Chapter

Myopia

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Abstract

Short-sightedness -myopia-, is the most common refractive error in the world. The number of myopic people is rising worldwide. It causes range from those that are genetically determined to those influenced by the external environment. Several risks factors have been described that increase the likelihood of an increase in myopia. Manifestations of myopia in the eye vary, but they affect almost the entire eyeball; whether it's the cornea, the anterior chamber, or the posterior segment of the eye. It is on the posterior segment that damage to the intraocular tissues can occur, which seriously endangers visual functions. Therefore, the prevention of myopia plays an important role in stabilizing and limiting its growth.

Keywords: myopia, axial length, retinal pigment epithelium defects, lacquer cracks, chorioretinal atrophy, myopic cone, myopic chorioretinal atrophy, myopic maculopathy, peripheral myopic degeneration, prevention

1. Introduction

Myopia (short-sightedness) is the most common refractive error of the eye, in which the rays of light refracted by the lens converge at a point in front of the retina, so there is no sharp image on the retina. Its manifestation is poor visibility of distant objects. To correct the blurred image created on the retina in the short-sighted eye, it is necessary to reduce the refractive power of the cornea, the lens, or both, so that the light rays converge more posteriorly to create a sharp image on the retina. Because the cornea represents approximately two-thirds of the total refractive power of the eye, in refractive surgery we try to increase its radius and reduce its thickness to correct myopia. Other options are correction with negative lenses in glasses or intraocular lens implantation.

In myopia, the distance from the nodal point (optic center) to the retina is greater than is found in an emmetropic eye, and therefore, the projected image will be larger than normal, unlike in those with hypertropia, in whom the refractive apparatus projects a smaller image [1].

According to the main cause, we divide myopia into axial, refractive and mixed. In axial myopia, the main cause is an increase in the axial (anteroposterior) length of the eye. The average axial length of the eye in the Caucasian population is 23.33 mm [2]. Within the average range of axial length, an increase in axial length by 1mm corresponds to a decrease of approximately 3 diopters in glasses.

In refractive myopia, the optical refractive power of the cornea and/or the lens is increased. It could be caused by a decreased radius of optical surfaces

(e.g., keratoconus, lenticonus). An increase in the refractive indices of the lens, such as that which occurs in nuclear cataract, could also cause refractive myopia. The mixed type of myopia occurs when both of the aforementioned causes are present together.

Based on the amount of myopia (the value of refraction in diopters), we can categorise light (up to -3 D), medium (up to -6 D) and high myopia (over -6 D).

In general, we classify myopia into two groups: non-pathological and pathological myopia. Non-pathological myopia is also commonly referred to as simple or school myopia. Simple myopia is usually up to -6D where the structures of the eye develop within normal limits without signs of degeneration of the sclera, retina or choroid which are typical of pathological myopia.

Pathological myopia (PM), also known as degenerative or malignant myopia, is characterised by a refractive error of at least -6 D, an axial length of more than 26.5 mm, and degenerative changes affecting the sclera, choroid and retina. These changes are concentrated in the areas from the ora serrata to the equator zone and at the posterior pole of the eye [3].

2. Prevalence

Myopia is a major global public health and socio-economic problem, the incidence of which has risen sharply around the world in recent decades [4]. Myopia is usually an underestimated eye disease. Although impaired vision due to myopia can often be corrected with visual aids such as glasses, contact lenses, or refractive surgery, uncorrected refractive error is still the leading cause of visual impairment worldwide, accounting for at least 33% of visual impairments [5–7]. A total of 153 million people over the age of 5 years are estimated to be visually impaired due to uncorrected myopia and other refractive errors, of which eight million will become blind. The incidence of myopia is increasing from west to east [8]. In the Central European Caucasian population, the prevalence of myopia is estimated at 23% [9], and in the young Asian population, it is up to 80-90% [10].

High myopia is associated with a risk of irreversible visual impairment and blindness due to higher risks of macular and retinal complications. Holden et al. showed that 25% of all myopic subjects would eventually develop pathological myopia and 50% of those with pathological myopia would have poorer vision until late adulthood [11]. Pathological myopia is one of the leading causes of vision loss in developed countries, especially in the younger population (in those younger than 50 years old). Older generations have shorter eyes on average relative to younger adults [2]. When comparing pathological myopia, adolescents and children have a significantly lower prevalence compared to adults. This supports the idea that myopic macular changes are time-dependent because of mechanical retinal tension caused by axial extension of the eye. It has been found that myopic changes of the macula and optic disc are commonly found in highly myopic eyes in young adults [12]. It is therefore likely that the disease burden of pathological myopia will increase in the future due to high myopia. The aging effect seen in myopia will contribute to this process [4].

According to a global prediction for 2050, the incidence of pathological myopia may increase to more than 200 million in the future [11]. Studies have reported that pathological myopia is a major cause of blindness or visual impairment in 7% of the Western population and 12-27% of the Asian population [4].

3. Biometric and anatomical changes

3.1 Biometric changes

Most cases of myopia are strongly related to increased axial length. Increased axial length may cause changes in many other biometrical parameters. These changes could be the result of proportional adjustment during emmetropisation or simply a result of an increase in anatomical space.

