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Commentary

Glaucoma: Evolving Perspectives on Pathophysiology and Management

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DESCRIPTION

Glaucoma has long been regarded as the "silent thief of sight," a chronic progressive optic neuropathy that remains asymptomatic until significant vision is lost. Globally, glaucoma is the second leading cause of blindness, affecting an estimated 80 million people, with numbers expected to rise as population's age. Unlike many eye diseases that can be reversed or stabilized with timely intervention, glaucoma-induced vision loss is irreversible, making prevention, early detection, and effective management critically important. The disease is not a singular entity but rather a group of disorders characterized by optic nerve damage and corresponding visual field loss, most often associated with elevated Intraocular Pressure (IOP), though not exclusively.

The pathophysiology of glaucoma is complex and multifactorial. Elevated IOP has long been considered the primary risk factor, resulting from impaired aqueous humor outflow through the trabecular meshwork and Schlemm's canal. However, a growing body of research indicates that glaucoma involves more than just pressure-related mechanical damage. Vascular dysregulation, mitochondrial dysfunction, and immune-mediated processes have all been implicated in optic nerve degeneration. The recognition of normal-tension glaucoma, where optic nerve damage occurs despite IOP within the statistically normal range, underscores the multifaceted nature of the disease and the importance of considering factors beyond pressure.

Genetics has provided valuable insights into glaucoma susceptibility. Variants in genes such as *MYOC*, *OPTN*, and *CYP1B1* have been associated with specific forms of the disease, including juvenile open-angle glaucoma and primary congenital glaucoma. These discoveries not only enhance understanding of disease mechanisms but also open the door to potential gene-targeted therapies in the future. Family history remains a strong predictor of risk, highlighting the importance of early screening in at-risk populations.

Diagnosis of glaucoma relies on a combination of structural and functional assessments. Visual field testing remains a cornerstone, detecting characteristic patterns of vision loss such as arcuate scotomas and nasal steps. Optical Coherence Tomography (OCT) allows for detailed imaging of the retinal nerve fiber layer and optic nerve head, providing objective measurements of structural damage. Gonioscopy assists in distinguishing between open-angle and angle-closure glaucoma, the latter resulting from mechanical obstruction of the anterior chamber angle. Advances in imaging, such as OCT angiography, are shedding light on vascular changes in the optic nerve head and peripapillary region, offering new biomarkers for early detection.

Management of glaucoma has traditionally centered on lowering IOP, which remains the only proven modifiable factor. First-line treatment often involves topical medications, including prostaglandin analogs, beta-blockers, carbonic anhydrase inhibitors, and alpha agonists. These drugs reduce aqueous humor production or enhance outflow, effectively lowering pressure. However, adherence to long-term topical therapy is often suboptimal, with patients struggling due to side effects, cost, or difficulty in instilling drops.

Laser therapy provides another option, particularly Selective Laser Trabeculoplasty (SLT), which enhances aqueous outflow through the trabecular meshwork. SLT has gained popularity as both a primary and adjunctive therapy, offering efficacy comparable to medications with the advantage of reducing reliance on daily drops. Surgical interventions are considered when medical and laser therapies fail to control IOP adequately. Traditional procedures such as trabeculectomy and tube shunt implantation remain highly effective but carry risks of complications, including infection, hypotony, and bleb failure.

In recent years, Minimally Invasive Glaucoma Surgeries (MIGS) have emerged as an exciting advancement, offering safer and less invasive alternatives for lowering IOP. These procedures, which include trabecular micro-bypass stents, canaloplasty, and suprachoroidal shunts, are often combined with cataract surgery to enhance outcomes. While MIGS may not achieve the same degree of pressure reduction as trabeculectomy, their favorable safety profile and quicker recovery make them attractive for early to moderate disease.

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Beyond pressure management, neuroprotection has emerged as a potential therapeutic strategy. Since optic nerve degeneration involves multiple pathways, including excitotoxicity, oxidative stress, and mitochondrial dysfunction, interventions aimed at protecting retinal ganglion cells are under investigation. Agents such as brimonidine have shown some neuroprotective potential, while research into stem cell therapies and gene editing continues to expand.