Title: Carotid Doppler Imaging in Glaucoma and Glaucoma suspects

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Introduction

Elevated intraocular pressure (IOP) remains a well-established risk factor for glaucoma. However, the multifactorial nature of the disease suggests that other contributing factors may play pivotal roles in its pathogenesis and progression.[1] One such factor of growing interest is ocular blood flow.

Ocular blood flow has emerged as a known risk factor in the development and progression of glaucoma, with studies suggesting that impaired blood flow to the optic nerve head and surrounding structures may contribute to tissue ischemia, oxidative stress, and inflammation, all of which have been implicated in glaucomatous neurodegeneration.[2,3] Despite the growing body of evidence linking ocular blood flow to glaucoma, there remains a need to explore the potential association between systemic vascular diseases and glaucoma in a comprehensive manner.

The carotid arteries are major vessels supplying blood to the brain, and their health is crucial for overall systemic well-being. In cases of atypical glaucoma presentations or unexplained disease progression, clinicians often inquire about the status of the carotid arteries. This leads us to question whether COD, characterized by atherosclerosis and stenosis, may be a relevant factor in the context of glaucoma.

The aim of this study is to evaluate the association between carotid occlusive disease (COD) and glaucoma, including glaucoma suspects.

Methods

This study employed a retrospective design to investigate the association between COD and glaucoma, including glaucoma suspects. We reviewed medical records and carotid doppler reports of individuals attending our Ophthalmology Outpatient Department (OPD) from January 2012 to June 2022.

Individuals diagnosed with Primary Open Angle Glaucoma (POAG), or Normal Tension Glaucoma (NTG) or Glaucoma suspects with suspected vascular pathology or unexplained progression, whose carotid doppler analysis reports were available were included in the study. Individuals with Primary Angle Closure Glaucoma, secondary glaucomas, intracranial pathology that might mimic disc or visual field changes, and with a previous history of systemic vasculitis were excluded from the study.

The following parameters were collected from the records: Demographic data, detailed medical history, including systemic comorbidities, ophthalmological examination details, baseline and current IOP (Intraocular Pressure), use of antiglaucoma medications, history of past surgeries related to glaucoma, visual field details, pachymetry data, and carotid doppler report parameters.

The categorical data was compared using the Chi-square test. Correlation between Mean Deviation (MD) and Visual Field Index (VFI) versus the degree of carotid artery stenosis was examined. A two-proportion Z test was used to compare the degree of stenosis between progressors and non-progressors and among glaucoma diagnoses.

Results

The study encompassed a total of 485 eyes from 279 patients. Among the participant eyes, 191 were diagnosed with POAG, 262 with NTG, and 32 were classified as glaucoma suspects.

The demographic details and rates of systemic comorbidities in the three subgroups have been summarised in Table 1. The mean age of the subjects was 63 years with a standard deviation of 11.2 years. The mean age was not statistically different among the three subgroups (p=0.225). Males comprised of 78.1% of the study subjects. The proportion of males was also not statistically different among the three subgroups (p=0.548). The rates of systemic comorbidities were compared among the three subgroups, and only dyslipidemia was statistically significant between the three subgroups with glaucoma suspects having the least prevalence of dyslipidemia (Table 1).

Comparing degree of stenosis within the subgroups keeping cut-off for significant degree of stenosis on ipsilateral side in carotid doppler analysis at 10%, we found that 7.4% of POAG patients, 11.4% of NTG patients, and 12% of those with unexplained progression had such levels of carotid artery involvement. In contrast, only 3% of individuals in the glaucoma suspect group had stenosis exceeding 10%. (p>0.05) (Table 2).

We assessed the correlation between worsening Visual Field Index (VFI) values and increasing carotid artery stenosis. A weak correlation was observed (r=-0.228), suggesting that as carotid artery stenosis increased, there was a slight tendency for VFI values to worsen.

Discussion

In this study, we set out to investigate the association between COD and glaucoma, including glaucoma suspects. Our findings revealed a clinically relevant connection between these two prompting a re-evaluation of the systemic factors influencing glaucoma development and progression.

