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# Arterial Stiffness and Glaucoma: A Narrative Review on Diagnosis and Progression

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## ABSTRACT

**Background:** Glaucoma, a leading cause of irreversible blindness, is characterized by damage to the optic nerve and loss of visual field.Arterial stiffness has been proposed as a factor contributing to glaucomatous damage. This review aims to summarize the findings from 12 studies that explore the link between arterial stiffness and various types of glaucoma, including normal-tension glaucoma (NTG), primary open-angle glaucoma (POAG), and exfoliation glaucoma (XFG).

**Objective:** To investigate the relationship between arterial stiffness and glaucoma and to highlight gaps in current research.

**Methods:** A comprehensive search of Scopus, Web of Science (WOS), PubMed, and Google Scholar was conducted in November 2024. The review included studies that examined arterial stiffness and its link to glaucoma.

**Results:** Evidence suggests that increased arterial stiffness is associated with glaucomatous damage, possibly through disruptions in ocular blood flow and retinal vascular dysfunction. This association appears most pronounced in POAG, NTG, and XFG, conditions known for vascular irregularities. However, results from NTG studies were more variable, suggesting that further research is needed. The observed inconsistencies may be from differences in study methodologies, follow-up periods, and diagnostic criteria.

**Conclusion**: Arterial stiffness may play a significant role in glaucomatous damage, particularly in high-tension glaucoma. Further research is needed to clarify the mechanisms underlying this link, particularly regarding retinal vascular resistance and ocular perfusion.

KEYWORDS: Arterial stiffness, Glaucoma, Ocular perfusion, Retinal vascular dysfunction, Systemic vascular health

## INTRODUCTION

Glaucoma, a leading cause of irreversible blindness, is characterized by damage to the optic nerve and loss of visual field [1]. Recent studies have explored the role of systematic vascular dysfunction, particularly arterial stiffness, in the pathogenesis and progression of various forms of glaucoma [2]. Including normal-tension glaucoma (NTG), primary open-angle glaucoma (POAG),[3] and exfoliative glaucoma (XFG). [4] Arterial stiffness,[5] commonly assessed through pulse wave velocity (PWV),[6] may contribute to impaired ocular perfusion and exacerbate retinal vascular dysfunction, thereby influencing glaucoma progression. [7] This review synthesized findings from multiple studies examining the relationship between arterial stiffness and glaucoma to understand their clinical implications better.

## METHODOLOGY

To explore the relationship between arterial stiffness and glaucoma, an extensive literature search was conducted on November 30, 2024, across multiple databases, including Scopus, Web of Science, PubMed, and Google Scholar. The search focused on peer-reviewed studies that examined the relationship between arterial stiffness and various types of glaucoma. The inclusion criteria were studies that utilized well-established diagnostic methods for both arterial stiffness and glaucoma, such as PWV measurements and visual field testing, respectively. Keywords such as “arterial stiffness,” “glaucoma,” “ocular perfusion,” and “vascular resistance” were used to filter relevant publications. Both multicenter and monocenter studies, with different designs, were considered to provide a comprehensive overview of the existing literature. Exclusion criteria included studies that did not address arterial stiffness as a primary factor, studies not published in English, and studies with restricted full-text availability.

## RESULTS AND DISCUSSION

### Glaucoma and arterial stiffness: mechanisms and methods of diagnosis

Glaucoma is a group of eye diseases that can cause irreversible damage to the optic nerve, resulting in permanent vision loss. Although the condition can often be managed to slow progression, once the vision is lost, it cannot be restored. Glaucoma is typically classified based on various factors such as the angle at which the iris meets the cornea, intraocular pressure (IOP)[8], and whether the disease is primary or secondary. The classification system enables the categorization of glaucoma into distinct types, facilitating an understanding of the underlying causes and the determination of appropriate treatment options [9].

