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Glaucoma

Relationship Between Omega-3 Fatty Acids and Glaucoma Risk in Patients With Dry Eye Disease: A Multinational Retrospective Cohort Study

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Purpose: To evaluate whether omega-3 fatty acid supplementation is linked to a reduced glaucoma risk in individuals with dry eye disease.

Methods: This retrospective cohort study included adults with dry eye disease from a multinational database between 2013 and 2023. Individuals who received omega-3 were classified into the omega-3 group, and individuals who never received omega-3 were defined as the control group. The omega-3 and control groups were 1:1 propensity score matched for age, sex, race, smoking status, comorbidities, and corticosteroid use. Incident total glaucoma, ocular hypertension, primary open-angle glaucoma (POAG), normal-tension glaucoma, primary angle-closure glaucoma, and the use of first-line glaucoma medications were observed across a 5-year follow-up period.

Results: A total of 14,168 participants with dry eye disease were included in the final analysis. Compared with the control group, individuals who received omega-3 fatty acid prescriptions experienced lower risks of total glaucoma (hazard ratio [HR], 0.48; 95% confidence interval [CI], 0.42–0.54), ocular hypertension (HR, 0.57; 95% CI, 0.43–0.75), POAG (HR, 0.45; 95% CI, 0.33–0.63), normal-tension glaucoma (HR, 0.41; 95% CI, 0.19–0.88), primary angle-closure glaucoma (HR, 0.45; 95% CI, 0.21–0.94), and the use of first-line glaucoma medications (HR, 0.65; 95% CI, 0.53–0.80). The lower risks of ocular hypertension and POAG associated with omega-3 use remained consistent across those aged 60 years or older, females, Whites, and other demographic categories.

Conclusions: Omega-3 fatty acid supplementations may have the potential to decrease glaucoma risk in individuals with dry eye disease.

Translational Relevance: Clinically, omega-3 supplementation in patients with dry eye disease may decrease disease burden.

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Introduction

Glaucoma is the worldwide leading cause of irreversible vision loss.[1] Patients with primary open-angle glaucoma (POAG) have been found to exhibit reduced levels of blood docosahexaenoic acid (DHA) and eicosapentaenoic acid, two major omega-3 fatty acids.[2] Omega-3 has been shown to benefit ocular conditions such as dry eye disease,[3,4] age-related macular degeneration,[5] and cataract.[6] Among these, the strongest evidence supports the use of omega-3 for reducing symptoms of dry eye disease, with recommended daily doses ranging from 420 to 3000 mg.[7,8] Although studies have shown that omega-3 fatty acids may protect retinal ganglion cells and lower intraocular pressure (IOP), it remains unclear whether the use of omega-3 fatty acids directly decreases the risk of glaucoma development compared with nonusers.

Animal studies have demonstrated that omega-3 fatty acids may decrease glaucoma risk through multiple mechanisms, including lowering IOP, regulating ocular blood flow, providing neuroprotection, and mitigating oxidative stress and inflammation.[9–12] Clinical studies have also reported an association between omega-3 supplementation and decreases in IOP. A randomized controlled trial conducted by Downie et al.[13] involved 105 participants with dry eye disease and normal baseline IOP, who were randomized to receive either oral omega-3 supplementation or placebo for a duration of 3 months. Individuals in the omega-3 group experienced a significantly greater decrease in IOP compared with those in the placebo group.[13] Similarly, another study involving 19 eyes with POAG found that omega-3 supplementation led to a significant improvement in the mean deviation of the visual field compared with baseline.[14] However, these studies primarily assessed short-term IOP changes, involved small sample sizes, and did not directly assess whether omega-3 intake decreases the risk of glaucoma onset relative to placebo.

A cross-sectional study using data from the 2005–2008 National Health and Nutrition Examination Survey database provided preliminary insight, indicating that higher daily dietary intake of omega-3 fatty acids was associated with a lower risk of glaucoma development.[15] However, due to the absence of longitudinal cohort studies with extended follow-up durations, it remains unclear whether omega-3 supplementation confers a protective effect against glaucoma. Therefore, cohort studies are warranted to investigate the potential long-term benefits of omega-3 supplementation in reducing glaucoma risk.

We conducted a retrospective cohort study using a multinational database to examine the comparative risk of glaucoma between individuals with dry eye disease who received omega-3 supplementation and those who did not. By leveraging a large, diverse population and applying a 5-year follow-up period, this study aimed to provide more robust evidence to inform whether omega-3 supplementation may contribute to a reduced risk of glaucoma.

