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Reframing Glaucoma: Beyond Intraocular Pressure As A Pressure-Centric Disease

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Abstract

Purpose*: To evaluate new researches which shows that glaucomatous optic neuropathy results from multiple factors that include neurodegenerative changes and vascular problems and biomechanical effects.*

Methods*: A detailed review of available research and clinical studies about retinal ganglion cell degeneration and vascular dysregulation and optic nerve head biomechanics while studying structural–functional dissociation and outcomes of intraocular pressure–lowering treatments was done.*

Results*: Research shows that retinal ganglion cell death and ocular blood supply problems and lamina cribrosa vulnerability and trans-synaptic degeneration all play roles in disease development. The structural–functional dissociation between visual function and anatomical changes demonstrates why pressure-focused evaluation methods fall short. The variable treatment responses and diverse clinical presentations of glaucoma find better explanation through a phenotype-based classification system.*

Conclusion: *Glaucoma should be recognized as a multifactorial optic neuropathy which extends beyond the traditional definition of elevated intraocular pressure. A comprehensive conceptual framework emerges from combining pressure reduction with awareness of vascular and biomechanical and neurodegenerative factors which could lead to new diagnostic and treatment developments.*

Keywords: *Glaucoma; intraocular pressure; neurodegeneration; optic nerve head biomechanics; ocular perfusion; normal-tension glaucoma*

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I. Introduction: The Limits Of A Pressure-Centric View Of Glaucoma

Glaucoma care has revolved around one core metric for more than a hundred years,that is the intraocular pressure.There has been solid evidence behind the idea that elevated eye pressure sits at the center of this disease, since it's pretty much the only risk factor we can actually modify to change how things unfold.Every current glaucoma therapy is all about driving IOP down [1–3].

If we consider landmark studies like the Ocular Hypertension Treatment Study and Early Manifest Glaucoma trial,they told us that , if we lower the pressure, and we will shrink chances of developing glaucoma while slowing vision loss at any stage [4–6]. It does sounds straightforward enough on paper, but once we step outside controlled trials and look at what actually happens in clinics every day,we can see that high IOP can not be the culprit for entire optic nerve damage.

Plenty of people develop classic optic nerve damage from glaucoma even though their pressures are comfortably within normal territory; meanwhile others keep losing vision despite hitting those so-called "target" numbers [7–9]. Then there are outliers who walk around for decades with sky-high IOP yet never show any real signs of glaucomatous changes [4,10]. Clearly, how vulnerable someone is to pressure-related injury varies wildly. All this pokes holes in our old reliance on IOP as the be-all end-all marker,it just doesn't capture all that's happening beneath the surface.

Normal tesnion glaucoma patients lose retinal ganglion cells and develop cupping plus visual field loss, the same grim markers as typical high-pressure open-angle cases,even though their pressures always fall inside textbook limits [7,11].

OCT often spots thinning or outright loss in nerve fiber layers before anyone detects vision problems; sometimes it works backwards too: patients have clear visual decline, but no matching structural changes yet [14–16]. So there is a visible disconnect between anatomy and function . So now researchers are thinking and today we may frame glaucoma as an ongoing neurodegenerative disorder marked by death of retinal ganglion cells plus axonal degeneration, with effects moving way beyond what goes on inside just the eyeball itself [17–19]. There is more to think here as both bench research and actual patient studies tell us that culprits like poor blood flow regulation, impaired ocular perfusion, fragile exits where nerves thread through support structures, mitochondrial malfunctions,you name it, all tangled together in this complex web called glaucoma [20–24].

What we're left with instead is an expanded perspective, a model that is trying to explain why patients look so different from each other clinically in terms of varying speeds of symptom worsening; unpredictable responses to standard therapies; stubborn progression long after treatment goals seem ticked off on paper [2,25].

II. Glaucoma As A Neurodegenerative Optic Neuropathy

There's now a mountain of both lab-based and real-world evidence that firmly recasts glaucoma as a long-term neurodegenerative disease, not merely something sparked by high intraocular pressure. Again and again, if you peek under the microscope,whether in people or animal models, what jumps out is apoptotic RGC death; these neurodegenerative changes are clearly driving the bus here . Quigley's group threw an interesting wrench into things when they found that axonal damage actually rears its head before you ever spot RGC cell body loss[26–28].

This lands glaucoma right alongside other central nervous system diseases on the spectrum of neurodegeneration [29,30]. So where does this all begin? It turns out, everything starts falling apart when axonal transport gets jammed at the lamina cribrosa. Without this critical delivery route keeping growth factors flowing, RGCs lose their safety net and start dying off [31,32].

Trans-synaptic degeneration has emerged as another clue cementing glaucoma's place among genuine neurodegenerative disorders. MRI scans and diffusion tensor imaging shows that people with glaucoma show obvious structural shifts not just in their optic nerves, but also further upstream,in places like the lateral geniculate nuclei and even spilling over into visual cortex regions [33–35]. In other words, glaucomatous injury refuses to stay boxed in within the eye; it radiates outward, a pattern eerily familiar from other brain diseases.Several pathways have been implicated in glaucomatous damage,including mitochondrial dysfunction running rampant, oxidative stress building up, glutamate-fueled excitotoxicity making matters worse, along with chronic neuroinflammation [36–39].

If mitochondria go off-script inside retinal ganglion cells,those cells become easy targets for metabolic distress, which partly explains why some people keep declining even if their IOP hovers at normal or only slightly raised levels [40,41]. Here comes an important twist, not everyone bounces back just by lowering IOP alone. Clinical findings reveal that dropping pressure can definitely ease mechanical burden on fragile neurons

by helping restore axonal movement,but crucially, it doesn't address downstream neuron injury or outright cell death [42,43]. That leaves scientists hunting for genuinely protective therapies aimed at safeguarding RGC health no matter what happens with IOP; yet so far there hasn't been rock-solid evidence from large trials showing these approaches deliver major benefits to patients [44,45].

Bottom line is that seeing glaucoma through this broader lens, as progressive optic neuropathy built on top of neurodegeneration,means pressure acts more like an adjustable risk dial that speeds up nerve harm if your eyes are vulnerable; but whether, or how,the disease unfolds is shaped by a vast mix of biomechanical stresses blended with vascular oddities and unique cellular frailties playing out differently across individuals [2,19,25].

