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Intracranial Pressure in Primary Open Angle Glaucoma, Normal Tension Glaucoma, and Ocular Hypertension: A Case–Control Study

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Abstract

PURPOSE—To compare intracranial pressure (ICP) in subjects with primary open-angle glaucoma (POAG), normal-tension glaucoma (NTG; subset of POAG), and ocular hypertension (OHT) with that in subjects with no glaucoma.

METHODS—The study was a retrospective review of medical records of 62,468 subjects who had lumbar puncture between 1985 and 2007 at the Mayo Clinic. Of these, 57 POAG subjects, 11 NTG subjects (subset of POAG), 27 OHT subjects, and 105 control subjects met the criteria and were analyzed. A masked comparison of the relationship between ICP and other ocular and nonocular variables was performed by using univariate and multivariate analyses.

RESULTS—ICP was significantly lower in POAG compared with age-matched control subjects with no glaucoma (9.1 ± 0.77 mm Hg vs. 11.8 ± 0.71 mm Hg; $P < 0.0001$). Subjects with NTG also had reduced ICP compared with the control subjects (8.7 ± 1.16 mm Hg vs. 11.8 ± 0.71 mm Hg; $P < 0.01$). ICP was higher in OHT than in age-matched control subjects (12.6 ± 0.85 mm Hg vs. 10.6 ± 0.81 mm Hg; $P < 0.05$).

CONCLUSIONS—ICP is lower in POAG and NTG and elevated in OHT. ICP may play an important role in the development of POAG and NTG and in preventing the progression of OHT to POAG. Further prospective and experimental studies are warranted to determine whether ICP has a fundamental role in the pathogenesis of glaucoma.

The glaucomas represent a variety of pathophysiologic processes that result in characteristic visual field loss and characteristic optic nerve changes. Elevated intraocular pressure (IOP) is an important risk factor in the development of glaucoma, but elevated IOP is not present in all forms of glaucoma (e.g., normal-tension glaucoma; [NTG]). Furthermore, an elevated IOP does not necessarily cause development of the disease. Patients with elevated IOP but no change in the appearance of the optic nerve are classified as having ocular hypertension (OHT), and only a small percentage of individuals with OHT will ever have glaucoma.[1] The precise mechanisms by which intraocular pressure (IOP) contributes to optic nerve damage remains unclear.

The optic nerve is exposed not only to IOP in the eye, but also to intracranial pressure (ICP), as it is surrounded by cerebrospinal fluid (CSF) in the subarachnoid space. The average IOP

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is 10 to 21 mm Hg, whereas the average ICP is 5 to 15 mm Hg.[2] The lamina cribrosa separates these two pressurized regions[3] and the pressure drop that occurs across the lamina cribrosa (IOP − ICP) is known as the translaminar pressure difference and is typically directed posteriorly. Recent data indicate that ICP is lower in patients with primary open-angle glaucoma (POAG) than in those with no glaucoma, and the resulting increase in the translaminar pressure difference may play an important role in the pathogenesis of the glaucomas.[4] The CSF pressure as assessed by lumbar puncture correlates with ICP; therefore, we use the terms ICP and CSF pressure interchangeably, as is done in clinical practice.[5]

In this study, we compared ICP measurements in patients with POAG, NTG (a subset of POAG), and OHT with age-matched control subjects with no glaucoma. Because a prospective study of ICP measurement in patients carries ethical considerations, we chose to study this relationship retrospectively by using the long-standing integrated comprehensive multispecialty database of the Mayo Clinic.

METHODS

This is a retrospective study of medical records of patients with POAG, NTG (a subset of POAG), and OHT and two age-matched control groups who had undergone lumbar puncture (LP) with measurement of ICP and analysis of CSF. This study was approved by the Mayo Clinic Institutional Review Board.

Patient Selection

A computerized search of all patients who underwent LP at Mayo Clinic between 1985 and 2007 was used as the initial dataset. This list was cross-referenced by ICD-9 codes, to identify all patients with POAG, NTG, suspected glaucoma, OHT, cataract, presbyopia, hyperopia, or myopia diagnosed by an ophthalmologist (ICD-9 codes: 365, 365.11, 365.12, 365.0, 365.10, 365.04, 366.10, 366.14, 366.15, 366.16, 366.17, 367.4, 367.1, and 367.0). Inclusion criteria included ICP measurement, normal findings in a CSF analysis, no medical diagnoses known to affect ICP, no surgical procedures known to affect ICP, documentation of systemic and topical medications, and no medications known to affect ICP (e.g., systemic carbonic anhydrase inhibitors). In addition, all subjects were required to have a recorded eye examination that included measurement of IOP and estimation of cup-to-disc ratio by an ophthalmologist.

POAG—Subjects were considered to have POAG if it was diagnosed by an ophthalmologist and showed characteristic optic nerve changes and visual field loss consistent with glaucoma. The POAG group included all subjects who met criteria for NTG.

NTG—Subjects were included in the NTG subset if NTG was diagnosed by an ophthalmologist, and they showed the characteristic optic nerve changes and visual field loss consistent with glaucoma. All recorded IOPs were less than or equal to 21 mm Hg and either pretreatment IOP was documented or a diurnal curve was performed.

