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PERIPAPILLARY ALTERATIONS IN IDIOPATHIC NORMAL PRESSURE HYDROCEPHALUS

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Purpose: To evaluate the peripapillary area in eyes of patients with idiopathic normal pressure hydrocephalus (iNPH) before and after shunt surgery.

Methods: Twenty patients with iNPH were prospectively recruited. Enhance depth imaging-optical coherence tomography (EDI-OCT) was performed to image the peripapillary region. Using a 360° 3.4 mm diameter peripapillary circle scan, the peripapillary choroidal thickness was manually measured and compared with 20 healthy age-matched controls. Peripapillary choroidal thickness was assessed before and after at least 6 months from ventriculoperitoneal shunt surgery in 12 patients.

Results: Mean age of patients with iNPH was 75 ±7.4 years, and 45% were females. Mean peripapillary choroidal thickness was increased in patients with nonshunted iNPH compared with healthy individuals (113 ± 39 vs. 82 ± 43 μm, $P = 0.026$). Also, OCT scans in the peripapillary region showed a set of recurrent alterations, such as subclinical optic disc edema (30%), choroidal folds (40%) peripapillary intraretinal cysts (30%), peripapillary atrophy (85%), peripapillary pigment epithelium alterations (45%), and pachyvessels (70%). After 79 ± 29 weeks from ventriculoperitoneal shunt surgery, 84% (10 out of 12) of patients with iNPH presented a reduction in peripapillary choroidal thickness (111 ± 47 vs. 95 ± 49, $P = 0.011$). This reduction was associated with a subjective improvement of the neurologic symptoms in 9 out of 10 of patients, and resolution of optic disc edema (75%), intraretinal cysts (66%), and choroidal folds (20%).

Conclusion: The ophthalmologic findings observed in patients with iNPH may be attributed to a framework of venous overload choroidopathy. Shunt surgery relieved peripapillary choroidal congestion, leading to improvements in OCT parameters.

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Idiopathic normal pressure hydrocephalus (iNPH) is a neurologic disorder characterized by the gradual development of gait impairment, cognitive decline, and urinary incontinence.[1] It is most commonly observed in the elderly population, with a prevalence ranging from 0.2% to 6% in patients older than 70 years.[2] The syndrome's hallmarks are ventricular dilation at neuroimaging in the context of normal intracranial pressure (ICP). The main pathophysiology responsible for iNPH is a reduction in cerebrospinal fluid (CSF) absorption, secondary to impaired conductance from the ventricles or impaired CSF resorption across the arachnoid granulations.[3] Surgical treatment consists of CSF shunting to alleviate symptoms resulting from enlarged ventricles, and ventriculoperitoneal (VP) shunt is the widest surgical procedure performed, achieving a success rate of up to 85%.[4–6]

Previous studies demonstrated an increased superficial venous pressure and a subsequent reduced venous drainage secondary to ventricular dilation in iNPH, occurring within the context of impaired CSF dynamics.[7–9] Using spectral domain-optical coherence tomography (OCT), we recently observed an increased subfoveal choroidal thickness and total choroidal area in the macula of patients with iNPH when compared with healthy individuals, suggesting that increased venous pressure may result in increased pressure in the vortex veins and subsequently in decreased venous outflow from the choroid, thus potentially leading to choroidal congestion.[10]

Several ocular diseases appear to be associated with venous outflow problems in the choroid, including central serous chorioretinopathy, peripapillary pachychoroid syndrome (PPS), and spaceflight-associated neuro-ocular syndrome (SANS). These conditions are marked by chronic venous insufficiency, causing enlargement of choroidal vessels, elevated pressure within the capillaries, and subsequent leakage and damage to the overlying retina. The term "venous overload choroidopathy" has been proposed to define the underlying pathogenesis of these disorders, which share a common set of ocular abnormalities.[11,12]

In venous overload choroidopathies, both the macula and the peripapillary region present alterations, including choroidal folds, disc edema, and peripapillary intraretinal cysts.[11,12] Hence, assessing the peripapillary area in iNPH may provide insights into the optic nerve response and adjacent structure to impaired CSF reabsorption and choroidal congestion. In addition, it might serve as an important tool for assessing the response to shunt surgery. Therefore, the present study aimed to examine the peripapillary region in patients with iNPH before and after VP shunt surgery and to compare the results with a group of age-matched healthy individuals.

Methods

Study Population

The present prospective study was performed at the Unit of Ophthalmology, University of Bologna, in collaboration with the multidisciplinary PRO-HYDRO study group. Patients were recruited between November 2021 and October 2023. The study adhered to the tenets of the Declaration of Helsinki, and it was approved by the Ethics Committee of Bologna, Italy (Cod CE: 809/2021).

The multidisciplinary group reviewed the medical charts and the available brain images of suspected patients with iNPH.[13] Eligible patients underwent brain magnetic resonance imaging, and they were assessed during an outpatient visit. Patients showing clinical symptoms and neuroimaging findings consistent with iNPH were included in the inpatient program and underwent CSF tap-test. The CSF tap-test is a diagnostic procedure performed in patients with iNPH that consists in removing 30 mL to 50 mL of CSF via a lumbar puncture[14] The CSF opening pressure was measured at the time of the lumbar puncture. Subsequently, during a consensus case conference, the multidisciplinary group established the diagnosis of "probable" iNPH and determined which patients were suitable candidates for VP shunt surgery.[15] Patients diagnosed with "probable" iNPH and indicated for VP surgery underwent ophthalmologic assessments both before and after shunt surgery at the Unit of Ophthalmology, University of Bologna.