III. Vascular Dysregulation And Ocular Perfusion In Glaucoma

Vascular dynamics are actually woven right into the core of glaucomatous optic neuropathy, especially in cases where the disease pops up even though intraocular pressure (IOP) is sitting pretty at normal or low levels. Here's what challenges our conventional wisdom?when ocular blood flow stumbles, it blows open that old "pressure explains everything" narrative[46-48]. Ocular perfusion pressure,which boils down to the gap between arterial blood pressure and IOP, plays a decisive role in whether the optic nerve head gets the circulation it desperately needs.. Time and again, major studies have consolidated that as perfusion pressure drops, not only does glaucoma crop up more often, but it also tends to speed ahead with alarming momentum[49-51].

Normal-tension glaucoma (NTG) really puts this vascular angle under a spotlight. People living with NTG frequently grapple with broader vascular oddities, like recurring migraines, Raynaud phenomenon flare-ups, or spells of peripheral vasospasm,all clues pointing toward an underlying fragility within their circulatory systems[52-54]. Flammer and his team coined "primary vascular dysregulation" to capture this exact scenario: flawed regulation leads to patchy blood flow and repeated episodes of ischemia–reperfusion injury taking aim right at the optic nerve head itself. Make no mistake, these unpredictable shifts in supply can nudge axonal damage forward even if your average IOP looks completely unremarkable.Another twist worth highlighting is that nocturnal systemic hypotension, that drop in blood pressure while you're asleep,is now seen as a major accelerant for glaucoma progression[55,56].

Thanks to ambulatory monitoring tech, we know those steep nighttime dips in BP walk hand-in-hand with worsening visual fields, especially among NTG patients[57-59]. The reason why does this matter is because, during sleep hours, reduced ocular perfusion pressure teams up with sluggish autoregulatory mechanisms, a double hit that leaves the optic nerve unusually exposed to harm[56,57]. This isn't just theory, it has real-world stakes for people on aggressive antihypertensive regimens,the very medication protecting your heart could end up blindsiding your eyes during those crucial overnight hours without anyone catching on until damage sets in. State-of-the-art imaging like optical coherence tomography angiography has poured fuel on this fire by revealing progressively sparser vessels around both peripapillary and macular zones as glaucoma tightens its grip, a trend too glaring to dismiss as severity ramps up[60-62].

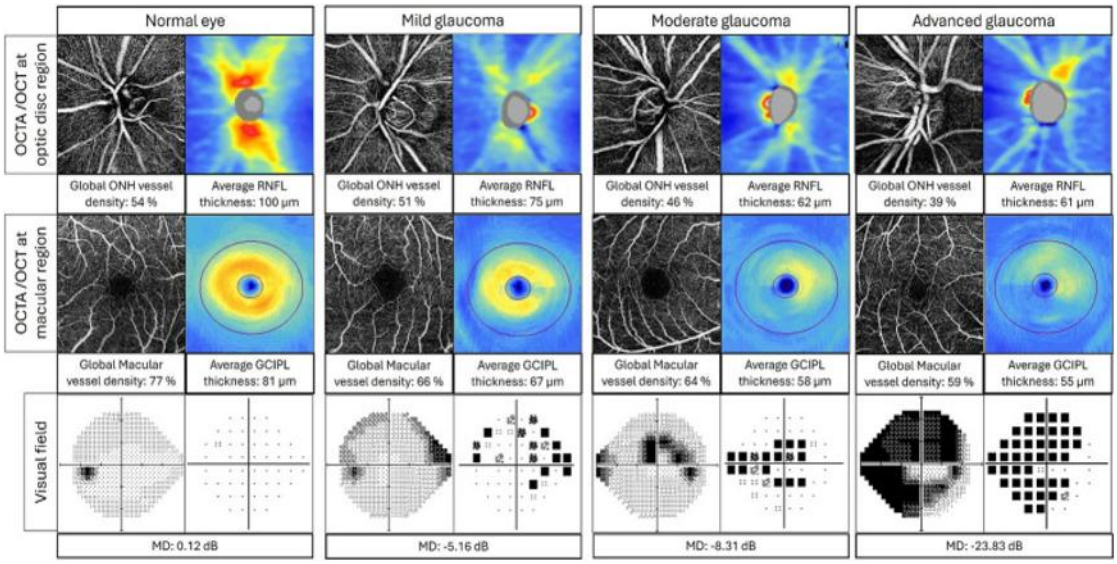

Figure 1. How do microvascular, structural and functional markers interact as glaucoma moves through its different phases. Here's a look: you'll see OCTA scans revealing vessel density around both the optic nerve (peripapillary) and the macula, alongside OCT maps tracking RNFL and GCIPL thickness. Visual field charts for eyes ranging from normal to mild, moderate and advanced glaucoma are right there for comparison.. As the disease ramps up, blood vessels thin out further and neural layers shrink,but as you can see in image of moderate and advanced glaucoma,the RNFL and GCIPL has a floor effect but vessel density does not so vessel density goes more hand-in-hand with worsening visual field loss.All of this is reproduced from Shen et al[93]., Frontiers in Medicine, 2024 (Creative Commons Attribution/CC BY license).

Whether these vascular changes light the fuse for neural injury or merely keep pace alongside ,it remains unsettled,but either way they drive home how closely linked vascular health is with neuronal survival when we talk about glaucoma. Taking a step back paints an interesting picture-baseline differences in systemic BP, not to mention each individual's unique approach to regulating vessel tone,help explain why two people having identical IOPs can still wind up worlds apart when it comes to vision loss outcomes[65,66]. That reality makes one thing crystal clear, relying solely on pressure-centric risk models means missing entire chapters of what's really going on beneath the surface.

