REVIEW

Idiopathic intracranial hypertension: expanding our understanding

Keira Markey[a,b], *Christopher Hutchcroft*[b] *and Hedley Emsley*[a,b]

Purpose of review
Idiopathic intracranial hypertension (IIH) affects predominantly overweight women of childbearing age, causing chronically-disabling headaches and visual loss. Weight loss remains the most effective management strategy, but innovative treatments and randomized control trials (RCTs) remain few. This paper will review recent IIH research.

Recent findings
Pregnancy-related complications, but not losses, are increased in IIH, while symptom severity is not affected. Weight loss of 24% results in normalization of intracranial pressure (ICP) and improvement in papilledema. Prolonged periods of papilledema result in delayed thinning of the ganglion cell layer. Less-invasive telemetry has improved understanding of the positional effects on ICP with rises seen in the supine and lateral positions. Exenatide, a GLP-1 agonist, may reduce ICP and improve symptoms. Venous sinus stenting is increasingly popular but its benefits over CSF diversion remain unclear.

Summary
Early involvement of obstetric care is recommended with pregnancy in IIH. Early intervention is required to avoid chronic papilledema that confers worse visual outcomes. Positional changes may affect ICP readings. The use of novel ICP telemetric devices has significant potential in future disease monitoring. The dual benefits of weight loss and ICP reduction with exenatide have significant potential in IIH management. Surgical RCTs are still required.

Keywords
headache, idiopathic intracranial hypertension, intracranial pressure, obesity, papilledema

INTRODUCTION

Idiopathic intracranial hypertension (IIH) typically presents in women of childbearing age with visual disturbances, papilledema and headaches resulting from raised intracranial pressure (ICP) of unknown cause. Obesity is strongly associated with IIH development but for mechanistically unclear reasons. Secondary causes of intracranial hypertension include space-occupying lesions, hydrocephalus and cerebral venous sinus thrombosis (CVST), whilst other causes such as anaemia, tetracyclines, vitamin A excess and retinoids are less well understood.

With limited epidemiological data, the true incidence of IIH is not clear but is thought to be around 0.5–2 in 100 000 per year in the general population, while in those with a typical IIH phenotype, the incidence is 12–20 in 100,000 per year [1]. Around 5% are considered atypical, consisting of men, children and individuals of normal body mass index (BMI).

The cause of IIH, by definition, remains unknown, but in recent years, there have been a number of studies looking at a distinct metabolic profile including changes in 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1), affecting the local availability of active cortisol [2,3]. Androgen profiling when compared with polycystic ovarian syndrome (PCOS), a common comorbidity, shows a unique but similar metabolic phenotype [4].

Recent UK consensus guidelines [5] emphasize the separate investigation and management of visual dysfunction and headaches. Weight loss is by far the most effective method of reducing raised ICP in typical IIH, but maintaining this is challenging [6].

[a]Lancaster Medical School, Bailrigg, Lancaster University, Lancashire and [b]Department of Neurology, Lancashire Teaching Hospitals NHS Foundation Trust, Royal Preston Hospital, Preston, UK

Correspondence to Dr Keira Markey, Lancaster Medical School, Bailrigg, Lancaster University, Lancashire LA1 4YW, UK.
E-mail: k.markey@lancaster.ac.uk

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KEY POINTS

- IIH is a distinct metabolic phenotype from obesity alone.
- Loss of a quarter of total body weight is required for normalization of intracranial pressure.
- Chronic papilledema should be avoided as it is associated with long-term retinal neuronal loss.
- Venous sinus stenting has grown in popularity, but randomized control trials compared with CSF diversion are needed.
- Less-invasive ICP monitoring and novel therapeutics, for example, GLP-1 agonists, for lowering pressure are welcomed developments.

A recent multicentre 5-year randomized control trial (RCT) comparing bariatric surgery and a dietary programme (IIH:WT) showed ICP improvements with weight loss but no significant effect on visual or headache secondary outcomes, although it was underpowered for this purpose [7].

