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Original Research

The relationship between glaucoma and an electronic frailty index with the cumulative incidence of healthcare encounters for falls and fractures in older adults☆,☆☆

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A R T I C L E I N F O

Keywords:
Frailty
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A B S T R A C T

Objective: To compare the association of glaucoma and glaucoma suspect diagnoses with frailty, quantified via an electronic frailty index (eFI), and to evaluate whether a glaucoma diagnosis moderates the association between frailty and the cumulative risk of acute healthcare encounters for incident falls or fractures.
Design: Retrospective study of electronic health record (EHR) data.
Subjects, Participants, and/or Controls: Adults ≥65 years old with an ICD-10 diagnosis code for glaucoma or glaucoma suspect who had a calculable eFI score as of 10/1/2017.
Methods: Ordinal logistic regression was used to examine the cross-sectional association between glaucoma (predictor) and frailty status (outcome) based on the eFI. The relationship of glaucoma and frailty with the cumulative incidence of hospital or emergency room visits for injurious falls or fractures over time was modeled using cause-specific recurrent event survival models that account for censoring and the competing risk of death.
Main Outcome Measures: Frailty status based on the eFI and cumulative incidence of falls or fractures.
Results: Glaucoma patients were significantly more likely to be frail compared to glaucoma suspects (adjusted odds ratio=1.36, 95 % CI(1.16, 1.60)). Both pre-frailty and frailty were associated with an increased risk of incident falls/fractures in older adults: prefrail (hazard ratio=2.07, 95 % CI (1.40, 3.06)), frail (hazard ratio=3.35, 95 % CI (2.24, 5.03)), but there was no interaction of frailty with glaucoma status on falls/fractures risk. Also, the risk of incident falls/fractures did not significantly differ between glaucoma versus glaucoma suspects.
Conclusions: Glaucoma patients were more likely to be frail or pre-frail based on an EHR-derived index than glaucoma suspects. Both pre-frailty and frailty were associated with increased cumulative risk of injurious falls or fractures but there was no interaction of frailty with glaucoma. Frailty based on the eFI was better at discriminating who is at risk of acute healthcare utilization for falls/fractures than a glaucoma diagnosis.

1. Introduction

Glaucoma is the most common cause of irreversible blindness worldwide and is projected to impact 111.8 million people by the year 2040 [1]. Several clinical and population-based studies have suggested an association between a glaucoma diagnosis and risk of falls [2–7]. However, the underlying pathophysiologic mechanisms explaining this relationship are complex and not well understood. Moreover, a majority of these studies have collected self-reported falls [7–9], many of which may not result in any serious injury. Little has been done to investigate whether patients with glaucoma are more likely than patients without glaucoma or glaucoma suspects to suffer injurious falls or fractures that could result in an emergency room or inpatient hospitalization, and higher healthcare utilization and costs. According to Hoffman, et al. fall-related injuries in particular are estimated to cost $9389 per instance, with an average out-of-pocket cost of $1363 [10]. Prager et al. found

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that patients with glaucoma incurred an additional $2903 (95 % CI ($2247, $3558)) in overall annual health costs, [11] though the amount attributable to fall-related injuries was not specified.

The mechanisms linking glaucoma to falls are also complex and multifactorial, and currently, the literature is mixed as to whether functional mobility mediates the relationship between glaucomatous visual impairment and fall risk [7,12]. Several recent studies have postulated that poor vision in general may be associated with frailty, a condition with a high prevalence of impaired mobility function, though the intricacies of the relationship between frailty and visual impairment have not been well-characterized [13–17]. Whether frailty may be related to glaucoma or whether there may be an interaction between frailty and glaucoma with the risk of injurious falls and fractures in older adults is unclear. One study failed to find an association between increased cup to disc ratio or elevated intraocular pressure, which are risk factors for glaucoma, and either cognitive or physical frailty [18]. Another study showed that frailty but not pre-frailty was cross-sectionally associated with a glaucomatous appearing optic nerve on graded color photographs [19].

Frailty is a multi-system pathologic clinical syndrome that is more prevalent in older adults and is characterized by weakness and decreased physiologic reserve [20]. Frailty has been associated with a number of downstream adverse outcomes, including falls, hospitalizations (including increased hospital utilization and cost), institutionalization, and mortality [21–25]. The prevalence of frailty among older adults ranges from 24 % in the community [26] to 70 % in institutionalized settings [27], and is expected to increase as the U.S. population ages.