IV. Biomechanics Of The Optic Nerve Head And Lamina Cribrosa Susceptibility

The lamina cribrosa, the meshwork where retinal ganglion cell axons slip out of the eye , remains on the front lines, exposed not just to pressure, but also to a whole host of other stresses that aren't strictly about intraocular pressure[67–69]. It has been a dilemma that why people with similar IOP readings can end up with wildly different disease outcomes. It usually comes down to their unique lamina architecture,how it's built, its material properties, and ongoing tweaks in connective tissue over time. Experimental work paired with clinical observations has really consolidated this fact that an uptick in IOP leads straight to backward bowing (posterior deformation), thinning out, and shifting of the lamina cribrosa itself.This isn't just academic, those changes heap mechanical strain onto both nerve fibers and microvasculature [70–72]. Now here's where things get even more interesting, finite element modeling steps in and tells us these internal stress patterns don't simply track with IOP values alone; they hinge on factors like scleral stiffness, how thick or thin that laminar region is, and exactly how stretchy and elastic those tissues are [73,74]. Taken as a whole, all this evidence pushes a broader idea into focus: glaucoma isn't just about high pressure per se,it stems from an imbalance between local

biomechanics and whatever absolute IOP happens to be present. We see this play out when structural deformation shows up at so-called normal pressures, especially if someone's connective tissue is unusually flexible or their matrix configuration deviates from the norm [75,76]. This helps in explaining that in normal-tension glaucoma cases individual susceptibility gets dictated by each person's own local tissue landscape.

But another twist is that, as people age, shifts in scleral or laminar rigidity can either ramp up or tone down personal risk profiles over time [77,78]. Thanks to advances like enhanced-depth imaging or swept-source OCT tech we're now able to peek inside living eyes directly; these methods let clinicians spot subtle focal defects or localized thinning,and posterior migration, in the lamina cribrosa itself which are classic signatures seen in glaucomatous eyes [79–81]. Longitudinal patient tracking drives home one big message that warping of this structure usually kicks off early,sometimes before you catch any loss in retinal nerve fiber layer thickness or visual field function at all. [82,83].

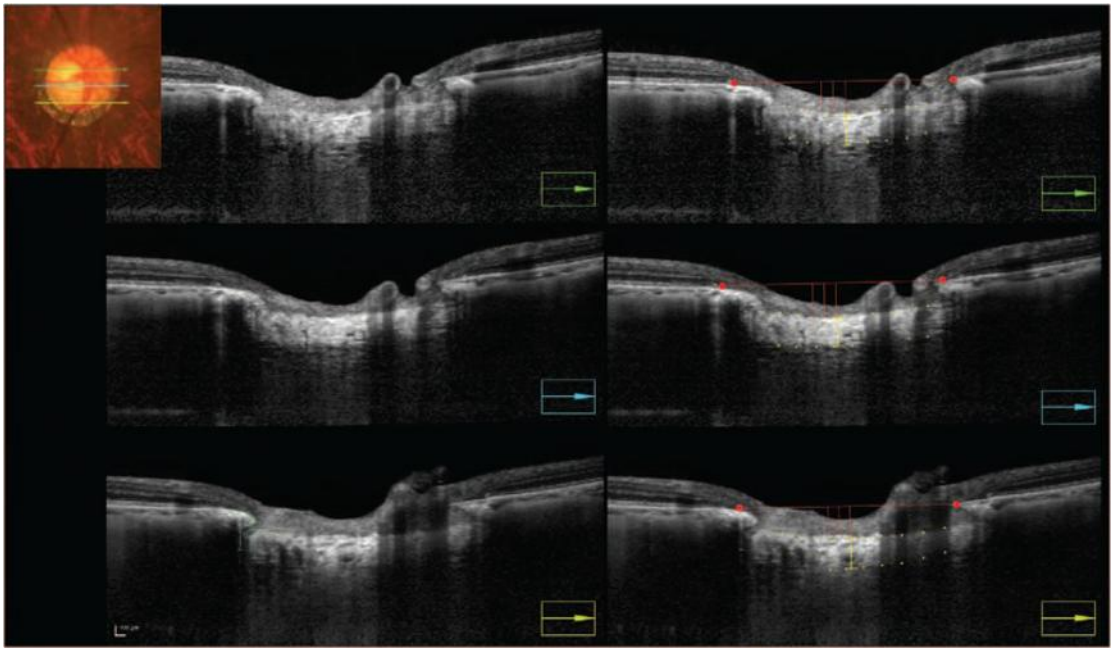

Figure 2. Here's a closer look at the lamina cribrosa, captured with enhanced depth imaging spectral-domain optical coherence tomography (EDI-SD-OCT) of the optic nerve head, an approach that really lets you appreciate both LC structure and how these measurements are actually made. Now, when we talk about a focal LC defect, what we mean is any break in that typical U- or W-shaped curve along the front edge of the lamina cribrosa (outlined in green). To count as genuine, this disruption needs to show up on at least two neighboring B-scans,not just a one-off blip. To pin down lamina cribrosa depth (LCD): we have to measure straight down from the Bruch's membrane opening reference plane, that red line connecting either side of Bruch's membrane,to where it hits the anterior surface of the LC.

They check this at three specific spots: above, right through the middle horizontally, and below. As for lamina cribrosa thickness (LCT), they're gauging how thick that layer is by measuring from its front to back borders, always perpendicular to its anterior surface for accuracy. The average LCD and LCT values come from crunching those numbers across all three locations, a simple mean calculation does the trick here. This whole methodology comes straight out of Lee SH et al.[76], Investigative Ophthalmology & Visual Science, 2020 (shared under Creative Commons Attribution–NonCommercial–NoDerivatives 4.0 License),

It gets worse because mechanical forces at play interact constantly with blood flow dynamics within the optic nerve head. Whenever that structural scaffold gives way,capillary circulation drops off; ischemia worsens; limited blood supply makes recovery sluggish,a feedback loop where vascular compromise amplifies neural injury through metabolic stress [84,85]. From a clinical angle, the biomechanical model tosses aside any notion that targeting some magic "ideal" IOP will safeguard every patient equally well.

Not everyone fits neatly into that box; certain eyes are flat-out more delicate and demand lower pressure goals due to heightened sensitivity while others weather higher numbers without falling apart [69,86].