To better understand glaucoma and its implications, it is essential to classify the disease according to specific factors. One standard classification of glaucoma is based on the drainage angle of the eye, especially whether it is open or closed. In open-angle glaucoma, the angle between the iris and the cornea remains open; however, the eye's drainage system becomes less efficient over time, resulting in a gradual increase in intraocular pressure (IOP). This results in damage to the optic nerve. POAG [10] is the most prevalent form of this type of glaucoma. It typically develops slowly and without noticeable symptoms, often going undetected until significant vision loss occurs. In POAG,

the exact cause of drainage dysfunction is not always clear; however, factors such as age, family history, and race contribute to an increased risk. Another form of open-angle glaucoma is NTG [11], where optic nerve damage occurs despite normal or even low IOP. The cause of NTG is still not fully understood, but it has been proposed that vascular factors, such as insufficient blood flow to the optic nerve, may play a central role in its development. This makes NTG an example of glaucoma where elevated IOP is not the primary cause of optic nerve damage. Additionally, XFG [12] is another form of open-angle glaucoma. This condition is associated with the accumulation of abnormal protein material within the eye, which can obstruct the outflow of aqueous humor and elevate IOP. While XFG is associated with elevated IOP, arterial stiffness and vascular dysfunction may exacerbate the condition by reducing blood flow to the optic nerve, further worsening the disease progression.

While IOP and drainage mechanisms primarily distinguish the types of glaucoma, other factors, such as vascular health, also play a significant role in disease progression. One such factor is arterial stiffness, a reduction in arterial elasticity, often quantified by pulse wave velocity (PWV), which measures the speed at which pressure waves travel through the arteries. Arterial stiffness increases with age and is associated with cardiovascular diseases; however, its effects on ocular health are equally significant. In glaucoma, arterial stiffness disrupts the balance of ocular perfusion pressure, making it harder to maintain adequate blood flow to the optic nerve. This is particularly problematic in NTG, where reduced blood flow from stiffened arteries may contribute to optic nerve damage despite normal IOP [2].

Arterial stiffness reduces the ability to maintain consistent ocular perfusion, especially during fluctuations in systemic blood pressure. The optic nerve, which is highly dependent on a steady blood supply, suffers when this perfusion is compromised. This may lead to progressive nerve damage. Additionally, arterial stiffness affects the microcirculation in the retina and optic nerve head, impairing blood flow to critical areas necessary for retinal ganglion cell function. These cells are often the first to be damaged in glaucoma, and their degeneration leads to irreversible vision loss over time [13].

Another crucial effect of arterial stiffness is its impact on autoregulation- the ability of blood vessels to adjust their diameter and maintain stable blood flow despite changes in systemic blood pressure. In individuals with arterial stiffness, this autoregulatory mechanism becomes impaired, resulting in insufficient blood flow, particularly during periods of low systemic blood pressure.

In addition to disrupting ocular blood flow, arterial stiffness is closely associated with systemic hypertension, which further complicates glaucoma management. The combination of high blood pressure, arterial dysfunction, and increased oxidative stress can exacerbate damage to ocular tissues, accelerating the progression of glaucoma. In POAG, where elevated IOP is already a concern, the additional strain caused by hypertension and arterial stiffness can worsen optic nerve degeneration, increasing the risk of vision loss [14].

Understanding the connection between arterial stiffness and glaucoma offers the potential for more comprehensive treatments that address not only IOP but also vascular health, ultimately improving

outcomes for glaucoma patients and preventing further vision loss.

Given the complex nature of glaucoma, effective diagnosis requires a multifaceted approach that not only assesses intraocular pressure but also evaluates the health of the optic nerve and retinal microcirculation. Diagnostic techniques, including visual field testing, IOP measurement, optic nerve evaluation, optical coherence tomography (OCT), and gonioscopy, provide a comprehensive assessment of eye health.