Opinions on corneal changes in myopia are controversial. Several analyses revealed only a weak correlation between increasing corneal refractive power (steeper radius of curvature) and increasing degree of myopia, while others do not indicate any correlation or opposite relationship [2]. Long-term studies suggest that changes in corneal curvature during childhood and early adulthood are minimal and unrelated to the extent of myopia progression. Although corneal thickness does not change with refractive error, a decrease in corneal hysteresis (an estimate of corneal biomechanical strength or viscoelasticity) has been observed with an increase in the degree of myopia in children and adults [4, 13].

Changes in the depth of the anterior chamber in childhood are indirectly related to changes in the thickness of the lens (the thinner the lens, the deeper the anterior chamber). The anterior chamber is usually deeper in myopes compared to emmetropes, whilst, conversely, the lens is thinner in myopes [14].

In contrast to the anterior segment, changes in the posterior segment (especially the vitreous, choroid and sclera) are more pronounced in myopes compared to non-myopic eyes. The axial length, or more precisely the depth of the vitreous cavity, is the primary biometric contributor to the refractive error. The axial length of the eyeball and the depth of the vitreous cavity increases in emmetropic children by approximately 0.16 mm per year from 6 to 10 years of age, decelerating to 0.05 mm per year from 11 to 14 years [15]. In short-sighted children aged 6 to 11 years (corrected by spectacles or contact lenses), average growth rates of approximately 0.30 mm per year have been reported, with larger vitreous cavities and axial elongations observed in younger women with myopic parents [16]. The extent of myopia correction slows the rate of eye growth and the progression of myopia during childhood, in some cases by up to 50% [4].

3.2 Choroid

The choroid supplies oxygen and nutrients to the outer layers of the retina, and also regulates intraocular pressure and eye temperature. High myopia is associated with profound changes in the choroid. In the process of myopization, the eye elongates but does not form additional tissue, therefore, the sclera, choroid and retina are stretched and thinned. The choroid thickness differs from normal at extreme axial lengths (extremely short and long) [17]. The choroid thickness decreases with increasing myopia and axial length in both adults and children. The most pronounced thinning is in the foveal area compared to non-myopic subjects [18]. Significant choroidal thinning is observed in high myopia and in eyes with posterior staphyloma and may contribute to atrophy and myopic maculopathy. Areas of completely missing choroidal vessels could be found in very high myopes. Myopic maculopathies are a variety of lesions, all of which involve vascular changes, namely diffuse chorioretinal atrophy, irregular chorioretinal atrophy, macular atrophy, lacquer cracks, and myopic choroidal neovascularization [4].

A colour Doppler ultrasonographic study showed that choroidal circulation was reduced in highly myopic eyes due to its marked thinning [19]. Because the choroid

supplies oxygen and nutrition to the retinal pigment epithelial cells (RPE) and outer layers of the retina, impaired choroidal circulation may be partly responsible for retinal dysfunction associated with vision loss [20].

The reduction in choroid thickness occurs with age in both non-myopes and myopes. In the elderly, the choroid may also show reduced thickness in a process known as age-related choroidal atrophy (ARCA) [21]. These patients have a normal axial length but show tessellation of the fundus and peripapillary atrophy of the beta zone, much the same as older high myopes. Eyes with reduced choroid thickness as part of ARCA are more likely to have pseudodrusen, whilst highly myopic eyes almost never have pseudodrusen. Based on studies, ARCA was defined as a reduction in choroidal thickness due to age of less than 125 μm [20].

3.3 Sclera

Anatomical changes occurring in the collagen fibers of the sclera contribute to the axial elongation of the eye, as well as the formation and progression of staphyloma. Scleral thinning associated with axial myopia is primarily limited to the posterior pole of the eye due to the redistribution of scleral tissue. Myopia causes several changes in the composition of the sclera. There is a general loss of collagen and proteoglycans. At the onset of myopia, the ongoing synthesis of type I collagen is decreased, and existing collagens and proteoglycans are degraded by matrix metalloproteinases [20].

Scleral thinning around the optic nerve head makes myopic eyes more susceptible to glaucoma damage. Histological studies have shown that scleral thinning associated with axial length elongation is most pronounced near the posterior pole, while scleral thickness anterior to the equator does not differ significantly between eyes of different axial lengths [22]. Slight anterior scleral thinning occurs during accommodation, especially in myopic eyes, probably due to the biomechanical forces of the ciliary muscle [23].

3.4 Retina

Retinal changes in myopia are closely related to the changes in the sclera and choroid. RPE cells are flatter and larger, and in some places, pigment cells and photoreceptors are replaced by Müller cells. The Bruch membrane shows various changes, including thinning and ruptures.

4. Complications

In summary, anatomical changes occurring during myopia are:

- increasing axial length, anterior chamber depth and vitreous cavity depth
- decreasing retinal, choroidal and scleral thickness
- the vessels of the retina, choroid, ciliary body narrow and lengthen
- there is mechanical tension and focal ruptures of the Bruch's membrane-RPE-choriocapillaris complex
- increase in lamina cribrosa defects around the optic nerve head.