In terms of medical management, the options are still currently limited to acetazolamide and topiramate, both having carbonic anhydrase activity suspected to reduce cerebrospinal fluid (CSF) secretion, and occasionally other diuretics. The IIH Treatment Trial (IIHTT) was a multicentre U.S.-based, double-blinded RCT that evaluated acetazolamide against placebo; both groups also received a dietary intervention. Those with active IIH and mild to moderate visual loss were included in the study. There were significant improvements in visual field perimetric mean deviation (PMD), lumbar puncture (LP) opening pressure, weight loss and papilledema grade when comparing groups at 6 months [8]. An open-label crossover trial comparing acetazolamide and topiramate showed no significant differences in outcomes but with greater weight loss in the topiramate group [9]. In animal studies, topiramate reduced ICP more effectively [10] and is also a prophylactic treatment in migraine.

Surgical options are generally reserved for fulminant or rapid visual loss with no current evidence providing efficacy of one over another. CSF diversion, by either ventriculoperitoneal or lumboperitoneal shunt, is still the most popular option in the USA and UK [11]. However, there is an increasing trend towards venous sinus stenting (VSS). Optic nerve sheath fenestration (ONSF) is utilized in certain centres, but much less frequently with limited efficacy studies performed thus far.

The aim of this study is to review recent novel research in IIH with a focus on updated knowledge in epidemiology, pathophysiology, diagnostics and disease management.

EPIDEMIOLOGY

Recent epidemiological studies have sought to shed further light upon the wider health implications for the predominantly young, obese and female IIH population. Mollan *et al.* [12] (Table 1) evaluated the burden of depression and anxiety in IIH in a large database review, occurring with increased frequency compared to the normal population but at similar levels to migraine. A smaller study did not find an association with IIH but instead with younger age, headache and elevated BMI [13] (Table 1). In those with established comorbid psychiatric disorders compared to those without, visual outcomes in IIH were found to be worse, both at baseline and after a further 6 months [14–21] (Table 1).

Given the largely female population in IIH, peripartum morbidity is a frequent consideration. Thaller *et al.* [15▪] (Table 1) reviewed pregnancy complications and outcomes in IIH using a UK national dataset. IIH incidence was 3.1 per 100 000. Preeclampsia, gestational diabetes and Caesarean sections occurred more frequently in IIH, but pregnancy losses matched the national average. Involving obstetricians at an earlier stage of peripartum care in IIH may be beneficial.

A further prospective cohort study by Thaller *et al.* [16] (Table 1) evaluated long-term visual and headache outcomes in four IIH cohorts based on their pregnancy status. Diagnosis of IIH in pregnancy was rare but associated with potentially more severe papilledema. Pregnancy itself made no difference in overall headache or visual outcomes.

Prognostication in IIH is incredibly important to select the right time and correct patients for invasive surgical treatments. Thaller *et al.* [17▪] (Table 1) reviewed the IIH:Life database and compared medically managed patients to their surgical cohort. For vision, worse papilledema at onset conferred greater ganglion cell layer (GCL) neuronal loss, delayed for up to 12 months. Monitoring GCL thickness longitudinally, by optical coherence tomography (OCT), may be beneficial to guide intervention when papilledema persists. Weight gain unsurprisingly had the greatest impact on visual outcomes emphasizing the importance of weight loss strategies. Previous migraine history and daily headaches at presentation conferred a worse headache prognosis.

Donaldson *et al.* [18] (Table 1) looked further into the characteristics of the atypical IIH cohort demonstrating a lower prevalence of headaches in older patients. Men also tended to have worse visual