V. Structural–Functional Dissociation In Glaucoma

One of the biggest headaches is how structural changes in the eye don't always sync up with what's happening to a person's vision. Here's the thing, despite all our high-tech imaging tools and advanced visual field tests, it's still pretty routine to find folks whose OCT scans reveal nerve fiber thinning while their day-to-day sight seems totally fine, or flip it around,people showing clear dips in visual ability even though their structural scans look unremarkable. This disconnect ,what we call structural–functional dissociation exposes some glaring blind spots in how we diagnose glaucoma, making it clear this disease isn't just a one-trick pony; there are layers upon layers involved [87–89]. Looking at patient data over time paints an interesting picture:OCT measurements tracking retinal nerve fiber layer (RNFL) thinning usually flag trouble earlier than standard visual field tests do, especially during those first warning signs or when someone just starts raising suspicions for glaucoma [90–92]. This fits perfectly with what autopsy studies tell us,you have to lose a hefty chunk of retinal ganglion cells before automated perimetry even hints anything's wrong [29,93].

Things get tricky as disease advances,eg.in moderate or late-stage glaucoma, sometimes people start losing vision function without seeing any further RNFL thinning on their OCTs. Why does that happen?because at that point, RNFL thickness hits a so-called "floor effect", it bottoms out so much that OCT can't pick up on additional axonal loss anymore [94–96]. Meanwhile because visual fields reflect combined output from every remaining neuron still hanging in there, scores might keep dropping even while structure appears stable,or frozen in place. This split between what we measure structurally and functionally throws a wrench into figuring out whether someone's truly under control, it shatters any illusion that stability in one area automatically means safety across the board.

The important part is that you can't swap OCT and perimetry like interchangeable parts,they each differ not just in sensitivity, but also how well they track change over time. Structural imaging tends to be more dependable early on for diagnosis; later down the line though, functional testing becomes your best friend for spotting ongoing damage. Add on normal test-to-test fluctuations ,not forgetting other unrelated eye or brain issues creeping into results,that's a lot of noise clouding interpretation [99–101]. Structural–functional mismatch also lays bare why relying solely on intraocular pressure (IOP) as an outcome measure falls short. Even eyes staying within "target" IOP might worsen anyway since factors like blood flow problems or mechanical strain driving cell death aren't magically fixed by lowering pressure alone [16,102].

What should clinicians take away from here? trusting IOP as proof everything's okay is risky business, it calls out loud and clear for using several kinds of data together instead. Which brings us right back around: new approaches now try bridging these gaps by merging both types of information into unified assessment models.. Recent research shows combining event-based trends with mapping techniques linking structure-function patterns,as well as region-specific correlation models, can sharpen our radar for catching real progression sooner rather than later [103–105].

VI. Why Intraocular Pressure Lowering Still Works—And Why It Is Not Enough

Multiple major randomized controlled trials have hammered home the point: lower IOP leads to fewer cases of visual field loss across different types of glaucoma, and bigger reductions yield even better results [4–6,106]. So here's the thing,high IOP is one risk we can genuinely target, which explains why keeping it in check remains front and center in how doctors manage glaucoma today.

But not every eye starts with high pressures.Look at normal-tension glaucoma: data from the Collaborative Normal-Tension Glaucoma Study showed a 30% drop in IOP caused disease progression to slow down significantly for these patients [12,107]. That isn't some statistical blip; cutting pressure shields against vision loss whether we're talking about primary open-angle glaucoma, ocular hypertension, or even late-stage disease [5,108].

How much someone benefits from lower IOP?plenty of people see their condition worsen anyway, even after hitting textbook targets for pressure reduction. The numbers don't lie: clinical trials keep turning up cases where folks still lose structure or function despite aggressive management over years [6,9,109].Why does this gap exist? a few culprits lurk beneath the surface. Lowering IOP relieves mechanical stress on the optic nerve head and helps restore axonal transport (which matters), but it can't undo past harm to retinal ganglion cells or halt neurodegeneration already underway [42,43]. If blood flow regulation is shaky, or if an eye just can't handle biomechanical strain,pressure control by itself falls short . And once injury sets off mitochondrial dysfunction and weakens cellular resilience further[55,84,110].

The odds of reversing damage stay pretty slim because things are rarely black-and-white here, and after years spent chasing magic "target" numbers,the medical field no longer buys into a universal "target IOP" for everyone with glaucoma [36,40]. Now when experts say "target pressure," they mean something flexible: an individualized benchmark that gets adjusted depending on how fast someone is progressing and what specific risks they bring to the table [2,111]. Acknowledging these limitations doesn't degrade the importance of controlling IOP ; if anything, it underlines its central role while making clear that expecting miracles from pressure alone isn't realistic. Sure enough,lessening mechanical load through lower IOP curbs some damage, but doesn't reliably put neurodegeneration in reverse once it starts rolling [19,25].

VII. Toward A Phenotype-Driven Model Of Glaucoma

The phenotype-centered approach flips the script by focusing on how every individual tends to have their own primary pathway that leads straight to optic nerve trouble[2,19,25]But here's the thing,not everyone ends up with damage for identical reasons; sometimes high intraocular pressure (IOP) is front and center, other times disrupted blood flow or vascular hiccups take over, or maybe there's just increased biomechanical fragility even if IOP numbers look textbook-normal [55,69,84]. Add neurodegenerative factors into the mix, mitochondrial glitches and less cellular resilience,and suddenly you've got multiple ways these phenotypes can play out [36,40,112]. If we zoom out like this and reconsider everything through that lens, classic pressure-driven glaucoma is only part of an entire landscape. Patients whose IOP shoots up, but who've got resilient blood vessels and sturdy support tissues usually respond well to conventional pressure-lowering approaches. But on the flip side,people with normal-tension glaucoma plus dips in nighttime blood pressure (nocturnal hypotension), extra-flexible lamina cribrosa tissue or systemic vascular issues, they often keep sliding downhill despite aggressive IOP drops [12,57,76]. That drives home why trying to shoehorn everyone into "one-size-fits-all" treatments misses so much nuance; tailoring risk assessment becomes non-negotiable. This phenotyping idea also helps clarify why structural loss doesn't always neatly line up with functional decline,and why treatment results can be unpredictable from case to case. Sometimes structural problems show up before vision changes hit because neuroaxonal injury sneaks in early; other times function plummets while scans still look clean due

to limits in today's imaging tech [94,97,103]. If clinicians start treating these findings as genuine phenotypic expressions instead of blaming measurement error or quirks in testing protocols, it could seriously sharpen both diagnostic accuracy and therapeutic fine-tuning.