Methods

Data Source

This retrospective cohort study used deidentified electronic health records from the TriNetX Global Collaborative Network, which aggregated data from more than 160 health care institutions across 21 countries. TriNetX offered a web-based platform with integrated tools for database access and analysis, containing information on patient demographics, diagnosis records, medication prescriptions, and laboratory results. Diagnoses and medications were coded using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), the Anatomical Therapeutic Chemical classification system, or other standardized coding systems, with ICD-9-CM codes automatically mapped to ICD-10-CM. The platform enabled direct data extraction, analysis, and results generation.

To protect patient privacy, TriNetX adhered to the U.S. Health Insurance Portability and Accountability Act. Outcome counts involving 10 or fewer patients were masked and reported as 10 to ensure confidentiality. The study protocol was approved by the Institutional Review Board of Taichung Veterans General Hospital under the registration number CE24430C-1, which permits retrospective data collection and analysis using the TriNetX Analytics Network. The requirement for patient informed consent was waived because TriNetX did not involve direct interaction with human participants, and patient identities cannot be identified from the records.

Study Population

Adults aged 18 years or older with a diagnosis of dry eye disease who either received or never received prescriptions for omega-3 fatty acid supplements were included. Participants were required to have at least 1 year of follow-up after the index date. Individuals were excluded if they had a history of any subtypes of glaucoma diagnosis, prior use

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of glaucoma medications, laser trabeculoplasty, or autoimmune conditions such as rheumatoid arthritis, systemic lupus erythematosus, sarcoidosis, Sjögren syndrome, Crohn's disease, or ulcerative colitis. These autoimmune diseases were excluded because they may contribute to dry eye symptoms and are commonly treated with systemic corticosteroids, which may increase the risk of glaucoma. The detailed diagnostic codes used for the inclusion and exclusion criteria are provided in Supplementary Table S1.

Exposure Definition

The study population was further classified into the omega-3 group and the control group. The omega-3 group included participants who received their first prescription for omega-3 fatty acids between 2013 and 2023. To enhance the likelihood of continual use, individuals in the omega-3 group were required to have at least one additional prescription within 1 year after the initial prescription. The date of the first prescription was designated as the index date for the omega-3 group.

The control group consisted of participants who were never prescribed omega-3 fatty acids at any time recorded in the TriNetX database. For the control group, the index date was defined as the date of their dry eye disease diagnosis. The diagnostic codes used to identify omega-3 prescriptions are listed in Supplementary Table S1.

Outcome Measures

The outcomes of interest included total glaucoma, ocular hypertension, POAG, normal-tension glaucoma (NTG), primary angle-closure glaucoma (PACG), and the initiation of first-line glaucoma medications (beta-blockers, prostaglandin analogues, brimonidine, brinzolamide, dorzolamide, and netarsudil). Individuals were followed from 3 months after the index date to minimize reverse causation bias, and were censored at the outcome occurrence, the end of the study period, loss to follow-up (defined as the date of the last recorded clinical encounter within the study period), or 5 years after the index date, whichever occurred first. The diagnostic codes used to define each outcome can be found in Supplementary Table S1.

Statistical Analyses

A 1:1 propensity score matching was conducted between the omega-3 and control groups using a greedy nearest-neighbor algorithm without replacement. A caliper of 0.1 pooled standard deviations was applied, and the cohorts were randomly shuffled before matching. A standardized mean difference of less than 0.1 was considered indicative of well-balanced baseline demographics. Matching covariates were collected within 1 year before the index date and included age at index, sex (male), race (White, Black or African American, Asian), ethnicity (Hispanic or Latino, not Hispanic or Latino), smoking history, comorbidities (hypertension, ischemic heart disease, cerebrovascular disease, heart failure, diabetes mellitus, dyslipidemia, overweight or obesity, and obstructive sleep apnea), and prior corticosteroid use. The diagnostic codes used to identify these covariates are listed in Supplementary Table S1.

All analyses were performed in June 2025 using the TriNetX web-based platform. A matched Cox proportional hazards model was applied to evaluate the risk of glaucoma in the omega-3 group compared with the control group, with results presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Kaplan-Meier analysis was used to estimate the cumulative incidence of outcomes based on survival probabilities. Additional stratified analyses were conducted by age group (<40, 40–59, ≥60 years), sex (female, male), race (White, Black or African American, Asian), and the presence or absence of hypertension, diabetes mellitus, and hyperlipidemia. To address potential reverse causation bias, we conducted sensitivity analyses by excluding outcome cases that occurred within 1, 6, 9, or 12 months after the index date, in contrast with the main analysis, which excluded cases within the first 3 months.

Statistical analyses were conducted using a combination of programming languages and software libraries. These included Java version 11.0.16 with the Apache Commons Math 3.6.1 library, R version 4.0.2 (The R Foundation for Statistical Computing, Vienna, Austria) with the Hmisc (v1.1) and Survival (v3.2-3) packages, and Python 3.7 equipped with several analytical and visualization libraries such as lifelines (v0.22.4), matplotlib (v3.5.1), numpy (v1.21.5), pandas (v1.3.5), scipy (v1.7.3), and statsmodels (v0.13.2). Additional analytical methodologies used in the TriNetX platform were proprietary and protected as trade secrets.