OHT—Subjects were considered to have OHT if it was diagnosed by an ophthalmologist and they had a documented IOP greater than 21, a normal-appearing optic nerve, and no visual field loss consistent with glaucoma. If a subject with OHT had a vertical cup-to-disc ratio of 0.3 or less, visual field analysis was not required for inclusion.

Control Groups—Two age-matched nonglaucoma control groups were established: one control group for comparison with POAG and the NTG subset and another for comparison with the OHT group. Separate control groups were established *before* data collection because

of the lower anticipated age range in the OHT group. The age criterion for the POAG and NTG control group was greater than 55 years. The age criterion for the OHT control group was between 30 and 70 years. Additional criteria for inclusion in either control group was an examination by an ophthalmologist, documentation of cup-to-disc ratio, and no history of glaucoma, elevated IOP, or optic nerve abnormality. For the control groups, inclusion diagnoses were cataract, presbyopia, myopia, or hyperopia.

All subjects had lumbar puncture as part of a work-up that was unrelated to ophthalmic findings, and conversely none of the subjects were referred for eye examination because of the results of lumbar puncture. Subjects evaluated for disorders known to affect the optic nerve (e.g., optic neuritis, pseudotumor cerebri) were excluded. Subjects taking oral carbonic anhydrase inhibitors were excluded because of the known effects of these medications on ICP. All inclusion and exclusion criteria were applied by an observer masked to ICP.

Data Collection

Data collected included sex, age at the time of LP, indication for LP, opening CSF pressure, CSF analysis, medical history, ocular history, surgical history, medications, IOP closest to LP date, months between IOP measurement and LP, maximum IOP, ocular history, ocular medications, refractive error, and visual field evaluation. In a modification of the method described by Quigley et al.,[6] visual field loss was divided into four stages of severity. This method described severity ranging from stages 0 to 8. We deemed grades 0 to 2 to be normal; 3 and 4, mild; 5 and 6, moderate; and 7 and 8, severe. A visual field grade ≥ 3 was used as the inclusion criterion for POAG or the NTG subset and the exclusion criterion for OHT.

Lumbar Puncture

A standard lumbar puncture technique was used for all patients. Patients were placed in the lateral decubitus position and either the L3–L4 or L4–L5 interspace was identified and anesthetized. A 3.5-in., 20-gauge spinal needle with a three-way stop-cock was inserted into the subarachnoid space. A 550-mm manometer was attached to the stopcock, and the column of CSF was allowed to equilibrate. The patient was asked to remain still and not speak. The meniscus of the CSF was read and reported in mm H_2O. This value was converted to mm Hg to allow comparison with IOP and for data analysis (1 mm Hg = 13.6 mm H_2O).

Statistical Analyses

The prestudy power calculation with $\alpha = 0.05$ and $\beta = 0.80$ revealed that a sample size of 49 in each group would be necessary to detect a mean ICP difference of 2 mm Hg at the 95% CI between the groups, assuming that mean ICP is 13 ± 3.0 mm Hg[2] and mean IOP is 16 ± 4 mm Hg.

Data were presented as the mean ± SD for continuous variables and as frequency and percentage for categorical variables. The significance of the difference between groups was assessed with independent-sample *t*-tests. Linear regression analysis was used to determine the significance of the relationship between predictors and ICP. Multivariate linear regression was performed by using all recorded variables to determine whether POAG and NTG were independently associated with lower ICP and whether OHT was independently associated with a higher ICP. These variables included group designation (POAG, OHT, POAG control, or OHT control), age, sex, indication for LP (altered mental status, rule-out meningitis, headache, normal pressure hydrocephalus, seizure, stroke, peripheral neuropathy, and other), medical history (diabetes, hypertension, stroke), systemic medication use (diuretic, β-blocker, angiotensin converting enzyme inhibitors, other antihypertensives, and glucocorticoids), topical antiglaucoma medications (β-blockers, prostaglandin analogues, α-agonists, and topical carbonic anhydrase inhibitors), CSF protein concentration, CSF glucose concentration, cup-

to-disc ratio, maximum IOP, and IOP closest to the date of lumbar puncture. Analysis of covariance was also performed.

RESULTS

Between the years 1985 and 2007, 62,468 lumbar punctures were performed at the Mayo Clinic. Of these, 164 subjects had a diagnosis of POAG, 69 NTG, and 97 OHT, and 746 had a diagnosis of cataract, presbyopia, myopia, or hyperopia. Inclusion criteria were met for 57 in the POAG group, 11 in the NTG subset, 27 in the OHT group, 66 in the age-matched control group for POAG, and 39 in the age-matched control group for OHT. (Table 1) Patient demographics, medications, and the most common reasons for lumbar puncture are listed in Table 2. Demographics were generally similar between groups although the average age of POAG and NTG subjects was higher than OHT. Nearly all subjects in both groups were Caucasian. Altered mental status was a more common indication for lumbar puncture in the NTG and OHT groups compared with the control groups.