Just so there's no confusion: adopting a phenotype-first mindset isn't about throwing out tried-and-true therapies,it means threading them into broader care strategies built around each patient profile. Pressure reduction still anchors every type of glaucoma management; what shifts is how doctors set expectations based on distinctive patterns they spot [6,111]. Keeping tabs on systemic blood pressures, including those nighttime lows,as well as checking for sleep apnea or other vascular risk contributors might also give certain patients an edge [59,65,113]. Now here's where technology starts making serious waves: cutting-edge imaging has started prying open doors that used to stay slammed shut. Merging sharper lamina cribrosa scans with deeper vascular details from OCT-angiography, and tracking both structure and function longitudinally,is finally letting us tease apart subtypes beyond just chasing IOP stats alone [60,79 ,104].

We may not be at the stage where machines spit out bulletproof clinical phenotypes yet, but honestly ,reframing glaucoma as a phenotype-driven optic neuropathy finally brings clinical thinking into sync with the messy, unpredictable nature of biology itself.Lowering intraocular pressure is important for sure, that remains the mainstay for now,but folks are finally acknowledging there's much more beneath the surface: those non-pressure factors aren't going away anytime soon. [2,25,111].

When patients keep declining despite low eye pressures it should be our cue to pan out,systemic vascular issues like nocturnal hypotension, sleep apnea, heart trouble or even autonomic dysfunction all come into play here [57,59,65,113]. Turns out these elements matter more than we once realized.With clearer lamina cribrosa views plus OCT angiography metrics, and by tying anatomy straight back to function,we're edging closer to spotting high-risk phenotypes sooner while sharpening our ability to detect true progression [60,79,104,114]. Mix long-term imaging data with functional tests and clinical clues inside AI models and suddenly predicting who lands in hot water doesn't seem so far-fetched, though let's be real: these algorithms still have plenty of hurdles before they become part of routine care [115,116].

There's also mounting energy around treating glaucoma as an honest-to-goodness neurodegenerative disease,which keeps pushing neuroprotection and maybe even neuroenhancement therapies onto center stage. Early signals look promising preclinically; unfortunately not one agent has cleared the finish line yet in major trials [44,45,117].

All signs point toward needing smarter ways of measuring trial results that actually reflect reality rather than just tracking IOP drops alone, especially when vascular or degenerative drivers fuel progression over pure pressure overload. Right now there's no agreed-upon "gold standard" composite endpoint blending structure-function-vascular measures for monitoring meaningful change [103,118].

VIII. Summary

For years, glaucoma has been seen mostly through the lens of elevated intraocular pressure, pressure's always been the headline act. Treatments have long revolved around keeping that eye pressure in check, since it's the one variable doctors can reliably influence. But here's the thing: this focus on pressure doesn't really account for all the quirks and inconsistencies you see in real-world cases of glaucoma.. It turns out, plenty of people develop glaucoma even when their intraocular pressure is well within normal range, and others experience worsening disease despite textbook-perfect pressure control,not to mention the variety in how damage actually shows up.

Instead, it should be understood as an ongoing optic neuropathy involving several culprits working together, retinal ganglion cell loss, faulty blood flow to ocular tissues, weakened biomechanics at the optic

nerve head, plus trans-synaptic degeneration throughout parts of the visual system.. So we're dealing with more than meets the eye; relying solely on pressure readings leaves too much out. Still, no one's saying lowering intraocular pressure isn't valuable, it remains an essential tool,but now it sits alongside other factors inside a broader biological network.

Switching gears toward a phenotype-driven model (one that brings vascular changes, biomechanical weaknesses and neurodegeneration into play with traditional pressure concerns) makes far more sense when trying to explain why two patients can look so different or respond differently to treatment. This shift nudges clinicians toward tailoring goals for each patient, personalized targets rather than one-size-fits-all numbers,and allows for smarter interpretation of disease progression as well as clearer expectations about outcomes.

IX. Conclusion

Until now, glaucoma has mostly been tackled through the narrow focus of intraocular pressure, IOP,the tried-and-true metric everyone's leaned on, mainly because decades of data back up how much lowering IOP helps. Still, here's where things get complicated: not every case fits that template. The reality is messier than textbooks let on; you've got normal-tension glaucoma in the mix and patients who keep sliding downhill even when their pressures look textbook-perfect. That alone should make us pause before blaming IOP as the sole villain in this story. These days, though, a wider perspective is catching on.

Glaucoma isn't just a numbers game about pressure; it's an ongoing optic nerve disease with multiple moving parts. Sure, intraocular pressure remains front and center, it hasn't lost its relevance,but it's only one piece of a puzzle that also includes neurodegeneration, quirks in blood flow, and mechanical strain inside the eye itself. When you start thinking about all these overlapping factors, which honestly fits real-world cases better, suddenly some head-scratchers make more sense, like why certain people develop visible changes to their optic nerve without losing vision right away or why others do fine for years before problems show up. So yes,we're no longer stuck seeing IOP as the be-all-end-all here.

This shift toward tailoring care by each patient's specific profile means clinicians can set custom targets for therapy and monitoring, a far better approach if you ask me,and gives everyone involved clearer expectations around what "success" really looks like. Looking forward, clinical practice will need to absorb new advances from cutting-edge scans and laboratory discoveries, think advanced analytics bridging into everyday decision-making. Treating glaucoma as something bigger than just chasing numbers finally cracks open possibilities for individualized medicine based on biology instead of averages,and paves the way for sharper diagnostics plus smarter treatments down the line.

References

[1]. Weinreb RN, Aung T, Medeiros FA. The Pathophysiology And Treatment Of Glaucoma: A Review. JAMA. 2014;311:1901–1911.

[2]. European Glaucoma Society. Terminology And Guidelines For Glaucoma, 5th Edition. Br J Ophthalmol. 2021;105(Suppl 1):1–169.

[3]. Quigley HA. Glaucoma. Lancet. 2011;377:1367–1377.

[4]. Kass MA, Heuer DK, Higginbotham EJ, Et Al. The Ocular Hypertension Treatment Study. Arch Ophthalmol. 2002;120:701–713.

[5]. Heijl A, Leske MC, Bengtsson B, Et Al. Reduction Of Intraocular Pressure And Glaucoma Progression. Arch Ophthalmol. 2002;120:1268–1279.