Results

After applying the inclusion and exclusion criteria, 7084 individuals who received omega-3 and 831,142 individuals who never received omega-3 were identified as eligible. After propensity score matching, the final analysis included 7084 participants in the omega-

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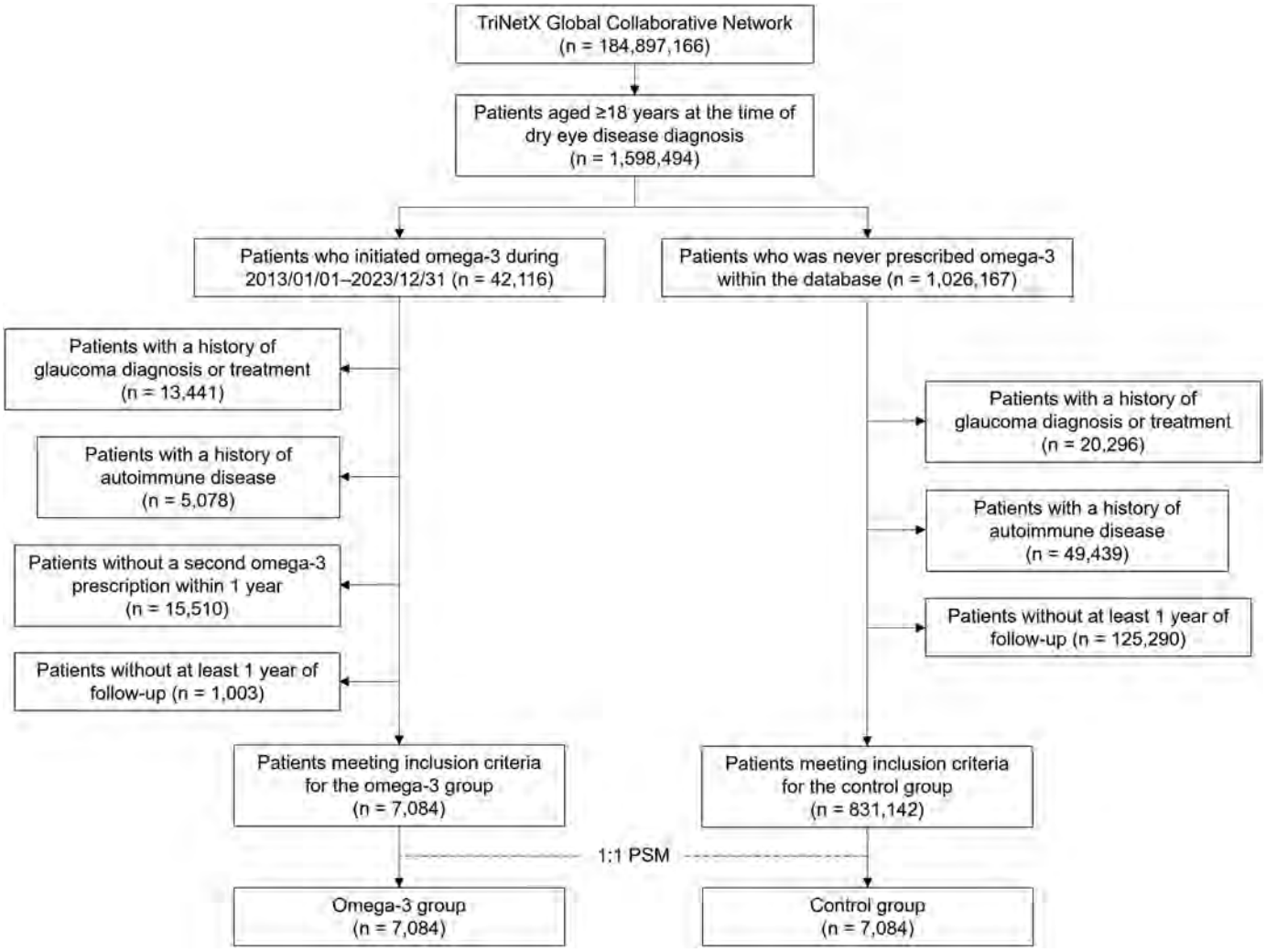


Figure 1. Participant selection. The flowchart outlines the participant selection process based on the inclusion and exclusion criteria. PSM, propensity score matching.

3 group and 7084 participants in the control group (Fig. 1). The mean ± standard deviation participant age was 62.7 ± 14.9 years in the omega-3 group and 62.5 ± 14.5 years in the control group. The mean ± standard deviation follow-up duration was 3.6 ± 1.4 years for the omega-3 group and 3.8 ± 1.3 years for the control group. Baseline characteristics were well balanced between the two groups, with all standardized mean differences below 0.1 (Table).

