Chapter 6
Lamina Cribrosa

Lina Siaudvytyte

The lamina cribrosa, a multi-layered sieve-like structure in the optic nerve head, has been proposed as a primary site of axonal damage in glaucoma [1]. The lamina cribrosa provides structural and functional support to the retinal ganglion cells axons as they pass from the relatively high-pressure intraocular space to a low-pressure region in the retrobulbar space. The collagenous beams of the lamina cribrosa provide mechanical support for the nerve fiber bundles, while nutritional support is provided by extracellular matrix components, glial cells such as astrocytes, blood vessels within lamina beams, and axonal transport [2, 3]. It also allows central retinal vein to leave the eye and central retinal artery to enter the intraocular space. Consideration of the anatomy of the lamina cribrosa and peripapillary sclera suggests that the classic mechanical and vascular mechanisms of glaucomatous injury are inseparably related [4].

Studies analyzing the importance of lamina cribrosa began to surface through post mortem studies of glaucomatous eyes [1, 5]. Histological studies found regional differences in lamina cribrosa architecture, showing that glaucomatous eyes had larger lamina cribrosa pores in the superior and inferior poles with narrow connective tissue beams compared to the nasal and temporal regions of the lamina cribrosa [1, 6]. Experimental studies showed posterior deformation and outward migration of lamina cribrosa in response to a chronic intraocular pressure (IOP) elevation [7–9]. With the development of the enhanced depth imaging technique using optical coherence tomography (EDI-OCT), changes in lamina cribrosa have been studied in vivo. Several studies showed that the lamina cribrosa is thinner in glaucomatous eyes compared with healthy controls [10–12]. Seo et al. demonstrated a wide variation of laminar depth in healthy subjects (range 193.08–826.81 μm, with a mean 402 (101.46) μm) [13]. Furthermore, males had significantly deeper located lamina

L. Siaudvytyte (✉)
Eye Clinic, Lithuanian University of Health Sciences, Kaunas, Lithuania
e-mail: lina.siaudvytyte@lsmuni.lt

I. Januleviciene, A. Harris (eds.), *Biophysical Properties in Glaucoma*,
https://doi.org/10.1007/978-3-319-98198-7_6

cribrosa than females, in agreement with a previous findings that males tend to have a larger cup depth than females [14]. You et al. found that focal lamina cribrosa defects (laminar holes or disinsertions) were associated with neuroretinal rim loss and acquired pits of the optic nerve. They concluded that these defects can be visualized more effectively on EDI-OCT images than by clinical examination [15]. Other authors suggested that focal lamina cribrosa defects might be associated with focal retinal nerve fiber damage [16]. In another study, focal laminar defects were associated with disc hemorrhages, diagnosis of normal tension glaucoma (NTG) and more advanced glaucoma status [17]. Faridi et al. showed that focal lamina cribrosa defects were strongly associated with glaucomatous visual field progression [18].

Several studies investigated the structure-function relationship between the morphology of the lamina cribrosa and glaucoma severity [19–24]. Kim et al. found significant correlations between laminar depth, laminar thickness and glaucoma severity, with greater severity associated with increasing laminar depth and decreasing laminar thickness. Furthermore, only laminar depth was associated with visual field mean deviation in NTG group, whereas laminar thickness and IOP were correlated with visual field mean deviation in high tension glaucoma (HTG) group. Authors concluded that the pathogenesis of NTG and HTG might differ [22]. Park et al. found that the laminar thickness was significantly thinner from the early and mid-stages of glaucoma in NTG compared with HTG subjects. Authors suggested that thinner lamina cribrosa in NTG group might have contributed to the development of retinal ganglion cell damage in a normal IOP range [20]. Ren et al. revealed relation between the anterior laminar depth and visual field status in early glaucoma or ocular hypertension (OHT) patients. In their study, the laminar depth increased with worse visual field status in younger eyes but not in older eyes [19]. Rho et al. reported age-related differences in laminar displacement in 8 of 12 clock-hour positions in primary open-angle glaucoma (POAG) but interestingly found no age-related differences in laminar displacement in NTG patients [24]. Other studies demonstrated linear [21] or logarithmic [20] correlation between the laminar thickness and retinal sensitivity in OAG.