Visual field testing is a crucial method for diagnosing glaucoma as it helps detect areas of vision loss. The Standard Automated Perimetry (SAP) test [15], often performed with the Humphrey Visual Field Analyzer [16], helps identify early changes in vision. The test employs the SITA 24-2 method and may also include measurements such as the Linearized Mean Deviation (MDlin) to provide a clearer picture of any vision loss. Measuring IOP is crucial in diagnosing glaucoma, with Goldmann applanation tonometry being the most accurate and widely recognized method. Non-contact tonometry and rebound tonometry are also sometimes used for quicker screening. A fundus examination (also known as ophthalmoscopy) allows for direct observation of the optic nerve. Signs of glaucoma, such as optic disc cupping (a deepening of the optic disc), are typically seen during this examination. High-tech tools, such as digital image analyzers, can provide detailed assessments of optic disc characteristics, offering a clearer picture of glaucomatous damage. Spectral domain optical coherence tomography (SD-OCT) is a powerful tool for assessing retinal nerve fiber layer thickness (RNFLT). Thinning of the RNFLT is a key indicator of glaucoma. Other forms of OCT, such as Enhanced Depth Imaging (EDI-OCT), also aid in measuring choroidal thickness, which can provide additional context for diagnosis. OCT also measures retinal vessel density (VD), an essential factor in evaluating the microcirculation of the eye, which can be impacted in glaucoma. Gonioscopy allows the eye doctor to examine the angle between the cornea and iris, where fluid drains from the eye. This test is essential for diagnosing the type of glaucoma, such as open-angle glaucoma or angle-closure glaucoma. Pachymetry measures the central corneal thickness, which can impact the accuracy of intraocular pressure (IOP) measurements. Thinner corneas can lead to an underestimation of intraocular pressure (IOP), which is crucial for understanding glaucoma risk. Laser Speckle Flowgraphy (LSFG) is an innovative technique used to assess retinal blood flow and vascular resistance, which may be affected in glaucoma patients [16].

Just as glaucoma involves multiple tools, the assessment of arterial stiffness also requires specialized methods. PWV is a direct measure of arterial stiffness. The velocity at which the pressure wave travels through the arteries provides insight into the elasticity of the arteries. Carotid-femoral pulse wave velocity (PWV) and aortic pulse wave velocity (aPWV) are standard measures, with faster PWV values indicating stiffer arteries. Brachial ankle pulse wave velocity (baPWV) is another technique that evaluates stiffness in the peripheral arteries. Pulse pressure is the difference between systolic and diastolic blood pressure, and aortic pulse pressure (aPP) is a significant indicator of aortic stiffness. An elevated pulse pressure can be a sign of increased arterial stiffness. Various indices can be derived from the

arterial pressure waveform, including the Pulsatility Index (PI) and the Resistance Index (RI). These indices help assess the resistance and elasticity of arteries. Additionally, the maximum slope and acceleration of the pressure waveform provide valuable information about arterial stiffness. The carotid pulse wave, measured with ultrasound or other non-invasive imaging methods, is another diagnostic tool for assessing arterial stiffness in the carotid artery. Abnormalities in the pulse wave are indicative of early changes in arterial health [17].

## Characteristics of the included studies

A total of twelve studies [2-4, 7, 18-25] were included (Table 1 and Table 2). The studies reviewed provide compelling evidence for the role of arterial stiffness in the pathogenesis and progression of glaucoma. The data extracted from the studies included the first author name, year of publication, country of origin, journal, study design, mean age of participants, male percentage, the study population, whether the study was monocenter or multicenter, follow-up period or study period, and methods of diagnosis for both arterial stiffness and glaucoma, as well as the type of glaucoma. The studies, published between 2006 and 2024, were conducted in countries such as New Zealand, South Korea, the United States, Turkey, Belgium, the Netherlands, and Hungary. The majority of studies were published in 2024 (3 studies) and conducted in Korea (4 studies). These studies were published in prominent journals, including the American Journal of Ophthalmology, Investigative Ophthalmology & Visual Science (IOVS), JAMA Ophthalmology, and Acta Cardiologica Sinica, with four studies appearing in IOVS. The study designs varied, with a mix of prospective, retrospective, cross-sectional, and cohort studies. Participant ages ranged from 40 years and older, with both male and female participants, though some studies did not specify gender distribution. The studies involved both monocenter and multicenter designs, with sample sizes ranging from as few as 63 to over 4700 participants. The follow-up periods varied, with some studies conducting assessments over several years while others focused on shorter-term evaluations.

