Unmet needs and research priorities in glaucoma

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Abstract

Despite advancements in diagnostics and treatment, glaucoma remains a leading cause of irreversible blindness worldwide, with significant unmet research needs. This review explores key research priorities identified by clinicians and patients to optimize research resource allocation within the ophthalmic community.

The European Glaucoma Society (EGS) and the collaborative efforts of the American Glaucoma Society and the American Society of Cataract and Refractive Surgery (ASCRS) have highlighted critical areas of glaucoma research. These include improving screening methods, developing early detection biomarkers, advancing innovative treatments, and enhancing patient adherence. Additionally, rehabilitation, education, and awareness are essential for improving patient quality of life.

Aligning research with patient and clinician needs ensures impactful advancements in glaucoma care, guiding future research and funding toward effective, patient-centered solutions.

Keyword: glaucoma, research, European Glaucoma Society (EGS), American Glaucoma Society (AGS), American Society of Cataract and Refractive Surgery (ASCRS).

Necesidades no cubiertas y prioridades de investigación en glaucoma

Resumen

A pesar de los avances en el diagnóstico y el tratamiento, el glaucoma sigue siendo una de las principales causas de ceguera irreversible en todo el mundo con importantes necesidades de investi-

gación no cubiertas. Esta revisión explora las principales prioridades de investigación identificadas por clínicos y pacientes para optimizar la asignación de recursos de investigación dentro de la comunidad oftalmológica.
La Sociedad Europea de Glaucoma (EGS) y los esfuerzos de colaboración de la Sociedad Americana de Glaucoma y la Sociedad Americana de Catarata y Cirugía Refractiva (ASCRS) han puesto de relieve áreas críticas de investigación en el campo del glaucoma. Entre ellas se incluyen la mejora de los métodos de cribado, el desarrollo de biomarcadores de detección precoz, el avance de tratamientos innovadores y la mejora en la adhesión de los pacientes. Además, la rehabilitación, la educación y la concientización son esenciales para mejorar la calidad de vida de los pacientes.
Alinear la investigación con las necesidades de los pacientes y los médicos garantiza avances significativos en el tratamiento del glaucoma, orientando la pesquisa y la financiación futuras hacia soluciones eficaces y centradas en el paciente.
Palabras clave: glaucoma, investigación, European Glaucoma Society (EGS), American Glaucoma Society (AGS), American Society of Cataract and Refractive Surgery (ASCRS).

Necessidades não atendidas e prioridades de pesquisa em glaucoma

Resumo

Apesar dos avanços no diagnóstico e tratamento, o glaucoma continua sendo uma das principais causas de cegueira irreversível no mundo, com necessidades significativas de pesquisa não atendidas. Esta revisão explora as principais prioridades de pesquisa identificadas por médicos e pacientes para otimizar a alocação de recursos de pesquisa na comunidade oftalmológica.
A Sociedade Europeia de Glaucoma (EGS) e os esforços colaborativos da Sociedade Americana de Glaucoma e da Sociedade Americana de Catarata e Cirurgia Refrativa (ASCRS) destacaram áreas críticas de pesquisa no campo do glaucoma. Isso inclui melhorar os métodos de triagem, desenvolver biomarcadores de detecção precoce, avançar em tratamentos inovadores e melhorar a adesão do paciente. Além disso, reabilitação, educação e conscientização são essenciais para melhorar a qualidade de vida dos pacientes.
Alinhar a pesquisa com as necessidades de pacientes e médicos garante avanços significativos no tratamento do glaucoma, orientando pesquisas e financiamentos futuros para soluções eficazes e centradas no paciente.
Palavras-chave: glaucoma, pesquisa, Sociedade Europeia de Glaucoma (EGS), Sociedade Americana de Glaucoma (AGS), Sociedade Americana de Catarata e Cirurgia Refrativa (ASCRS).

Introduction

Glaucoma is a multifactorial progressive optic neuropathy that leads to irreversible vision loss[1]. It is estimated that approximately 76 million people worldwide were affected by glaucoma in 2020, and this number is projected to be over 110 million in 2040, posing a significant burden on both patients and healthcare systems[2]. From the patient's perspective, glaucoma leads to progressive visual dysfunction, affecting daily activities, and, when combined with treatment side effects, significantly impacts their quality of life. On the other hand, the chronic nature of glaucoma and the need for continuous monitoring and treatment, places a significant burden on healthcare systems. As the population ages, this burden will only intensify, making the need for early diagnosis and effective management a critical priority[3]. Despite advancements in technology, such as the optical coherence tomography (OCT) for diagnosis and monitoring, and the introduction of Minimally Invasive Glaucoma Surgery (MIGS) devices for treatment, many fundamental questions about optimal glaucoma management remain unanswered[4].