Some studies analyzed lamina cribrosa changes after glaucoma surgery procedures [25–29]. Reduction of laminar depth following trabeculectomy was described at 6 months and over 2 years postoperatively [25–27, 29]. Reis et al. reported that both anterior laminar surface displacement and thickening of prelaminar tissue occurred after surgical IOP reduction in glaucoma patients (18 patients underwent trabeculectomy, 4–tube shunt implantation) [30]. Barrancos et al. revealed that reversal cupping after non-penetrating deep sclerectomy was mainly due to changes in prelaminar tissue thickness, whereas lamina cribrosa changes in position were less pronounced [28]. Other authors concluded that reversal cupping after non-penetrating deep sclerectomy was first of all caused by the anterior movement of lamina cribrosa [29].

References

1. Quigley HA, Addicks EM, Green WR, Maumenee AE. Optic nerve damage in human glaucoma. II. The site of injury and susceptibility to damage. Arch Ophthalmol (Chicago, IL: 1960). 1981;99(4):635–49.
2. Burgoyne CF, Downs JC, Bellezza AJ, Suh J-KF, Hart RT. The optic nerve head as a biomechanical structure: a new paradigm for understanding the role of IOP-related stress and strain in the pathophysiology of glaucomatous optic nerve head damage. Prog Retin Eye Res. 2005;24(1):39–73.
3. Dai C, Khaw PT, Yin ZQ, Li D, Raisman G, Li Y. Structural basis of glaucoma: the fortified astrocytes of the optic nerve head are the target of raised intraocular pressure. Glia. 2012;60(1):13–28.
4. Downs JC, Roberts MD, Burgoyne CF. Mechanical environment of the optic nerve head in glaucoma. Optom Vis Sci. 2008;85(6):425–35.
5. Yan DB, Coloma FM, Metheetrairut A, Trope GE, Heathcote JG, Ethier CR. Deformation of the lamina cribrosa by elevated intraocular pressure. Br J Ophthalmol. 1994;78(8):643–8.
6. Quigley HA, Addicks EM. Regional differences in the structure of the lamina cribrosa and their relation to glaucomatous optic nerve damage. Arch Ophthalmol (Chicago, IL: 1960). 1981;99(1):137–43.
7. Yang H, Downs JC, Bellezza A, Thompson H, Burgoyne CF. 3-D histomorphometry of the normal and early glaucomatous monkey optic nerve head: prelaminar neural tissues and cupping. Investig Ophthalmol Vis Sci. 2007;48(11):5068–84.
8. Yang H, Williams G, Downs JC, Sigal IA, Roberts MD, Thompson H, et al. Posterior (outward) migration of the lamina cribrosa and early cupping in monkey experimental glaucoma. Invest Ophthalmol Vis Sci. 2011;52(10):7109–21.
9. Roberts MD, Grau V, Grimm J, Reynaud J, Bellezza AJ, Burgoyne CF, et al. Remodeling of the connective tissue microarchitecture of the lamina cribrosa in early experimental glaucoma. Invest Ophthalmol Vis Sci. 2009;50(2):681–90.
10. Jonas JB, Berenshtein E, Holbach L. Anatomic relationship between Lamina Cribrosa, intraocular space, and cerebrospinal fluid space. Investig Ophthalmol Vis Sci. 2003;44(12):5189–95.
11. Quigley HA, Hohman RM, Addicks EM, Massof RW, Green WR. Morphologic changes in the lamina cribrosa correlated with neural loss in open-angle glaucoma. Am J Ophthalmol. 1983;95(5):673–91.
12. Ren R, Wang N, Li B, Li L, Gao F, Xu X, et al. Lamina cribrosa and peripapillary sclera histomorphometry in normal and advanced glaucomatous Chinese eyes with various axial length. Invest Ophthalmol Vis Sci. 2009;50(5):2175–84.
13. Seo JH, Kim T-W, Weinreb RN. Lamina cribrosa depth in healthy eyes. Invest Ophthalmol Vis Sci. 2014;55(3):1241–51.
14. Cheung CY, Chen D, Wong TY, Tham YC, Wu R, Zheng Y, et al. Determinants of quantitative optic nerve measurements using spectral domain optical coherence tomography in a population-based sample of non-glaucomatous subjects. Invest Ophthalmol Vis Sci. 2011;52(13):9629–35.
15. You JY, Park SC, Su D, Teng CC, Liebmann JM, Ritch R. Focal lamina cribrosa defects associated with glaucomatous rim thinning and acquired pits. JAMA Ophthalmol. 2013;131(3):314–20.
16. Tatham AJ, Miki A, Weinreb RN, Zangwill LM, Medeiros FA. Defects of the lamina cribrosa in eyes with localized retinal nerve fiber layer loss. Ophthalmology. 2014;121(1):110–8.
17. Park SC, Hsu AT, Su D, Simonson JL, Al-Jumayli M, Liu Y, et al. Factors associated with focal lamina cribrosa defects in glaucoma. Invest Ophthalmol Vis Sci. 2013;54(13):8401–7.