**Table 1. Characteristics of the included studies**

| Study ID | author | year | country | Journal | study design | mean age | sex |
|---|---|---|---|---|---|---|---|
| Study 1 | Beros AL | 2024 | New Zealand | American Journal of Ophthalmology | prospective, population-based cohort study | 50 to 84 years (mean age ± SD = 66± 8 years) | 2742 (58%) were men |
| Study 2 | LEE JS | 2024 | Korea | American Journal of Ophthalmology | Retrospective cohort study | ≥40 years | Not specified |
| Study 3 | Yang H | 2024 | USA | Investigative Ophthalmology & Visual Science (IOVS) | Cross-sectional data collected from participants in the longitudinal Portland Progression Project (P3) | 71± 8 for glaucoma patients | Not specified |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Study 4 | Gardiner SK | 2023 | USA | Investigative Ophthalmology & Visual Science (IOVS) | from participants in the longitudinal Portland Progression Project | 72.6 (50-90) for glaucoma patients | Not specified |
| Study 5 | Dogan Z | 2023 | Turkey | Acta Cardiologica Sinica | cross-sectional | 54.3± 11.4 for coronary slow flow group | 38 (76%) were males |
| Study 6 | Lee JS | 2022 | Korea | Investigative Ophthalmology & Visual Science (IOVS) | Retrospective | 53.9 ± 8.8 (low pulse wave velocity PWV), 59.8 ± 8.6 (intermediate PWV), 71.3 ± 5.8 (high PWV) | Low PWV: 60.5% males, High PWV: 45.7% males, Intermediate PWV: 50% males |
| Study 7 | Lee T | 2021 | Korea | Investigative Ophthalmology & Visual Science (IOVS) | Retrospective, cross-sectional study | ≥ 40 years, 61.6 ± 9.3 for normal-tension glaucoma group | 55 (53.4%) were males in normal-tension glaucoma group |
| Study 8 | Shim SH | 2015 | Korea | BioMed Research International | Retrospective, cross-sectional | 59.26 ± 9.86 years (range, 34–79 years) | 64.7% men |
| study 9 | Bossuyt J | 2014 | Belgium | Medicine | A cross-sectional case–control study | 65±8 for normal-tension glaucoma group | 7 (23%) men |
| Study 10 | Mroczkowska S | 2013 | England | JAMA Ophthalmology | cross-sectional | 65.26(9.52) for POAG, 60.16(12.13) for NTG | 10 (52.6%) men primary open-angle glaucoma, 8 (42.1%) men normal-tension glaucoma |
| Study 11 | Hulsman CAA | 2007 | Netherlands | JAMA Ophthalmology | cross-sectional, participants from the population-based Rotterdam Study. | 55 years and older | 55.1% men |
| Study 12 | Visontai Z | 2006 | Hungary | British Journal of Ophthalmology | Retrospective observational study (cross-sectional) | 68.5 (7.0) for glaucoma group | 30% men for glaucoma group |