The ultimate purpose of health research is to enhance patient care and improve outcomes. In order to achieve this goal, it is imperative that research addresses questions that are important to both clinicians and patients[4]. While clinicians may prioritize the more clinical aspects, such as intraocular pressure (IOP) management and preventing optic nerve damage, patients may be more likely to focus on maintaining vision,

reducing treatment side effects, and addressing the psychological impact of living with glaucoma. Incorporating patients' insight into research agendas ensures that future advancements in glaucoma align with the practical needs of those affected by the disease. To this effect, the European Glaucoma Society (EGS) established a task force comprising both clinicians and patients to identify the most relevant research priorities in glaucoma. Identification of research priorities in glaucoma would ultimately inform researchers but also funding bodies, so that their actions and decisions on planning and funding research would take those research priorities into account[4].

On the other hand, the collaboration between the American Glaucoma Society (AGS) and the American Society of Cataract and Refractive Surgery (ASCRS) is another significant step toward identifying research priorities for future glaucoma research. These organizations work together with patients, researchers, clinicians, and other stakeholders to better understand and alleviate the clinical burdens associated with the disease. In their efforts, they have identified six key areas of unmet needs in glaucoma research. This dynamic list is designed to be regularly reviewed and updated, ensuring that it remains relevant as needs are addressed and new challenges emerge. By focusing on these specific areas, the AGS and ASCRS strive to align research efforts with the practical needs of those affected by glaucoma, ultimately enhancing patient care and improving outcomes in this field[5].

Key areas of unmet needs according to AGS-ASCRS

Efforts to enhance glaucoma care should include improving screening techniques and methods to ensure more accurate diagnoses. This involves minimizing both false positives and false negatives in glaucoma diagnosis and developing targeted screening strategies for populations at high risk[5]. This is especially relevant considering that research has shown that undiagnosed glaucoma accounts for an estimated more than 50% of all glaucoma cases, while up to 60% of documented cases are overdiagnosed[6-12]. Additionally, advancements in telemedicine are essential for expanding access to care and facilitating remote consultations. Moreover, there is a need to refine the assessment and characterization of primary open angle glaucoma (POAG), particularly focusing on more precise definitions of the disease and its staging. These improvements collectively aim to provide better outcomes for individuals at risk for or affected by glaucoma[5].

A top priority in glaucoma research is the development of highly sensitive and reliable biomarkers to predict the likelihood of developing POAG, detect its early stages, and track its progression. The focus should lie on early diagnosis and identifying patients most at risk for fast disease progression. Another important goal is the creation of safe and precise technologies for continuous 24-hour monitoring of IOP. Additionally, the development of advanced tools to assess visual function and retinal ganglion cell health with greater precision is critical. These technologies should prioritize early detection of changes in the disease and be designed to be user-friendly for patients.

According to the AGS-ASCRS group, gaining a deeper understanding of non-IOP-related factors that influence the susceptibility, onset, and progression of POAG is of critical importance. These factors include vascular perfusion, cellular and molecular pathways, ocular biomechanics, the health of retinal ganglion cell bodies and their axons, and the role of genetic predispositions. Equally vital is the need to explore IOP-related factors contributing to POAG. This includes understanding the effects of nocturnal IOP, fluctuations in IOP, and the mechanisms of IOP control. Research should focus on how these elements impact the disease at tissue, cellular, and molecular levels[5].

In the area of glaucoma therapeutics, a key focus is enhancing treatment effectiveness by improving patient compliance and medication adherence. The development of sustained-release drug delivery systems is a crucial area where resources should be allocated, as these innovations would significantly reduce the need for patients to administer medication regularly, thereby easing

the treatment burden and enhancing adherence. Additionally, pharmacogenetic approaches aim to identify the most effective drugs for individual patients based on their genetic profile. Further research is also being directed toward developing new, more effective therapies for lowering IOP, a crucial factor in controlling glaucoma progression. In addition to IOP-lowering therapies, a key focus of glaucoma therapeutics research should be the development of treatments that address non-IOP-related factors. This includes exploring neuroprotective therapies, neural regeneration techniques, and innovative approaches such as stem cell therapy and cell reprogramming, which aim to repair or regenerate damaged retinal ganglion cells. Additionally, biomechanical reinforcement strategies should be investigated to strengthen ocular structures and prevent further damage. Equally important is the need to advance both invasive and non-invasive surgical techniques that improve patient outcomes while reducing long-term failure rates. By prioritizing these areas of research, ophthalmic community can work towards more effective and durable solutions for glaucoma management, ultimately enhancing vision preservation and quality of life for patients[5].

A significant area of focus for improving patient outcomes in glaucoma is enhancing the quality of life (QoL) for individuals living with glaucoma. According to the AGS-ASCRS group, one of the critical unmet needs is to improve vision rehabilitation services for patients with advanced glaucoma-related vision loss, ensuring they receive the support necessary to adapt and maintain their independence. Furthermore, refining the definitions and characterization of clinically relevant progression in POAG is essential, as this directly influences vision-related quality of life. Understanding how disease progression affects daily functioning can inform better treatment strategies. In addition, the development of a glaucoma-specific QoL questionnaire is needed to accurately measure the true impact of the disease on patients' lives. Such a tool would not only assist in assessing individual patient needs but also help standardize research efforts, enabling more comprehensive and effective studies aimed at improving outcomes for those affected by glaucoma[5].

