pellucid marginal degeneration (PMD) is a rare, bilateral, asymmetric, ectatic disorder of the cornea most commonly associated with an arcuate band of thinning in the inferior peripheral cornea approximately 1 mm from the limbus. The thinning usually occurs in the 4- to 8-o’clock position and can be severe, with as much as 80% stromal loss, resulting in corneal protrusion. The point of maximal protrusion in PMD occurs in the region of cornea just superior to the thinned region. This is in contrast to the more common ectatic disorder, keratoconus, in which apical protrusion occurs within regions of thinned central and paracentral cornea.

Differentiating PMD from keratoconus is important for prognosis and management (Table 1). Although both keratoconus and PMD cause reduced visual acuity, Descemet’s frowns, and acute hydrops, PMD is not associated with several classic keratoconus findings, including Munson’s sign (a V-shaped deformation of the lower eyelid when gaze is directed downward), Rizutti’s phenomenon (sharply focused beam of light near the nasal limbus on lateral illumination), apical corneal scarring, Fleisher’s rings (hemosiderin deposition in basal epithelium), or reduced central corneal thickness. Moderate PMD can usually be differentiated from keratoconus via slit-lamp examination given the classic location of crescentic thinning. However, early in the disease process, the signs are subtle and cases of advanced PMD can involve the entire inferior cornea and be difficult to differentiate from keratoconus. Patients with PMD may present with acute hydrops or corneal perforation as a result of progressive thinning, although this presentation is more common in keratoconus.

ABSTRACT

PURPOSE: To review and evaluate current and future directions in the diagnosis and surgical management of pellucid marginal degeneration (PMD), including penetrating keratoplasty, full-thickness crescentic wedge resection (FTCWR), deep anterior lamellar keratoplasty (DALK), crescentic lamellar wedge resection (CLWR), crescentic lamellar keratoplasty, tuck-in lamellar keratoplasty (TILK), toric phakic intraocular lens (PIOL) implantation, intrastromal corneal ring segment implantation (ICRS), corneal collagen cross-linking (CXL), and combined therapies. This is the first review article looking at the literature specific to PMD.

METHODS: Review of published studies.

RESULTS: Reported data for each treatment is presented. Penetrating keratoplasty is the treatment of last resort in PMD and is effective, but with considerable complications. DALK provides visual outcomes similar to penetrating keratoplasty without the risk of immune-mediated graft rejection, but its complexity and relative novelty limit its acceptance. FTCWR has good visual outcomes, but with significant astigmatic drift. CLWR is effective, but lacks long-term results. Crescentic lamellar keratoplasty and TILK are effective, but technically difficult and without long-term results. Toric PIOL implantation is effective, but ectasia progression is a concern. ICRS implantation can delay penetrating keratoplasty and improve contact lens tolerance, but does not treat the underlying process. CXL demonstrates effectiveness without complications, although data are limited and long-term results are needed. Combining treatments such as ICRS, CXL, toric PIOL implantation, and refractive surgery is promising, but additional studies are needed to investigate their efficacy and safety.

CONCLUSIONS: Although little is understood about the etiology, pathophysiology, epidemiology, and genetics of PMD, new treatments are improving visual outcomes and reducing complications. Corneal collagen cross-linking is especially exciting because it halts disease progression. Combined treatments and improved screening could eliminate the need for surgical management in most cases of PMD.

Current Options in the Management of Pellucid Marginal Degeneration

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Although PMD and other ectatic disorders such as keratoconus and keratoglobus have some distinguishing phenotypic characteristics, it is unclear whether each is an individual disease entity or simply a variation in presentation of the same disease.2-4,7 Several authors propose that PMD is an inferior manifestation of keratoconus, whereas others report combinations of PMD, keratoconus, and keratoglobus coexisting in the same cornea.1,11-15 Whatever the case, the word “pellucid” means “clear” and refers to the clarity of the diseased cornea (or the absence of corneal scarring) despite protrusion and ectasia.16