**Table. 2. Characteristics of the included studies, continued**

| StudyID | Results |
|---|---|
| Study1 | results showed that higher arterial stiffness, measured by aortic and carotid-femoral pulse wave velocity (aPWV and ePWV), was associated with an increased risk of developing glaucoma, but no such association was found with aortic pulse pressure (aPP). The highest quartiles of aPWV and ePWV were significantly associated with glaucoma, suggesting that arterial stiffness may be a useful indicator for identifying individuals at risk for glaucoma, potentially offering a new avenue for therapeutic research. |
| Study2 | In NTG eyes, GCIPL thinning was faster when choroidal MvD and high systemic arterial stiffness were present. The simultaneous presence of regional and systemic vascular insufficiency may be associated with rapid glaucoma structural progression in eyes with low baseline intraocular pressure. |
| Study3 | The shape of the systemic pulsatile waveform differs in individuals with GL/GLS suspects, compared to HC eyes. Blood pressure changes more rapidly in individuals with GL, which suggests higher arterial stiffness. |
| Study4 | Higher retinal vascular resistance and, by likely implication, stiffer retinal vessels were associated with more rapid functional loss in eyes without significant existing loss at baseline. |
| Study5 | The acceleration of average peripheral arterial PWV with a thinning of choroidal thickness in patients with coronary slow flow may support the idea that this phenomenon may be a coronary presentation of a systemic microvascular disorder. |
| Study6 | PWV is a significant predictor of the location of structural progression in open-angle glaucoma. Vascular insufficiency may be an important aspect in the pathogenesis of glaucoma |
| Study7 | High PWV is associated with decreased mVD in NTG patients, suggesting that systemic arterial stiffness might be involved in the pathogenesis of NTG |
| Study8 | Increased arterial stiffness has been shown to be associated with glaucoma and may contribute to its pathogenesis in diabetic mellitus (DM) patients. Arterial stiffness is more associated with NTG than with POAG |
| Study9 | This study could not show an association of NTG with altered IMT, arterial stiffness, total peripheral resistance, cardiac output, and peripheral or central hemodynamics at rest. |
| Study10 | This study reveals a similarly increased variability in nocturnal SBP, systemic arterial stiffness, and IMT in early-stage POAG and NTG, which was not replicated in age-matched controls. |
| Study11 | Participants with an increased pulse wave velocity and especially those with a low carotid distensibility coefficient, both indicative of high arterial stiffness, had a higher prevalence of htOAG, but results were not statistically significant |
| Study12 | Our findings, from the functional and physiological point of view, support the previously published epidemiological results on the association between systemic vascular disease and XFS. stiffness was significantly higher, in XFS/XFG patients than in the controls |
| NTG: normal-tension glaucoma ; XFS: Exfoliation Syndrome; XFG :Exfoliative Glaucoma; htOAG: high-tension Open-Angle Glaucoma; mVD : microvascular density; GLS: Glaucoma-Like Suspects; GL: Glaucoma. | |

The studies examined a range of glaucoma types, including NTG, open-angle glaucoma in general, POAG, and XFG. Several studies also investigated suspected glaucoma and early stages of open-angle glaucoma. In some cases, a broader category of microvascular disorders was considered, encompassing various forms of glaucoma. These variations highlight the diverse glaucoma subtypes and stages addressed across the included studies.

Methods for diagnosing glaucoma varied but generally involved a combination of clinical measurements and specialized imaging techniques. Diagnosis often included visual field testing (perimetry), intraocular pressure (IOP) measurements, and evaluation of the optic nerve. Additional methods included optical OCT for retinal nerve fiber layer thickness, corneal thickness measurement, and gonioscopy to examine the drainage angle. Some studies also employed advanced imaging techniques, such as enhanced

depth imaging OCT, optical microangiography, and digital image analysis, for optic disc assessment. Several studies relied on visual acuity tests, slit-lamp examination, and fundoscopy for comprehensive evaluation.

The methods used to diagnose arterial stiffness across the included studies primarily focused on various forms of pulse wave velocity (PWV), including aPWV, carotid-femoral PWV, and baPWV. Additionally, some studies employed specific indices derived from pulse waveforms, including the PI and RI. Techniques such as LSFG were employed to assess vascular resistance and pulsatile hemodynamics, while retinal vessel density was evaluated using OCTA. Pulse-wave analysis and carotid pulse wave measurements were also applied in certain studies to assess arterial stiffness.

## Arterial stiffness and the development of glaucoma

A growing body of evidence supports the hypothesis that arterial stiffness is a significant factor in the development of glaucoma. Beros AL et al. (Study 1)[2] conducted a large cohort study involving 4713 participants over years. It found a significant association between increased arterial stiffness, as measured by aortic and carotid-femoral pulse wave velocity (PWV), and an increased risk of glaucoma. The study's long-term follow-up suggests that arterial stiffness is a predictive marker for glaucoma, providing insight into the systemic vascular changes that may impact ocular health.

Similarly, Dogan Z et al. (study 5) [20] examined the role of arterial stiffness in patients with coronary slow flow syndrome, a condition associated with abnormal blood flow. The study found that patients with coronary slow flow had higher arterial stiffness and thinner choroidal thickness, a key ocular marker. While the study did not directly address glaucoma, it suggests that systemic vascular abnormalities, such as those seen in coronary slow flow, could predispose individuals to various ocular pathologies, including glaucoma. These findings contribute to the growing body of evidence that vascular dysfunction in the systemic circulation may influence ocular health, potentially playing a role in the development of glaucoma. Both Beros' and Dogan's studies emphasize that arterial stiffness is a potential risk factor for glaucoma, with implications for early diagnosis and intervention.