The measurement of frailty has evolved over time since the syndrome was initially described. Multi-dimensional frailty indices based on the theory of deficit accumulation have shown excellent prognostic capability for prediction of adverse health outcomes [28–31]. Clegg et al. developed an electronic frailty index (eFI) capable of identifying and staging frailty in older adults solely leveraging data from the EHR [32]. Within our institution, this approach has been adapted with an eFI integrated within the EHR (Epic, Verona, WI) since October 2019 on all patients 55 years or older. This eFI implementation leverages routine encounters, diagnosis codes, laboratory, medication, vital signs, and Medicare Annual Wellness Visit data housed within the EHR. The eFI has been examined across a myriad of settings and populations, including pre-operative screening, de-prescribing in patients with type 2 diabetes, and examining the relationship between frailty and socioeconomic disadvantage with healthcare utilization [33–35].

The goal of this study was to compare the relationship of glaucoma and glaucoma suspect diagnoses with frailty, quantified via the eFI. A secondary goal was to examine whether a glaucoma diagnosis contributes to the association between frailty and the risk of acute emergency room or hospitalization encounters for incident falls and fractures as captured in the EHR. Our overarching hypothesis was that patients with a glaucoma diagnosis would be more likely to be frail than older adults with glaucoma suspect diagnoses and that the association between frailty and falls may be moderated by glaucoma.

2. 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 or glaucoma suspect (Supplemental Table 1) [36] between 10/1/2015 – 10/1/2017, with follow-up through 2022. The index date was chosen to avoid the system-wide conversion from ICD-9 to ICD-10 codes on 10/1/2015. Patients with any baseline diagnosis of glaucoma in at least one eye during the 2015–2017 look-back window were categorized as having a glaucoma diagnosis. Patients were categorized as a glaucoma suspect if they had a stable glaucoma suspect diagnoses in at least one eye but did not develop any glaucoma diagnosis in either eye. In the current study, we leveraged cumulative EHR data from the preceding 2 years to estimate a single eFI score as of 10/1/2017. At minimum patients needed to have at least two outpatient encounters during that 2-year window with a measured blood pressure in order to be able to estimate the eFI. Details of the eFI calculation can be found in the supplemental material of Pajewski et al., with recent updates to the scoring algorithm described in Khanna et al. (Supplemental Table 2) [37]. Frailty status based on the eFI was categorized as Fit (FI≤0.10), Pre-Frail (0.10<FI≤0.21), and Frail (0.21<FI) [38,39]. Institutional Review Board (IRB) approval was obtained. A waiver of informed consent was provided due to the retrospective nature of this analysis.

EHR and Humphrey visual field imaging (Zeiss Meditec, Inc.) from a random subset of patients with glaucoma were manually reviewed to ascertain reliability and glaucoma severity based on the American Academy of Ophthalmology Preferred Practice Pattern Guidelines [40,41]. Patients were categorized as having severe (both superior and inferior hemifields or central 10 degrees) vs. Moderate (one hemifield and not involving central 10 degrees) vs. No field loss in the worse eye. Over three years of follow-up, we also examined the cumulative incidence of emergency department (ED) visits or inpatient hospitalizations with a diagnosis of a fall or fracture (Supplemental Table 3). A new ED visit or inpatient hospital event for fall or fracture was defined as an event that occurred more than 1 month after a prior fall or fracture.