There is little certainty about the etiology and pathophysiology of PMD, although studies have confirmed that PMD demonstrates progression over time.1-4 Histopathological studies demonstrate stromal thinning, an irregular Bowman’s membrane, Bowman’s membrane breaks, increased stromal polysaccharides, epithelial edema, Descemet’s folds, and an absence of inflammatory cells.17 Electron microscopy further reveals irregularly arranged stroma and the presence of extracellular, granular, electron-dense deposits.15,18

Although no formal categorization of PMD severity exists, published studies consistently use the subjective terms early, moderate, and advanced to describe progressive stages of the disease.3,7,19

There have been no formal epidemiological studies of PMD, although the general consensus in the literature is that PMD is a rare disorder that is more prevalent than keratoglobus but less prevalent than keratoconus.2-4,7 The disease occurs more often in males, but afflicts all ethnicities without geographic discrimination.1,9,10 There is no known genetic inheritance pattern in PMD, although isolated studies describe corneal ectasia and moderate to high astigmatism in the asymptomatic family members of patients with PMD.13,14,20-22 Patients with PMD usually present between the second and fifth decades of life, whereas keratoconus commonly presents during puberty.

Penetrating keratoplasty remains the treatment of last resort in advanced PMD. However, recent advances in the surgical management of PMD make it possible to postpone and possibly avoid penetrating keratoplasty altogether. The purpose of this article is to review and evaluate current and future directions for the diagnosis and management of PMD. This is the first review article looking at the literature specific to PMD.

**DIAGNOSIS**

Classically, diagnosis of PMD was made based on slit-lamp findings of inferior corneal thinning in an arcuate or crescentic pattern and a “beer-belly” side-profile contour (Figure 1). Today, technological advances allow detailed analysis of corneal topography and can assist in the diagnosis of PMD.

Topographical findings indicative of PMD include a flattened vertical meridian with abnormal inferior steepening in the corneal periphery (as much as 20 diopters [D] in advanced cases) that extends to the inferior or oblique meridians in a “crab-claw,” “kissing doves,” or “butterfly” appearance (Figure 2).2,4,23 However, a “crab claw” pattern on corneal topography alone is insufficient for diagnosis of PMD because keratoconus can create similar findings.8 More detailed analysis with slit lamp, topography, and pachymetry is suggested to assess corneal thickness and improve the accuracy of PMD diagnosis.24

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**TABLE 1**

<table>
<thead>
<tr>
<th>Clinical Parameter</th>
<th>Pellucid Marginal Degeneration</th>
<th>Keratoconus</th>
<th>Keratoglobus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etiology</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Onset</td>
<td>2nd to 5th decade</td>
<td>Puberty</td>
<td>At birth</td>
</tr>
<tr>
<td>Location of thinning</td>
<td>1 to 2 mm from limbus</td>
<td>Central, paracentral</td>
<td>Generalized</td>
</tr>
<tr>
<td>Location of protrusion</td>
<td>Superior to thinning</td>
<td>Apical, same as thinning</td>
<td>Generalized, globular</td>
</tr>
<tr>
<td>Scarring</td>
<td>Absent</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td>Reduced VA from astigmatism, rarely acute hydrops</td>
<td>Unilateral reduced VA from myopia and astigmatism, acute hydrops</td>
<td>Rupture with mild trauma, very rarely acute hydrops</td>
</tr>
<tr>
<td>Signs</td>
<td>“Beer belly” side profile, slowly progressive arcuate band of thinning</td>
<td>Conical ectasia, VS, MS, RP, FR, oil drop red reflex, “scissoring” reflex</td>
<td>Globular ectasia</td>
</tr>
<tr>
<td>Topography</td>
<td>Steepening of inferior cornea, “crab claw,” “butterfly,” or “kissing dove”</td>
<td>Irregular astigmatism, asymmetric bow-tie, skewed radial axis &gt; 30°</td>
<td>Generalized steepening</td>
</tr>
</tbody>
</table>

VA = visual acuity; VS = Vogt striae; MS = Munson’s sign; RP = Rizzuti’s phenomenon; FR = Fleisher’s rings

*Topographic findings alone are not sufficient for diagnosis of pellucid marginal degeneration and should be correlated with slit-lamp and pachymetric findings to improve specificity.*