Table 1. Summary of epidemiology studies reviewed

Author	Study type	Aim	Population	Control	Key findings
Mollan *et al.* [12]	Retrospective national cohort	Depression and anxiety in IIH	IIH ($n=3411$)	Migraine ($n=30\,879$) No migraine ($n=33\,495$)	Increased depression and anxiety in IIH vs. general population with no migraine (adjusted hazard ratio for depression 1.38 [98% CI 1.20–1.58] and anxiety 1.4 [1.19–1.64]). Similar rates were seen for IIH and migraine (adjusted hazard ratio for depression 0.98 [98% CI 0.86–1.13] and anxiety [0.83–1.14]).
Donaldson *et al.* [13]	Retrospective cohort	Frequency of anxiety and depression	IIH ($n=100$)	Healthy ($n=100$). Age and sex matched.	No significant association between symptoms and IIH. Depression and anxiety severity was associated with raised BMI, younger age and headache presence. Depression and anxiety did not affect final vision outcome.
Korsbaek *et al.* [14]	Prospective cohort	Relationship between symptom severity and psychiatric disease	New onset IIH ($n=189$)	None	At baseline, 45% with psychiatric disease had worse visual outcomes, compared to those who did not (PMD -8 vs. -6 dB, $P=0.04$) and 6 months (-5.5 vs. -4 dB; $P<0.01$).
Thaller *et al.* [15▪]	Retrospective national dataset	Pregnancy complications in IIH	IIH ($n=17\,587$)	National population. PCOS	IIH pregnancy losses were the same as the national population but higher losses were seen in PCOS. Higher preeclampsia and gestational diabetes (5.3 and 2.7-fold) in IIH. Twice the number of C-sections were performed in IIH.
Thaller *et al.* [16]	Prospective longitudinal cohort (2012–2021)	Long-term clinical outcomes associated with pregnancy status.	IIH ($n=377$) First-time pregnant Established pregnancy Pregnancy prior to IIH Not pregnant	None	Pregnancy made no significant difference to IIH symptom severity. Being diagnosed with IIH in pregnancy is rare.
Thaller *et al.* [17▪]	Prospective longitudinal cohort (2012–2021)	Prognostic indicators for medically managed IIH	Medically managed IIH ($n=426$)	Surgically-managed IIH ($n=64$)	Acetazolamide used in 27%, topiramate in 9% and other diuretics in 4%. Analgesic use was more common in chronic headaches. IIH relapse rates were low (3.2%). Increasing BMI had the biggest impact on visual outcomes. The greater the papilledema, as measured by RNFL, the greater the macular GCL loss. There was a delay of over 12 months to reveal declines. A history of migraine and daily headaches at diagnosis predicts having a worse headache prognosis.
Thaller *et al.* [19]	Prospective observational cohort	Asymptomatic IIH: visual and headache outcomes	Asymptomatic IIH ($n=36$)	Symptomatic IIH ($n=307$)	Incidental papilledema was found in 121 patients. A similar visual prognosis in asymptomatic and symptomatic populations. Two-thirds eventually became symptomatic.

Table 1 (*Continued*)

Author	Study type	Aim	Population	Control	Key findings
Donaldson *et al.* [18]	Retrospective review	Compared the clinical presentation between typical and atypical IIH cohort.	Typical IIH ($n=193$)	Atypical (men, low BMI $<26\,kg/m^2$, >40 years at diagnosis) ($n=50$)	Headache was reported less often by older patients (42.9 vs. 77.2%). PMD was worse in male patients at presentation (-10.16 ± 10.4 vs. -4.52 ± 5.53; $P=0.05$) and a trend towards being worse at follow-up but not statistically significant [-9.97 ± 10.74 vs. $-3.97 \pm /-5.77$]]. Best predictor of final visual loss was PMD at presentation.
Bsteh *et al.* [20]	Retrospective database	Prognostic impact of migraine in IIH.	IIH with migraine ($n=45$)	IIH with nonmigrainous headache ($n=36$)	Headache improvements were lower in IIH migraine vs. nonmigraine (67 vs. 89%; $P=0.019$). Headache resolution was lower in migraine vs. nonmigraine (11 vs. 33%; $P=0.015$).
Svart *et al.* [21]	Prospective cohort	Compared phenotypes and symptoms of secondary pseudotumor cerebri to IIH	Typical IIH ($n=120$)	Secondary pseudotumor cerebri ($n=28$)	28.6% medication cause, 28.6% systemic cause, 17.9% associated with OSA, 14.3% CVST. Childbearing-aged, obese females were still the predominant phenotype with PTC.

CVST, cerebral venous sinus thrombosis; GCL, ganglion cell layer; IIH, idiopathic intracranial hypertension; OSA, obstructive sleep apnoea; PCOS, polycystic ovarian syndrome; PMD, perimetric mean deviation; PTC, pseudotumor cerebri; RNFL, retinal nerve fibre layer.

fields at presentation, but final visual outcomes were no different to the typical IIH patient.

CAUSE AND PATHOPHYSIOLOGY

How papilledema develops is unclear. Pircher *et al.* [22] performed a small retrospective study of medically refractory IIH with chronic papilledema on acetazolamide. CSF samples were analysed following ONSF for an abundant brain-derived protein, lipocalin-type prostaglandin D synthase (L-PGDS). Higher levels were found in the perioptic subarachnoid space (SAS), compared to lumbar puncture samples taken up to a month apart. Reduced local CSF flow and stasis was suggested, as uniform CSF distribution is expected. However, there was no control group for comparison.