[6]. Leske MC, Heijl A, Hussein M, Et Al. Factors For Glaucoma Progression And The Effect Of Treatment. Arch Ophthalmol. 2003;121:48–56.

[7]. Anderson DR, Drance SM, Schulzer M. Natural History Of Normal-Tension Glaucoma. Am J Ophthalmol. 2001;131:699–707.

[8]. Chauhan BC, Mikelberg FS, Balaszi AG, Et Al. Canadian Glaucoma Study. Arch Ophthalmol. 2008;126:1030–1036.

[9]. De Moraes CG, Liebmann JM, Greenfield DS, Et Al. Risk Factors For Visual Field Progression In Treated Glaucoma. Arch

Ophthalmol. 2011;129:562–568.

[10]. Gordon MO, Beiser JA, Brandt JD, Et Al. Predictive Factors For Conversion To Glaucoma. Ophthalmology. 2002;109:789–795.

[11]. Drance SM. Normal-Tension Glaucoma. Glaucoma. 1992;14:69–74.

[12]. Collaborative Normal-Tension Glaucoma Study Group. Comparison Of Glaucomatous Progression. Am J Ophthalmol. 1998;126:487–497.

[13]. Anderson DR, Normal Tension Glaucoma Study. Ophthalmology. 2003;110:1–2.

[14]. Hood DC, Kardon RH. A Framework For Comparing Structural And Functional Measures Of Glaucomatous Damage. Prog Retin Eye Res. 2007;26:688–710.

[15]. Leung CK, Cheung CY, Weinreb RN, Et Al. Evaluation Of Retinal Nerve Fiber Layer Progression. Ophthalmology. 2010;117:1554–1562.

[16]. Medeiros FA, Zangwill LM, Bowd C, Et Al. Detection Of Glaucoma Progression. Ophthalmology. 2009;116:219–227.

[17]. Quigley HA, Nickells RW, Kerrigan LA, Et Al. Retinal Ganglion Cell Death In Experimental Glaucoma. Invest Ophthalmol Vis Sci. 1995;36:774–786.

[18]. Nickells RW. Apoptosis Of Retinal Ganglion Cells In Glaucoma. Prog Brain Res. 2008;173:221–229.

[19]. Calkins DJ. Critical Pathogenic Events Underlying Progression Of Neurodegeneration In Glaucoma. Prog Retin Eye Res. 2012;31:702–719.

[20]. Flammer J, Orgül S, Costa VP, Et Al. The Impact Of Ocular Blood Flow In Glaucoma. Prog Retin Eye Res. 2002;21:359–393.

[21]. Mozaffarieh M, Flammer J. New Insights In The Pathogenesis Of Glaucoma. Surv Ophthalmol. 2007;52(Suppl 2):S162–S170.

[22]. Osborne NN, Casson RJ, Wood JP, Et Al. Retinal Ischemia: Mechanisms Of Damage. Prog Retin Eye Res. 2004;23:91–147.

[23]. Tezel G. Oxidative Stress In Glaucomatous Neurodegeneration. Prog Retin Eye Res. 2006;25:490–513.

[24]. Yu DY, Cringle SJ. Oxygen Distribution In The Optic Nerve Head. Prog Retin Eye Res. 2005;24:1–25.

[25]. Weinreb RN, Khaw PT. Primary Open-Angle Glaucoma. Lancet. 2004;363:1711–1720.

[26]. Quigley HA, Addicks EM. Chronic Experimental Glaucoma. Invest Ophthalmol Vis Sci. 1980;19:137–152.

[27]. Kerrigan LA, Zack DJ, Quigley HA, Et Al. TUNEL-Positive Ganglion Cells In Glaucoma. Arch Ophthalmol. 1997;115:1031–1035.

[28]. Garcia-Valenzuela E, Shareef S, Walsh J, Et Al. Programmed Cell Death Of Retinal Ganglion Cells. Invest Ophthalmol Vis Sci. 1995;36:2334–2342.

[29]. Quigley HA. Neuronal Death In Glaucoma. Prog Retin Eye Res. 1999;18:39–57.

[30]. Quigley HA, Mckinnon SJ, Zack DJ, Et Al. Retrograde Axonal Transport Of BDNF In Glaucoma. Invest Ophthalmol Vis Sci. 2000;41:3460–3466.

[31]. Pease ME, Mckinnon SJ, Quigley HA, Et Al. Obstruction Of Axonal Transport. Invest Ophthalmol Vis Sci. 2000;41:764–774.

[32]. Howell GR, Soto I, Ryan M, Et Al. Axonal Transport Defects In Glaucoma. J Neurosci. 2011;31:14000–14012.

[33]. Gupta N, Ang LC, Noël De Tilly L, Et Al. Human Glaucoma And Neurodegeneration. Arch Ophthalmol. 2006;124:639–645.

[34]. Gupta N, Greenberg G, De Tilly LN, Et Al. Atrophy Of The Lateral Geniculate Nucleus. Arch Ophthalmol. 2009;127:102–109.

[35]. Frezzotti P, Giorgio A, Motolese I, Et Al. Structural Brain Changes In Glaucoma. Ophthalmology. 2014;121:93–101.

[36]. Kong GY, Van Bergen NJ, Trounce IA, Et Al. Mitochondrial Dysfunction In Glaucoma. Clin Exp Ophthalmol. 2009;37:291–299.

[37]. Ju WK, Kim KY, Lindsey JD, Et Al. Elevated Hydrostatic Pressure Triggers Mitochondrial Fission. Invest Ophthalmol Vis Sci. 2008;49:5125–5133.

[38]. Tezel G, Yang X. Comparative Gene Expression Analysis In Glaucoma. Invest Ophthalmol Vis Sci. 2005;46:1060–1073.

[39]. Bosco A, Inman DM, Steele MR, Et Al. Neuroinflammation In Glaucoma. J Neurosci. 2008;28:10585–10594.

[40]. Osborne NN. Mitochondria: Their Role In Ganglion Cell Death. Exp Eye Res. 2010;90:750–757.

[41]. Lee S, Van Bergen NJ, Kong GY, Et Al. Mitochondrial Dysfunction And Glaucoma. Curr Opin Ophthalmol. 2011;22:75–80.