Data from Krachmer et al.2, Romero-Jimenez et al.6, and Jinabhai et al.7
Placido disk-based topography is limited in its ability to detect PMD because it can only evaluate the anterior cornea. The Orbscan II (Bausch and Lomb, Rochester, NY) uses stereo-triangulation slit-scanning and placido rings to measure anterior corneal topography and thickness. The resulting mean keratometric axial power map is useful in detecting PMD, but lacks specificity. Additional placido disk-based topographers that aid in PMD diagnosis include the Tomey Topographic Modeling System (Tomey Corp., Nagoya, Japan) and GALILEI Dual Scheimpflug Analyzer (Zeimer, Switzerland), which combines placido disk-based topography with a three-dimensional Scheimpflug camera.

The Pentacam (Oculus Optikgeräte, Wetzlar, Germany) uses Scheimpflug photography to measure pachymetry and topography. Pentacam’s ability to image the cornea in cross-section allows evaluation of both the anterior and posterior curvature, as well as corneal thickness. In PMD, the corneal thickness map produced by Pentacam shows horizontal thinning of the inferior cornea near the limbus (Figure 3). Belin et al. recommends that detailed anterior and posterior elevation maps, anterior curvature topography with indices, and full pachymetry maps with 12 mm of corneal coverage and thickness data be required for accurate diagnosis of PMD, especially when determining inclusion criteria for studies. Careful screening for PMD should also be performed prior to refractive surgery because cases of iatrogenic ectasia have been reported in patients with PMD following LASIK.

Figure 1. Slit-lamp photograph of pellucid marginal degeneration (PMD). Unlike keratoconus, where the area of maximal protrusion is within the area of thinning, maximal protrusion in PMD is immediately superior to the area of thinning, resulting in a “beer-belly” contour as seen in this side profile of a cornea with PMD.

Figure 2. Topographical representation of pellucid marginal degeneration. Note the superior flattening with inferior steepening most pronounced between the 4- and 8-o’clock positions, and the classic “kissing dove” or “crab claw” pattern.
The newer Visante Omni system (Carl Zeiss Meditec, Dublin, CA) uses both placido ring and optical coherence tomography (OCT) to provide topography, thickness data, and detailed images of the anterior segment. Srivannaboon et al. recently compared the Visante Omni to the Orbscan II and reported high agreement...
between systems with good repeatability and reproducibility. These results are promising, but additional studies are needed to establish the sensitivity and specificity of this technology in detecting specific pathologies such as PMD. The RTVue Premier (Optovue, Inc., Fremont, CA) provides a Fourier-domain OCT to examine corneal pachymetry at higher scanning speeds and improved repeatability of pachymetry maps.

**MANAGEMENT**

The management of PMD can be organized into cornea-independent, structural, full-thickness, and partial-thickness interventions (Figure 4). Cornea-independent interventions involve the use of lenses, which correct visual deficits without affecting the cornea and include non-surgical interventions (spectacles and contact lenses) and surgical interventions (toric intraocular lens [IOL] implantation). Structural interventions involve modification of the curvature or mechanical properties of the cornea using mechanical devices designed to change the shape of the cornea (intrastromal corneal ring segments [ICRS]) and procedures designed to strengthen the biological structure of the cornea (corneal collagen cross-linking [CXL]). Full-thickness interventions involve removal and replacement of all layers of the cornea with total cornea replacement (as in penetrating keratoplasty) and crescentic cornea replacement, where only the area of abnormally thinned cornea is removed. Partial-thickness interventions involve removal of the anterior layers of corneal stroma while preserving the host corneal endothelium and can be subdivided into total cornea replacement (as in deep anterior lamellar keratoplasty [DALK]) and crescentic cornea replacement (removal of the anterior layers of only the abnormally thinned cornea). The most common surgical treatments of PMD today are penetrating keratoplasty and DALK.