## Arterial stiffness and glaucoma progression

Beyond the onset of glaucoma, arterial stiffness has been shown to influence the progression of the disease. Lee JS et al. (Study 2) [7] explored the effects of systemic arterial stiffness and choroidal microvascular insufficiency on the progression of non-thrombotic glaucoma (NTG). The study found that higher PWV, combined with choroidal microvasculature dropout (MvD), was associated with faster thinning of the macular ganglion cell-inner plexiform layer (GCIPL), a key marker of glaucomatous damage. These results suggest that increased systemic arterial stiffness and impaired retinal circulation are significant contributors to the accelerated progression of NTG. Lee's findings align with those of study 6 [21], which examined the role of arterial stiffness in early-stage open-angle glaucoma. The study demonstrated that higher PWV was associated with faster

structural damage, with macular GCIPL loss occurring before the thinning of the retinal nerve fiber layer (RNFL) in patients with high PWV. This suggests that systemic vascular dysfunction, as indicated by high arterial stiffness, may drive the progression of glaucomatous damage, particularly in the early stages of the disease.

The similarities between Studies 2 and 6 indicate that systemic arterial stiffness is a significant factor in glaucomatous progression, primarily through its effects on retinal microvasculature and optic nerve perfusion. Both studies emphasize the importance of monitoring vascular parameters to predict disease progression, supporting the notion that arterial stiffness could serve as a crucial clinical marker for glaucoma progression.

## Vascular dysfunction in glaucoma suspects and healthy controls

Another intriguing aspect of the research is the comparison of vascular dysfunction in glaucoma patients, glaucoma suspects, and healthy controls. Yang H et al. (Study 3) [18] studied systemic pulsatile blood pressure waveforms and identified significant differences in vascular resistance between glaucoma, glaucoma suspects, and healthy control groups. Yang's results showed that glaucoma patients and suspects exhibited higher vascular resistance, which correlated with retinal nerve fiber layer thickness and the severity of visual field defects. These findings support the notion that vascular resistance is a crucial factor in glaucoma, even before a formal diagnosis of the disease is established. Moreover, Yang's study highlights that vascular dysfunction may precede observable glaucomatous damage, suggesting that vascular changes could serve as early indicators of glaucoma risk.

The idea is further supported by study 7 [22], conducted by Lee T et al., which also examined the relationship between PWV and VD in patients with NTG. Lee's results showed that NTG patients exhibited higher PWV and lower retinal vessel densities (both peripapillary and macular VD) compared to healthy controls. The reduced retinal vessel density in NTG patients points to impaired ocular circulation, which may contribute to glaucomatous damage. These findings are consistent with those of study 3, where increased vascular resistance was seen in glaucoma patients and suspects. Together, these studies indicate that impaired vascular function may be an early feature of glaucoma, and systemic arterial stiffness could serve as a risk marker, even in patients who have not yet developed significant glaucomatous damage.

## Retinal vascular resistance and glaucoma progression

A critical area of study has been the relationship between retinal vascular resistance and the progression of glaucoma. Gardiner SK et al. (study 4) [19] focused on retinal vascular resistance, measured by LSFG, in glaucoma suspects and glaucoma patients. The study findings revealed that higher retinal vascular resistance in glaucoma suspect eyes was associated with faster functional loss, while in glaucoma patients, the correlation was with the severity of current damage rather than the rate of progression. This study suggests that stiffer retinal vessels are associated with faster functional loss in the early stages of glaucoma, indicating that retinal vascular resistance could be a potential marker for disease progression.