The main objective of the present study was to assess the peripapillary area using spectral domain-OCT and to measure the peripapillary choroidal thickness (PPCT) and retinal nerve fiber layer (RNFL) thickness, comparing the results with healthy individuals. The secondary objective was to compare the peripapillary area, PPCT, and RNFL in patients with iNPH before and after a follow-up of at least 6 months from VP shunt surgery.

We excluded patients with a previous history of retinal detachment, uveitis or vitreoretinal diseases, ocular trauma, advanced cataract, age-related macular degeneration, corneal surgery, diabetic retinopathy, and an axial length $>$26 mm and $<$21 mm. A previous diagnosis of glaucoma or ocular hypertension was considered an exclusion criterion, as previous studies found a reduced PPCT in this population of patients.[16] We included a control group with ages ranging between 65 years and 85 years, selected using the identical exclusion criteria outlined for the iNPH group.

Clinical Assessment

A comprehensive ophthalmologic evaluation was performed before and after VP shunt surgery, including assessment of best-corrected visual acuity, refraction, slit-lamp examination, Goldmann applanation tonometer, cataract grading, and indirect

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ophthalmoscopy.[17] Axial length was assessed using the IOLMaster 700 (Carl Zeiss Meditec AG, Jena, Germany).

Optical Coherence Tomography Images Acquisition

All OCT assessments were conducted using the Heidelberg Spectralis spectral domain-OCT (Heidelberg Engineering, Heidelberg, Germany). Acquisitions were performed between 13.00 and 15.00. For the assessment of the peripapillary region, radial scans with multiple lines were centered on the optic disc (20°, 12-line, 16 automatic real-time). Data were retrospectively analyzed at the end of the study. Two readers (N.V., M.E.) conducted the qualitative evaluation of the OCT scans. In instances of disagreement, a third reader (M.R.) was consulted to make the final decision. To assess the PPCT, we used a standard protocol for RNFL evaluation, using a 360° 3.4 mm diameter peripapillary circle scan, as previously described.[18] The PPCT was measured manually from the hyperreflective line corresponding to the retinal pigment epithelium (RPE) to the inner surface of the sclera, at the center of the temporal, superior, nasal, and inferior segments. Two trained graders (M.E. and M.N.R.) performed the measurements, blinded to patients' characteristics. Measurements from the main reader (M.E.) were used for the analysis, and those from the second reader (M.N.R.) were used to calculate the intergrader agreement. We included in the study the eye with the best resolution from each patient with iNPH before and after shunt surgery to ensure precise measurements of the PPCT. The RNFL thickness was assessed using the same peripapillary circle scan for the same eye before and after shunt surgery.

Statistical Analysis

Normality was assessed using the Shapiro–Wilk test, and parametric tests were used for the analysis. Pearson correlation was used to assess the correlation between the PPCT measurements of the two eyes of the same patient. The inter-rater reliability was assessed using the intraclass correlation coefficient. The chi-square test was used for the analysis of categorical variables. *T*-test was used to compare demographic data, PPCT, and RNFL between iNPH and healthy patients. A paired *t*-test was used to compare PPCT, RNFL, spherical equivalent, and axial length after shunt surgery. *P* values <0.05 were considered statistically significant. Statistical analysis was performed using International Business Machines (IBM) ped Statistical Package for Social Sciences version 26.

Results

Demographic Data

Twenty eyes of 20 patients with iNPH were included, 12 right eyes (60%) and 8 left eyes (40%). Demographic data are reported in Table 1.

Ophthalmologic Findings

None of the patients reported any subjective visual disturbances at the time of the visit or in the previous months, and no evident alterations were observed at the fundoscopy examination. However, the OCT assessment revealed the presence of subclinical optic disc edema (ODE) in 6/20 of patients (Frisen = 0 in five patients, Frisen = 1 in one patient, based on ophthalmoscopy[19]) (bilateral in 6/6 cases), peripapillary choroidal folds in 8/20 patients (bilateral in 7/8 patients), peripapillary atrophy of RPE and ellipsoid zone with a band of signal hyper transmission in 17/20 (bilateral in 14/17), peripapillary intraretinal cysts in the temporal side of the optic disc in 6/20 patients (bilateral in 1/6 patients), alterations of the RPE in the peripapillary region in 9/20, and pachyvessels in 14/20 patients. In three patients, choroidal folds were associated with subclinical ODE, whereas in five patients, they were observed as an isolated finding. All cases with intraretinal cysts were associated with peripapillary atrophy. Only one patient presented all the above-mentioned signs, and every patient presented at least one of the five clinical findings. No differences were observed according to the sex of patients. The OCT acquisitions were performed after a mean of 7 ± 2 weeks from the CSF tap test (Table 1, Figures 1 and 2).