**CORNEA-INDEPENDENT INTERVENTIONS**

**Non-surgical Interventions.** Many options exist for the treatment of early and moderate PMD. Most patients with PMD are treated non-surgically with spectacles or contact lenses. Soft and hybrid contact lenses can be used in early PMD, but lose their effectiveness

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**TABLE 2** Study Outcomes by Surgical Technique in the Management of Pellucid Marginal Degeneration

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>Total Eyes (Total Pts)</th>
<th>Procedure</th>
<th>Complication (%)</th>
<th>Astigmatism (Δ Astigmatism) (D)</th>
<th>Final CDVA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MacLean et al. (1997)</td>
<td>10 (9)</td>
<td>FTCWR</td>
<td>Inferior pannus (30), choroidal detachment (10), corneal hydrops (10), wound leak (10), astigmatic drift (100)</td>
<td>1.4 (-12.4)</td>
<td>&lt; 20/30 (100)</td>
</tr>
<tr>
<td>Biswas et al. (2000)</td>
<td>6 (6)</td>
<td>FTCWR</td>
<td>NR</td>
<td>8.9 (-2.14)</td>
<td>&lt; 20/40 (67)</td>
</tr>
<tr>
<td>Busin et al. (2008)</td>
<td>10 (10)</td>
<td>FTCWR, CTRI</td>
<td>Minimal astigmatic drift</td>
<td>4.6 (-10.5)</td>
<td>&lt; 20/40 (80)</td>
</tr>
<tr>
<td>Cameron (1992)</td>
<td>5 (4)</td>
<td>CLWR</td>
<td>Inferior vascularization and pannus (100), recurrence of thinning (20)</td>
<td>2.62 (NR)^a</td>
<td>&lt; 20/40 (80)</td>
</tr>
<tr>
<td>Javadi et al. (2004)</td>
<td>15 (9)</td>
<td>CLWR</td>
<td>NR</td>
<td>4.30 (-14.7)</td>
<td>&lt; 20/40 (71)</td>
</tr>
<tr>
<td>Maccheron et al. (2012)</td>
<td>7 (6)</td>
<td>CLWR</td>
<td>Microperforation (14), suture infiltrates (34),</td>
<td>6.84 (-9.1)^c</td>
<td>&lt; 20/40 (57)^b</td>
</tr>
<tr>
<td>Rasheed &amp; Rabinowitz (2000)</td>
<td>5 (5)</td>
<td>CLK, PK</td>
<td>Worsening with-the-rule astigmatism (80%)</td>
<td>4.24 (+1.02)</td>
<td>&lt; 20/40 (60)</td>
</tr>
<tr>
<td>Sridhar et al. (2004)</td>
<td>2 (2)</td>
<td>CLK</td>
<td>NR</td>
<td>10.3 (-5.35)</td>
<td>20/200, 20/125 (NR)</td>
</tr>
<tr>
<td>Millar et al. (2008)</td>
<td>2 (1)</td>
<td>DALK</td>
<td>None reported</td>
<td>NR</td>
<td>&lt; 20/30 (100)</td>
</tr>
<tr>
<td>Al-Torbak (2013)</td>
<td>16 (16)</td>
<td>DALK</td>
<td>Perforation (12)</td>
<td>NR</td>
<td>20/50</td>
</tr>
<tr>
<td>Fronterre et al. (1991)</td>
<td>4 (2)</td>
<td>EK</td>
<td>Folds beneath cap graft (100)</td>
<td>6.75 (approximately -1.7)</td>
<td>20/25 (100)</td>
</tr>
<tr>
<td>Kaushal et al. (2008)</td>
<td>12 (12)^c</td>
<td>TILK</td>
<td>None reported</td>
<td>3.23 (-2.7)</td>
<td>&lt; 20/80 (100)</td>
</tr>
<tr>
<td>Camoriano et al. (2012)</td>
<td>10 (5)</td>
<td>tpIOL</td>
<td>Severe glare and halos (10)</td>
<td>-0.58 (6.13) SE</td>
<td>&lt; 20/40 (100)</td>
</tr>
</tbody>
</table>