The mean ICP was 9.6 ± 3.1 mm Hg in POAG and 9.3 ± 3.2 mm Hg in the NTG subset compared with 12.7 ± 3.9 mm Hg in age-matched control subjects for POAG (and the NTG subset; Fig. 1A). In the OHT group, the mean ICP was 13.2 ± 3.8 mm Hg compared with 11.5 ± 3.3 mm Hg in age-matched control subjects for OHT. A statistically significant difference in the mean ICP was found between the POAG and control groups ($P < 0.0001$); the NTG subset and control group ($P < 0.01$); OHT and POAG ($P < 0.0001$); and OHT and the NTG subset ($P < 0.01$). No difference in ICP was found between OHT and age-matched control subjects, but a trend toward significance was present ($P = 0.06$). However, after multivariate analysis, a significant difference ($P < 0.05$) was found between the OHT and age-matched control groups (Fig. 1B). Analysis of covariance showed a significant difference ($P < 0.001$) between POAG and control subjects and borderline significance ($P < 0.038$) between OHT and control subjects, when the Bonferroni correction of the α-level for three tests was used. No difference in ICP was found between the control groups. Linear regression analysis showed that cup-to-disc ratio did not correlate with IOP, ICP, or the translaminar pressure difference. Visual field severity did not correlate with maximum IOP, ICP, or translaminar pressure difference.

Univariate analysis showed that the following LP indications were associated with a lower ICP: increasing age, increased cup-to-disc ratio, normal pressure hydrocephalus, zoster, and stroke. Headache and seizure as indications for LP were associated with a higher ICP. Group differences in ICP were assessed by using multivariate analysis and showed a continued association between ICP and the following indications for LP: headache, seizure, and stroke. Multivariate analysis showed no relationship between ICP and any other variables. After correction of the mean ICP of each group for variables predictive of ICP, the significant difference between POAG, the NTG subset, and controls persisted. A significant difference between the OHT and control groups became apparent ($P < 0.05$; Fig. 1B). Multivariate analysis using all recorded variables confirmed these findings indicating that POAG and NTG are independently associated with lower ICP, and OHT is independently associated with a higher ICP.

The mean translaminar pressure difference (IOP − ICP) in each group was calculated using both the maximum recorded IOP (IOP max − ICP) and the IOP at the date closest to lumbar puncture (IOP closest to LP date − ICP). POAG, the NTG subset, and OHT all had an elevated translaminar pressure difference when compared with the respective control groups. (Fig. 2) The mean translaminar pressure difference using maximum recorded IOP (IOP_{max} − ICP) was 11.6 ± 11.0 mm Hg in POAG and 7.4 ± 4.8 mm Hg in the NTG subset compared with 3.3 ± 4.0 mm Hg in age-matched control subjects ($P < 0.01$). In the OHT group, the mean translaminar pressure difference (IOP_{max} − ICP) was 11.5 ± 5.1 mm Hg compared with 5.2 ±

3.8 mm Hg in age-matched control subjects ($P < 0.05$). The mean translaminar pressure difference using IOP closest to LP date (IOP closest to LP date − ICP) was 6.1 ± 5.6 mm Hg in POAG and 5.0 ± 4.4 mm Hg in the NTG subset compared with 1.9 ± 4.4 mm Hg in age-matched control subjects ($P < 0.05$). In the OHT group, the mean translaminar pressure difference (IOP closest to LP date − ICP) was 8.4 ± 5.5 mm Hg compared with 4.4 ± 3.5 mm Hg in the age-matched control group ($P < 0.05$).

CSF protein concentration was significantly lower in the POAG group (58.1 vs. 68.1, $P < 0.05$) and the NTG subset (45.5 vs. 68.1, $P = 0.01$) compared with that in the control subjects (Table 2, Table 3). Otherwise CSF protein and glucose analysis, IOP at the time of LP, and refractive state of the eye were similar between groups (Table 4).

Since the data reported herein include data from our previous analysis (1996–2007),[4] we compared the current dataset (1985–1996) with the previously acquired dataset (1996–2007). No difference in mean ICP was found between the previous POAG dataset (1996–2007) and the current POAG dataset (1985–1996; 9.2 mm Hg vs. 9.7 mm Hg, respectively; $P = 0.28$). No difference was found between the control subjects in the previous dataset (1996–2007) and those in the current dataset (1985–1996; 11.6 mm Hg vs. 12.7 mm Hg, respectively; $P = 0.17$). Similar to our previously published results, a significant difference in ICP was found in this current dataset when comparing POAG (1985–1996) with control subjects (1985–1996; 9.6 mm Hg vs. 12.7 mm Hg, respectively; $P < 0.05$; Fig. 3).

DISCUSSION

An imbalance between the anterior (IOP) and posterior (ICP) fluid pressures on the optic nerve appears to have a role in glaucomatous optic nerve damage. Pressure differences between the two compartments, known as the translaminar pressure difference,[7] may lead to abnormal function and potential nerve damage due to changes in axonal transport, deformation of the lamina cribrosa, or altered blood flow. In this retrospective study, we found ICP to be 3 to 4 mm Hg lower in patients with POAG, and its subset NTG, when compared with control subjects with no glaucoma and patients with OHT. These findings suggest that POAG and NTG may act as a compartment syndrome and be influenced by ICP as well as IOP. For perspective, the 3 to 4 mm Hg difference in ICP between those with glaucoma and those without (control and OHT) is similar to the difference in IOP between POAG and control subjects in large population-based studies.[8,9] In addition, a difference of 4 mm Hg in IOP can mean the difference between stability and progression of glaucoma.[10–12]

The present study confirmed observations from our previous study that ICP is lower in POAG patients compared with a nonglaucomatous control group.[4] Mean ICP of the POAG group was no different between the previous dataset and the current dataset. No difference in mean ICP was found between controls in the previous dataset and controls in the current dataset (Fig. 3).