Peripapillary Choroidal Thickness and Retinal Nerve Fiber Layer in Patients With Idiopathic Normal Pressure Hydrocephalus Versus Healthy Age-Matched Individuals

The mean PPCT was significantly increased in patients with nonshunted iNPH compared with controls before shunt surgery ($P = 0.026$, difference of 31 μm). The difference was statistically significant in every sector except for the inferior sector ($P = 0.157$). No statistically significant differences in RNFL thickness were observed in each sector between patients with iNPH and controls (Table 2 and Figure 3).

Assessment After Shunt Surgery

Twelve patients with iNPH underwent VP shunt surgery after a mean of 11.2 ± 11.5 weeks from the

Table 1. Clinical Data and OCT Findings are shown.

	Nonshunted iNPH (n = 20)
Clinical data	
Age, years, mean ± SD	75 ± 7.4
Sex females, n (%)	9 (45%)
Pseudophakic, number (%)	5 (25%)
Cataract, number (%)	6 (30%)
NO2–NC2	4 (20%)
NO3–NC3	2 (10%)
BCVA LogMar, mean (range)	0.1 (0.2–0)
SE, diopters, mean (range)	+0.15 (+2.25–1.75)
Axial length mm, mean ± SD	23 ± 1
IOP mmHg, mean ± SD	16.1 ± 3.6
ICP cmH_2O, mean ± SD	14.7 ± 5.2
Time from onset of neurologic symptoms and ophthalmologic assessment years, mean (SD)	3.1 ± 2.3
OCT findings	
Subclinical optic disc oedema, n (%)	6 (30%)
Bilateral	6 (100%)
Choroidal folds, n (%)	8 (40%)
Bilateral	7 (87%)
Peripapillary intraretinal cysts, n (%)	6 (30%)
Bilateral	1 (16%)
Peripapillary atrophy, n (%)	17 (85%)
Bilateral	14 (82%)
Peripapillary RPE alterations, n (%)	9 (45%)
Bilateral	5 (55%)

BCVA, best-corrected visual acuity; IOP, intraocular pressure; SE, spherical equivalent; ICP, incracranial pressure; OCT, optical coherence tomography.

first ophthalmologic assessment, and they were reevaluated after a mean of 79 ± 29 weeks from shunt surgery (range 27–134 weeks). None of the patients reported an improvement or worsening of visual functions after surgery. In one patient, choroidal folds resolved after shunt surgery; in two patients, intraretinal cysts were resolved at the follow-up assessment; in three patients, there was a resolution of the ODE. Overall, 84% (10 out of 12) of patients with iNPH presented a reduction in PPCT after shunt surgery, and the mean PPCT was reduced compared with the preoperative status ($P = 0.011$, difference of 16 μm). This reduction was statistically significant in all quadrants except for the inferior quadrant. Moreover, in 9 out of 10 patients (90%), the reduction of PPCT was associated with a subjective improvement of the neurologic symptoms. However, one over two patients without a reduction of the PPCT reported a subjective improvement of the neurologic symptoms ($P = 0.166$) (Table 3 and Figure 4). No differences in PPCT and RNFL were observed between shunted iNPH and controls (see **Table, Supplemental Digital Content 1**, http://links.lww.com/IAE/C534, which shows differences in OCT parameters between the two groups). The two readers had a good to excellent agreement in PPCT measurements in every sector (see **Table, Supplemental Digital Content 2**, http://links.lww.com/IAE/C535, which shows the intraclass correlation coefficient between the two graders). Also, we found a strong correlation when we compared the measurement of the two eyes of the same patients (r = 0.912, $P < 0.001$).

Discussion

The main result of the present study was that mean PPCT was increased in patients with nonshunted iNPH compared with controls. Also, OCT scans performed in the peripapillary region showed a set of recurrent alterations in patients with nonshunted iNPH as subclinical ODE (30%), choroidal folds (40%), peripapillary intraretinal cysts (30%), peripapillary atrophy (85%), peripapillary RPE alterations (45%), and pachyvessels (70%). Furthermore, we found that after VP shunt surgery, 84% of patients with iNPH presented a reduction in PPCT, associated with a subjective improvement of the neurologic symptoms in 90% of patients. Moreover, in one patient, choroidal folds were not visible after shunt surgery; in two patients, the intraretinal cysts were absent at the follow-up assessment; and in three patients, there was a resolution of the ODE.

The primary pathophysiologic factor responsible for iNPH is a decrease in CSF absorption.[20–22] Previous researches indicated that individuals with iNPH exhibit reduced intracranial superficial venous drainage, which consists of veins that primarily drain the cerebral cortex and the superficial white matter, and elevated venous pressure, resulting in decreased CSF absorption through the arachnoid granulations.[7–9] Furthermore, as aging progresses, intracranial compliance gradually diminishes, leading to stiffer CSF circulatory pathways and increased venous pressure.[23] Therefore, insufficient CSF absorption because of outflow resistance can result in CSF accumulation, further promoting ventricular dilatation driven by high CSF pulsatility in iNPH.[20] The present results support the hypothesis that increased intracranial venous pressure in iNPH may result in decreased venous outflow from the choroid, with subsequent retrograde increased pressure in the vortex veins, thus potentially leading to choroidal congestion. These findings are consistent with our previous study reporting increased total macular choroidal area and subfoveal choroidal thickness in iNPH eyes.[10]