CDVA = corrected distance visual acuity; FTCWR = full-thickness crescentic wedge resection; NR = none reported; CTRI = corneal tunnel relaxing incision; CLWR = crescentic lamellar wedge resection; CLK = crescentic lamellar keratoplasty; PK = penetrating keratoplasty; DALK = deep anterior lamellar keratoplasty; EK = epikeratoplasty; TILK = tuck-in lamellar keratoplasty; tpIOL = toric phakic intraocular lens; SE = spherical equivalent; D = diopters

^aExcluding one eye that experienced recurrence of thinning.
^bFollow-up duration and thus outcomes varied among study participants.
^cPopulation includes 8 patients with combined keratoconus/pellucid marginal degeneration and 4 patients with keratoglobus.
as the disease progresses. In moderate PMD, the development of irregular astigmatism and progressive corneal irregularity often necessitates the use of large diameter rigid gas permeable lenses. Specialized contact lenses such as reverse geometry lenses and “bi-toric” lenses have proven useful in the management of moderate PMD. Customized soft contact lenses have theoretical potential in treating moderate PMD given their success in keratoconus. In advanced PMD, the scleral contact lens is a non-surgical treatment of last resort. However, tolerance is an issue with scleral contact lenses because the lenses are uncomfortable, expensive, difficult to apply, complicated to manufacture, and qualified scleral contact lens fitting experts are scarce.

**Surgical Interventions.** Toric IOls can be implanted in either the anterior or posterior chamber, either with or without natural lens extraction (toric phakic IOls [PIOLs]), and allow for correction of refractive error and astigmatism independent of cornea alteration. Camoriano et al. recently reported improved visual acuity and astigmatism with toric PIOL implantation for PMD in 10 eyes with severe glare and halos requiring explantation in just one eye (Table 2). Studies in patients with keratoconus have demonstrated the safety and efficacy of toric PIOL implantation in larger patient populations. The greatest concerns with using toric PIOL in patients with PMD are rotational stability and ectasia progression after lens implantation. Because patients with PMD are often young at the time of potential lens implantation, if ectasia progression continues following implantation, it may result in the need for spectacle correction despite lens placement. Thus, patient selection is important to ensure acceptable visual outcomes. For patients with advanced PMD who experience contact lens intolerance, toric PIOL can potentially be combined with spectacles. However, acceptable vision may be unattainable due to high irregular astigmatism and higher-order aberrations. Finally, the reversible nature of toric PIOL implantation, although less than ideal, is an advantage to consider with this modality.

**STRUCTURAL INTERVENTIONS**

**Mechanical Devices.** ICRS are semicircular polymethylmethacrylate rings implanted in peripheral

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### TABLE 3

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>Total Eyes (Total Pts)</th>
<th>Intervention</th>
<th>Complication (%)</th>
<th>Cylinder (Δ Cyl) (D)</th>
<th>K (Δ K) (D)</th>
<th>Final CDVA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mularoni et al. (2005)</td>
<td>8 (8)</td>
<td>ICRS</td>
<td>NR</td>
<td>-1.72 (4.59)</td>
<td>42.46 (1.49)</td>
<td>≤ 20/40 (100)</td>
</tr>
<tr>
<td>Ertan &amp; Bahadir (2006)</td>
<td>9 (6)</td>
<td>ICRS via FS</td>
<td>NR</td>
<td>-0.94 (1.47)</td>
<td>46.90 (1.3)</td>
<td>20/20 (55)</td>
</tr>
<tr>
<td>Pinero et al. (2009)</td>
<td>21 (15)</td>
<td>ICRS</td>
<td>Visual deterioration with eventual explantation (19)</td>
<td>-3.21 (2.15)</td>
<td>43.19 (1.76)</td>
<td>20/30 mean, range: 20/70 to -20/15 (NR)</td>
</tr>
<tr>
<td>Kubalaglu et al. (2010)</td>
<td>16 (10)</td>
<td>Single ICRS</td>
<td>White deposits around segments (12.5)</td>
<td>-2.38 (2.01)</td>
<td>46.08 (3.62)</td>
<td>≤ 20/40 (72.7)</td>
</tr>
</tbody>
</table>