The present study also included OHT and NTG. We wondered whether elevated ICP in subjects with OHT would provide a protective effect for the optic nerve by decreasing the translaminar pressure difference. Using the raw data, a trend toward significance was found in ICP between OHT and control subjects (13.2 ± 3.8 mm Hg vs. 11.5 ± 3.3 mm Hg; $P = 0.06$). After using multivariate analysis to correct ICP based on variables predictive of ICP, a significant difference between ICP in OHT and controls was found (12.6 ± 0.85 mm Hg vs. 10.6 ± 0.81 mm Hg; $P < 0.05$). This suggests the elevated ICP in OHT may counterbalance the elevated IOP, potentially preventing or slowing glaucomatous optic nerve damage in this patient population (Table 4).

Conversely, a reduced ICP in patients with NTG may increase the risk of glaucoma compared with that in control subjects, which is supported by both the raw data and statistically adjusted

data. Even though the NTG sample number is low with only 11 subjects, this group had the lowest mean ICP, suggesting that a low ICP may be a risk factor for development of NTG.

Numerous studies have demonstrated that axonal transport is reduced at the lamina cribrosa in glaucoma.[13–17] Jonas et al.[7,18,19] have shown that the lamina cribrosa is thinner (201 μm vs. 457 μm) and posteriorly bowed in glaucomatous human eyes, suggesting that a posteriorly directed force acts on the lamina cribrosa. Of interest, it has been demonstrated that although peripheral nerves can withstand very high *absolute* pressures of 3800 mm Hg, pressure *gradients* of only 4.5 mm Hg/100 μm reduce axonal transport in rabbit nerves.[20,21] Although we were able to measure only the translaminar pressure difference (IOP − ICP; Fig. 2), we suggest that the translaminar pressure gradient (the pressure difference across a specific distance) acting across the lamina cribrosa in combination with the inherent structural and physiological properties of the lamina (thickness, rigidity, elasticity, and blood flow) may be fundamental to the pathogenesis of POAG and NTG. This notion may explain why only a small percentage of patients with OHT convert to glaucoma, despite a high translaminar pressure difference. One must keep in mind that IOP was measured in the sitting position and ICP was measured in the lateral decubitus position. Ideally, IOP and ICP would be measured simultaneously in a standard position; therefore, our calculated translaminar pressure difference is only a surrogate for the actual translaminar pressure difference. The posteriorly directed force generated by a pressure difference across the lamina cribrosa may explain why the lamina cribrosa is bowed posteriorly in glaucoma. However, recent data indicate that the lamina is actually thicker (but still posteriorly displaced) at the earliest detectable stage of experimental glaucoma in monkeys. [22,23]

Cerebrospinal fluid dynamics are not well understood. The CSF pressure as assessed by lumbar puncture correlates with ICP; therefore, we have used the terms ICP and CSF pressure interchangeably, as is done in clinical practice.[5] However, ICP specifically refers to pressure within the cranial vault, whereas the more general term CSF pressure represents pressures throughout the central neuroaxial system. Both ICP and CSF pressure represent a column of fluid, therefore positional changes have a significant effect on the retrolaminar CSF pressure and subsequently change the translaminar pressure difference. [24–26] Positional changes are also known to affect IOP.[27–29] Furthermore, the orbital tissue pressure may transmit pressure forces that influence the retrolaminar CSF pressure. [30,31] It is possible, though difficult to explain, that optic nerve damage leads to a feedback mechanism that lowers ICP. If this were that case, lower ICP would be a downstream effect of glaucomatous damage and not a potential cause. This mechanism would also explain why ICP is not low in OHT subjects. We also found that nonspecific protein concentrations were lower in both POAG and NTG. Our retrospective design did not allow further pursuit of this finding; however, it is possible that optic nerve damage leads to a reduction in specific proteins or that a deficiency in specific proteins within the CSF may lead to or augment glaucomatous damage.

Several limitations exist within our study. “Snapshot” measurements of IOP and ICP likely do not represent the long-term pressure variations in either the eye or the subarachnoid space. Therefore, interpretation of the data can only be correlative, since changes in IOP or ICP over time may affect the development and progression of glaucoma. In addition, NTG and POAG subjects had characteristic glaucomatous changes to the optic nerve; however, we analyzed data using the documented cup-to-disc ratio which has known limitations.[32,33] Contrary to our previous study,[4] linear regression analysis showed that cup-to-disc ratio did not correlate with IOP, ICP, or the translaminar pressure difference. The lack of correlation may be the result of using IOP to categorize patients into POAG, NTG, OHT or control groups. Also, we were not able to correlate disease severity with ICP. Obviously, a prospective study would eliminate many of these concerns and allow us to characterize the ophthalmic examination and the patient population more precisely.