These changes can lead to complications associated either with high or pathological myopia. Most typical are those related to the posterior pole of the eye because of the prolongation of the axial length and thus the stretching of the posterior pole and the formation of staphyloma. Scleral ectasia affecting the posterior pole of the eye is relatively common and usually leads to a poor visual prognosis. Most complications associated with myopic maculopathy can lead to irreversible damage to photoreceptors, leading to decreased central visual acuity [24].

4.1 Posterior staphyloma

The presence of posterior staphyloma is the most characteristic finding of pathological myopia. A staphyloma is a circumscribed bulging of the scleral wall that has a radius of curvature smaller than the surrounding curvature of the eyewall. A primary (simple) staphyloma is an area that has only one radius of curvature. Combined staphyloma consist of two or more staphyloma.

Posterior staphyloma is characterised by the presence of a sudden sharply demarcated margin. Compared to the normal retina, the bulged area is relatively pale and is associated with increased visibility of choroidal vessels. Staphyloma depth correlates with the extent of scleral thinning. Posterior staphyloma is often associated with chorioretinal atrophy. In fact, these two symptoms are the most common macular finding associated with myopia, occurring in approximately 20-23% of highly myopic eyes in adults [24]. Increasing age and axial length are relevant risk factors associated with the occurrence of pathological changes in highly myopic patients, as well as with the occurrence of staphyloma. The posterior staphyloma deepens with age, changes its shape, and thus increases the number of combined staphyloma. The prevalence of posterior staphyloma increases with age; it occurs in 53.5% of highly myopic patients aged 60-86 years [24].

The first classification of posterior staphyloma was suggested by Curtin in 1977 [25]. Ohno-Matsui modified and simplified the classical Curtin classification. The new classification stratifies posterior staphyloma into 6 types according to their location and extent [26].

Due to the extreme thinning of the choroid in highly myopic eyes, the curvatures of both the retina and Bruch's membrane closely mimic the curvature of the sclera. However, this is not the case with emmetropic eyes, because the choroid is much thicker [26]. Many authors have evaluated the role of staphyloma in the development of chorioretinal atrophy. Clinical quantification of posterior staphyloma showed that shorter staphyloma depth was associated with poorer best-corrected visual acuity and a higher occurrence of myopic choroidal neovascularization. On the other hand, larger staphyloma has been associated with a higher prevalence of cone formation, RPE defects, lacquer cracks, and chorioretinal atrophy [27].

4.2 Tilted disc syndrome

With an inferior staphyloma, the nerve is usually at the border of the staphyloma and has an inclined appearance. This appearance is called tilted optic disk syndrome. Tilted disc syndrome (TDS), also known as Fuch's Coloboma, is a congenital anomaly that occurs in up to 3.5% of the population [28]. It is an abnormality consisting of inferonasal tilting of the optic disc. It may cause superior bitemporal visual field defects. These defects could be confused with chiasmal lesions; however, the visual

field defects in TDS can cross the vertical meridian. Other types of defects in TDS include altitudinal or arcuate defects. They may be confused with glaucomatous changes.

4.3 Myopic cone

A myopic cone is one of the first signs to develop on the posterior pole in myopic eyes. It has the appearance of a pale and sharply demarcated crescent-shaped area. This is the area of the translucent sclera which is created by the pulling and thinning of the retina and choroid from the optic nerve. It tends to increase with increasing myopia and axial length. Myopic cone and tessellated fundus are the earliest lesions that develop in eyes with pathological myopia, and these lesions can also be seen in children and young individuals. A myopic cone without the occurrence of other pathologies has no effect on visual acuity.

4.4 Myopic maculopathy

Myopic maculopathy is described by a simplified and systematic classification based on a meta-analysis of pathological myopia (META-PM) [29]. Myopic maculopathy lesions have been categorized into five categories from 0 to 4: 0. no myopic retinal lesions; 1. tessellated fundus; 2. diffuse chorioretinal atrophy; 3. patchy chorioretinal atrophy and 4. macular atrophy. Two additional categories were added to them and were included as 'plus signs': lacquer cracks and myopic choroidal neovascularization (CNV). Fuchs' spots were categorized under the term myopic CNV. The reason for the separate listing of additional lesions ("plus signs") is that they are associated with central vision loss, however, they do not fall into any main category, and they may develop or coexist with any of the categories of myopic maculopathy described above.

Myopic choroidal neovascularisation is a vision-threatening complication in many ocular diseases, including pathological myopia [30]. Pathological myopia is the most common cause of CNV in people under the age of 50 and is the second most common cause of CNV after age-related macular degeneration (AMD) [4]. Approximately 5-11% of patients with pathological myopia develop CNV, usually type 2 [4, 31].

Lacquer cracks are spontaneous cracks in Bruch's membrane-RPE-choriocapillaris complex. After the spontaneous resorption of subretinal hemorrhages caused by these ruptures, we can observe lacquer cracks in the corresponding area of previous bleeding. They appear clinically as fine, linear, irregular, yellowish subretinal lines at the posterior pole of highly myopic eyes. They occur most frequently in the macular area.