Finally, improving the relationship between clinicians and the public is essential for advancing glaucoma care, and a key aspect of this is public education. Raising awareness about glaucoma and its potential consequences can significantly impact patient outcomes. Educating the community about the importance of regular clinical wellness visits, including comprehensive glaucoma screening, is crucial for early detection and timely intervention. By fostering a better understanding of the disease and encouraging proactive health measures, clinician-scientists can empower individuals to take charge of their eye health, ultimately leading to improved management of glaucoma and reduced rates of vision loss[5].

EGS research priorities

The EGS undertook a significant project aimed at establishing a prioritized list of research goals in glaucoma, with input from both clinicians and patients across various European countries.

The project was structured in a three-phase manner, starting with a two-round electronic Delphi survey to gather insights and build consensus. An in-depth workshop followed, to refine and finalize the list of research priorities. Notably, the electronic surveys were conducted separately for clinicians and patients, allowing each group to independently express their views on the key areas of unmet needs in glaucoma research. This collaborative effort by the EGS reflects a commitment to integrating diverse perspectives to guide future research in glaucoma[4].

In detail, the three phases of this study focused on integrating diverse viewpoints to establish research priorities that reflect both clinical and patient-centered concerns. Phase I involved an electronic survey aimed at identifying key research priorities from both groups. This survey reached patients across 27 European countries in six different languages while the same survey was distributed to EGS members-—ophthalmologists specializing in glaucoma care. The

responses from this initial survey formed a comprehensive list of potential research questions. This was followed by the second phase focused on ranking these identified priorities. In this phase, both patients and clinicians were asked to evaluate and rank the importance of each research question using a Likert scale. This ranking process helped to highlight the issues that mattered most to both patients and healthcare professionals, creating a preliminary hierarchy of research needs. The study then continued in phase III, which consisted of a one-day workshop that brought together patients and clinicians to discuss and reach a consensus on the top ten research priorities. This collaborative meeting aimed to finalize the most crucial areas for glaucoma research, guiding future efforts to align with the needs and perspectives of those directly impacted by glaucoma[4].

In the first phase, both patients and clinicians highlighted several critical areas for glaucoma research, revealing shared priorities as well as distinct perspectives. Patients placed a strong emphasis on improving screening and early diagnosis, indicating a desire for more accessible and accurate methods to detect glaucoma at an early stage. They also expressed significant interest in treatments that could restore lost vision and halt further sight loss, alongside an emphasis on better understanding risk factors and developing eye drops with fewer side effects. Additionally, patients prioritized improved educational resources to better understand their condition and treatment options[4].

Clinicians, while also valuing early diagnosis and screening, prioritized research in neuroprotection to safeguard vision by preventing damage to the optic nerve. They advocated for stronger evidence supporting MIGS and improvements in surgical treatments overall. Clinicians highlighted the need for new tools to identify patients at high risk of progression, as well as sustained-release treatments that require less frequent dosing, which could improve patient adherence. Advanced technologies, including artificial intelligence, were also seen as promising tools for enhancing diagnostic and treatment capabilities. This alignment in some areas and divergence in others reflects the complementary priorities that both groups bring to the advancement of glaucoma care[4].

In the second phase, an electronic survey helped refine and rank the initial priorities identified by both patients and clinicians, revealing several shared concerns. Both groups highlighted the need for better ways to stop sight loss, improve detection of worsening glaucoma, and enhance surgical options or find alternatives to surgery[4].

A key finding of the research process was the distinct differences in priorities between patients and clinicians. Patients placed high importance on treatments that reduce the need for eye drops and surgery, as well as interventions to help maintain their independence. In contrast, clinicians prioritized areas like wound healing modulation and the use of artificial intelligence in glaucoma management, which were not emphasized by patients. This divergence highlights the unique perspectives each group brings to glaucoma care and underscores the need for a balanced approach in research and treatment development[4].

The consensus reached in Phase III identified the top ten research priorities for glaucoma, grouped into three main areas: treatment, diagnosis and follow-up, and pathophysiology. In treatment, key priorities include finding better ways to stop sight loss, developing treatments to restore vision, creating new or improved medical treatments, advancing surgical or laser options like MIGS, and ensuring treatments with fewer side effects. Under diagnosis and follow-up, priorities focused on detecting disease progression more effectively, enhancing diagnostic tests such as visual field and imaging, and improving early screening to prevent late diagnosis. In understanding pathophysiology, the priorities emphasized uncovering the underlying causes of glaucoma, including genetic risk factors, and exploring treatments beyond IOP reduction, such as neuroprotection. This prioritized roadmap reflects a balanced approach to advancing glaucoma research across key dimensions[4].

Conclusion

In conclusion, the findings from both the EGS and AGS-ASCRS studies provide a valuable framework for shaping future glaucoma

research efforts, highlighting critical areas that need attention to improve patient care. By systematically identifying unmet needs and establishing shared priorities among clinicians and patients, these studies offer a strategic guide for funding bodies and the wider research community. Focusing on these priorities can accelerate advancements in diagnostic tools, treatment options, and understanding of glaucoma's underlying mechanisms, ultimately paving the way for more effective, patient-centered care. This collaborative approach to setting research priorities is essential to driving innovations that can significantly impact the lives of individuals affected by glaucoma.

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