In summary, our data show that ICP is lower in POAG and NTG and higher in OHT compared with the control level. ICP may play an important role in the development of POAG and NTG and in preventing the progression of OHT to POAG. Analyses of other datasets and examination of this phenomenon in experimental models would be helpful to elucidate possible disease mechanisms. Although potentially controversial, a prospective human study would provide the most definitive means to confirm or refute the findings presented in this retrospective study.

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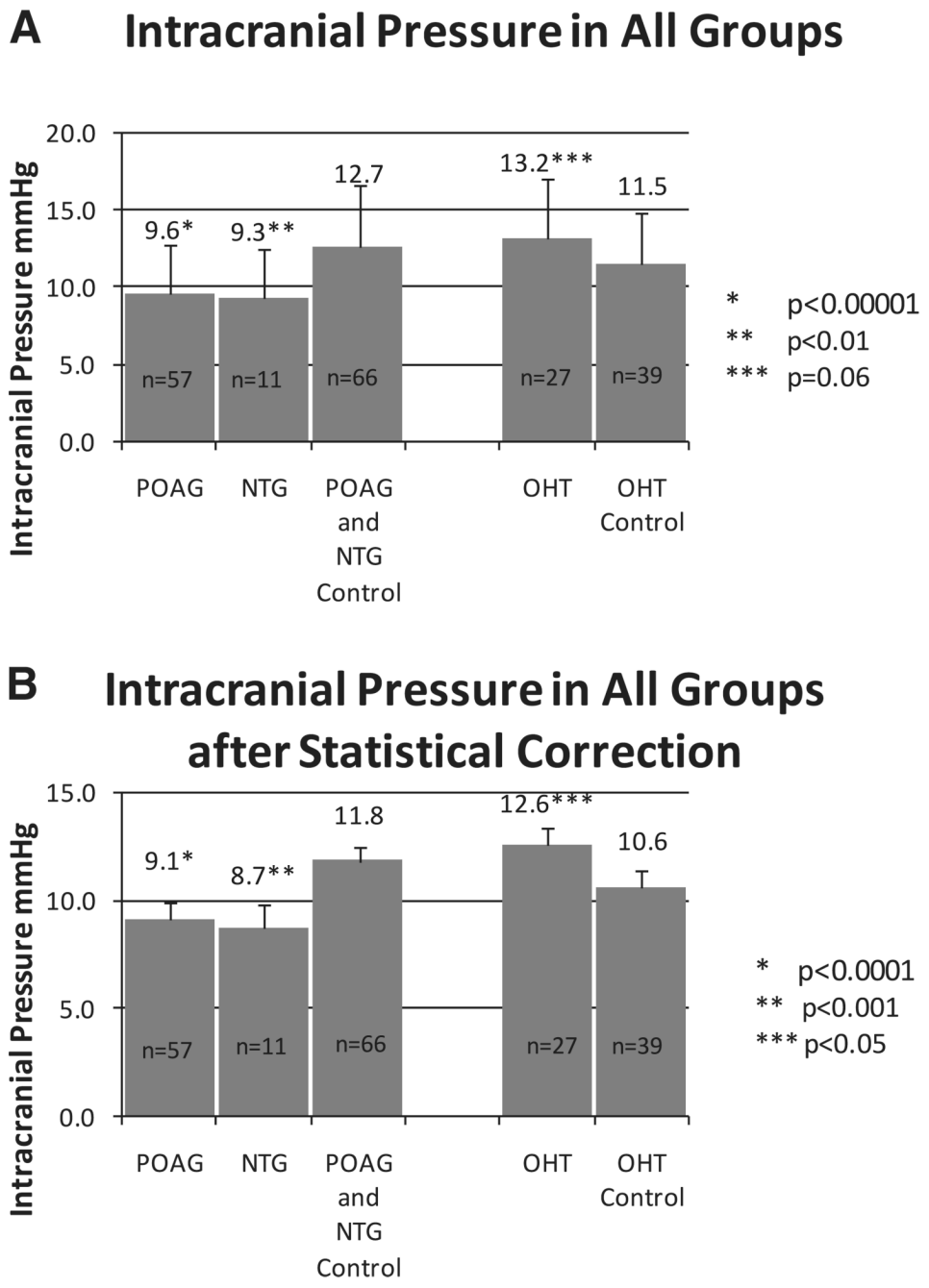

FIGURE 1.

(**A**) Uncorrected intracranial pressure in all groups. (**B**) After correction of the mean ICP of each group for variables predictive of ICP, the significant difference between POAG, the NTG subset and controls persisted and a significant difference between OHT and the control became apparent.

