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ORIGINAL RESEARCH

An Electronic Frailty Index Based on Deficit Accumulation May Predict Glaucomatous Visual Field Progression

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Purpose: To investigate whether an electronic frailty index (eFI) is associated with visual field loss in glaucoma.

Patients and Methods: We identified 1163 subjects ≥65 years old with glaucoma (1082 right eyes and 1042 left eyes) who had a calculable baseline eFI, and who had reliable visual fields at baseline and final follow-up. Multivariable linear regression models adjusting for demographic and clinical variables were used to assess the association between eFI and mean deviation at baseline and the change in mean deviation over time in each eye.

Results: Being pre-frail or frail was not associated with baseline MD, except in the right eye where being pre-frail was associated with a higher baseline MD. Increasing level of eFI was negatively correlated with change in MD ($p<0.05$ both eyes), but not baseline MD. Moreover, being frail was significantly associated with a more significant decline in MD in both eyes (Right eye: Beta −0.89, 95% CI (−1.71, −0.063), p=0.035; Left eye: Beta −1.25, 95% CI (−2.17, −0.34), p=0.007). Notably, baseline IOP was not associated with MD at baseline or the change in MD in the multivariable models.

Conclusion: Glaucoma patients who are frail may be at higher risk of experiencing visual field decline, independent of baseline IOP. Future studies should investigate whether interventions to improve frailty can decrease risk of glaucoma progression.

Keywords: glaucoma, electronic frailty index, visual field

Introduction

Glaucoma is a progressive optic neuropathy that can result in irreversible blindness. Intraocular pressure (IOP) is currently the only modifiable risk factor to delay the onset and progression of glaucoma. Nevertheless, many people with glaucoma have IOP in the normal range, and yet still experience disease progression.[1–3] Consequently, it is not always clear which patients with glaucoma will progress and there are likely other factors besides IOP that could contribute to glaucoma progression and visual impairment. There is a clear clinical need to identify risk factors beyond IOP that might identify adults more likely to experience glaucoma progression and visual impairment.

One promising connection is the relationship between visual dysfunction and the geriatric syndrome of frailty. Frailty is a multi-system pathologic clinical syndrome of older adults that is characterized by weakness and decreased physiologic reserve.[4] It has been associated with numerous adverse outcomes including falls, hospitalizations, institutionalization, and mortality.[5–9] Glaucoma patients who are frail have increased acute healthcare utilization,[10] including ER visits or hospitalizations for falls and fractures.[11] A recent study using NHANES data described a cross-sectional association between visual field loss and frailty in older adults, where patients with either unilateral (adjusted odds ratio = 2.07, 95% CI (1.42, 3.02)) or bilateral (adjusted odds ratio = 1.74, 95% CI (1.20, 2.52))

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visual field loss were more likely to be classified as frail compared to patients without visual field loss.[12] Another study in China suggested that older adults with visual impairment are more likely to show physical deconditioning consistent with frailty.[13] However, it is unclear whether visual problems contribute to the development of frailty, or whether being frail may increase the risk of visual decline or degrade performance on visual field assessments. Moreover, there has not been a study to investigate the association of frailty with progression of glaucomatous eye disease.

The measurement and definition of frailty have evolved since the syndrome was initially described by Fried et al.[14] Multi-dimensional frailty indices based on the theory of deficit accumulation have shown excellent prognostic capability for prediction of adverse health outcomes.[15–17] In addition, several groups in multiple countries have shown that routine structured data within the electronic health record (EHR) can be leveraged to construct an electronic frailty index (eFI) capable of identifying and staging frailty.[18] Within our health system, our local eFI implementation incorporates routine encounters, diagnosis codes, laboratory, medication, vital signs, and Medicare Annual Wellness Visit data within the EHR (Epic, Verona, WI) and can be passively calculated in patients during routine encounters in the healthcare system. The eFI has been shown to be a useful tool for predicting acute care utilization, falls, fractures, and mortality.[19,20] We have also previously described an association between frailty based on the eFI and glaucoma, and higher incidence of emergency room or hospital encounters for falls/fractures among frail older adults with glaucoma or glaucoma suspect diagnoses.[21]

In this study, we hypothesized that there would be an association between frailty and glaucomatous field loss and that frail patients, as quantified by eFI, would be more likely to demonstrate glaucomatous progression on visual fields. If so, this could suggest that eFI could be used as a prognostic tool for identifying glaucoma patients at risk of progressive vision loss.