Providing further evidence of compartmentalization, Berberat *et al.* [23] retrospectively assessed diffusion-weighted MRI flow rates in the ON SAS in five IIH patients with papilledema, compared to 11 healthy controls. The IIH group showed significantly reduced flow rate ratio (0.55 ± 0.08 vs. 0.63 ± 0.05; $P<0.05$). How flow rates relate to papilledema severity requires exploration.

Changes to the neurogliovascular interface were seen in frontal grey matter biopsies taken during CSF diversion in IIH ($n=13$), when compared to a neurosurgical control group ($n=12$). The cohorts were not age, sex or BMI-matched and some took acetazolamide, but increased astrogliosis was found in the IIH group. Aquaporin-4 levels, associated with CNS fluid regulation and glymphatic function, were no different [24].

Several exploratory untargeted metabolomic studies, involving female patients with active IIH:WT study showed dysregulation of amino acid and lipid metabolism in CSF and serum samples. Mechanistically how this relates to IIH is uncertain [25]. A similar study by the same group employed nuclear magnetic resonance spectroscopy demonstrating lower urea, raised lactate:pyruvate ratio and acetate levels in the CSF at baseline. These subsequently reversed after 12 months of intervention. Increases in urea correlated with improved ICP and headache severity, suggestive of possible compensatory changes in CSF osmolarity. Acetate reductions over time correlated with markers of headache improvement, possibly relating to trigeminal sensitisation [26].

11β-HSD1 activity was assessed systemically through quantification of urinary metabolites and in adipose tissue in active IIH ($n=27$) compared to age and BMI-matched controls ($n=17$). Adipose explants in IIH have markedly higher 11β-HSD1 activity (2.2-fold) compared to controls. Following bariatric surgery, significant reductions in activity

between baseline and 12 months, correlated positively with ICP ($r = 0.43$, $P = 0.02$). A distinct metabolic phenotype is suggested in IIH compared to obesity alone, but the relationship to CSF dynamics needs elucidating [27].

A prospective cohort study of 80 treatment-naive IIH patients without PCOS assessed sella radiological appearances and pituitary hormone profiles. Hormonal abnormalities were seen in 37.5%, with 20% having reduced systemic cortisol, not related to the presence of partial or empty sella (68.8%) [28]. Kassubek *et al.* [29] retrospectively evaluated hypothalamic morphology and satiety hormones in IIH patients ($n = 33$) vs. healthy matched controls ($n = 40$). Only melatonin was significantly different in groups after BMI matching. In IIH, the anterior hypothalamus was significantly smaller and the posterior larger. Comparing hypothalamic morphology to migraineurs may be of interest given its purported involvement during migraine attacks.

Two systematic reviews evaluating secondary causes of raised ICP, causing pseudotumor cerebri (PTC) have been performed recently. Yu *et al.* [30] looked at anaemia in a meta-analysis, but this consisted of predominantly case reports ($n = 62$) and five observational studies. There was a high number of atypical patients with only two-thirds being female. A higher prevalence of anaemia was noted in IIH vs. controls [relative risk 1.44; 95% confidence interval (95% CI) 1.08–1.92]. Treatment of anaemia improved IIH symptoms in over half without requiring ICP-lowering interventions. Only one included study directly compared those with anaemia to those without. This is in contrast to a prospective cohort study by Svart *et al.* [21] where medication, systemic problems and CVST were common reasons for PTC development, but the cohort remained phenotypically similar to typical IIH. Datta *et al.* [31] systematically collated cases of raised ICP associated with levothyroxine. The cohort were atypical with a mean age of 13 years and one-third being male. Marked hypothyroidism and high initial levothyroxine doses were associated with development of PTC, but participant numbers were small. It is also unclear if discontinuation alone would result in improvements as additional medical management was provided. Overall, secondary causes should be considered in both typical and atypical-presenting patients with papilledema.

DIAGNOSTICS

Machine learning to analyse visual field patterns was employed on study data from IIHTT [8]. Further analysis on clinic patient data by unsupervised methods, known as archetypal analysis, modelled visual loss patterns and their potential for vision prognostication. Unlike IIHTT patients, those with severe visual loss (PMD >7 dB) were included. Over half demonstrated a regional defect. The main visual field loss patterns, seen in the clinic cohort, included global depression with enlarged blind spots in the clinic cohort, but near-normal fields when combined with IIHTT [32].