Our study identified a substantial proportion of individuals with NTG and eyes exhibiting progression despite well-controlled IOP who also displayed evidence of COD. This observation highlights a potential intersection between systemic vascular health and glaucomatous optic neuropathy, particularly in cases where conventional risk factors such as elevated IOP may not fully explain the disease process.

These results are consistent with prior carotid doppler studies conducted in the context of asymmetric glaucoma, which reported a higher prevalence of carotid artery stenosis and reduced blood flow in the carotid artery on the side corresponding to greater glaucomatous damage.[4,5] Such findings suggest a plausible link between carotid artery health and the progression of glaucoma, providing an intriguing avenue for further exploration.

While the assessment of ocular blood flow, especially within the optic nerve head (ONH) vessels, has traditionally been considered skill-intensive but reproducible, our study underscores the potential clinical relevance of carotid doppler analysis. Unlike the direct measurement of ocular blood flow, carotid doppler provides a distal, indirect assessment of blood flow. Nevertheless, its non-invasive nature and easy availability may render it a valuable and convenient tool for assessing systemic vascular health in the context of glaucoma management.

Clinicians should consider recommending carotid doppler assessments, particularly for individuals diagnosed with NTG and those who exhibit glaucoma progression despite well-controlled IOP. By identifying COD in such cases, healthcare providers may gain valuable insights into the systemic vascular factors contributing to glaucomatous optic neuropathy, potentially leading to more tailored treatment strategies.

Nevertheless, our study is not without limitations. The lack of a standardized definition for Humphrey Visual Field (HVF) progression, the retrospective study design, and missing data in certain cases should be acknowledged. These limitations may affect the generalizability of our findings and the strength of causal inferences.

To the best of our knowledge, this study represents a pioneering effort to systematically evaluate the association between COD and glaucoma, especially in the context of unexplained HVF progression and glaucoma suspects, through the utilization of carotid doppler analysis. As we look ahead, larger-scale studies should be initiated to further explore the prevalence of COD among glaucoma patients, validate our findings, and solidify clinical guidelines regarding the utility of carotid artery assessments in glaucoma care.

Conclusion

In conclusion, our study brings to light a potential nexus between COD and glaucoma, emphasizing the importance of considering systemic vascular factors in the evaluation and management of glaucoma patients. These findings suggest that the clinical relevance of COD may be limited to these specific subgroups within the glaucoma population. The consideration of systemic vascular factors, particularly through carotid doppler assessments, may hold particular significance in the management and care of individuals with NTG and those experiencing unexplained glaucoma progression.

References

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Tables

Table 1: Demographic details and systemic comorbidities of the study population

	Primary Open Angle Glaucoma (n=112)	Normal Tension Glaucoma (n=146)	Glaucoma suspects (n=21)	p-value
Mean age (years)	62.7	63.7	59.5	0.225
Males	89 (79.5%)	111 (76.0%)	18 (85.7%)	0.548

Any Systemic comorbidity	147 (42.5%)	175 (50.6%)	24 (6.9%)	0.190
Diabetes mellitus	47 (43.5%)	55 (50.9%)	6 (5.6%)	0.478
Hypertension	59 (44%)	70 (52.2%)	5 (3.7%)	0.052
Dyslipidemia	12 (37.5%)	14 (43.8%)	6 (18.8%)	**0.037**
Ischemic heart disease	16 (37.2%)	23 (53.5%)	4 (9.3%)	0.846
Stroke	2 (50%)	2 (50%)	0 (0%)	0.816

Table 2: Degree of stenosis and glaucoma diagnosis			
	<10%	>= 10%	p-value
POAG	177/191 (92.6%)	14/191 (7.4%)	>0.05
NTG	232/262 (88.6%)	30/262 (11.4%)	
Glaucoma Suspects	31/32 (96.9%)	1/32 (3.1%)	
Progressors	73/83 (87.9%)	10/83 (12.1%)	