Association Between Omega-3 and Risk of Glaucoma

Among 14,168 participants included in the final analysis, 354 (5.00%) in the omega-3 group developed total glaucoma compared with 739 (10.43%) in the control group, corresponding with a significantly lower risk of total glaucoma (HR, 0.48; 95% CI, 0.42–0.54). In addition, 80 patients prescribed omega-3 fatty acids (1.13%) developed ocular hypertension during the 5-year follow-up period, compared with 144 (2.03%) in the matched control group. Individuals prescribed omega-3 fatty acids had a significantly lower risk of ocular hypertension compared with those who did not receive omega-3 (HR, 0.57; 95% CI, 0.43–0.75). Within the same population, 53 participants (0.75%) in the omega-3 group and 120 (1.69%) in the control group developed POAG. Omega-3 users had a significantly lower risk of POAG compared with non-users (HR, 0.45; 95% CI, 0.33–0.63).

Similarly, individuals in the omega-3 group also experienced a lower incidence of NTG (HR, 0.41; 95% CI, 0.19–0.88), PACG (HR, 0.45; 95% CI, 0.21–0.94), and the need for first-line glaucoma medications (HR, 0.65; 95% CI, 0.53–0.80) compared with those in the control group (Fig. 2). Individuals who

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Table. Baseline Characteristics of the Study Population

	Before Propensity Score Matching			After Propensity Score Matching		
	Omega-3	Control	SMD	Omega-3	Control	SMD
Total number	7084	831,142		7084	7084	
Age (years)	62.7 ± 14.9	58.3 ± 15.4	0.295	62.7 ± 14.9	62.5 ± 14.5	0.016
Male sex	1947 (27.5)	251,694 (30.3)	0.062	1947 (27.5)	1940 (27.4)	0.002
Ethnicity						
Hispanic or Latino	848 (12.0)	67,424 (8.1)	0.129	848 (12.0)	867 (12.2)	0.008
Not Hispanic or Latino	3937 (55.6)	563049 (67.7)	0.252	3937 (55.6)	4019 (56.7)	0.023
Race*						
White	4150 (58.6)	484,517 (58.3)	0.006	4150 (58.6)	4224 (59.6)	0.021
Black	1243 (17.5)	108,185 (13.0)	0.126	1243 (17.5)	1286 (18.2)	0.016
Asian	342 (4.8)	74,608 (9.0)	0.164	342 (4.8)	339 (4.8)	0.002
Smoking	266 (3.8)	10,545 (1.3)	0.159	266 (3.8)	255 (3.6)	0.008
Comorbidities						
Hypertension	3933 (55.5)	247,460 (29.8)	0.539	3933 (55.5)	3980 (56.2)	0.013
Ischemic heart disease	1167 (16.5)	55,330 (6.7)	0.311	1167 (16.5)	1139 (16.1)	0.011
Cerebrovascular disease	647 (9.1)	31,799 (3.8)	0.217	647 (9.1)	635 (9.0)	0.006
Heart failure	680 (9.6)	22,090 (2.7)	0.292	680 (9.6)	595 (8.4)	0.042
Diabetes mellitus	2130 (30.1)	131,189 (15.8)	0.345	2130 (30.1)	2128 (30.0)	0.001
Dyslipidemia	2275 (32.1)	140,587 (16.9)	0.359	2275 (32.1)	2314 (32.7)	0.012
Overweight or obesity	1417 (20.0)	79,387 (9.6)	0.298	1417 (20.0)	1437 (20.3)	0.007
Obstructive sleep apnea	923 (13.0)	46,511 (5.6)	0.258	923 (13.0)	888 (12.5)	0.015
Corticosteroid	3412 (48.2)	228,061 (27.4)	0.438	3412 (48.2)	3499 (49.4)	0.025

SMD, standardized mean difference.

*The racial and ethnic classifications (e.g., White, Black or African American, Asian) are directly taken from the original terminology provided in the TriNetX database. Specifically, "Black and African American" has been shortened to "Black" due to space constraints.

Values are mean ± standard deviation or number (%).

received omega-3 supplements demonstrated a significantly lower cumulative incidence of ocular hypertension, POAG, NTG, PACG, and the need for first-line glaucoma medications over the 5-year follow-up period compared with those in the control group. All outcomes showed statistically significant differences between the omega-3 and control groups, with log-rank *P* values of less than 0.05. The corresponding survival curves are presented in Figure 3.