2.1. Statistical analysis

We used ordinal logistic regression models to estimate the cross-sectional association between a glaucoma diagnosis (independent variable) and frailty based on eFI (outcome) as of 10/1/2017. In a random subset of glaucoma patients, we analyzed the relationship between glaucoma severity in the eye with more advanced disease and frailty. Next, we used the mean cumulative count estimator (MCC), which estimates the average number of events (incident or recurrent) per individual over a specified time interval, to estimate and visualize the cumulative incidence of emergency room or inpatient hospitalizations for an injurious fall or fracture that occurred after 10/1/2017 among glaucoma vs. glaucoma suspects and among frail vs. pre-fail vs. fit individuals. First, separate unadjusted models were constructed, and then both glaucoma and frailty status were placed in the same adjusted multivariable survival model. We also examined models that included a statistical interaction between glaucoma diagnosis and frailty status. To address potential confounding effects within the context of recurrent events, we used the gap-time model proposed by Prentice, Williams, and Peterson [42]. Both the MCC estimator and the gap-time survival model account for censoring and the competing risk of death. Also, since eFI summarizes many aspects of health status (e.g. co-morbidities, physical and cognitive function, etc.), we considered a very limited number of covariates in analyses, namely age, sex, race/ethnicity, and the number of outpatient encounters during 2015–2017 to attempt to account for informed presence bias [43]. A p-value <0.05 was considered statistically significant. Statistical analyses were conducted in R Statistical Computing Environment (R Core Team, Vienna, Austria) or SAS v9.4 (SAS, Cary, NC).

3. Results

We identified 4147 older adults with an ICD-10-CM diagnosis code for glaucoma or glaucoma suspect who also had a calculable eFI score as of 10/1/2017. Table 1 compares the patient characteristics of those with an ICD-10 diagnosis of glaucoma versus glaucoma suspect. The distributions of sex and race were similar for the two groups, but glaucoma cases were slightly older. We had 2710 total glaucoma cases and 1437 glaucoma suspects with a calculable eFI score using data from the 2-year lookback (2015–2017). Among older adults with a glaucoma diagnosis, 630 (23.2 %) were classified as fit, 1375 (50.7 %) were classified as pre-frail, and 705 (26 %) were classified as frail. Among glaucoma suspects, 480 (33.4 %) were classified as fit, 681 (47.4 %) were classified as pre-frail, and 276 (19.2 %) were classified as frail. Glaucoma patients were

Table 1
Patient study characteristics stratified by glaucoma status.

Characteristic	Glaucoma Suspect (N = 1437)	Glaucoma (N = 2710)	P value
Age, years, mean (SD)	74.9 (7.1)	77.6 (7.8)	<0.001
Male sex, No. (%)	560 (39.0 %)	1117 (41.2 %)	0.17
Race/Ethnicity, No. (%)			<0.001
White	1135 (79.0 %)	2000 (73.8 %)	
Black	237 (16.5 %)	614 (22.7 %)	
Hispanic	29 (2.0 %)	35 (1.3 %)	
Other	36 (2.5 %)	61 (2.3 %)	
No. of outpatient visits in last 2 years, median [IQR]	7 [3, 14]	5 [3, 10]	<0.001
Frailty status based on eFI, No. (%)			<0.001
Fit (eFI≤0.10)	480 (33.4 %)	630 (23.2 %)	
Pre-frail (eFI>0.10 & eFI≤0.21)	681 (47.4 %)	1375 (50.7 %)	
Frail (eFI>0.21)	276 (19.2 %)	705 (26.0 %)	
Died during follow-up	115 (8.0 %)	272 (10.0 %)	0.04

SD = Standard deviation; IQR = interquartile range; eFI = electronic frailty index.