Visual field pointwise analysis was evaluated in IIH:WT [7] patients and compared to PMD as an alternative way of monitoring visual field outcomes. However, most showed no improvement if less than 10 dB over 24 months with the baseline mean PMD already being mild (-3.6 ± 3.7), therefore offering no superiority to detect subtle visual changes over PMD itself [33].

Several recent studies [34,35] have looked at changes in optic nerve sheath diameter and optic disc elevation, as measured by orbital ultrasound B-scans, both showing a significant difference compared to healthy controls. B-scans can have potential variations resulting in a so-called 'blooming' effect, affecting measurement accuracy [36]. A-scans are recommended but can be difficult to interpret [37].

El-Haddad *et al.* [38] assessed optic disc vessel density using OCT-angiography, after CSF diversion. However, there were multiple exclusions including myopia, smoking and alcohol use, affecting generalisability. Optic disc vessel density was decreased in all patients, and positively correlated with decreased CSF opening pressure ($r = 0.527$; $P = 0.000$), potentially providing further visual monitoring options.

MRI brain reports can be suggestive of raised ICP, but it is currently unclear how sensitive or specific these findings are, especially if a patient is asymptomatic. Tascioglu *et al.* [39] retrospectively compared a small group of adult IIH patients with radiological features of raised ICP and healthy controls, balanced for age and sex. Optic nerve tortuosity, protrusion and posterior globe flattening (Fig. 1) were the most reliable features for differentiating IIH from the control groups. A scoring system (TopFLAT) was developed with high sensitivity, specificity and good positive and negative predictive values. A larger prospective study would be useful to help guide further investigations based on imaging findings alone.

Currently, lumbar punctures provide a one-off pressure reading with continuous monitoring requiring a highly invasive ICP bolt. Mitchell *et al.* [40▪] utilized a less-invasive telemetric device that was inserted in the right frontal region of IIH patients with active disease. There was a rise in ICP while lying flat and a decrease of 51% when standing. ICP also rose when moving from supine to lateral decubitus by 13%. This is an important consideration when measuring ICP via lumbar puncture.