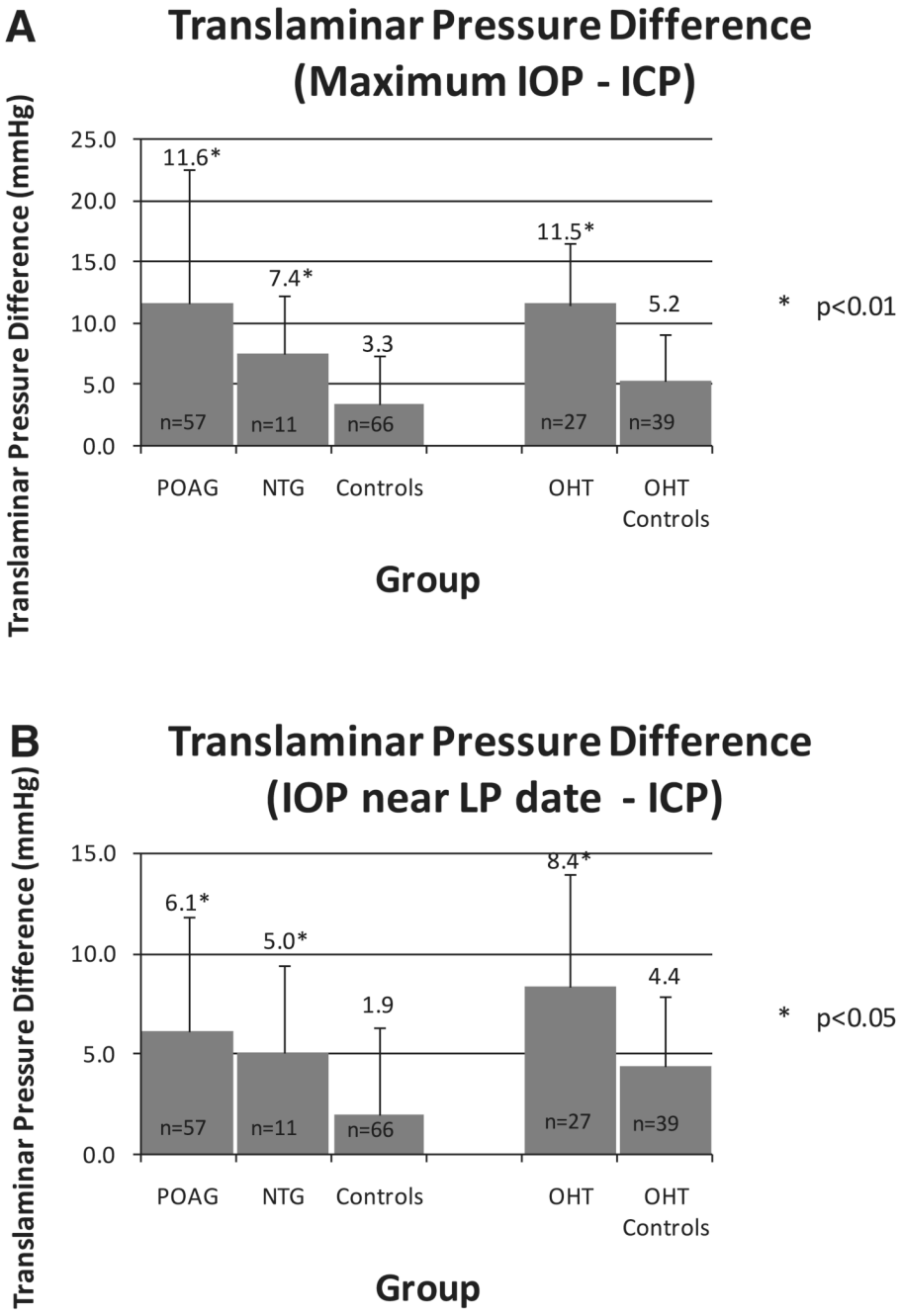

FIGURE 2.

The translaminar pressure difference (TLPD) was higher in POAG, the NTG subset, and OHT. TLPD was calculated by subtracting ICP from maximum IOP (**A**) and by subtracting ICP from IOP (**B**) near the time of LP.