ICRS = intracorneal ring segment; cyl = cylinder; K = keratometry; CDVA = corrected distance visual acuity; NR = none reported; FS = femtosecond laser; D = diopters

### TABLE 4

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>Total Eyes (Total Pts)</th>
<th>Intervention</th>
<th>Complication (%)</th>
<th>Cylinder (Δ Cylinder) (D)</th>
<th>Postop K (Preop K) (D)</th>
<th>Final CDVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spadea (2010)</td>
<td>1 (1)</td>
<td>CXL</td>
<td>NR</td>
<td>(1.40)</td>
<td>47.60/54.00; (47.40/55.30)</td>
<td>20/63</td>
</tr>
<tr>
<td>Kymionis et al. (2009)</td>
<td>2 (1)</td>
<td>PRK, CXL</td>
<td>NR</td>
<td>Right: -2.50 (5.50), Left: -5.50 (3.00)</td>
<td>“Improved”</td>
<td>Right: 20/25, Left: 20/32</td>
</tr>
<tr>
<td>Kymionis et al. (2010)</td>
<td>1 (1)</td>
<td>ICRS, PRK, CXL</td>
<td>NR</td>
<td>-4.00 (3.00)</td>
<td>44.92/39.01; (46.73/38.67)</td>
<td>20/25</td>
</tr>
</tbody>
</table>
corneal stroma outside the visual axis. These ring segments create an arc-shortening effect in the stroma, which flattens the cornea. The procedure for ICRS implantation involves creation of a radial stromal tunnel either manually or via femtosecond laser followed by insertion of the ICRS. Originally designed for refractive correction, ICRS have been used successfully in keratoconus and PMD for delaying penetrating keratoplasty and improving contact lens tolerance. Studies show that ICRS placement is a safe, reversible, and relatively conservative approach to surgical management in early and moderate PMD (Table 3). However, ICRS placement has several limitations, including regression over time, unpredictable visual outcomes, and the rare occurrence of corneal melt. In addition, placement of ICRS does not address the underlying cause of thinning and instability, so disease progression continues.

Kubaloglu et al. and Ertan and Bahadir have reported good outcomes with placement of single ICRS in corneas with PMD. Because the degree of corneal flattening depends on the thickness and diameter of ring segments, a single, wider segment may produce more flattening with less induced astigmatism. Sharma et al. demonstrated that single-segment ICRS placement provided significantly better outcomes than double-segment ICRS in peripheral keratoconus. Although the location of corneal thinning makes ensuring adequate peripheral thickness perhaps more critical in patients with PMD, the similarities between keratoconus and PMD give reason to believe that these results could be mirrored in patients with PMD. Future studies should compare single- and double-segment ICRS implantation in patients with PMD.

Interventions Changing Biological Structure. CXL is the creation of covalent bonds between collagen molecules, which results in increased strength of the collagen scaffold and greater corneal stiffness. The CXL procedure is minimally invasive and involves the application of riboflavin drops to the eye, either with or without epithelial debridement to maximize penetration. The treated eye is then exposed to ultraviolet-A light at energy levels ranging from 3 to 30 mW/cm² for time intervals of 3 to 30 minutes. Only case reports demonstrate successful CXL in PMD (Table 4). The efficacy, safety, and complications of CXL have been more widely reported in keratoconus, with studies consistently showing improved astigmatism and stabilization of corneal degeneration since 1999. However, CXL produces only minimal improvement in topography and visual acuity. Safety is an important issue for CXL. Although CXL has been widely studied around the world with good
safety and efficacy, approval in the United States is still pending because long-term results have not yet been established.63,70-72 Snibson has cautioned that measures should be undertaken to ensure limbal stem cells be protected from ultraviolet-A exposure.66 Finally, the safety of CXL in PMD may be uniquely challenging due to the perilimbal location of ectatic thinning.