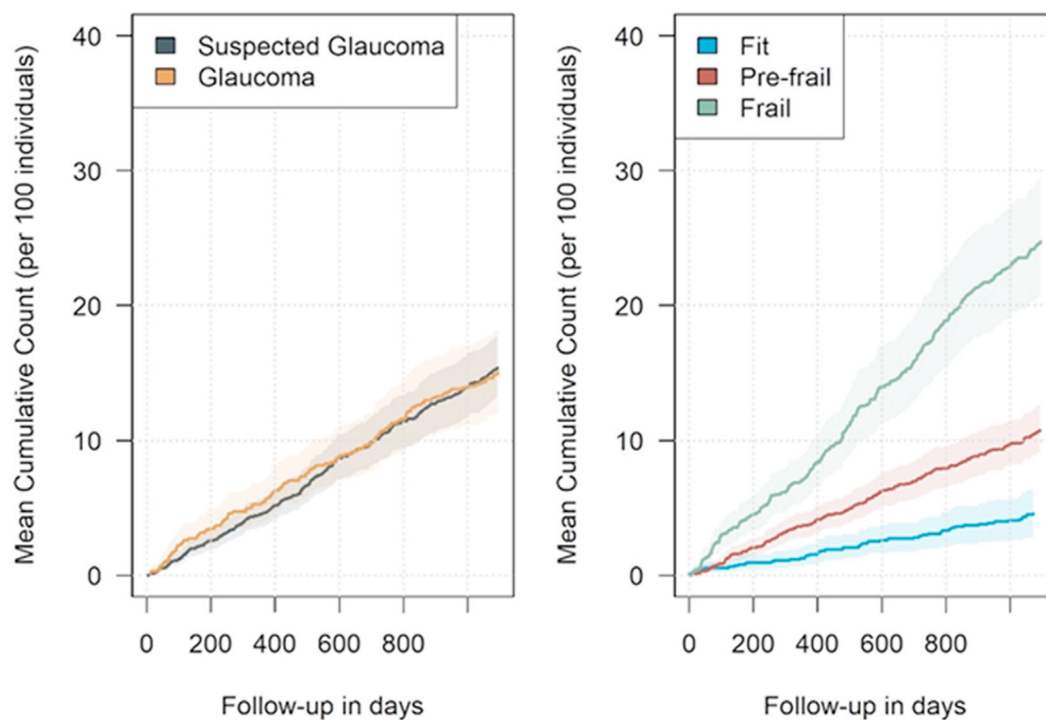

Fig. 1. Incidence of falls and fractures by glaucoma diagnosis and frailty status.

older and a higher proportion were black compared to the glaucoma suspects ($p < 0.05$).

From our analysis of the overall cohort, we found that older adults with glaucoma were significantly more likely to be classified as frail compared to glaucoma suspects (adjusted odds ratio = 1.36, 95 % CI (1.16, 1.60)), adjusting for age, sex, and race/ethnicity. Within the chart review subset of patients (N = 207), those with severe glaucoma were more likely to be categorized as frail based on the eFI compared to those with either mild or moderate glaucoma in the worse eye (26.3 % vs 20.2 %, odds ratio = 1.40, 95 % CI (0.69, 2.90)) though this was not statistically significant ($p > 0.05$).

Fig. 1 shows a graphical representation of the cumulative incidence of falls/fractures for glaucoma vs. glaucoma suspect patients (left graph) and for frail vs. pre-frail vs. fit patients (right graph). Table 2 describes the unadjusted and adjusted Hazard Ratios (HR) for incident falls/fractures by frailty status and comparing glaucoma to glaucoma suspect patients. Glaucoma and glaucoma suspect patients classified as prefrail (HR = 2.38, 95 % CI (1.60, 3.53)) or frail (HR = 5.81, 95 % CI (3.90, 8.70)) were significantly more likely to experience an incident fall or fracture in unadjusted analyses. Patients with a glaucoma diagnosis were slightly more likely to have an incident fall/fracture than those with a glaucoma suspect diagnosis, but this was not statistically significant. In the adjusted model which included glaucoma status, eFI, age, sex, and race/ethnicity, both pre-frail (HR = 2.07, 95 % CI (1.40, 3.06)) and frail (HR = 3.35, 95 % CI (2.24, 5.03)) patients had a significantly higher risk of falls/fractures compared to fit patients. However, there was not a significant difference in the incidence of falls or fractures between glaucoma and glaucoma suspect patients. We also explored models that included a statistical interaction between glaucoma diagnosis and frailty status (results not shown). There was no statistical evidence that the association of pre-frailty (p = 0.12) or frailty (p = 0.51) varied as a function of glaucoma diagnosis.

4. Discussion

This study used an electronic frailty index within the electronic medical record to demonstrate that patients with glaucoma are more likely to be frail than glaucoma suspects. We also showed that in this cohort of patients with either a glaucoma or suspect diagnosis, frail older adults were at a much higher risk of emergency room visits or hospitalizations

Table 2

Multivariable modeling for incident emergency room or hospital encounters for fall/fracture including frailty status and glaucoma diagnosis.

	Unadjusted[a]		Adjusted[b]	
	Hazard Ratio	95 % CI	Hazard Ratio	95 % CI
Frailty status (Reference=Fit)				
Pre-frail (0.10 < eFI ≤ 0.21)	2.38	1.60 - 3.53	2.07	1.40 – 3.06
Frail (eFI > 0.21)	5.81	3.90 - 8.70	3.35	2.24 – 5.03
Glaucoma (Reference = Glaucoma Suspect)	1.09	0.85 - 1.40	1.03	0.81 – 1.31

[a] Unadjusted models for frailty and glaucoma were fit separately.