Stratified Analysis

The lower risk of ocular hypertension associated with omega-3 use compared with controls was also observed across multiple subpopulations, including individuals aged 60 years or older (HR, 0.56; 95% CI, 0.39–0.80), females (HR, 0.59; 95% CI, 0.41–0.86), White individuals (HR, 0.37; 95% CI, 0.24–0.55), those without hypertension (HR, 0.62; 95% CI, 0.40–0.95), those with hypertension (HR, 0.54; 95% CI, 0.38–0.77), and those with hyperlipidemia (HR, 0.42; 95% CI, 0.24–0.74). These findings are detailed in Supplementary Figure S1.

Omega-3 use was also linked to a significantly lower risk of POAG across various groups, including those aged 60 years or older (HR, 0.51; 95% CI, 0.34–0.75), females (HR, 0.43; 95% CI, 0.28–0.67), males (HR, 0.47; 95% CI, 0.28–0.82), White individuals (HR, 0.27; 95% CI, 0.16–0.47), participants without hypertension (HR, 0.34; 95% CI, 0.21–0.56), those with hypertension (HR, 0.51; 95% CI, 0.34–0.78), participants without diabetes mellitus (HR, 0.58; 95% CI, 0.38–0.87), those with diabetes mellitus (HR, 0.50; 95% CI, 0.28–0.88), participants without hyperlipidemia (HR, 0.43; 95% CI, 0.29–0.64), and those with hyperlipidemia (HR, 0.49; 95% CI, 0.28–0.87). These findings are outlined in Figure 4.

Sensitivity Analysis

After excluding outcome events that occurred shortly after treatment initiation, the results remained

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Outcome	Omega-3		Control		Hazard Ratio (95% CI)
	Event (n)	Total (n)	Event (n)	Total (n)	
Total glaucoma	354	7,084	739	7,084	0.48 (0.42–0.54)
Ocular hypertension	80	7,084	144	7,084	0.57 (0.43–0.75)
POAG	53	7,084	120	7,084	0.45 (0.33–0.63)
NTG	≤10	7,084	23	7,084	0.41 (0.19–0.88)
PACG	≤10	7,084	23	7,084	0.45 (0.21–0.94)
First-line medications	143	7,084	225	7,084	0.65 (0.53–0.80)

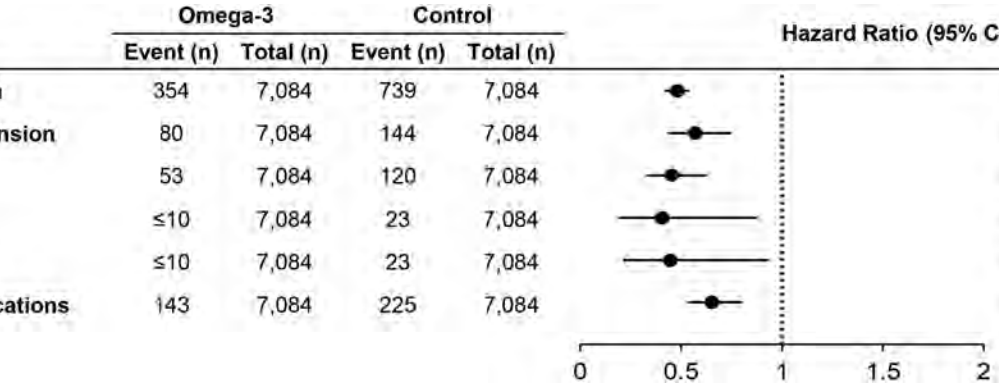


Figure 2. Associations between omega-3 and glaucoma-related outcomes. The risk of total glaucoma, ocular hypertension, POAG, NTG, PACG, and first-line medication use between the omega-3 and control groups. A lower HR indicates a reduced risk of the outcome associated with the omega-3 groups compared with the control group. For privacy, the TriNetX platform conceals exact event numbers for groups with 10 or fewer events.