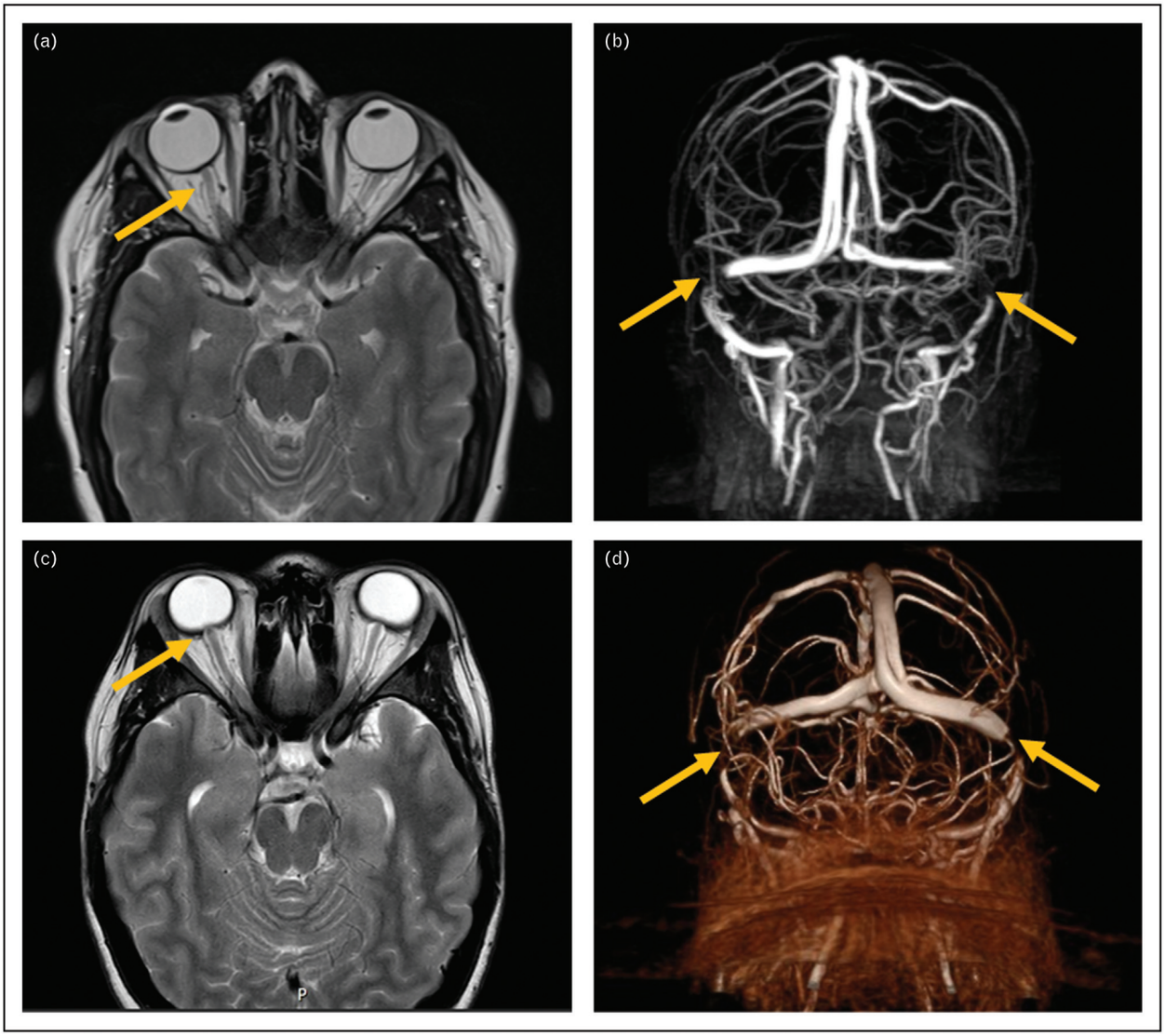

FIGURE 1. Radiological features of raised intracranial pressure. (a) Yellow arrow: optic nerve tortuosity on MRI T2. (b) Yellow arrows: bilateral transverse sinus stenosis on MRI venogram. (c) Yellow arrow: flattened globe, protruding optic nerve and increased perioptic subarachnoid space CSF signal on MRI T2. (d) Yellow arrows. Bilateral transverse stenosis on MRI venogram 3D reconstruction.

MEDICAL MANAGEMENT

Effective and targeted treatment of headache burden in IIH remains an unmet need, with Adderley *et al.* [41] finding that patients with IIH were twice as likely to be prescribed opiates than migraine alone, and three times more likely than population controls. In addition, IIH patients were more frequently trialled with preventive medications, implying a higher likelihood of refractory headaches.

Nevertheless, the rapid proliferation in recent, targeted migraine therapies such as calcitonin gene-related peptide (CGRP) mAbs, antagonists ('gepants') and 5HT1F receptor agonists ('ditans') has shown significant promise for potential transposition into treatment of IIH migrainous-phenotype headaches.

Focus has also fallen on the potential use of exenatide, a GLP-1 receptor agonist developed for use in diabetes, to reduce both ICP and secondary symptom burden in IIH. A small ($n = 15$) randomized, placebo-controlled, double-blinded trial by Mitchell *et al.* [42▪▪] measured ICP response to exenatide in IIH via telemetric monitoring. An initial drop in ICP of 5.7 cmH_2O compared to placebo was then sustained at a mean reduction of 5.6 cmH_2O at 12 weeks. Additionally, the exenatide arm showed a mean improvement in visual acuity of an additional 5 letters on the LogMAR chart and 7.7 less headache

days. Mechanistically, this may be separate to weight loss, as none was reported amongst the participants.

SURGICAL MANAGEMENT

Previously, CSF diversion was the primary surgical management option for rapid, progressive or fulminant visual loss in IIH. Khunte *et al.* [43] performed a large U.S. database review that included 7535 adult IIH patients to assess surgical trends in IIH. The findings showed that VSS procedures increased by 80% per year while the number of CSF diversion procedures have reduced by 54%.

The relationship between changes in the pressure gradient following VSS insertion and at 3 months, the effect on papilledema, was assessed by Yang *et al.* [44] There was no nonsurgical control to compare to the natural disease course. At 1 month, 79.3% showed an improvement to grade 0–1 and 95.7% at 3 months. Details regarding the degree of improvement were lacking. The study did highlight that a pressure of 22.75 mmHg could be used to consider alternative surgical interventions and that lower gradients may be more amenable to VSS. However, Estiaghi *et al.* [45], including 44 patients with unilateral or bilateral TSS (Fig. 1), suggested that the degree of stenosis did not correlate with visual prognosis.