In highly myopic eyes, atrophy of the retinal pigment epithelium may occur. It is assumed that the pathophysiology is similar to age-related choroidal atrophy [20]. This fundoscopic finding is described as tessellated fundus. It has no effect on central visual acuity.

Diffuse chorioretinal atrophy appears as a vaguely demarcated yellowish lesion on the posterior pole of the eye in highly myopic patients. It begins to appear around the optic disc and spreads to the entire macular area. Its incidence increases with age as well as with increased axial length. It begins to appear around the age of 40 [32].

Patchy chorioretinal atrophy appears as a gray-white, clearly demarcated lesion in the macular area or around the optic disc. It is characterized by complete atrophy of the RPE, choroid and outer layers of the retina. It has a characteristic white colour because the sclera is visible through the transparent retinal tissue. With increasing

age, areas of irregular atrophy enlarge and cluster with each other. Patchy chorioretinal atrophy causes the formation of absolute scotomas. Extra-foveal patches rarely involve the fovea and central visual acuity is spared [20].

In macular atrophy, progressive choroidal atrophy is followed by loss of retinal pigment epithelium and outer retinal layers. These areas of atrophy eventually merge to form large geographical areas of atrophy. Macular atrophy is similar to patchy chorioretinal atrophy, but is cantered on the fovea, which significantly impairs the central vision.

4.5 Dome-shaped macula

The dome-shaped macula (DSM) is an anterior bulging of the macula of >50μm above the level of the outer RPE line on the posterior staphyloma associated with high myopia and a posterior staphyloma. It can be visualized by OCT [33]. Several theories have been proposed, but the exact pathophysiology of DSM remains unclear. It was thought to be either due to coarsening of the choroid, collapse of the posterior wall of the eye, or vitreomacular traction. More recent evidence suggests that it seems to be related to a localized scleral thickening. The presence of DSM is associated with an increased risk of complications. Eyes with complications have a thinner choroid, thicker sclera, and higher dome height [33]. Complications include serous retinal detachment, CNV, epiretinal membrane, lamellar and full-thickness macular hole, and foveal or extra-foveal retinoschisis.

4.6 Myopic traction maculopathy

In 2014, Panozzo and Mercanti introduced the term myopic traction maculopathy (MTM) to describe the spectrum of foveal traction changes in highly myopic eyes. MTM included the following alterations: foveoschisis/maculoschisis/retinoschisis (FS/MS/RS), retinal/foveal detachment (RD/FD), lamellar macular holes (LMH) and full-thickness macular holes (FTMH) with (MHRD) or without RD [34].

The presence of posterior staphyloma in highly myopic patients plays a key role in the subsequent development of MTM, as the elasticity of the retina cannot compensate for the posterior scleral bulging. This rigidity of the retina can be caused by many factors, including vascular rigidity, the presence of epiretinal membrane (ERM), vitreomacular traction syndrome (VMTS), cortical vitreous remnants, or incomplete posterior vitreous detachment. The internal limiting membrane (ILM) could also be thickened or stiffened [20, 35].

Myopic foveoschisis (FS) can be diagnosed ophthalmoscopically in some cases, but OCT examination is necessary to make a correct diagnosis and to monitor development. Myopic foveoschisis involves the gradual separation of the retinal layers, which remain joined by Müller cells [20]. Several classifications have been proposed for FS. Some are based on the location or amount of its extension. Others are based on the involvement of different retinal layers [35]. Most patients with FS may be relatively asymptomatic, especially when the eyes do not develop more serious complications, such as a macular hole. FS can last for many years without significantly affecting vision. Some patients complain of metamorphopsia before a decrease in visual acuity. Regular OCT examination should be performed in highly myopic eyes with posterior staphyloma. For eyes with stable disease, observation is a sufficient approach.

The progression of FS can lead to complications, including foveal detachment, lamellar macular holes (LMH) and full-thickness macular holes. LMH is a common

finding on OCT in asymptomatic myopic patients. Surgery is only necessary for the presence of clear vitreous traction or decreased visual acuity. Epiretinal proliferation associated with myopic LMH tends to be more prevalent and is more adherent to the posterior hyaloid than in non-myopic eyes [36]. Some authors perform fovea-sparing ILM peeling to protect the fovea. This approach is helpful in myopic FS with vitreomacular traction, where forces exerted during the peeling could damage weakened fovea and lead to FTHM [37].

The development of FTMH in myopic eyes is associated with significant visual impairment. Anteroposterior and tangential traction of the vitreous on the macula is closely related to the development of MH. In the presence of posterior staphyloma, which promotes retinal layer cleavage, myopic MH is commonly associated with FS, which is an important difference compared to emmetropic MH. Overall, the presence of concomitant FS indicates a worse anatomical and functional prognosis, which may even lead to retinal detachment.