[b] The final adjusted multivariable model included both frailty and glaucoma status as well as age, sex, race/ethnicity, and number of outpatient encounters.

for incident falls or fractures, but that a glaucoma diagnosis did not moderate the risk. These data suggest that frailty drives fall risk in older adults with a highly prevalent visual disorder, estimated to affect 2–7 % of older white adults and 4.6–9.8 % of older black adults in the United States over the age of 65 [44]. Use of the eFI, which can be passively calculated in the EHR, could help to identify older adults at risk for acute healthcare utilization related to injurious falls and could be leveraged to develop targeted interventions to reduce this risk.

Older adults with glaucoma were significantly more likely to be frail based on eFI compared to older adults with glaucoma suspect diagnoses, even when adjusting for age, sex, and race/ethnicity. Also, glaucoma patients with more severe visual deficits were more likely to be frail based on the eFI in a random subset, though the smaller sample limited the statistical significance. Shang et al. similarly found that near and distance visual impairment was associated with a higher prevalence of frailty, independent of confounders [45]. Since the eFI definition of frailty was based on deficit accumulation, this could suggest that patients with vision-threatening diseases like glaucoma are more likely to have multiple serious health co-morbidities [20,32,38,39]. A recently published study using US National Health and Nutrition Examination Survey data described a cross-sectional association with frailty but not pre-frailty being associated with a grading of probable or definite glaucoma on color optic disc photographs [19]. Mendelian randomization models have also shown that genetically predicted frailty was associated with increased odds of several subtypes of glaucoma such as primary open angle, primary angle closure glaucoma, and exfoliation glaucoma, but not normal tension glaucoma [19]. Others have failed to find an association between vertical cup to disc ratio or elevated intraocular pressure, which are risk factors for glaucoma, and cognitive frailty or physical frailty [18]. Some of the reasons for these differences could be the different definitions of glaucoma being utilized. For example, gradings of color photographs relying on cup to disc ratio and other features are not sensitive or specific for glaucoma, as eyes with large optic nerve heads can have physiologic cupping while it can be difficult to detect cupping in eyes with small optic nerve heads. Eyes with myopia can also be difficult to interpret on color photographs. Similarly, high intraocular pressure is not synonymous with glaucoma as some types of glaucoma have low intraocular pressure and some individuals have high intraocular pressure but do not have glaucoma. Our study utilized ICD-10 codes to define glaucoma based on ophthalmic examination and testing by eye providers, rather than relying on risk factors for glaucoma or color imaging.

After adjusting for age, sex, and race/ethnicity, and accounting for the competing risk of death, being pre-frail or frail was also strongly associated with a higher cumulative incidence of ED visits or hospitalizations for falls or fractures among glaucoma and glaucoma suspects in our study. Similarly, frailty has been associated with acute healthcare utilization in other studies [46–48]. Theou et al. found that patients with mild/moderate frailty had a higher number of hospitalizations (adjusted incidence rate ratio 1.57, 95 % CI (1.11, 2.20)) and hospital days (incidence rate ratio 1.48, 95 % CI (1.32, 1.66)) [46]. Chang, et al. also did a meta-analysis demonstrating that frail older persons were at the highest risk for hospitalizations compared to pre-frail and fit older adults [47]. Halawa et al. showed that compared to nonfrail/prefrail individuals, moderate-to-severely frail individuals had higher rates of inpatient and ED encounters (incident rate ratio = 5.03, 95 % CI (2.36, 10.71) [48]. They also found that in individuals with glaucoma, moderate-to-severely frail Medicare beneficiaries had higher rates of acute care setting utilization and lower rates of outpatient care compared to nonfrail/prefrail beneficiaries [48]. Given that frailty is a marker of poor health and predicts numerous adverse health outcomes, our findings are similarly important as the eFI could be used to identify which glaucoma or glaucoma suspect patients may be at risk of higher acute care utilization for falls or fractures in particular.