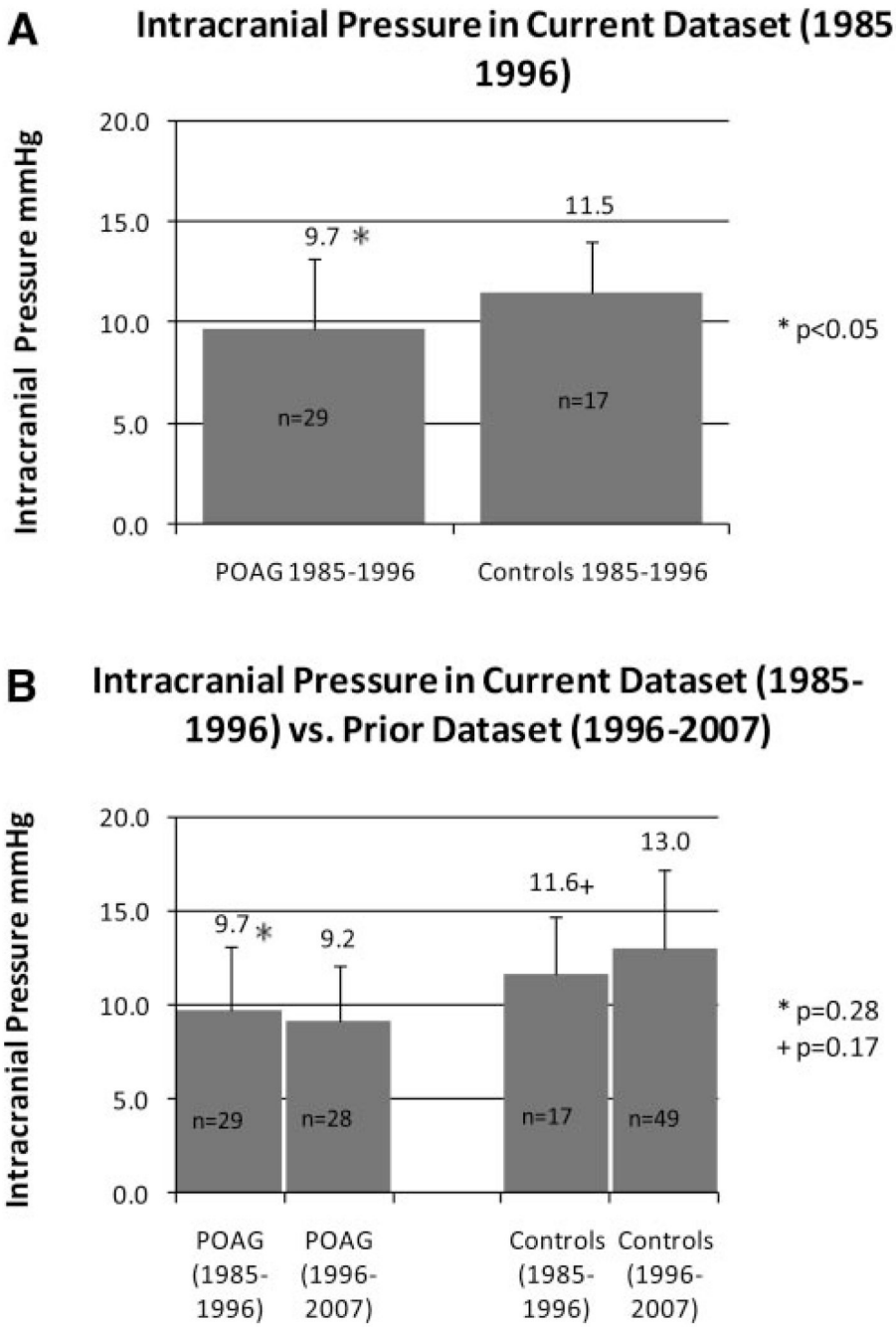

FIGURE 3.

(**A**) ICP comparison in the current dataset. (**B**) ICPs in the current dataset (1985–1996) compared with those in the previous dataset (1996–2007).

TABLE 1

Inclusion Criteria

	POAG (Include NTG)	NTG (Subset of POAG)	Age-Matched Control for POAG and NTG	OHT	Age-Matched Control for OHT
Total identified	233	69	746	97	734
Total excluded	176	58	680	70	695
Reason for exclusion					
No ICP	98	34	253	36	232
Did not meet eye criteria	70	21	10	25	17
Abnormal CSF, PMH, or PSH	8	3	21	9	23
Did not meet age criterion	0	0	396	0	423
Total included	57	11	68	27	39

Data are the number of patients and control subjects.

TABLE 2

Patient Characteristics

	POAG (Includes NTG)	*P* vs. Age-Matched Control	NTG (subset of POAG)	*P* vs. Age-Matched Control	Age-Matched Control for POAG and NTG	OHT	*P* vs. Age-Matched Control	Age-Matched Control for OHT
n	57		11		86	27		39
Males	24 (42)	0.716	3 (27)	0.329	31 (47)	15 (56)	0.617	18 (46)
Females	33 (58)	0.716	8 (73)	0.329	35 (53)	12 (44)	0.617	21 (54)
Age, y (±SD)	70.5 (±12.9)	0.242	68.0 (±17.1)	0.960	68.2 (±8.6)	55.4 (±18.6)	0.926	55.0 (±11.3)
Indication for lumbar puncture								
Altered mental status	24 (42)	0.084	7 (64)	0.029	17 (26)	9 (33)	0.006	2 (5)
Headache	9 (16)	0.013	2 (18)	0.718	18 (27)	8 (30)	0.783	10 (26)
Meningitis	4 (7)	0.379	0 (0)	0.593	8 (12)	1 (4)	0.639	3 (8)
Normal pressure hydrocephalus	4 (7)	0.703	0 (0)	1.000	3 (5)	0 (0)	0.509	2 (5)
Seizure	0 (0)	0.081	0 (0)	1.000	5 (8)	0 (0)	0.134	4 (10)
Stroke	2 (4)	1.000	1 (9)	0.467	3 (5)	2 (7)	0.563	1 (3)
Peripheral neuropathy	3 (5)	0.711	0 (0)	1.000	6 (9)	3 (11)	0.504	8 (21)
Radiculopathy	5 (9)	0.732	0 (0)	1.000	4 (6)	2 (7)	1.000	3 (8)
Carcomatosis	2 (4)	0.596	0 (0)	1.000	1 (2)	0 (0)	1.000	1 (3)
Herpes zoster	1 (2)	0.463	0 (0)	1.000	0 (0)	0 (0)	1.000	0 (0)
Eye medications								
β-Blocker	25 (44)	<0.001	5 (45)	<0.001	0 (0)	4 (15)	0.024	0 (0)
Prostaglandin	17 (30)	<0.001	4 (38)	<0.001	0 (0)	3 (11)	0.064	0 (0)
α-Agonist	9 (16)	<0.001	0 (0)	1.000	0 (0)	2 (7)	0.164	0 (0)
Carbonic anhydrase inhibitor	2 (4)	0.212	0 (0)	1.000	0 (0)	0 (0)	1.000	0 (0)
Other eye drops	10 (18)	<0.001	1 (9)	0.143	0 (0)	3 (11)	0.064	0 (0)
Prednisolone	0 (0)	0.499	0 (0)	1.000	2 (3)	0 (0)	1.000	0 (0)
Glaucoma surgery	12 (21)	<0.001	3 (27)	0.002	0 (0)	0 (0)	1.000	0 (0)
Medical history								
Diabetes	12 (21)	0.644	2 (18)	1.000	11 (17)	4 (15)	0.705	4 (10)
Hypertension	19 (33)	0.101	2 (18)	0.100	32 (48)	10 (37)	0.095	7 (18)
Stroke	3 (5)	1.000	1 (9)	0.467	5 (8)	2 (7)	0.563	0 (0)
Systemic medications								