The goal of surgical treatment is complete closure of FTHM, as well as to maintain or improve visual acuity. The gold standard of treatment is posterior vitrectomy, posterior hyaloid dissection, and ILM peeling. It is important to remove the entire vitreous from the macular surface. Vitreoschisis is common in myopic patients. ILM peeling in highly myopic eyes is a demanding surgical manoeuvre due to several factors, including greater axial length, retinal thinning, weak staining of ILM and difficulty identifying the exact location of the MH. Many surgeons perform a full ILM peeling across the macula to the vascular arcades in an effort to maximize the relief of tangential tractions. Several alternative techniques have been proposed to achieve a successful closure, especially in FTMH with FS. One of these techniques is the inverted ILM flap method [38]. This technique has several modifications where the ILM layer is placed inside or above the MH bed to anatomically close the macular hole [39]. At the end of surgery, it is important to perform the fluid-air exchange to prevent the ILM flap from slippage. Macular buckling surgery is another method of treating MTM. It relieves anterior-posterior traction by placing a buckle under the posterior pole and pushing it anteriorly. It could be made more effective by combination with pars plana vitrectomy [40].

4.7 Peripheral retinal degenerations

The main peripheral retinal degeneration changes associated with pathological myopia are lattice degenerations, white with/without pressure, pigment degenerations, paving stone degeneration and retinal holes. Each of these degenerations has its distinct morphology and prevalence, which varies with age and axial length. The dynamic interaction between the vitreous and the retina plays an important role in the development, appearance, and progression of these peripheral retinal degenerations. The combination of abnormal vitreoretinal adhesions, posterior vitreous traction, and vitreous liquefaction can lead to rhegmatogenous retinal detachment in highly myopic eyes. Early detection of peripheral retinal changes associated with high myopia through careful ophthalmoscopic examination or examination with a wide-angle viewing system is very important in preventing the most dangerous complication of peripheral degeneration—retinal detachment. Paving stone degeneration or pigment degeneration is considered a benign lesion without an increased risk of complications. Lattice or snail track degenerations are the most dangerous in terms of vitreoretinal adhesions, tear creation and subsequent rhegmatogenous retinal detachment. The most common peripheral degeneration in myopic adults and children is

lattice degeneration [41, 42]. Whether or when to treat lattice degeneration in adult eyes has been a source of controversy. Prophylactic treatment for asymptomatic peripheral retinal degenerations in adults is not recommended [42, 43]. There is not sufficient data to strongly support prophylactic treatment of asymptomatic lesions [43]. However, treatment of lattice in the other eye of patients with rhegmatogenous retinal detachment reduces the risk of retinal detachment in the second eye from 5.1% to 1.8%. In addition, prophylactic treatment did not reduce the risk of detachment in the higher risk eyes with high myopia or extensive lattice [44]. Laser photocoagulation is the most common procedure in prophylactic treatment of peripheral degenerations. Buckles or encircling bands are sometimes used for prophylaxis.

4.8 Myopic optic neuropathy and glaucoma

Axial myopization leads to significant changes in the optic nerve head: enlargement of all three layers of the optic disc (Bruch membrane, choroidal and scleral orifice of the optic disc); enlargement and fusion of excavation; lengthening and thinning of the lamina cribrosa, peripapillary sclera and choroid, and rotation of the optic disc around the vertical axis. These changes, among others, such as the loss of the neuroretinal rim margin and thinning of the retinal nerve fiber layer (RNFL), make it difficult to distinguish between myopic changes and glaucoma-related changes. At the same time, these changes may make optic nerve head more vulnerable, which could explain the increased prevalence of glaucomatous optic neuropathy in highly myopic eyes [4]. Myopia is a risk factor for glaucoma. Eyes with high myopia had a sixfold increased risk of having primary open-angle glaucoma [45]. Highly myopic glaucoma eyes may have significantly lower IOP thresholds for optic nerve damage [4]. These factors make myopic glaucoma hard to diagnose and treat.

5. Risk factors

Myopia is a complex multifactorial disorder affected by genetic and environmental factors. Although genetic factors are the strongest influence, exposure to the environment plays an important role. Environmental factors can include occupational activities, work on computer displays and other light-emitting devices (electron microscopes, photographic equipment, lasers, etc.), stress and eye strain [20, 46].

Another explanation for the different perspectives on the role of genetic factors in myopia is the sensitivity of the human eye to very small changes in its anatomical structure. Small deviations from the normal structure could cause significant refractive errors. This is the reason why it is difficult to determine strength of the influence for specific genetic or environmental factors.

Genes in the proximity of loci associated with refractive error play different functions, including as neurotransmitters (GJD2, RASGRF1, GRIA4, etc.), involvement in retinoic acid metabolism (RDH5, RGR, RORB), and ion channel activity (KCNQ5, KCNJ2, KCNMA1, CACNA1D), or are involved in ocular and central nervous system development (SIX6, CHD7, ZIC2, and PRSS56). Although their individual effect is small, the overall effect of these genes may be highly coordinated [47]. Other genes associated with myopia encode extracellular matrix-related proteins (COL1A1, COL2A1 and MMP1, MMP2, MMP3, MMP9, MMP10) [4]. The PAX6 gene has a suggestive association with high myopia [48]. Any of these genes could cause a disruption in the balance between growth of the eye and emmetropization.