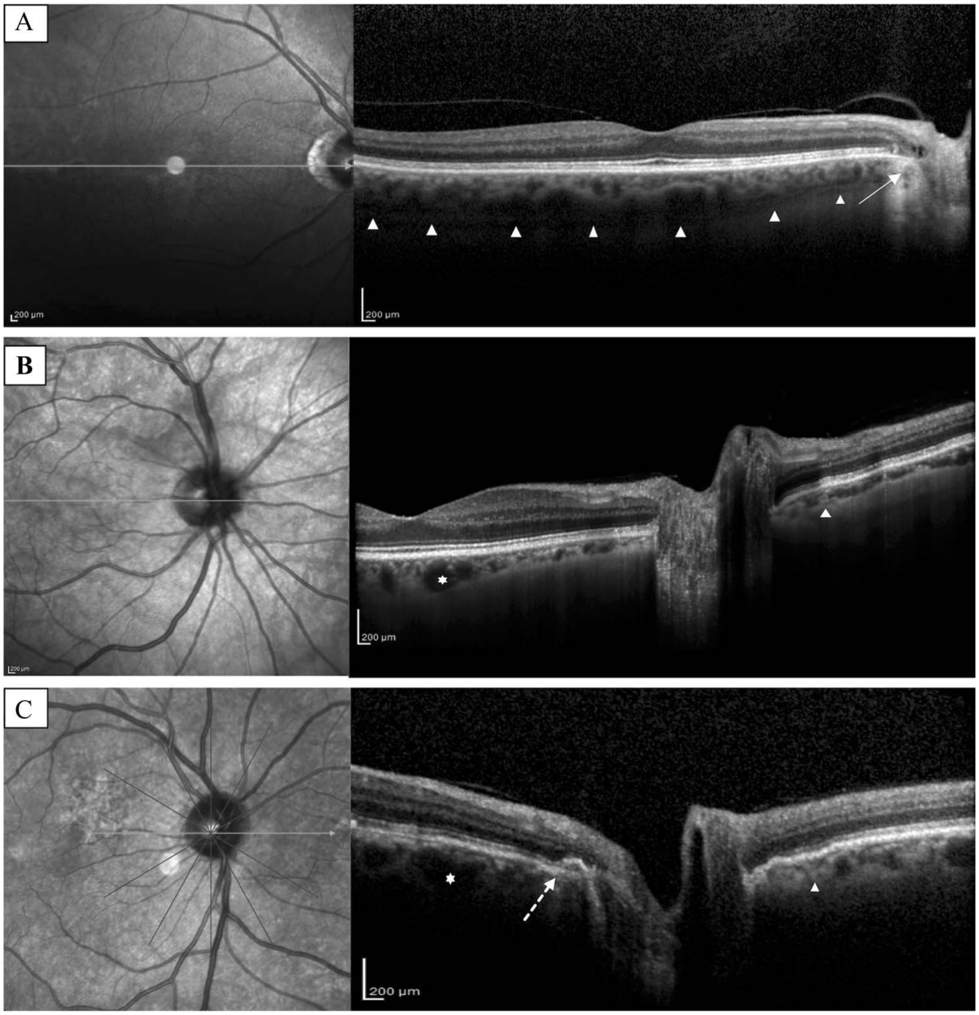

Fig. 1. Representative examples of peripapillary alterations in patients with iNPH before shunt surgery. **A.** Right eye of a 73-year-old man before shunt surgery. Note the peripapillary intraretinal cysts (white arrow) above the peripapillary retinal atrophy. Choroidal thickness with pachyvessels is outlined with white arrowheads. **B.** Right eye of a 65-year-old woman before shunt surgery. Note the optic disc edema (ODE), the choroidal folds (white arrowhead), and the pachyvessel in the macula (white asterisk). **C.** Right eye of a 66-year-old man before shunt surgery. Note retinal pigment epithelium (RPE) alterations in the peripapillary temporal area (dashed white arrow), the choroidal folds in correspondence of the choroidal vessels (white arrowhead), and the pachyessel (white asterisk).

Also, we observed that VP shunt surgery determined a significant decrease in mean PPCT, indicating that interventions restoring CSF dynamics might alleviate choroidal congestion. Moreover, the reduction was associated with a subjective neurologic improvement in 90% of patients. Despite the limited number of patients, these findings highlight the role of OCT in the assessment of patients with iNPH and the response to shunt surgery. In a previous study, Afonso et al reported lower values of subfoveal choroidal thickness and PPCT in six patients with nonshunted iNPH compared with healthy controls.[24] Also, they reported higher values of PPCT and subfoveal choroidal thickness in six shunted iNPH compared with a different cohort of patients with nonshunted iNPH, and the analysis did not involve the same individuals both before and after shunt surgery.

Furthermore, the OCT findings observed in iNPH eyes exhibit numerous resemblances to other venous overload choroidopathies.[11] Despite sharing some OCT characteristics with those observed in iNPH, central serous chorioretinopathy is defined by the accumulation of subretinal fluid in the macula, typically occurring at a younger age and showing a male predominance. Also, choroidal folds and ODE are not commonly present in central serous chorioretinopathy. Peripapillary pachychoroid syndrome has been recently described by Phasukkijwatana et al as a clinical variant of central serous chorioretinopathy.[12] Overlapping characteristics between PPS and iNPH include the older age of patients, the presence of peripapillary intraretinal cysts, focal RPE atrophy at the disc margin, choroidal folds, and ODE. However, in iNPH, we did not observe a male predominance and subretinal fluid in the macula, which are common features in PPS.