[42]. Levin LA. Retinal Ganglion Cell Death And Neuroprotection. Prog Retin Eye Res. 1999;18:39–57.

[43]. Levin LA, Danesh-Meyer HV. Neuroprotection In Glaucoma. Eye. 2010;24:1142–1149.

[44]. Osborne NN, Desantis L, Bae JH, Et Al. Failure Of Neuroprotection In Clinical Glaucoma Trials. Prog Brain Res. 2008;173:409–421.

[45]. Sena DF, Ramchand K, Lindsley K. Neuroprotection For Treatment Of Glaucoma. Cochrane Database Syst Rev. 2010;2:CD006539.
[46]. Harris A, Kagemann L, Ehrlich R. Measuring And Interpreting Ocular Blood Flow. Surv Ophthalmol. 2008;53:543–557.
[47]. Hayreh SS. Blood Supply Of The Optic Nerve Head. Prog Retin Eye Res. 2001;20:563–593.
[48]. Flammer J, Konieczka K. Retinal Venous Pressure. Prog Retin Eye Res. 2015;46:133–158.
[49]. Leske MC, Wu SY, Hennis A, Et Al. Risk Factors For Incident Glaucoma. Ophthalmology. 2008;115:85–93.
[50]. Leske MC, Connell AM, Wu SY, Et Al. Ocular Perfusion Pressure. Am J Ophthalmol. 1995;119:789–797.
[51]. Bonomi L, Marchini G, Marraffa M, Et Al. Vascular Risk Factors. Ophthalmology. 2000;107:1287–1293.
[52]. Drance SM, Douglas GR, Wijsman K, Et Al. Systemic Vascular Abnormalities. Arch Ophthalmol. 2001;119:121–128.
[53]. Kaiser HJ, Flammer J, Wenk M, Et Al. Blood-Flow Velocities In NTG. Am J Ophthalmol. 1997;123:359–361.
[54]. Gherghel D, Orgül S, Gugleta K, Et Al. Vascular Dysregulation. Surv Ophthalmol. 2004;49:13–29.
[55]. Flammer J, Mozaffarieh M. What Is Primary Vascular Dysregulation? Surv Ophthalmol. 2008;53(Suppl 1):S56–S62.
[56]. Flammer J. The Vascular Concept Of Glaucoma. Surv Ophthalmol. 1994;38(Suppl):S3–S6.
[57]. Hayreh SS, Podhajsky P, Zimmerman MB. Nocturnal Hypotension. Am J Ophthalmol. 1999;128:1–14.
[58]. Graham SL, Drance SM. Nocturnal Hypotension And NTG. Ophthalmology. 1999;106:1656–1663.
[59]. Charlson ME, De Moraes CG, Link A, Et Al. Nocturnal Systemic Hypotension. Ophthalmology. 2014;121:2004–2012.
[60]. Yarmohammadi A, Zangwill LM, Diniz-Filho A, Et Al. OCT Angiography In Glaucoma. Ophthalmology. 2016;123:2368–2382.
[61]. Jia Y, Morrison JC, Tokayer J, Et Al. OCT Angiography Of Optic Nerve Head. Invest Ophthalmol Vis Sci. 2012;53:6820–6828.
[62]. Wang X, Jiang C, Ko T, Et Al. Vessel Density And Glaucoma Severity. Ophthalmology. 2016;123:2498–2508.
[63]. Harris A, Siesky B, Zarfati D, Et Al. The Role Of Ocular Blood Flow. Surv Ophthalmol. 2008;53:560–575.
[64]. Costa VP, Harris A, Anderson D, Et Al. Ocular Perfusion Pressure. Acta Ophthalmol. 2014;92:E252–E266.
[65]. Choi J, Kim KH, Jeong J, Et Al. Circadian Blood Pressure. Ophthalmology. 2007;114:2182–2188.
[66]. Hayreh SS. Management Of NTG. Prog Retin Eye Res. 2011;30:152–175.
[67]. Burgoyne CF, Downs JC, Bellezza AJ, Et Al. The Optic Nerve Head As A Biomechanical Structure. Prog Retin Eye Res. 2005;24:39–73.
[68]. Burgoyne CF. A Biomechanical Paradigm For Glaucoma. Exp Eye Res. 2011;93:120–132.
[69]. Downs JC, Roberts MD, Burgoyne CF. Mechanical Environment Of The Optic Nerve Head. Invest Ophthalmol Vis Sci. 2008;49:207–215.
[70]. Bellezza AJ, Rintalan CJ, Thompson HW, Et Al. Deformation Of The Lamina Cribrosa. Invest Ophthalmol Vis Sci. 2003;44:623–630.
[71]. Yang H, Downs JC, Bellezza A, Et Al. Three-Dimensional Lamina Cribrosa Changes. Invest Ophthalmol Vis Sci. 2007;48:4597–4607.
[72]. Sigal IA, Flanagan JG, Tertinegg I, Et Al. Finite Element Modeling Of The Optic Nerve Head. Invest Ophthalmol Vis Sci. 2004;45:4378–4387.
[73]. Sigal IA, Flanagan JG, Ethier CR. Factors Influencing Optic Nerve Head Biomechanics. Invest Ophthalmol Vis Sci. 2005;46:4189–4199.
[74]. Roberts MD, Liang Y, Sigal IA, Et Al. Influence Of Scleral Stiffness. Invest Ophthalmol Vis Sci. 2010;51:133–141.
[75]. Park HY, Park SH, Park CK. Lamina Cribrosa Defects In NTG. Ophthalmology. 2013;120:1975–1981.
[76]. Lee EJ, Kim TW, Weinreb RN. Lamina Cribrosa Morphology In Glaucoma. Ophthalmology. 2014;121:2131–2140.
[77]. Girard MJ, Dahlmann-Noor A, Rayapureddi S, Et Al. Age-Related Changes In Scleral Biomechanics. Invest Ophthalmol Vis Sci. 2011;52:8250–8258.
[78]. Coudrillier B, Tian J, Alexander S, Et Al. Biomechanics Of The Sclera. J Biomech. 2012;45:254–262.
[79]. Park SC, De Moraes CG, Teng CC, Et Al. Enhanced-Depth Imaging OCT. Ophthalmology. 2012;119:3–9.
[80]. Kiumehr S, Park SC, Dorairaj S, Et Al. In Vivo Lamina Cribrosa Imaging. Ophthalmology. 2012;119:1269–1278.
[81]. Lee EJ, Kim TW, Kim M, Et Al. Focal Lamina Cribrosa Defects. Ophthalmology. 2014;121:189–199.