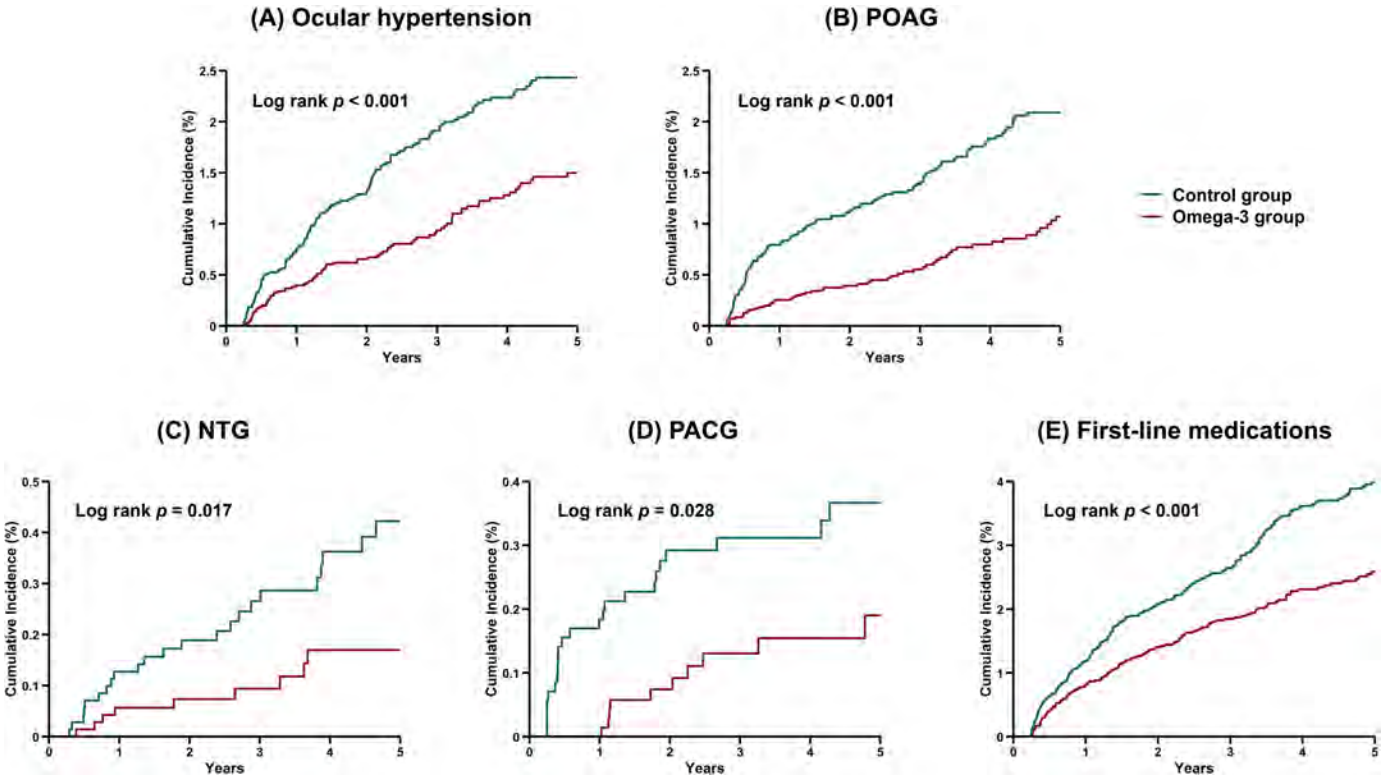


Figure 3. Cumulative incidence of outcomes in omega-3 and control groups. The 5-year cumulative incidence of outcomes in the omega-3 and control groups is presented. The *red line* represents patients in the omega-3 group, and the *blue line* represents those in the control group.

consistent with the primary analysis. Omega-3 supplementation continued to be associated with a lower risk of ocular hypertension compared with the control group, even when cases diagnosed within 1 month (HR, 0.61; 95% CI, 0.47–0.80), 3 months (HR, 0.57; 95% CI, 0.43–0.75), 6 months (HR, 0.56; 95% CI, 0.42–0.74), 9 months (HR, 0.60; 95% CI, 0.45–0.81), and 12 months (HR, 0.64; 95% CI, 0.47–0.86) of treatment initiation were excluded (Supplementary Fig. S2).

Similarly, omega-3 use was linked to a lower risk of POAG compared with the control group, with the association remaining significant after excluding events occurring within 1 month (HR, 0.49; 95% CI, 0.35–0.67), 3 months (HR, 0.45; 95% CI, 0.33–0.63), 6 months (HR, 0.49; 95% CI, 0.35–0.68), 9 months (HR,