FULL-THICKNESS INTERVENTIONS

**Total Cornea Replacement.** Penetrating keratoplasty is the treatment of last resort in PMD and is considered when contact lenses can no longer be tolerated or fail to provide adequate correction of visual acuity.9 This procedure involves replacement of the diseased cornea with donor corneal tissue. Although penetrating keratoplasty has a record of good results in PMD, these patients are generally poor candidates for penetrating keratoplasty because the location of corneal thinning requires large grafts (8.5 to 9.5 mm) to be positioned close to the limbus, increasing the risk of neovascularization, suture complications, secondary glaucoma due to angle structure damage, and graft rejection.1,3,73 In addition, penetrating keratoplasty results in irregular astigmatism that can be difficult to correct given the discrepancy between donor and recipient corneal thicknesses.11 Long-term graft survival is also an important issue, especially in young patients. Penetrating keratoplasty is also difficult to justify conceptually in PMD because the central cornea and endothelium is essentially unaffected by the disease. Because of these considerable concerns, additional surgical treatments have been developed with the goal of postponing or preventing penetrating keratoplasty.

**Crescentic Cornea Replacement.** Full-thickness crescentic wedge resection is a modification of penetrating keratoplasty that involves removal of only the abnormally thinned cornea followed by re-approximation and suturing of the normal-thickness residual corneal edges (Figure 5).74,75 This procedure has the advantages of not requiring donor tissue (thus avoiding the risk of graft rejection inherent in penetrating keratoplasty), preserving the normal central cornea, a stronger wound, and shorter visual rehabilitation times.76 Studies have demonstrated good visual outcomes with full-thickness crescentic wedge resection in PMD, but astigmatic drift is a concern (Table 2). In a 2008 study of 10 eyes, Busin et al. combined full-thickness crescentic wedge resection with corneal relaxing incisions and reported minimal long-term astigmatic drift.76 However, with advancements in surgical management of PMD, the small sample sizes of these studies and the risks associated with open globe surgery make full-thickness crescentic wedge resection a less appealing option.25,75,76

**PARTIAL-THICKNESS INTERVENTIONS**

**Total Cornea Replacement.** DALK is a modified approach to total cornea transplantation that spares the corneal endothelium. Studies reporting DALK outcomes in PMD are few and of limited sample size (Table 2).77,78 Studies in diseases of the anterior cornea indicate that DALK provides visual outcomes similar to penetrating keratoplasty without the risk of immune-mediated graft rejection.79-81 The documented benefits of DALK include a shorter time to suture removal, a shorter course of topical steroid treatment, reduced endothelial cell loss, and fewer postoperative complications.80 The surgical complexity and relative novelty of DALK are its biggest limitations. Several techniques have been described for separating corneal stroma from Descemet’s membrane, all of which have significant learning curves. DALK can also cause opacification of interface layers within the cornea leading to decreased visual acuity. Femtosecond laser technology has been used in combination with described surgical techniques with good outcomes and could represent the future direction and possible standardization of DALK technique.82 Currently, the need for more extensive study and the technical difficulty of this procedure limits its mainstream acceptance.

**Crescentic Cornea Replacement.** Crescentic lamellar wedge resection is similar to full-thickness crescentic wedge resection, but only the abnormally thinned stroma is removed, followed by re-approximation of the residual, normal-thickness stromal edges (Figure 5).83,84 Like full-thickness crescentic wedge resection, crescentic lamellar wedge resection does not require donor tissue. The main advantage of crescentic lamellar wedge resection over full-thickness crescentic wedge resection is the maintenance of a closed globe.85 Several small studies have confirmed the efficacy of crescentic lamellar wedge resection in PMD (Table 2).83-85 Recently, Maccheron and Daya performed corneal wedge resection with partial or total lamellar dissection with the aim of improving corneal symmetry and optical clarity by shortening the vertical circumference of the cornea in eyes with combined PMD/keratoconus or keratoglobus.85 The result was a statistically significant improvement in visual acuity with reduced astigmatism, although follow-up duration and outcomes varied among study participants.