6. Prevention

The relationship between time outdoors and myopia onset has been documented in several epidemiologic studies [49]. A randomized trial of 952 schoolchildren in China showed that an intervention of 40 minutes per day spent outdoors decreased myopia onset by 9% after 3 years [50]. In animal studies, experiments in chicken and non-human primate animal models have shown that high illuminance levels of light (>15,000 Lux) can slow or even stop the development of experimentally induced myopia [49]. However, this amount of illuminance might be retinotoxic in the long term [51]. To achieve healthy exposure to daylight, an effort should be made to increase children's time spent outdoors with physical activity. These measurements could not only slow down myopia but increased physical activity could prevent obesity and its own health-related complications.

There are many other possible interventions to reduce the progression of myopia. In terms of refraction, atropine, pirenzepine and progressive addition spectacle lenses were effective. For axial length, atropine, orthokeratology, peripheral defocus modifying contact lenses, pirenzepine, and progressive addition spectacle lenses were effective. The most effective interventions are muscarinic antagonists, such as atropine and pirenzepine [52]. All used doses (high-dose (1% and 0.5%), moderate-dose (0.1%) and low-dose of (0.01%)) of atropine are effective [52]. High doses induce clinical symptoms such as changes in pupil size and accommodation and displayed a rapid rebound effect with myopia when the treatment was stopped [53]. On the other hand, low-dose atropine (0.01%) does not show the same rebound effect seen in higher doses and has fewer visual side effects [49]. The ATOM2 clinical trial showed that over 5 years, atropine 0.01% eye drops were more effective in slowing myopia progression with fewer visual side effects compared to higher doses of atropine. Furthermore, atropine 0.01% also caused minimal pupil dilation (0.8 mm), minimal loss of accommodation (2-3 D), and no near visual loss compared with higher doses [54].

Another way to prevent the progression of myopia is contact lenses with added myopic defocus. These lenses are bifocal soft contact lenses with a series of alternating defocusing and correction zones. The correcting zones match the distant prescription, while the defocusing zones have myopic defocus. Myopia progressed 25% slower in children in the bifocal lens group compared with those in the control group with single-vision soft contact lenses [55]. In another study, they achieved greater control in myopia progression (59%) and axial elongation (52%) with bifocals relative to single-vision 1-day contact lenses [56]. However, the quality of vision offered by these lenses may be reduced due to their myopic defocus which may result in poorer compliance [49].

Orthokeratology (OK) is a clinical technique to flatten the central cornea moderately while steepening the peripheral cornea using contact lenses (CLs) worn overnight [49]. OK lenses showed moderate effects on the change in axial length (AL) compared with single-vision spectacle lenses/placebo over a year [52]. The OK technique is less popular, probably due to the frequent discomfort of wearing lenses overnight and the risk of infectious keratitis. There is no relevant data on rebound effects of this method.

The therapeutic effect of bifocal or other types of multifocal spectacles on myopia progression has been evaluated in several trials. The correction of Myopia Evaluation Trial 2 (COMET 2) showed that the progressive-addition lenses used in this study were found to have a statistically but not clinically significant effect of slowing myopia progression in children with high accommodative lag and near esophoria [57]. A trial with bifocals, without and with prism, showed that both bifocal groups had

less axial elongation (0.25 mm and 0.28 mm, respectively) than the single-vision lens group. It suggested that prismatic bifocals are more effective for myopic children with insufficient accommodation [58].

Myopia is a significant public health challenge, particularly in the urban environments of Asian countries. Whilst novel methods are emerging to control the progression of myopia, their principles are still unclear. A combination of these methods could yield a cumulative effect. Further studies are needed to confirm these assumptions.

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References

[1] Yanoff M, Duker JS. Ophthalmology E-Book. Elsevier Health Sciences. Amsterdam, Netherlands: Elsevier B.V. (Corporate Office); 2018

[2] Popov I et al. Analysis of biometric parameters of 2340 eyes measured with optical biometer Lenstar LS900 in a Caucasian population. European Journal of Ophthalmology. 2022;**32**(1):213-220

[3] Wilkinson CP, Hinton DR, Sadda SR, Wiedemann P. Ryan's Retina E-Book. Elsevier Health Sciences. Netherlands, Amsterdam: Elsevier B.V. (Corporate Office); 2017

[4] Ang M, Wong TY. Updates on myopia: A clinical perspective. London, UK: Springer Nature; 2020. p. 305

[5] Popov I, Popova V, Sekac J, Krasnik V. Does every calculation formula fit for all types of intraocular lenses? Optimization of constants for tecnis ZA9003 and ZCB00 is necessary. Medicina (Mex.). 2021;**57**(4):319

[6] Sherwin JC et al. Uncorrected refractive error in older British adults: The EPIC-Norfolk Eye Study. The British Journal of Ophthalmology. 2012;**96**:991-996