Interestingly, the OCT peripapillary alterations that we reported in the eyes of patients with iNPH share similar features and possible common pathophysiologic mechanisms with SANS, a condition observed in

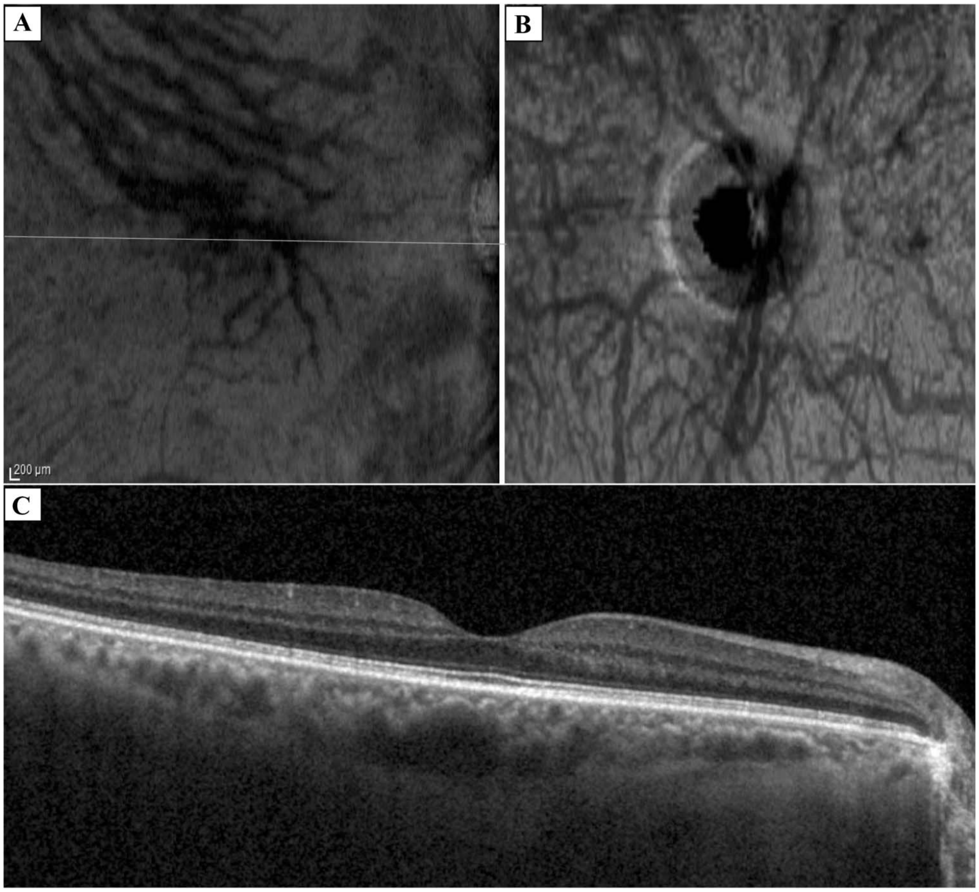

Fig. 2. En-face optical coherence tomography (OCT) in the right eye of a patient affected by iNPH before shunt surgery. **A.** Note the pachyvessels in the macula crossing the fovea. **B.** Note the choroidal vessels in the peripapillary region. **C.** Note the corresponding pachyvessels in the linear OCT scan passing through the fovea.

Table 2. Assessment of Patients With Nonshunted iNPH Compared With Healthy Controls

	iNPH Preshunt (n 20)	Healthy Controls (n 20)	*P*
Demographic data			
Age, mean ± SD	75 ± 7.4	77 ± 4.1	0.189
Sex female, n (%)	9 (45%)	11 (55%)	0.527
BCVA, mean (range)	0.1 (0.2–0)	0.1 (0.2–0)	0.874
Pseudophakic, number (%)	5 (25%)	4 (20%)	0.973
Variable	**Mean ± SD**	**Mean ± SD**	
PPCT, μm			
Mean	113 ± 39	82 ± 43	**0.026**
Superior	125 ± 41	92 ± 44	**0.024**
Inferior	115 ± 46	91 ± 54	0.157
Nasal	91 ± 31	64 ± 40	**0.031**
Temporal	119 ± 56	79 ± 53	**0.033**
RNFLs thickness, μm			
Mean	99 ± 14	97 ± 7	0.695
Temporal-superior	141 ± 27	129 ± 21	0.112
Temporal	72 ± 18	75 ± 10	0.640
Temporal-inferior	140 ± 24	139 ± 20	0.856
Nasal-superior	106 ± 18	106 ± 19	0.699
Nasal-inferior	107 ± 28	112 ± 19	0.539
Nasal	74 ± 18	73 ± 10	0.850

BCVA, best-corrected visual acuity.