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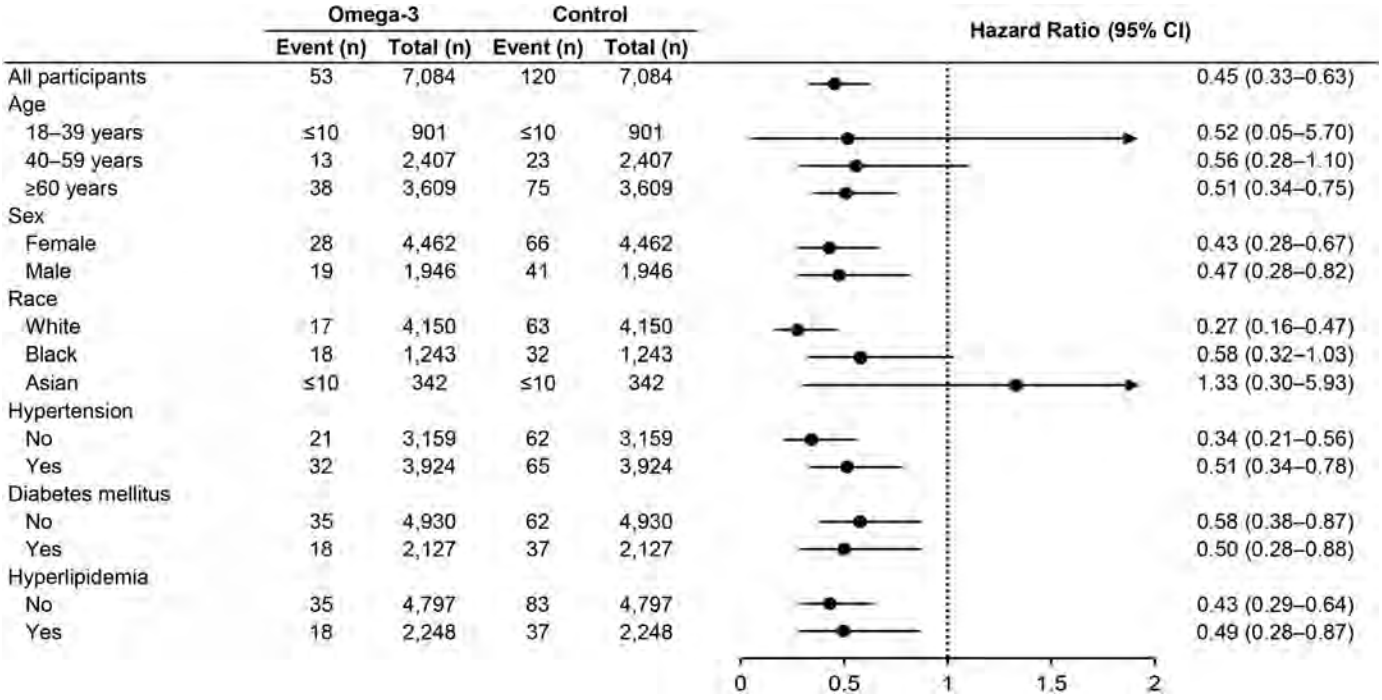


Figure 4. Stratified associations between omega-3 and POAG. The graph shows the risk of POAG between the omega-3 and control groups, stratified by multiple factors. A lower HR indicates a reduced risk of POAG in the omega-3 group compared with the control group. For privacy, the TriNetX platform conceals exact event numbers for groups with 10 or fewer events.

0.45; 95% CI, 0.32–0.64), and 12 months (HR, 0.46; 95% CI, 0.32–0.65) of treatment initiation (Supplementary Fig. S2).

Discussion

This multinational, retrospective cohort study involving 14,168 individuals with dry eye disease demonstrated that patients who received omega-3 fatty acids had lower risks of total glaucoma, ocular hypertension, POAG, NTG, PACG, and the need for first-line glaucoma medications compared with those who never received omega-3 fatty acids. The lower risk of ocular hypertension and POAG associated with omega-3 use was also observed in subpopulations aged 60 years or older, females, White, and other demographic characteristics.

Our findings are generally consistent with previous clinical studies. Omega-3 fatty acid supplementation has been associated with lower IOP in normotensive individuals[13] and decreased visual field loss in patients with POAG.[14] Similarly, a cross-sectional analysis using data from the 2005–2008 National Health and Nutrition Examination Survey database found that higher daily dietary intake of eicosapentaenoic acid and DHA was linked to a lower risk of developing glaucoma.[15] Weisinger et al.[16] conducted an animal study using guinea pigs and demonstrated that, after omega-3 depletion, retinal DHA levels increased after 5 weeks of canola oil (an omega-3–sufficient diet) supplementation and approached near-complete normalization after 10 weeks. These findings are consistent with the results of the present study, which showed that the risks of ocular hypertension and POAG were noticeably reduced after omega-3 supplementation. Taken together with our findings, these studies support the notion that omega-3 fatty acids may reduce the risk of glaucoma.

Mechanisms Potentially Underlying the Observed Association Between Omega-3 and Glaucoma Risk

Omega-3 fatty acids may decrease glaucoma risk by lowering the IOP, enhancing ocular blood flow, providing neuroprotection, and mitigating oxidative stress and inflammation.[9–12] Clinical studies have demonstrated that omega-3 intake is associated with reduced IOP,[13,14] and a rat study suggested that this IOP-lowering effect may result from increased aqueous outflow facility.[9]

