patients with pathological myopia.

Agns Glacet-Bemard et al., [201] noted that OCT can show various aspects of stage 3 macular holes.

Mrugacz M et al., [202] noted that optical coherence tomography can be employed to assess the retinal thickness and thus facilitate the detection of the evolution of alterations in myopia.

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Menchini U et al., [204] found that macular retinoschisis with stellate foveal appearance may rarely be associated with pathologic myopia. OCT was useful to establish the true extension of these macular changes.

Pollack AL and Brodie SE [205] estimated the rate of detection through routine dilated fundus examination of clinically significant fundus lesions in asymptomatic patients at 2.73% (95% confidence limits, 1.86%-3.80%). One tenth of these are beyond the view of the direct ophthalmoscope.

Yaniv Barkana, Noga Harizman, Yariv Gerber, Jaffrey M. Liebemann and Robert Ritch [198] observed a large range of differences in estimating disk size with Heidelberg retinal Tomography (HRT), optical coherence Tomography (OCT) and fundoscopy. This precludes interchangeable use of these measurements in clinical practice, and does not allow simple conversion formulas to be proposed i.e. Estimation of both absolute and relative disk size can only be defined separately for each measurement modality.

Weiss AH [203] noted that clinical conditions associated with unilateral high myopia can be identified in the majority of patients and often account for the associated visual impairment. 45 (94%) of the 48 patients had unilateral axial myopia.

Yoshinori Oie and Kazuyuki Emi et al., [167] observed that the probability of the fellow eyes with high myopia developing MHRD (Macular Hole resulted Retinal Detachment) was significantly higher than that of eyes without high myopia, which indicates that the fellow eyes should be examined and followed carefully. The incidence of MHRD among the highly myopic fellow eye was 12.8%. The average interval was 51 months. The Kaplan-Meier estimated probability of the fellow eye developing MHRD was 3.7% at 18 months and 8.0% at five years.