18. Faridi OS, Park SC, Kabadi R, Su D, De Moraes CG, Liebmann JM, et al. Effect of focal lamina cribrosa defect on glaucomatous visual field progression. Ophthalmology. 2014;121(8):1524–30.
19. Ren R, Yang H, Gardiner SK, Fortune B, Hardin C, Demirel S, et al. Anterior lamina cribrosa surface depth, age, and visual field sensitivity in the Portland Progression Project. Invest Ophthalmol Vis Sci. 2014;55(3):1531–9.
20. Park H-YL, Jeon SH, Park CK. Enhanced depth imaging detects lamina cribrosa thickness differences in normal tension glaucoma and primary open-angle glaucoma. Ophthalmology. 2012;119(1):10–20.
21. Inoue R, Hangai M, Kotera Y, Nakanishi H, Mori S, Morishita S, et al. Three-dimensional high-speed optical coherence tomography imaging of lamina cribrosa in glaucoma. Ophthalmology. 2009;116(2):214–22.
22. Kim M, Bojikian KD, Slabaugh MA, Ding L, Chen PP. Lamina depth and thickness correlate with glaucoma severity. Indian J Ophthalmol. 2016;64:358–63.
23. Furlanetto RL, Park SC, Damle UJ, Sieminski SF, Kung Y, Siegal N, et al. Posterior displacement of the lamina cribrosa in glaucoma: in vivo interindividual and intereye comparisons. Invest Ophthalmol Vis Sci. 2013;54(7):4836–42.
24. Rho CR, Park H-YL, Lee NY, Park CK. Clock-hour laminar displacement and age in primary open-angle glaucoma and normal tension glaucoma. Clin Exp Ophthalmol. 2012;40(4):e183–9.
25. Lee EJ, Kim T-W, Weinreb RN. Reversal of lamina cribrosa displacement and thickness after trabeculectomy in glaucoma. Ophthalmology. 2012;119(7):1359–66.
26. Lee EJ, Kim T-W, Weinreb RN, Kim H. Reversal of lamina cribrosa displacement after intraocular pressure reduction in open-angle glaucoma. Ophthalmology. 2013;120(3):553–9.
27. Lee SH, Yu D-A, Kim T-W, Lee EJ, Girard MJA, Mari JM. Reduction of the Lamina Cribrosa curvature after trabeculectomy in Glaucoma. Invest Ophthalmol Vis Sci. 2016;57(11):5006–14.
28. Barrancos C, Rebolleda G, Oblanca N, Cabarga C, Munoz-Negrete FJ. Changes in lamina cribrosa and prelaminar tissue after deep sclerectomy. Eye (Lond). 2014;28(1):58–65.
29. Krzyzanowska-Berkowska P, Melinska A, Helemejko I, Robert Iskander D. Evaluating displacement of lamina cribrosa following glaucoma surgery. Graefes Arch Clin Exp Ophthalmol. 2018;256(4):791–800.
30. Reis ASC, O'Leary N, Stanfield MJ, Shuba LM, Nicolela MT, Chauhan BC. Laminar displacement and prelaminar tissue thickness change after glaucoma surgery imaged with optical coherence tomography. Invest Ophthalmol Vis Sci. 2012;53(9):5819–26.