[7] Popov I, Valašková J, Krásnik V, Tomčíková D. Effect of multiple variables on the refractive error after cataract surgery. Ceska Slov. Oftalmol. Cas. Ceske Oftalmol. Spolecnosti Slov. Oftalmol. Spolecnosti. 2019;**74**:158-161

[8] Resnikoff S, Pascolini D, Mariotti SP, Pokharel GP. Global magnitude of visual impairment caused by uncorrected refractive errors in 2004. Bulletin of the World Health Organization. 2008;**86**: 63-70

[9] Popov I, Valašková J, Štefaničková J, Krásnik V. Prevalence of refractive errors in the Slovak population calculated using the Gullstrand schematic eye model. Ceska Slov. Oftalmol. Cas. Ceske Oftalmol. Spolecnosti Slov. Oftalmol. Spolecnosti. 2017;**73**:113-117

[10] Wu P-C, Huang H-M, Yu H-J, Fang P-C, Chen C-T. Epidemiology of Myopia. Asia-Pacific Journal of Ophthalmology. 2016;**5**:386-393

[11] Holden BA et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology. 2016;**123**:1036-1042

[12] Koh V et al. Myopic maculopathy and optic disc changes in highly myopic young asian eyes and impact on visual acuity. American Journal of Ophthalmology. 2016;**164**:69-79

[13] Huang Y et al. Corneal biomechanics, refractive error, and axial length in Chinese primary school children. Investigative Ophthalmology & Visual Science. 2011;**52**:4923-4928

[14] Shih Y-F, Chiang T-H, Lin LL-K. Lens thickness changes among schoolchildren in Taiwan. Investigative Ophthalmology & Visual Science. 2009;**50**:2637-2644

[15] Zadnik K et al. Normal eye growth in emmetropic schoolchildren. Optometry Vision Science Official Publication of American Academy of Optometry. 2004;**81**:819-828

[16] Saw SM et al. Eye growth changes in myopic children in Singapore. The British Journal of Ophthalmology. 2005;**89**:1489-1494

[17] Popov I, Popova V, Krasnik V. Comparing the results of vitrectomy and sclerectomy in a patient with

nanophthalmic uveal effusion syndrome. Medicina (Mex.). 2021;**57**(120)

[18] Xiong S et al. Choroidal thickness in 3001 Chinese children aged 6 to 19 years using swept-source OCT. Scientific Reports. 2017;**7**:45059

[19] Akyol N, Kükner AS, Ozdemir T, Esmerligil S. Choroidal and retinal blood flow changes in degenerative myopia. Canadian Journal of Ophthalmology. 1996;**31**:113-119

[20] Ohno-Matsui K, Wu PC, Yamashiro K, Vutipongsatorn K, Fang Y, Cheung CMG, et al. IMI pathologic myopia. Investigative Ophthalmology & Visual Science. 2021;**62**(5):5-5

[21] Spaide RF. Age-related choroidal atrophy. American Journal of Ophthalmology. 2009;**147**:801-810

[22] Jonas JB, Ohno-Matsui K, Panda-Jonas S. Myopia: Anatomic changes and consequences for its etiology. Asia-Pacific Journal of Ophthalmology. 2019;**8**:355-359

[23] Consejo A, Radhakrishnan H, Iskander DR. Scleral changes with accommodation. Ophthalmic & Physiologic Optics: The Journal of the British College of Ophthalmic Opticians Optometry. 2017;**37**:263-274

[24] Ruiz-Medrano J et al. Myopic maculopathy: Current status and proposal for a new classification and grading system (ATN). Progress in Retinal and Eye Research. 2019;**69**:80-115

[25] Curtin BJ. The posterior staphyloma of pathologic myopia. Transactions of the American Ophthalmological Society. 1977;**75**:67-86

[26] Ohno-Matsui K. Proposed classification of posterior staphylomas based on analyses of eye shape by three-dimensional magnetic resonance imaging and wide-field fundus imaging. Ophthalmology. 2014;**121**:1798-1809

[27] Steidl SM, Pruett RC. Macular complications associated with posterior staphyloma. American Journal of Ophthalmology. 1997;**123**:181-187

[28] Kim YC, Moon J-S, Park H-YL, Park CK. Three dimensional evaluation of posterior pole and optic nerve head in tilted disc. Scientific Reports. 2018;**8**:1121

[29] Ohno-Matsui K et al. International photographic classification and grading system for myopic maculopathy. American Journal of Ophthalmology. 2015;**159**:877-883

[30] Horkovicova K, Popov I, Tomcikova D, Popova V, Krasnik V. The natural history of retinal vascular changes from infancy to adulthood in Wyburn-Mason Syndrome. Medicina (Kaunas, Lithuania). 2020;**56**:E598

[31] Wong TY, Ferreira A, Hughes R, Carter G, Mitchell P. Epidemiology and disease burden of pathologic myopia and myopic choroidal neovascularization: An evidence-based systematic review. American Journal of Ophthalmology. 2014;**157**:9-25

[32] Tokoro T. Atlas of Posterior Fundus Changes in Pathologic Myopia. Japan: Springer; 1998