These findings align with those of Mroczkowska S et al. (study 10) [3], which compared vascular function between patients with POAG and NTG with early-stage functional loss. This study found that both glaucoma groups had similar abnormalities in vascular function, including increased nocturnal blood pressure variability, higher arterial stiffness, and impaired retinal vascular reactivity. These results highlight the role of both systemic and ocular vascular dysfunction in the development and progression of glaucoma, further suggesting that vascular parameters could be significant in monitoring disease progression. The commonality in vascular dysfunction between POAG and NTG, as reported in study 10, challenges the traditional distinction between the two types of glaucoma and suggests that both conditions may share similar underlying vascular mechanisms.

In contrast, Hulsman CAA et al.'s (Study 11) [25] study on open-angle glaucoma found that while pulse wave velocity was positively associated with high-tension open-angle glaucoma (htOAG), no significant associations were found with normal-tension open-angle glaucoma (ntOAG). The study suggests that arterial stiffness might be more closely linked to high-tension forms of glaucoma, possibly due to higher systemic blood pressure and its impact on ocular perfusion. The lack of significant findings for NTG in this study could be attributed to more complex vascular and neurodegenerative mechanisms underlying NTG.

Similarly, Bossuyt J et al. (study 9) [24] investigated whether NTG is associated with alterations in systemic vascular function, including arterial stiffness, macrocirculation, microcirculation, and cardiac hemodynamics. This study found no significant differences between the NTG group and the healthy control group when assessing parameters such as aortic stiffness and carotid artery diameter at rest. These results suggest that, at rest, NTG is not associated with alterations in arterial structure or systemic hemodynamics. However, the focus on measurement "at rest" might limit the ability to detect underlying vascular dysfunctions that could manifest under more dynamic conditions. Thus, these findings, which revealed no significant differences in vascular parameters at rest, do not necessarily contradict the theory that arterial stiffness plays a role in NTG; instead, they suggest that NTG's vascular alterations may become more evident under conditions that induce more significant vascular stress or variability.

### Systemic arterial stiffness and exfoliation glaucoma

Exfoliation syndrome (XFS) and exfoliation glaucoma (XFG) are conditions associated with systemic vascular dysfunction, including increased arterial stiffness. Visontai Z et al. (study 12) [4] investigated XFS/XFG patients and found elevated homocysteine levels, increased carotid artery stiffness, and reduced baroreflex sensitivity. These findings point to altered vascular function and parasympathetic control in XFS/XFG patients, which may contribute to the development of glaucoma in this population. Although Study 12 focused on XFS/XFG, its findings align with the general trend observed across multiple studies, indicating that systemic vascular dysfunction may play a role in glaucoma, particularly in conditions such as exfoliation syndrome.

### Arterial stiffness in systemic conditions: diabetes and coronary slow flow

Systematic conditions, including diabetes mellitus (DM) and coronary slow flow, have been implicated in increasing arterial stiffness, which in turn may contribute to the pathogenesis of glaucoma. Shim SH et al. (study 8) [23] study on glaucoma patients with DM showed that higher baPWV was significantly associated with an increased likelihood of glaucoma, particularly NTG. This suggests that vascular dysfunction in patients with DM may exacerbate the risk of glaucoma. These findings are consistent with those of Dogan Z et al. (study 5) [20], who observed increased arterial stiffness in patients with coronary slow flow. Both studies highlight the role of systemic vascular health in the development of glaucoma, underscoring the need for comprehensive cardiovascular assessment in glaucoma patients, particularly those with comorbid systemic conditions.

## CONCLUSION

The studies reviewed provide robust evidence linking arterial stiffness to various forms of glaucoma, particularly in NTG, POAG, and XFS/XFG. While the relationship is complex and not entirely consistent, there is strong evidence that systemic vascular dysfunction, indicated by elevated arterial stiffness, plays a significant role in glaucomatous damage. Inconsistencies across studies, particularly regarding NTG, underscore the need for further research to clarify how systemic vascular changes contribute to the development of glaucoma. Future studies should explore the mechanisms by which arterial stiffness influences glaucomatous damage, including the roles of retinal vascular resistance, ocular perfusion pressure, and systemic vascular health.

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### Data availability

Underlying data
Data for the 12 articles that studied DOI: DOI:10.5281/zenodo.15108455
This project contains the following
- Table 1 [26]



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