Usually, invasive venous manometry is performed to determine if the trans-stenotic pressure gradient is sufficient to proceed with stenting. An arbitrary figure of 8 mmHg is most frequently used. One small ($n = 24$) prospective study [46] used noninvasive MRI 4D flow to estimate pressure changes compared to manometry. There was agreement [0.9 (95% CI 0.78–0.95); $P < 0.001$] and accuracy of 0.96, which is promising and potentially warrants further assessment to avoid unnecessary invasive procedures.

VSS was directly compared to medical treatment in a nonrandomised prospective study of IIH patients by Raynald *et al.* [47]. Thirty-six patients, from 181, were matched by propensity scoring, which included age but not BMI or sex. There were improvements in papilledema and IIH-related symptoms in the VSS group, but the results were prone to selection bias and should be confirmed or refuted in a randomized trial.

Townsend *et al.* [48] reviewed 811 multicentre VSS procedures. Major complications occurred in only 1.7% and there was a single fatality. This figure correlates with another published meta-analysis of 2% and stent re-stenosis in 14% after 18.9 months [49]. Long-term data of stent failure or re-stenosis, as well as any evidence basis for clinical management of these scenarios, is currently lacking.

Hyder *et al.* [50] prospectively evaluated 51 IIH patients, in a single centre, who had undergone CSF diversion for sight-threatening symptoms. 98% had a ventriculoperitoneal shunt. Visual field PMD, OCT RNFL, GCL measurements and monthly headache days were recorded to establish the phenotype and recovery trajectory for these patients. RNFL and visual field PMD both improved over 12 months, but GCL thinning was observed. The longer the disease progressed, less improvements were seen. Unfortunately, there were missing visual field data and a risk of bias as those with severe visual loss would likely attend clinic routinely.

A sub-study of IIH:WT [7] found around 24% body weight loss was associated with normalisation of ICP ($<25\ cmH_2O$). The clinical relevance of a 'normal' ICP has yet to be determined with no significant improvements in headache or visual outcomes in IIH:WT. However, a greater degree of weight loss could be achieved with bariatric surgery, in particular the Roux-en-y gastric bypass technique [51▪]. Yet, another retrospective review by Okida *et al.* [52] looked at two groups: PTC having bariatric surgery ($n = 9$), and not having bariatric surgery ($n = 77$). There was a significant and sustained reduction in BMI from 0 to 48 months in the bariatric group (bariatric: 45.2 ± 7.6 to 33.3 ± 5.1; $P = 0.053$ vs. nonbariatric: 37.2 ± 6.5 to 37.5 ± 9.2; $P = 0.8767$), although baseline values were higher. It should be noted that the drop-out rates for follow-up in the nonbariatric group were high (79.2 vs. 43.3%).

LIFESTYLE MANAGEMENT

Given the well-known link between obesity and obstructive sleep apnoea (OSA), it is unsurprising that this condition might be more prevalent amongst the IIH patient population. Yiangou *et al.* [53] performed a further sub-study from the IIH:WT, assessing the prevalence of OSA and effectiveness of three screening questionnaires within a cohort of 46 women, as well as OSA's relationship with ICP and papilledema. Forty-seven percent of the cohort were found to have OSA, with the STOP-BANG questionnaire proving to have the highest sensitivity at 74%. OSA severity reduction had a nonsignificant relationship with ICP, when adjusting for BMI but a significant association with papilledema improvements, suggesting benefits of OSA identification and treatment independent of weight-loss related changes.

CONCLUSION

Summary of the main themes

In IIH, involvement of obstetrics early in pregnancy is advised to minimize potential complications.

Careful consideration of monitoring and potential surgical intervention is needed to avoid chronic papilledema and worse visual outcomes. Around a quarter of total body weight loss is required for normalization of ICP. Novel ICP monitoring and therapeutics, such as GLP-1 agonists, are exciting developments in diagnostics and management of IIH.

Future research directions

Evaluation of ICP-lowering surgical interventions is desperately needed. IIH intervention is a multinational RCT based in the UK that plans to assess CSF diversion against VSS in those with IIH and grade 3 or more papilledema. A similar study in Denmark is currently recruiting (clinicaltrials.gov NCT05050854). A larger RCT of Presendin (exenatide) vs. placebo is also underway (clinicaltrials.gov NCT05347147). Future evaluation of radiological findings of raised ICP and targeted treatment of headaches in IIH are required.

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Conflicts of interest

None.

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- ■ of special interest
- ■■ of outstanding interest

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