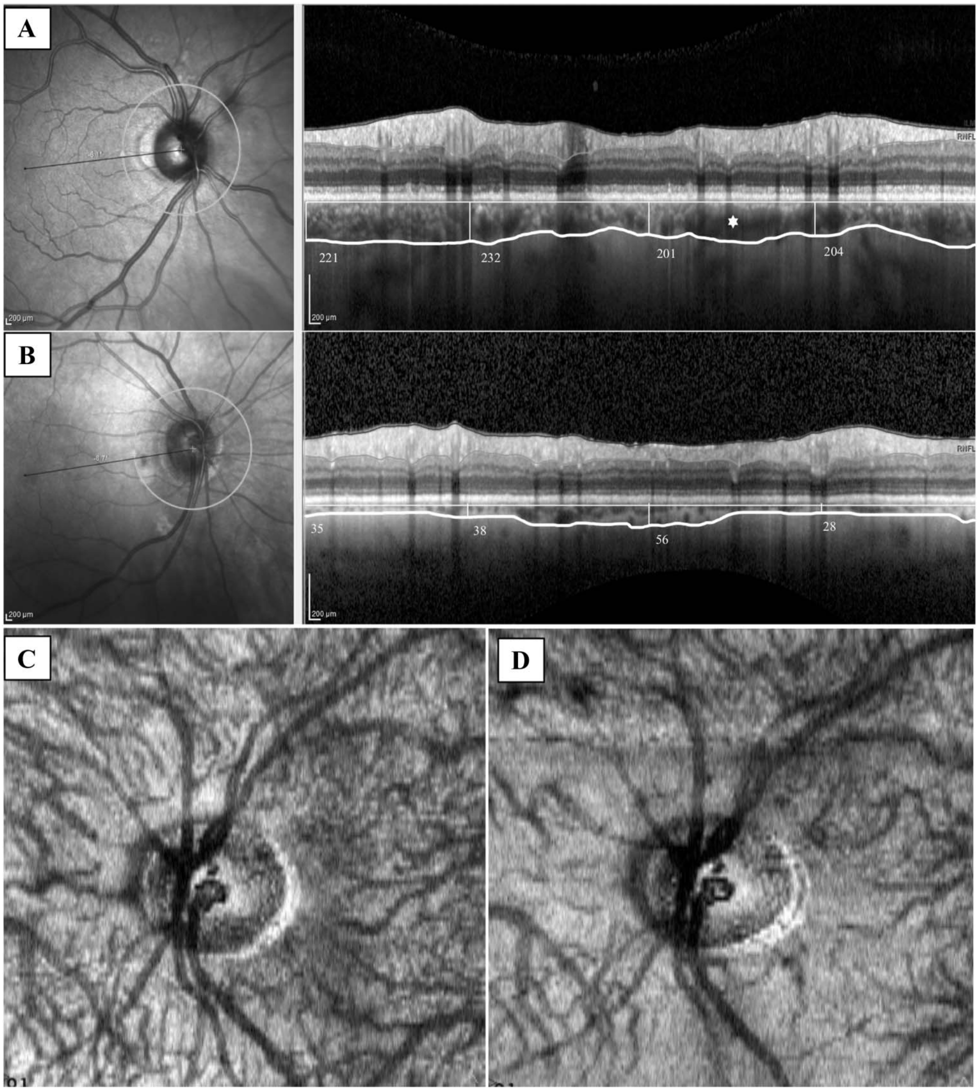

Fig. 3. Peripapillary choroidal thickness (PPCT) assessment. **A.** Right eye of a 72-year-old woman affected by iNPH before shunt surgery. The PPCT is shown for the different quadrants. Note the pachy-vessels (white asterisk). **B.** Right eye of a 73-year-old healthy woman. The PPCT is reduced compared with the patient with iNPH. **C.** En-face OCT angiography of the left eye of a 76-year-old man affected by iNPH before shunt surgery. Note the increased diameter of the choroidal vessels in the peripapillary area. The en-face image was taken with the optical coherence tomography angiography Optovue (Optovue Inc, Fremont, CA). Angio-disc 6 × 6 mm. Upper RPE offset 115, lower RPE offset 71, thickness 40. **D.** En-face optical coherence tomography angiography of the same eye after 13 months from shunt surgery. Note the reduction of the choroidal vessels after surgery. The image was taken with the same Optovue machine. Angio-disc 6 × 6 mm. Upper RPE offset 115, lower RPE offset 71, thickness 40.

astronauts during prolonged space missions.[25] Overlapping ocular findings between iNPH and SANS include the presence of peripapillary intraretinal cysts, peripapillary increased choroidal thickness, choroidal folds, and subclinical ODE in the absence of subretinal fluid in the macula.[25–27]

In SANS, the loss of hydrostatic pressure within the human body secondary to microgravity is thought to cause a cephalad fluid shift, resulting in venous stasis within the head and neck, altering normal CSF drainage.[28,29] It was hypothesized that elevated ICP was the primary cause of ODE.[30] However, further studies neither confirmed increased ICP in every case nor did they reveal the typical clinical presentation observed in intracranial hypertension.[31,32] Roberts et al, observed ventricular dilatation in patients with SANS following long-term missions in the absence of parenchymal atrophy, suggesting that SANS should be regarded as a form of normal pressure hydrocephalus.[32] However, despite certain resemblances between the two syndromes, iNPH is a progressive condition characterized by unique signs and symptoms that have not been observed in astronauts.[22]