While we observed a relationship between frailty and encounters for falls/fractures, the risk of these encounters was not statistically different between patients with glaucoma and GS diagnoses. The literature has generally suggested that visual problems, especially low visual acuity, are associated with higher fall and fracture risk [2,49–53]. However, our data raises the question of whether the risk of falls often attributed to glaucoma or poor vision may also be related to underlying vulnerability rather than visual impairment alone. One reason for the difference in our findings could stem from the definition of falls used since we only captured injurious falls and fractures that resulted in a hospital or emergency room encounter and did not capture self-reported falls or falls that did not produce an EHR encounter. However, by defining the fall outcome in this way, we eliminated the bias that may accompany subjective reporting, especially in frail older adults. Also, since visual changes related to glaucoma are typically gradual and peripheral, many patients may have preserved visual acuity until the end-stage of disease which could allow them to compensate. Moreover, the relationship of glaucoma to falls may need to account for their degree of physical activity which could impact their incident fall risk [54–56]. Patients with glaucoma/suspect diagnoses and worse visual field deficits have been shown to spend less time in away-from-home activities [54], and glaucoma patients in particular demonstrate more fragmented sessions of physical activity, lower activity levels during waking hours [55], and greater annual declines in daily steps [56]. When accounting for their lower steps by adjusting falls for the number of steps taken, Ramulu, et al. found that greater visual field damage was associated with a higher falls/step ratio [57]. However, investigating falls per step is a different outcome than incident falls since it accounts for the lower amount of physical activity performed. If glaucoma patients demonstrate less physical activity and are less likely to leave their homes, this could not only contribute to the development of frailty from muscle atrophy but also could account for a lower incidence of ED visits or hospitalizations related to falls or fractures captured in the EHR in this study. Another possibility is that patients went to a different hospital system for their care. A recent study using UK Clinical Practice Datalink found that individuals with glaucoma had a higher risk of a first fall than those with no glaucoma diagnosis, but this system has access to electronic data across hospitals

in the UK [53] and so was able to capture all hospital-based falls and fractures.

4.1. Limitations

This study has several limitations related to the retrospective nature of the analysis. This study is only generalizable to patients with a calculable eFI since they needed to meet the minimum criteria of at least 2 outpatient visits within our health system over a two-year window. Glaucoma patients without adequate connections to primary care could be systematically different from those with primary care and could be at higher fall risk. Another limitation is that we relied on ICD-10-CM diagnosis codes from the EHR. There is always a possibility of misclassification and incomplete data when utilizing large EHR datasets. Also, patients with pre-perimetric glaucoma were grouped with patients with moderate or severe glaucomatous field loss. This could have made it difficult to detect a difference in incident falls compared to patients with glaucoma suspect diagnoses. However, a large proportion of patients with glaucoma diagnoses do not have severity indicated, and not all patients had the same level of testing, which limited consideration of disease severity in a more granular manner. We did not include visual acuity in this analysis as it was difficult to standardize due to differences in testing (distance or near, with or without correction or pinhole), and was variably missing. Future studies should incorporate more sophisticated integration of acuity and visual field data to better understand the relationship of frailty with falls and glaucomatous visual changes. We did not try to control for the occurrence of other eye diseases or surgeries which could have occurred over the follow-up period and which could also impact visual function. Finally, we did not capture falls that occurred at home without hospital follow-up, and it is possible that some patients sought care at another hospital system after a fall. However, we do not have any reason to believe that there would be a systematic reason that the glaucoma and glaucoma suspects would differ in this regard.

5. Conclusions

In summary, glaucoma patients were significantly more likely to be frail than glaucoma suspect patients using an electronic frailty index. Both pre-frailty and frailty were associated with an increased risk of incident emergency room or hospital admissions for injurious falls or fractures but there was no statistical evidence that the association of pre-frailty or frailty varied as a function of glaucoma diagnosis. Overall, frailty based on the eFI was better at identifying who was at risk for higher healthcare utilization for falls or fractures than a glaucoma diagnosis. Future studies should consider whether the eFI can be used to determine who might benefit from targeted fall prevention strategies.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Walter Duy reports financial support was provided by Wake Forest Medical Student Research Program. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Walter D. Duy: Writing – review & editing, Writing – original draft, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **Nicholas M. Pajewski:** Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Jeff D. Williamson:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization. **Atalie C. Thompson:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.tjfa.2025.100051.

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