Materials and Methods

A retrospective single-center analysis of EHR data was performed for adults ≥ 65 years old who had an ICD-10-CM diagnosis for glaucoma (see Supplemental Table 1)[22] as of 10/1/2017. We selected this index date in order to avoid the system-wide conversion from ICD-9 to ICD-10 codes. The study was conducted in accordance with the Declaration of Helsinki, and IRB approval was obtained from Atrium Health Wake Forest Baptist Hospital. A waiver of informed consent was obtained due to the retrospective nature of the study. All data was anonymized and maintained with confidentiality.

The calculation of the eFI has been described previously by Pajewski et al.[19] All patients had at least two outpatient encounters with a measured blood pressure during a two-year lookback (10/1/2015-10/1/2017) which was the minimum criterion necessary to estimate eFI as of 10/1/2017. Extensive details of the eFI calculation can be found in the supplemental material provided by Pajewski et al[19,23] with recent updates to the scoring algorithm described in Khanna et al.[24] In brief, the eFI was calculated incorporating any of 54 deficits assessed at available outpatient visits drawing from diagnosis codes, vital signs, medications, laboratory measurements, and Annual Wellness Visit screening information.[19,23] Frailty status based on the eFI was categorized as Fit (eFI≤0.10), Pre-Frail (0.10<eFI≤0.21), and Frail (0.21<eFI).[19,23]

Included glaucoma cases had to have a reliable (false positive<15% and fixation loss<33%) typical glaucomatous visual field defect on a Humphrey visual field (Zeiss Meditec, Jena, Germany) during the baseline index period and they were followed through 2023. In addition, baseline IOP, age, sex, and race were collected. Demographic and clinical variables were stratified based on frailty status and compared using ANOVA or Kruskal–Wallis for continuous variables and Chi-square test for categorical variables. Spearman correlation was used to explore the association between eFI level and baseline MD or change in MD. Separate multivariable regression models were used to examine the association of baseline frailty based on eFI with 1) baseline mean deviation (MD) and 2) change in MD over time for each eye, controlling for demographic and clinical factors. All statistical analyses were conducted in StataMP (vs 18.0, StataCorp) and R Statistical Computing Environment (Core Team, Vienna, Austria). A p-value <0.05 was considered statistically significant.

Results

We identified 1163 subjects ≥65 years old with glaucoma (1082 right eyes and 1042 left eyes) who had a calculable eFI, and who also had reliable visual fields at baseline and final follow-up.

Table 1 characterizes the study population by frailty status within the affected eye. There was no significant difference in baseline age, baseline IOP, or total follow-up time by frailty status. There were some differences in sex and race breakdown by frailty status ($p<0.05$). In addition, there was a difference in the distribution of baseline MD in right eyes, and a difference in change in MD in left eyes. Increasing level of eFI was negatively correlated with change in MD in both eyes ($p<0.05$) but was not associated with the baseline MD in either eye ($p>0.05$).

Table 2 shows the adjusted association of eFI with baseline MD, and change in MD. Being pre-frail in the right eye was associated with a higher baseline MD; otherwise, being frail or pre-frail was not associated with the baseline MD. However, being frail was significantly associated with a more significant decline in MD in both eyes (Right eye: Beta −0.89, 95% CI (−1.71, −0.063), p=0.035; Left eye: Beta −1.25, 95% CI (−2.17, −0.34), p=0.007). Being pre-frail was also associated with a decline in MD in each eye, but this was not statistically significant ($p>0.05$). Of note, baseline IOP was not associated with MD at baseline or the change in MD in the multivariable models.

Discussion

In this cohort of older adults diagnosed with glaucoma, we observed a significantly greater decline in mean deviation on visual fields for those patients who were frail at baseline compared to patients who were fit, while adjusting for other demographic factors and baseline IOP. We also observed that increasing level of eFI was correlated with decline in MD, which could suggest a dose response. Overall, these data suggest that the eFI could be utilized during routine encounters with glaucoma patients to identify frailty which may increase their risk for progressive glaucomatous visual field loss.