As previously reported in PPS and SANS, peripapillary choroidal congestion might increase the hydrostatic pressure beneath the RPE, and the intraretinal cystic fluid may form through regions of peripapillary atrophy, determining a compartment-like effect on the peripapillary region.[12,32] These mechanisms might partially explain the presence of intraretinal cysts in iNPH eyes. In the present study, none of the patients presented increased values of ICP that could explain the presence of subclinical ODE. Thus, we believe that the subclinical ODE observed in iNPH was not

Table 3. Assessment of Patients With iNPH Before and After Ventriculo-Peritoneal Shunt Surgery

	iNPH Preshunt (n 12)	iNPH Postshunt (n 12)	*P*
Ophthalmologic assessment			
BCVA LogMar, mean (range)	0.1 (0.2–0)	0.1 (0.2–0)	0.934
IOP mmHg, mean ± SD	16.8 ± 3.5	16.5 ± 2.2	0.781
SE diopters, mean (range)	+0.25 (+2.25–1.75)	+0.50 (+2.25–1.75)	0.689
Axial length mm, mean ± SD	23.4 ± 0.6	23.4 ± 0.8	0.876
Variable	**n (%)**	**n (%)**	
Clinical findings			
Subclinical optic disc oedema	4 (33%)	1 (8%)	
Choroidal folds	5 (41%)	4 (33%)	
Intraretinal cysts	3 (25%)	1 (8%)	
PEDs	3 (25%)	4 (33%)	
Variable	**Mean ± SD**	**Mean ± SD**	
PPCT μm			
Mean	111 ± 47	95 ± 49	**0.011**
Superior	121 ± 47	99 ± 53	**0.039**
Inferior	117 ± 56	101 ± 58	0.096
Nasal	88 ± 37	78 ± 40	**0.019**
Temporal	119 ± 66	100 ± 66	**0.018**
RNFLs thickness μm			
Mean	99 ± 15	100 ± 10	0.773
Temporal-superior	142 ± 30	133 ± 13	0.245
Temporal	71 ± 17	71 ± 13	0.865
Temporal-inferior	141 ± 26	131 ± 27	0.095
Nasal-superior	105 ± 20	101 ± 23	0.304
Nasal-inferior	106 ± 25	118 ± 21	0.078
Nasal	74 ± 21	76 ± 19	0.238

BCVA, best-corrected visual acuity; IOP, intraocular pressure; SE, spherical equivalent; PED, pigment epithelial detachment.

secondary to increased ICP. In SANS and PPS, it has been proposed that choroidal congestion may contribute to the onset of ODE, determining a flow stasis within the prelaminar region of the optic nerve head. We hypothesize that the same mechanisms might also determine the presence of subclinical ODE in iNPH. In SANS, choroidal folds are thought to be secondary to choroidal expansion with hyperextension of choroidal collagen lamella, and they have been reported to persist for several years after the flight in certain crew members.[33,34] In patients with iNPH, we noted that the enlargement of choroidal vessels correlated with the occurrence of choroidal folds.

The key distinguishing feature between SANS and iNPH is that none of the patients with iNPH reported any visual disturbances. Also, it is noteworthy that the neuroradiologic presentation of iNPH does not include globe flattening, which is a feature of SANS and is considered one of the mechanisms responsible for the hyperopic shift; neither we found any significant difference in axial length and spherical equivalent before and after shunt surgery in patients with iNPH. In summary, despite recognizing the important differences between the two clinical conditions, SANS and iNPH seem to present similar ophthalmologic features, suggesting that potential common pathophysiologic mechanisms might be implicated in the alterations observed in the optic nerve and the papillary region.

The study's main limitation is the small cohort of patients. However, the cohort is well-documented for a rare condition. Moreover, we used only OCT scans to assess the peripapillary region, and multimodal imaging was not used in each patient. Further studies with a multimodal imaging approach will help to identify other signs of choroidal congestion and quantify the enlargement of the choroidal vessels in iNPH eyes, to confirm our findings. Also, the OCT acquisitions were performed after a mean of 7 weeks after the CSF tap test. As the daily CSF production is approximately 500 mL per day and the CSF tap test removes 30 mL to 50 mL of CSF, we believe that the effect of the CSF tap test might not have affected the values of ICP at the time of the OCT acquisitions.[35,36] Overall, our results indicate that OCT could serve as a valuable noninvasive tool for assessing patients with iNPH. Additional research is required to explore the potential of OCT for assessing patients with iNPH before and following shunt insertion and to investigate its utility as an adjunctive tool for predicting shunt response. Also, peripapillary choroidal congestion has been linked to visual impairment, including formation of intra- and subretinal fluid in the macula and