Crescentic lamellar keratoplasty involves the removal of abnormally thinned stroma followed by placement of a donor stromal graft (Figure 5).1,86-89 The advantages of crescentic lamellar keratoplasty include maintaining a closed globe and the fact that host endothelial cells are maintained, reducing the risk of graft rejection.86,88
Good visual results have been reported with crescentic lamellar keratoplasty in PMD with improved contact lens and spectacle tolerance (Table 2). The procedure has also been used to treat spontaneous corneal perforation in PMD. However, crescentic lamellar keratoplasty is a technically difficult procedure and induced astigmatism and opacification have been reported.

Other lamellar surgical techniques have been developed, but are less commonly used. Lamellar thermokeratoplasty involves thermal shrinkage of the host lamellar bed prior to placement of a donor lamellar cornea. Few data are reported for lamellar thermokeratoplasty in the literature. Epikeratoplasty or epikeratophakia is an onlay lamellar keratoplasty with good results reported in the treatment of PMD (Table 2). The procedure involves suturing a lens made of corneal tissue to the anterior cornea, correcting refractive abnormalities. However, with the advent of newer, more sophisticated PMD treatments, epikeratoplasty is rarely performed.

Tuck-in lamellar keratoplasty is a surgical technique developed for treatment of advanced corneal ectasias including concurrent keratoconus and PMD. The procedure involves creation of a peripheral, partial-thickness flange of posterior stromal tissue on the donor lenticule that is integrated into a 180° inferior stromal pocket in the host cornea (Figure 5). This technique is thought to provide additional tectonic support to the peripheral cornea. Kaushal et al. reported improved visual acuity and reduced astigmatism with no significant complications in 8 eyes that underwent tuck-in lamellar keratoplasty for combined keratoconus and PMD (Table 2). Potential future directions for tuck-in lamellar keratoplasty include using femtosecond laser technology for flange and stromal pocket creation. More long-term outcome data are also required for tuck-in lamellar keratoplasty to become mainstream.

Combination Therapies

Because CXL, toric PIOL implantation, and ICRS each target only one aspect of the PMD disease process, combined therapies have the potential to offer comprehensive treatment, correcting refractive error and astigmatism while halting ectatic progression (Table 4).

Kymionis et al. reported combining PRK and CXL in two eyes of one patient with PMD. Although topography-guided surface ablation is generally contraindicated in PMD due to the risk of accelerating ectatic change with iatrogenic thinning of the cornea, it is thought that CXL prevents this ectatic progression before it starts. Kymionis et al. reported improved keratometry, corrected distance visual acuity, and astigmatism with no intraoperative or short-term complications, although long-term follow-up is needed to ensure safety and ectasia stabilization. This study does raise the possibility that, in the future, patients at risk for iatrogenic ectasia could be pretreated with CXL prior to topography-guided surface ablation to avoid this dreaded complication.

Kymionis et al. also recently reported successful photorefractive keratectomy followed by same-day CXL in one patient with progression of PMD after ICRS implantation. By avoiding ICRS explantation, the patient was able to tolerate contact lenses postoperatively and an acceptable visual outcome resulted. Although the visual results were good and there were no reported complications at 12 months, more extended follow-up is required to assess the outcome of this combination of therapies.

Additional studies are necessary to investigate the efficacy and safety of combining PMD treatments such as ICRS, CXL, toric PIOL, and topography-guided surface ablation. Although studies of combined treatments in keratoconus can provide clues to the impact of these studies in PMD, independent studies are necessary before widespread acceptance is possible.

Conclusions

The diagnosis and management of PMD has seen considerable advancement in recent years. Although little is currently understood about the etiology, pathophysiology, epidemiology, and genetics of the disease, new treatments are improving visual outcomes and reducing complications. CXL is especially exciting given its ability to halt the progression of ectasia. Combined treatments and better screening could eliminate the need for surgical management of PMD in most cases. Future research aimed at discovering genetic markers for PMD and other ectatic disorders would allow early detection of affected patients and potentially lead to progression-altering treatment prior to visual distortion.

Author Contributions

Conception and design (MM, JNE, NLB); data collection (NLB); analysis and interpretation of data (MM, JNE, NLB, SMC); writing the manuscript (MM, JNE, NLB); critical revision of the manuscript (MM, JNE, SMC); administrative, technical, or material support (NLB, SMC); supervision (MM)

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