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A murine study found that short-term (7-day) dietary supplementation with omega-3 fatty acids (a mixture of eicosapentaenoic acid and DHA) helped to maintain endothelial function and vascular integrity in the ophthalmic artery, potentially decreasing glaucoma risk.[12] Omega-3 fatty acids may also offer neuroprotection. In one rat study, omega-3 deficiency was associated with greater retinal ganglion cell dysfunction, particularly under elevated IOP conditions.[17] Another mouse study showed that treatment with omega-3 polyunsaturated fatty acids, with or without timolol eye drops, resulted in significantly higher retinal ganglion cell densities compared with untreated controls.[11] The potential endothelial and neuroprotective effects of omega-3 may be reflected in our findings that omega-3 supplementation is associated with a lower risk of NTG, a condition whose pathogenesis is less dependent on elevated IOP and is more strongly linked to vascular dysregulation and neurodegenerative mechanisms.[18]

Omega-3 fatty acids also appear to reduce oxidative stress and inflammation, both central to glaucoma pathogenesis. This concept was supported by a study in which human trabecular meshwork cells were incubated in either an omega-3–containing medium or a standard medium, followed by exposure to H_2O_2 to induce oxidative stress. Human trabecular meshwork cells incubated with omega-3 were less susceptible to oxidative stress–induced mitochondrial dysfunction and exhibited lower expression of extracellular matrix components (fibronectin and plasminogen activator inhibitor-1) and inflammatory markers (interleukin-6 and nuclear factor κB) compared with those cultured under standard conditions.[19] Similarly, an animal study found that mice supplemented with omega-3 polyunsaturated fatty acids had reduced retinal expression of tumor necrosis factor-α and interleukin-8, further supporting the anti-inflammatory role of omega-3.[10] Collectively, the observed characteristics of omega-3 may contribute to a lower risk of glaucoma.

Clinical Implications

Our findings, derived from an extensive multinational database, reinforce existing evidence suggesting that omega-3 supplementation may offer protective effects against glaucoma. We specifically focused on a population with dry eye disease, because these patients share similar clinical indications for omega-3 use. Although patients prescribed omega-3 supplements might attend more frequent health care visits, potentially increasing surveillance and the detection rate of glaucoma, and the control group might include unrecorded over-the-counter users that attenuate the difference between groups, our analysis still revealed a significantly lower risk of glaucoma in the omega-3 cohort. The persistence of this association, even when accounting for these conservative biases, underscores the robustness of our findings. Additionally, the relatively large sample size enhances both the statistical power and the generalizability of our results. By applying propensity score matching across multiple covariates, we minimized baseline imbalances and potential biases.

Our stratified analyses provide insights into the potential differential effects of omega-3 fatty acids across various subpopulations. Although lower risks of ocular hypertension and POAG associated with omega-3 supplementation were observed in most subgroups, no statistically significant difference was found between the omega-3 and control groups among Asian participants. However, the wide CIs suggest that this finding might be attributable to the relatively small sample size rather than an absence of biological effect in the Asian population. Further studies investigating potential racial differences in the association between omega-3 supplementation and glaucoma are warranted.

Omega-3 fatty acids not only have potential benefits for glaucoma, but have also demonstrated lipid-lowering, atherosclerosis reduction, and heart rhythm stabilization effects,[20,21] as well as the potential to reduce ocular diseases including dry eye disease,[3,4] age-related macular degeneration,[5] and cataract.[6] Overall, given its wide-ranging health benefits, adequate omega-3 intake may support general health. Further studies are warranted to assess the applicability of our findings to other populations and to determine the optimal dosage for different individuals.

Limitations

Our study has several limitations. First, the underlying reasons for prescribing or obtaining omega-3 supplements may vary among individuals and could potentially influence the results. This is reflected in Table, where imbalanced baseline characteristics between the omega-3 and control groups were observed before propensity score matching. To reduce this bias, the omega-3 and control groups were matched on various covariates; however, the possibility of residual confounding cannot be completely excluded. Second, because TriNetX is a deidentified database that does not permit direct access to individual medical records, we could not independently verify glaucoma diagnoses. To address this issue, we included multiple outcomes,

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such as different glaucoma subtypes and the initiation of first-line glaucoma medications, to improve diagnostic specificity. Third, as an observational study, a direct causal relationship between omega-3 supplementation and reduced glaucoma risk cannot be established. We conducted a sensitivity analysis by excluding individuals diagnosed with glaucoma within 1 to 12 months after omega-3 initiation to minimize reverse causation. Fourth, because the TriNetX database lacks information on medication dosage, we were unable to ascertain the dose and formulation of omega-3 supplements received by patients; therefore, we could not evaluate whether a dose–response relationship exists between omega-3 use and glaucoma risk or determine the optimal dosage required for risk reduction. Future studies are needed to address these limitations.

Conclusions

In this multinational cohort of 14,168 patients with dry eye disease, omega-3 supplementation was independently associated with lower risks of ocular hypertension and several glaucoma subtypes. The consistency with findings from prior trials and biologic plausibility proposed by animal studies suggests that omega-3 intake may complement existing glaucoma preventive strategies. Randomized controlled studies are required to confirm causality and define optimal dosing.

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