[33] Jain M, Gopal L, Padhi TR. Dome-shaped maculopathy: A review. Eye. 2021;**35**:2458-2467

[34] Panozzo G, Mercanti A. Optical coherence tomography findings in myopic traction maculopathy. Archives of Ophthalmology. 2004;**1960**(122): 1455-1460

[35] Frisina R et al. Myopic traction maculopathy: Diagnostic and management strategies. Clinical Ophthalmology. 2020;**14**:3699-3708

[36] Lai T-T, Yang C-M. Lamellar hole-associated epiretinal proliferation in lamellar macular hole and full-thickness macular hole in high myopia. Retina. 2018;**38**:1316-1323

[37] Shimada N, Sugamoto Y, Ogawa M, Takase H, Ohno-Matsui K. Fovea-sparing internal limiting membrane peeling for myopic traction maculopathy. American Journal of Ophthalmology. 2012;**154**:693-701

[38] Hu X-T, Pan Q-T, Zheng J-W, Zhang Z-D. Foveal microstructure and visual outcomes of myopic macular hole surgery with or without the inverted internal limiting membrane flap technique. The British Journal of Ophthalmology. 2019;**103**:1495-1502

[39] Hirata A, Mine K, Hayashi K. Contractility of temporal inverted internal limiting membrane flap after vitrectomy for macular hole. Scientific Reports. 2021;**11**:20035

[40] Susvar P, Sood G. Current concepts of macular buckle in myopic traction maculopathy. Indian Journal of Ophthalmology. 2018;**66**:1772-1784

[41] Chen DZ et al. Peripheral retinal changes in highly myopic young Asian eyes. Acta Ophthalmology. 2018;**96**:e846-e851

[42] Bansal AS, Hubbard GB. Peripheral retinal findings in highly myopic children ≤10 years of age. Retina. 2010;**30**:S15-S19

[43] Wilkinson CP. Evidence-based analysis of prophylactic treatment of asymptomatic retinal breaks and lattice degeneration. Ophthalmology. 2000;**107**:12-15

[44] Folk JC, Arrindell EL, Klugman MR. The fellow eye of patients with phakic lattice retinal detachment. Ophthalmology. 1989;**96**:72-79

[45] Pan C-W et al. Differential associations of myopia with major age-related eye diseases: The Singapore Indian eye study. Ophthalmology. 2013;**120**:284-291

[46] Huang H-M, Chang DS-T, Wu P-C. The Association between near work activities and myopia in children—A systematic review and meta-analysis. PLoS One. 2015;**10**:e0140419

[47] Hysi PG, Wojciechowski R, Rahi JS, Hammond CJ. Genome-wide association studies of refractive error and myopia, lessons learned, and implications for the future. Investigative Ophthalmology & Visual Science. 2014;**55**:3344-3351

[48] Tang SM et al. PAX6 gene associated with high myopia: A meta-analysis. Optometry Vision Science Official Public American Academy of Optometry. 2014;**91**:419-429

[49] Saw S-M, Matsumura S, Hoang QV. Prevention and management of myopia and myopic pathology. Investigative Ophthalmology & Visual Science. 2019;**60**:488-499

[50] He M et al. Effect of time spent outdoors at school on the development of myopia among children in China: A Randomized Clinical Trial. JAMA. 2015;**314**:1142-1148

[51] Popov I et al. Effect of blue light filtering intraocular lenses on visual perception. Medicina (Mex.). 2021;**57**(559)

[52] Huang J et al. Efficacy comparison of 16 interventions for myopia control in children: A network meta-analysis. Ophthalmology. 2016;**123**:697-708

[53] Chia A et al. Atropine for the treatment of childhood myopia: Changes after stopping atropine 0.01%, 0.1% and 0.5%. American Journal of Ophthalmology. 2014;**157**:451-457

[54] Chia A, Lu Q-S, Tan D. Five-year clinical trial on atropine for the treatment of Myopia 2: Myopia control with atropine 0.01% eyedrops. Ophthalmology. 2016;**123**:391-399

[55] Lam CSY, Tang WC, Tse DY-Y, Tang YY, To, C. H. Defocus Incorporated Soft Contact (DISC) lens slows myopia progression in Hong Kong Chinese schoolchildren: A 2-year randomised clinical trial. The British Journal of Ophthalmology. 2014;**98**:40-45

[56] Chamberlain P et al. A 3-year randomized clinical trial of misight lenses for myopia control. Optometry and Vision Science Official Publication American Academy of Optometry. 2019;**96**:556-567

[57] Correction of Myopia Evaluation Trial 2 Study Group for the Pediatric Eye Disease Investigator Group. Progressive-addition lenses versus single-vision lenses for slowing progression of myopia in children with high accommodative lag and near esophoria. Investigative Ophthalmology and Visual Science. 2011;**52**:2749-2757

[58] Cheng D, Woo GC, Drobe B, Schmid KL. Effect of bifocal and prismatic bifocal spectacles on myopia progression in children: Three-year results of a randomized clinical trial. JAMA Ophthalmology. 2014;**132**:258-264