Table 1 Baseline Clinical and Social Demographics of Glaucoma Cohort

	Total	Frail	Pre-frail	Fit	p-value
Baseline age – mean (SD)					
Right Eye	74.7 (7.1)	75.1 (7.66)	74.7 (7.1)	74.2 (6.7)	0.3336*
Left Eye	74.5 (7.1)	75.0 (7.5)	74.6 (7.0)	73.8 (6.6)	0.1153*
Female sex – n(%)					
Right eye	649/1082 (60.0%)	167/251 (60.2%)	325/570 (57%)	157/261 (60.2%)	0.037
Left eye	617/1042 (59.2%)	158/231 (68.4%)	310/555 (55.9%)	149/256 (58.2%)	0.005
Black race – n(%)					
Right eye	276/1082 (25.5%)	79/251 (31.5%)	158/570 (27.7%)	39/261 (14.9%)	0.0001
Left eye	254/1042 (24.4%)	65/231 (28.1%)	152/555 (27.4%)	37/356 (10.4%)	0.0001
Baseline IOP (mmHg) – mean (SD)					
Right eye	16.7 (4.5)	16.3 (4.1)	16.8 (4.5)	16.8 (4.7)	0.3326*
Left eye	16.8 (4.7)	16.3 (4.7)	16.9 (4.7)	16.8 (4.7)	0.2107*
Total follow-up time (days)					
Right eye	1730.5 (753.6)	1653.6 (769)	1775.6 (734.2)	1705.9 (775.8)	0.0848*
Left eye	1731.0 (751.6)	1647.6 (773.0)	1774.3 (732.4)	1712.1 (768.8)	0.0884*
Baseline MD (dB) – mean (SD)					
Right eye	−5.46 (6.38)	−6.09 (6.70)	−4.97 (6.18)	−5.92 (6.41)	0.0135*
Left eye	−5.67 (6.35)	−5.84 (6.06)	−5.56 (6.30)	−5.78 (6.71)	0.4920*
Change in MD (dB) – mean (SD)					
Right eye	−1.44 (4.76)	−1.95 (4.90)	−1.43 (4.56)	−0.96 (5.01)	0.0628*
Left eye	−1.56 (5.15)	−2.25 (5.21)	−1.55 (4.88)	−0.98 (5.59)	0.0238*

Notes: *ANOVA or Kruskal–Wallis for comparison of continuous variables; Chi-square for comparison of categorical variables.
Abbreviations: SD, standard deviation; LS, least squares; NE, not estimable.

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Table 2 Multivariable Models of the Association of Baseline eFI With Baseline Mean Deviation and the Change in Mean Deviation, Adjusting for Baseline Clinical and Demographic Covariates

	Beta (95% Confidence Interval), p-value	
	Baseline Mean Deviation (dB)	**Change in Mean Deviation (dB)**
Baseline age		
Right eye	**−0.071 (−0.12, −0.02), p=0.01**	**−0.089 (−0.13, −0.048), p=0.001**
Left eye	−0.018 (−0.073, 0.037), p=0.52	**−0.086 (−0.132, −0.040), p=0.001**
Female sex		
Right eye	−0.71 (−1.49, 0.059), p=0.07	−0.36 (−0.21, 0.94), p=0.215
Left eye	**−1.33 (−2.12, −0.55), p=0.001**	−0.10 (−0.53, 0.74), p=0.752
Black race		
Right eye	**−1.43 (−2.32, −0.55), p=0.001**	−0.29 (−0.94, 0.37), p=0.393
Left eye	**−1.00 (−1.92, −0.095), p=0.030**	0.15 (−0.58, 0.088), p=0.687
Baseline IOP (mmHg)		
Right eye	−0.057 (−0.03, 0.14), p=0.203	−0.0129 (−0.078, 0.052), p=0.695
Left eye	−0.052 (−0.138, 0.034), p=0.233	−0.009 (−0.078, 0.060), p=0.795
Total follow-up time		
Right eye	-	**−0.001 (−0.001, −0.0005), p=0.001**
Left eye	-	**−0.001 (−0.002, −0.001), p=0.001**
eFI Right eye		
Frail	0.117 (−0.99, 1.23), p=0.837	**−0.89 (−1.71, −0.063), p=0.035**
Pre-frail	**1.20 (0.27, 2.14), p=0.012**	−0.33 (−1.03, 0.36), p=0.346
Fit	Reference	Reference
eFI Left eye		
Frail	−0.063 (−1.20, 1.07), p=0.913	**−1.25 (−2.17, −0.34), p=0.007**
Pre-frail	0.404 (−0.541, 1.35), p=0.402	−0.44 (−1.20, 0.32), p=0.252
Fit	Reference	Reference

Notes: Model for baseline mean deviation is adjusted for baseline age, female sex, black race, and baseline IOP. Model for change in mean deviation is adjusted for baseline age, female sex, black race, baseline IOP, and follow-up time. Significant associations ($p<0.05$) are bolded.