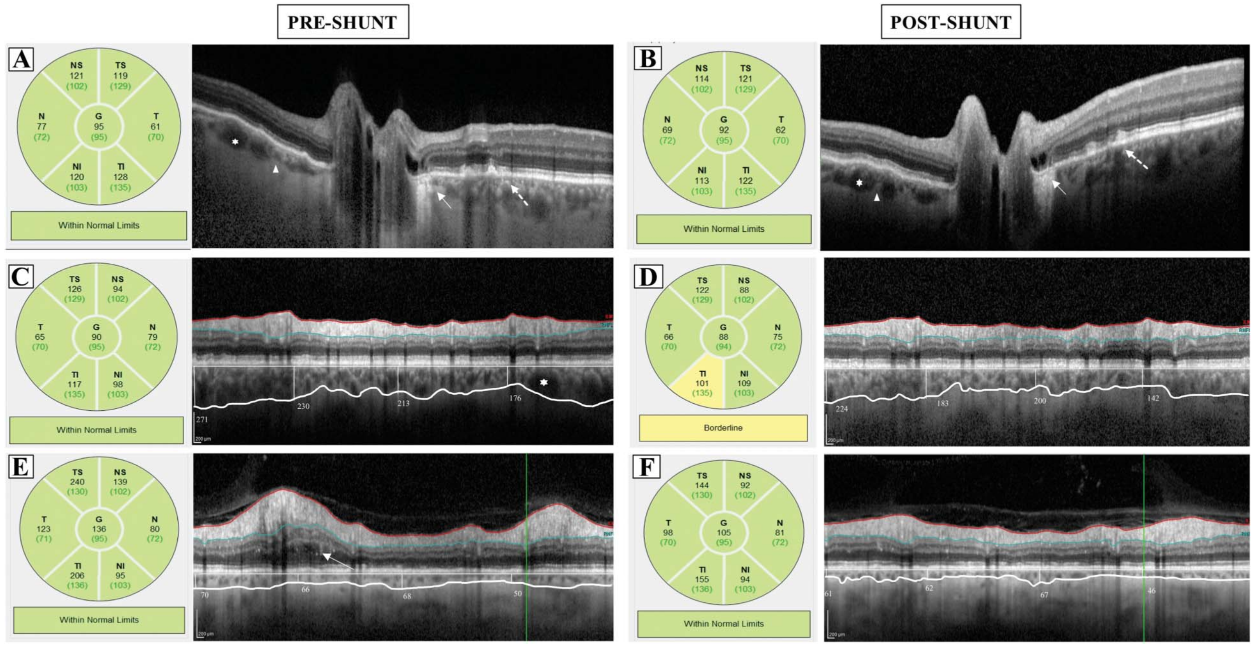

Fig. 4. Patients with iNPH before and after VP shunt surgery. **A.** Left eye of a 75-year-old man before shunt surgery. The patient presented with mild ODE, choroidal folds (white arrowhead), and pachyvessels (white asterisk). Note the peripapillary intraretinal cysts (white arrow) above the peripapillary retinal atrophy and RPE alterations in the peripapillary temporal area (dashed white arrows). The values of the RNFL thickness are shown. **B.** After 23 months from shunt surgery, there was a mild reduction of the ODE, but the choroidal folds and the pachyvessels were present (white arrowhead and white asterisk, respectively). Moreover, there was a reduction of the intraretinal cysts (white arrow). Note the RPE alterations in the peripapillary temporal area (dashed white arrows). There was no reduction of the PPCT after surgery, and the patient did not refer a subjective improvement of the neurologic symptoms (PPCT preshunt 212 μm. PPCT postshunt 213 μm). **C.** The right eye of a 68-year-old woman before shunt surgery. Note the pachyvessel (white asterisk). **D.** After 11 months from shunt surgery, there was a reduction of the PPCT, and the pachyvessel was not visible. The patient reported a subjective improvement of the neurologic symptoms. Also, there was a mild reduction of the RNFL thickness after surgery. **E.** The right eye of a 70-year-old-man before shunt surgery. Note the ODE with intraretinal cysts (white arrow). **F.** After 35 weeks from shunt surgery, there was a reduction of the ODE and RNFL thickness, a resolution of the intraretinal cysts, and a reduction of the PPCT. The patient reported a subjective improvement of the neurologic symptoms.

development of nonarteritic ischemic optic neuropathy.[12,37] Therefore, further studies with a larger cohort are needed to determine whether the choroidal congestion observed in iNPH is associated with visual alterations.

Conclusions

We described for the first time peripapillary alterations in patients with iNPH as increased PPCT, subclinical ODE, choroidal folds, peripapillary intraretinal cysts, peripapillary atrophy, and pachyvessels. We hypothesized that these findings could be the epiphenomenon of a "venous overload choroidopathy" since they might arise from chronic choroidal venous congestion in the context of impaired CSF dynamics. We observed that PPTC was reduced after shunt surgery, suggesting that interventions restoring CSF dynamics might alleviate choroidal congestion. Also, PPCT reduction after shunt was associated in 90% of patients with a subjective improvement of symptoms, suggesting that OCT might be a potential tool for noninvasively assessing the response to shunt surgery. Interestingly, iNPH ophthalmologic alterations present similarities with SANS, reflecting analogies in the pathophysiologic mechanisms between the two disorders. These findings may spark interest in understanding whether iNPH could serve as a model for studying potential ophthalmologic complications resulting from long-term exposure to microgravity environments and vice versa.

Key words: iNPH, shunt surgery, peripapillary choroid, choroidal congestion, spaceflight associated neuro-ocular syndrome.

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