[82]. Park HY, Park CK. Lamina Cribrosa Displacement Precedes RNFL Thinning. Ophthalmology. 2013;120:1046–1053.

[83]. Kim YW, Lee EJ, Kim TW. Laminar Deformation And Progression. Ophthalmology. 2015;122:1265–1273.

[84]. Girkin CA, Mcgwin G Jr, Mcneal SF, Et Al. Relationship Between Blood Pressure And Glaucoma. Invest Ophthalmol Vis Sci. 2004;45:3450–3456.

[85]. Harris A, Rechtman E, Siesky B, Et Al. Optical Coherence Tomography Angiography. Curr Opin Ophthalmol. 2017;28:206–212.

[86]. Caprioli J. Target Intraocular Pressure. Am J Ophthalmol. 2014;157:1–2.

[87]. Hood DC, Raza AS. On Improving The Use Of OCT In Glaucoma. Prog Retin Eye Res. 2014;39:1–22.

[88]. Medeiros FA, Alencar LM, Zangwill LM, Et Al. Prediction Of Glaucoma Progression. Ophthalmology. 2009;116:219–227.

[89]. De Moraes CG, Liebmann JM, Levin LA. Detection And Measurement Of Progression. Prog Retin Eye Res. 2017;56:58–73.

[90]. Wollstein G, Schuman JS, Price LL, Et Al. Optical Coherence Tomography Longitudinal Study. Arch Ophthalmol. 2005;123:464–470.

[91]. Mwanza JC, Oakley JD, Budenz DL, Et Al. Macular Ganglion Cell–Inner Plexiform Layer. Ophthalmology. 2011;118:241–248.

[92]. Leung CK, Ye C, Weinreb RN. Retinal Nerve Fiber Layer Imaging. Invest Ophthalmol Vis Sci. 2012;53:7945–7952.

[93]. Harwerth RS, Carter-Dawson L, Shen F, Et Al. Ganglion Cell Loss And Visual Field Sensitivity. Invest Ophthalmol Vis Sci. 2004;45:3152–3160.

[94]. Hood DC, Kardon RH. A Framework For Comparing Structural And Functional Measures. Prog Retin Eye Res. 2007;26:688–710.

[95]. Mwanza JC, Durbin MK, Budenz DL, Et Al. Glaucoma Diagnostic Accuracy. Ophthalmology. 2012;119:2188–2198.

[96]. Leite MT, Zangwill LM, Weinreb RN, Et Al. Structure–Function Relationships. Ophthalmology. 2012;119:1106–1113.

[97]. Gardiner SK, Johnson CA. Structure–Function Relationship In Glaucoma. Invest Ophthalmol Vis Sci. 2009;50:5282–5287.

[98]. Medeiros FA, Leite MT, Zangwill LM, Et Al. Predictive Models For Progression. Arch Ophthalmol. 2009;127:141–147.

[99]. Chauhan BC, Garway-Heath DF, Goñi FJ, Et Al. Practical Recommendations For Progression Detection. Ophthalmology. 2008;115:1347–1355.

[100]. Artes PH, O'Leary N, Hutchison DM, Et Al. Properties Of Visual Field Tests. Invest Ophthalmol Vis Sci. 2002;43:1484–1490.

[101]. Bengtsson B, Heijl A. Test–Retest Variability In Perimetry. Invest Ophthalmol Vis Sci. 1999;40:200–205.

[102]. Medeiros FA, Weinreb RN. Monitoring Glaucoma Progression. Ophthalmology. 2012;119:S25–S30.

[103]. Hood DC, Raza AS. Combined Structure–Function Index. Ophthalmology. 2013;120:244–253.

[104]. Zhang X, Loewen N, Tan O, Et Al. Progression Detection Using OCT. Invest Ophthalmol Vis Sci. 2014;55:718–724.

[105]. Mwanza JC, Budenz DL. New Approaches To Structure–Function Analysis. Curr Opin Ophthalmol. 2014;25:115–121.

[106]. Leske MC, Heijl A, Bengtsson B, Et Al. Long-Term Effects Of IOP Reduction. Arch Ophthalmol. 2007;125:119–126.

[107]. Collaborative Normal-Tension Glaucoma Study Group. The Effectiveness Of IOP Reduction. Am J Ophthalmol. 1998;126:498–505.

[108]. Chauhan BC, Mikelberg FS, Balaszi AG, Et Al. Canadian Glaucoma Study. Ophthalmology. 2008;115:1–9.

[109]. De Moraes CG, Liebmann JM, Greenfield DS, Et Al. Risk Factors For Progression Despite Treatment. Arch Ophthalmol. 2011;129:562–568.

[110]. Harris A, Siesky B, Patel P, Et Al. The Role Of Blood Flow In Glaucoma. Surv Ophthalmol. 2008;53:543–557.

[111]. Caprioli J, Coleman AL. Intraocular Pressure Targets. Ophthalmology. 2008;115:1460–1464.

[112]. Nickells RW. The Cell And Molecular Biology Of Glaucoma. Prog Brain Res. 2008;173:125–137.

[113]. Mojon DS, Hess CW, Goldblum D, Et Al. Sleep Apnea And Glaucoma. Ophthalmology. 2002;109:149–152.

[114]. Girkin CA, Mcgwin G Jr. Structural Biomarkers In Glaucoma. Prog Retin Eye Res. 2014;38:19–40.

[115]. Ting DSW, Pasquale LR, Peng L, Et Al. Artificial Intelligence And Ophthalmology. Ophthalmology. 2019;126:343–363.

[116]. Medeiros FA, Jammal AA, Thompson AC. AI In Glaucoma. Ophthalmology. 2020;127: S13–S20.

[117]. Sena DF, Lindsley K. Neuroprotection In Glaucoma. Cochrane Database Syst Rev. 2017;1:CD006539.

[118]. De Moraes CG, Hood DC, Thenappan A, Et Al. Modeling Glaucoma Progression. Ophthalmology. 2019;126:1350–1359.