	POAG (Includes NTG)	*P* vs. Age-Matched Control	NTG (subset of POAG)	*P* vs. Age-Matched Control	Age-Matched Control for POAG and NTG	OHT	*P* vs. Age-Matched Control	Age-Matched Control for OHT
Diuretic	9 (16)	0.608	4 (36)	0.063	8 (12)	5 (19)	0.749	6 (15)
β-Blocker	17 (30)	0.688	4 (36)	0.471	17 (26)	3 (11)	1.000	5 (13)
Ace inhibitor	12 (21)	0.644	4 (36)	0.210	11 (17)	2 (7)	0.290	7 (18)
Other antihypertensive	9 (16)	0.644	0 (0)	0.410	8 (12)	0 (0)	0.691	1 (3)
Prednisone	2 (4)	0.284	0 (0)	0.585	6 (9)	4 (15)	0.707	4 (10)

Unless indicated otherwise, data are number of subjects (%).

TABLE 3

Study Parameters in Patients with POAG or NTG and Control Subjects

	POAG (Including NTG)	*P* vs. Age-Matched Control	NTG (Subset of POAG)	*P* vs. Age- Matched Control	Age-Matched Controls for POAG and NTG
n	57		11		66
CSF Glucose (mg/dL)	65.1 ± 23.0	0.616	67.6 ± 14.5	0.659	62.2 ± 38.1
CSF Protein (mg/dL)	58.1 ± 23.0	0.038	45.5 ± 22.6	0.014	68.1 ± 28.2
Time between eye exam and LP (months)	14.2 ± 26.6	0.701	24.6 ± 42.9	0.160	12.3 ± 20.7
IOP near the time of LP OD (mm Hg)	15.2 ± 4.0	0.518	14.9 ± 3.0	0.871	14.8 ± 2.9
IOP near the time of LP OS (mm Hg)	15.5 ± 5.1	0.401	13.7 ± 3.1	0.290	14.8 ± 3.2
Maxmum IOP OD (mm Hg)	22.2 ± 6.4	0.000	17.3 ± 2.7	0.171	16.1 ± 2.7
Maxmum IOP OS (mm Hg)	22.6 ± 6.8	0.000	16.2 ± 2.4	0.862	16.4 ± 3.1
Cup-to-disk Ratio OD	0.7 ± 0.2	0.000	0.8 ± 0.1	0.000	0.3 ± 0.1
Cup-to-disk Ratio OS	0.7 ± 0.2	0.000	0.7 ± 0.2	0.000	0.3 ± 0.1
Visual field severity OD	3.6 ± 1.5		6.0 ± 1.5		
Visual field severity OS	3.3 ± 1.6		5.1 ± 2.2		

TABLE 4

Study Parameters in Patients with OHT and Control Subjects

	OHT	*P*	Age-Matched Control for OHT
n	27		39
CSF Glucose (mg/dL)	68.7 ± 25.7	0.483	64.7 ± 19.5
CSF Protein (mg/dL)	58.1 ± 24.9	0.361	52.3 ± 25.1
Time between eye exam and LP (months)	14.9 ± 25.2	0.975	15.1 ± 31.7
IOP near the time of LP OD (mm Hg)	20.9 ± 4.3	0.000	16.1 ± 2.2
IOP near the time of LP OS (mm Hg)	22.2 ± 4.0	0.000	15.7 ± 2.5
Maxmum IOP OD (mm Hg)	24.2 ± 4.5	0.000	16.7 ± 2.4
Maxmum IOP OS (mm Hg)	25.1 ± 3.6	0.000	16.8 ± 2.7
Cup to Disk Ratio OD	0.3 ± 0.1	0.887	0.3 ± 0.1
Cup to Disk Ratio OS	0.3 ± 0.1	0.558	0.3 ± 0.1
Visual Field Severity OD	0.7 ± 0.6		
Visual Field Severity OS	0.8 ± 0.6		