There have been several studies linking visual dysfunction with co-prevalent frailty. Shang et al found that near vision impairment (OR = 1.62, 95% CI (1.30, 2.00)) and distance vision impairment (OR = 1.59, 95% CI (1.30, 1.96)) were both associated with a higher prevalence of frailty independent of cofounders.[13] Shang's definition of frailty is based the Fried phenotype, and is comprised of physical measurement and subjective responses to assess exhaustion, weakness, inactivity, slowness and shrinking.[13,14] Visual field loss has also been associated with frailty in older adults, independent of visual acuity.[12,13] However, while we did see a possible relationship of baseline MD with frailty in the bivariate analysis, any cross-sectional relationship of frailty with baseline MD was not significant in the final adjusted models.

Whether visually impaired older adults are more likely to develop frailty or whether frailty could contribute to vision loss is not settled but is it possible that both can be true in the case of glaucoma. For example, a large study in China suggested that older adults with visual impairment were more likely to develop physical deconditioning consistent with the Fried definition of frailty.[13] This finding is consistent with other studies documenting a relationship between poor vision and mobility dysfunction, also observed in glaucoma, which may be related to restricted physical activity in older adults with limited vision.[25–27] However, we believe our study is the first to suggest that frailty could also predict visual decline in glaucoma. Reasons for this may be multifactorial. For example, given that frail glaucoma patients have been shown to have higher acute and lower outpatient healthcare utilization,[10] it could be that frail glaucoma patients are not as closely monitored by their ophthalmologist. Hospitalizations could contribute to periods of time where patients have

inconsistent drop compliance and missed outpatient visits for disease monitoring. Gaps in care are a well-documented concern among glaucoma patients, and frail patients are more likely to experience gaps in care.[28]

Although baseline IOP was not significantly associated with MD in this study, patients were undergoing usual care which included their usual medication management. It is well-known that uncontrolled or elevated IOP and IOP fluctuation can contribute to visual field progression in glaucoma.[29,30] However, most IOP fluctuation is likely undocumented especially in patients who miss appointments or spend periods of time in the hospital, which is common among frail patients.[19,31] Thus, it is possible that periods of poor IOP control may be playing a role. Also, frail older adults have weaker grip strength,[32] and could have more difficulty self-administering eyedrops. Future studies are needed to investigate if frailty is related to IOP control and other reasons that frailty may be linked to visual field decline.

For example, it is also possible that frailty as estimated by the eFI may be contributing to glaucomatous progression through comorbid diagnoses used to estimate eFI, such as hypertension or diabetes mellitus. Dielemans et al have shown that hyperglycemia associated with diabetes mellitus and hypertension are associated with elevated IOP.[33,34] Vergroesen et al have shown a potentially harmful association between calcium channel blocker use and increased IOP, leading to increased glaucoma prevalence.[35] Frail individuals may also have poor vascular health which could contribute to poor perfusion of the optic nerve. It is also possible that frail individuals may exhibit worse performance on automated perimetry, which could contribute to worse mean deviation. In this study, we manually reviewed the patient notes and fields to confirm glaucoma diagnosis and glaucomatous progression. While the reasons that frailty and visual field decline are linked is not known, our findings do suggest that the eFI could be used in a clinical context to identify glaucoma patients at higher risk of visual field decline, even independent of their IOP at the time of the visit. Such patients may benefit from closer monitoring and other ancillary support to help ensure they receive their glaucoma medications while hospitalized or get rescheduled for appropriate care after a hospitalization or period of illness. Future studies should test whether interventions to improve or prevent frailty also impact patients' ability to manage their glaucoma.

Limitations

Our study has several limitations related to the retrospective nature of the study. These data are only generalizable to older adults with a calculable eFI in our hospital system. Patients needed to meet a minimum of two outpatient primary care visits to have enough data to calculate the eFI as of the index date. Thus, glaucoma patients who received their primary care at a neighboring institution were not included in our sample. In addition, glaucoma patients without follow-up data were not included. While baseline IOP was not significantly associated with MD, we did not investigate changes in IOP over time as we were only interested in whether the baseline eFI, IOP, or other demographic factors could be used clinically to predict who is at risk for visual field loss. Future studies should consider whether frailty is related to IOP longitudinally and whether trends in IOP or IOP spikes may mediate the relationship between frailty and glaucoma progression.

Conclusions

Frail older adults with glaucoma were at greater risk of glaucomatous visual field loss over time. The electronic frailty index may be used during clinic to identify who is at risk of glaucomatous progression and may benefit from closer monitoring, tighter IOP control, or other support or interventions to ensure timely follow-up care and thus slow the rate of glaucomatous progression and lower their risk of visual impairment.

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Disclosure

The authors report no conflicts of interest in this work.

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