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ORIGINAL ARTICLE - CSF CIRCULATION

Is endoscopic third ventriculostomy safe and efficient in the treatment of obstructive chronic hydrocephalus in adults? A prospective clinical and MRI study

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Abstract

Background In case of suspected normal pressure hydrocephalus, MRI is performed systematically and can sometimes highlight an obstruction of the flow pathways of the CSF (aqueductal stenosis or other downstream obstruction). It seems legitimate for these patients to ask the question of a treatment with endoscopic third ventriculostomy (ETV), even if the late decompensation of an obstruction may suggest an association with a CSF resorption disorder. The aim of this study was to evaluate clinical and radiological evolution after ETV in a group of elderly patients with an obstructive chronic hydrocephalus (OCH).

Methods ETV was performed in 15 patients with OCH between 2012 and 2017. Morphometric (callosal angle, ventricular surface, third ventricular width, and Evans' index) and velocimetric parameters (stroke volume of the aqueductal (SVa) CSF) parameters were measured prior and after surgery with brain MRI. The clinical score (mini-mental status examination (MMSE) and the modified Larsson's score, evaluating walking, autonomy, and incontinence) were performed pre- and postoperatively.

Results SVa was less than 15 μL/R-R in 12 out of the 15 patients; in the other three cases, the obstruction was located at a distance from the middle part of the aqueduct. Fourteen out of 15 patients were significantly improved: mean Larsson's score decreased from 3.8 to 0.6 ($P \leq 0.01$) and mean MMSE increased from 25.7 to 28 ($P = 0.084$). Evans' index and ventricular area decreased postoperatively and the callosal angle increased ($P \leq 0.01$). The mean follow-up lasted 17.9 months. No postoperative complications were observed.

Conclusion ETV seems to be a safe and efficient alternative to shunt for chronic hydrocephalus with obstruction; the clinical improvement is usual and ventricular size decreases slightly.

Keywords Ventriculostomy · Normal pressure hydrocephalus · Chronic hydrocephalus · Aqueductal stenosis · Endoscopy · Third ventricle · MRI

Introduction

Normal pressure hydrocephalus (NPH) is a neurological disorder partially reversible if it is treated with appropriate surgery. The term of "chronic hydrocephalus" should be used instead of the classical NPH, first described by Adams and Hakim [1]. In fact, this term does not match the actual hydrodynamic profile of patients with chronic hydrocephalus [6, 7]. In case of suggestive clinical signs of the classical triad of symptoms, i.e., gait disturbance, cognitive impairment, and urinary incontinence, a radiological evaluation with MRI is crucial. Ventricular dilatation, measured by Evans's index and the ventricular surface according to a methodology described previously [3] are usually evaluated. Hydrocephalus is most often communicating, without visible obstruction on the CSF pathways; however, signs of obstructive hydrocephalus can sometimes be observed.

Among the "direct signs," one or more membranes in the middle part of the aqueduct of the mesencephalon of Sylvius can be highlighted as well as a more distal obstruction like

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subependymoma of the lowest part of the fourth ventricle. Indirect signs include dilatation of the proximal part of the aqueduct, flattening and extreme thinning of the floor of the third ventricle, and a decrease in the pulsatility of the lamina terminalis [23]. Furthermore, a rarefaction of the CSF of the convexity is sometimes observed (both in the lateral sulcus and in the vertex), unlike the chronic communicating hydrocephalus. In this case, the lateral sulcus and the calcarin sulcus are the only dilated sulcus, with a disproportionately enlarged subarachnoid space.

Endoscopic third ventriculocisternostomy (ETV) emerged as an effective alternative to shunt in patients with obstructive hydrocephalus. Compared with a ventriculoperitoneal shunt [10], the septic risk of ETV is almost null, no hyperdrainage was described, and the risk of obstruction is lower. However, late decompensation of a probably old aqueduct stenosis may raise the question of association with CSF resorption disorders and patients who underwent ETV could experience a temporary clinical improvement, requiring a further positioning of a permanent shunt to control the disease [26]. Therefore, the aim of this study was to assess clinical and radiological evolution after ETV in a group of elderly patients with obstructive chronic hydrocephalus (OCH).

Method

Patients and MRI

This prospective study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the ethics committee of the Amiens University Hospital, where the full study protocol can be accessed (n° ID RCB: 2011-A01633-38), with funds from the interregional clinical research hospital program (IR11). Participants were recruited between May 2012 and November 2017. Written informed consent was obtained from all participants.

All subjects were over 18 and had ventriculomegaly, defined by Evans' index greater than 0.3. All patients had an obstruction in the flow paths of the CSF: aqueductal stenosis was found in 14 cases; one patient had an obstruction of the lowest part of the fourth ventricle due to a probable subependymoma. Clinical evaluation was performed with Mini-Mental State Examination (MMSE) [11] and a combined score based on Larsson's work [22] which evaluates gait (since normal gait: 0 point to wheelchair: 5 points), autonomy (since independence: 0 point to hospitalized patient: 4 points) and urinary incontinence (1 point if present). The patients had no particular neurological antecedents.

All the patients were operated on by the same neurosurgeon, an endoscopic third ventriculostomy (ETV) was performed. The patients' heads were positioned in a neutral position, immobilized by Mayfield clamp and then flexed 30°. A right pre-coronal burr hall was performed; an endoscope with a working channel was introduced. The floor of the third ventricle was gently perforated by the tip of the scissors and the stoma was dilated by a NeuroBalloon [14]. At the end of the procedure, the endoscope was retracted while checking for no bleeding on the surgical approach.

Brain MRI was performed at 3 T (Achieva, Philips, Best, The Netherlands) and included the following sequences for each patient: 3D T1w, 3D heavily T2w TSE Brainview, phase contrast imaging (in and through planes at the level of the aqueduct). Sequences parameters are summarized in Table 1.

Image analysis

Evans' index and the ventricular area were calculated on the pre- and postoperative 3D T1w images on an axial section situated 1 cm above the bi-commissural line (Fig. 1). The ventricular area was semi-automatically segmented and calculated using the Osirix MD software on the 3D T1w sequence. The callosal angle was measured in a coronal section perpendicular to the midline of the bi-commissural line. Third ventricular width was measured in the same coronal section, at the level of the bi-commissural line. Stroke volume of the cerebrospinal fluid (CSF) was evaluated through the aqueductal (SVa). Posttreatment was realized using the Flow Software that can be downloaded for free at www.tidam.fr [2]. Complete posttreatment took less than 10 min by MRI.

Clinical follow-up

Clinical evaluation was performed after 3 months. Postoperative improvement was defined by at least 3 points more to MMSE or 2 points less to Larsson's modified score [22] or a postoperative Larsson's modified score of 0 and MMSE of 30. Patients were reviewed in postoperative consultations at 3 months, 1 year, and then every 2 years.

Statistical analysis

Wilcoxon matched pairs signed-rank tests were done to compare quantitative data between pre- and postoperative evaluation.

Statistical testing was done at the two-tailed α level of 0.05. Data were analyzed using GraphPad Prism version 6.00 for Mac OsX (GraphPad Software, La Jolla, CA, USA, www.graphpad.com).

Table 1 Sequences parameters

Sequence	TR	TE	Voxel size	FOV	Slices	Flip angle
3d T1	9.8 ms	4.6 ms	0.88 × 1.19 × 1 mm	200 × 239 × 176	176	8°
T2 Brainview	2500 ms	700 ms	1.1 × 1.1 × 2.2 mm	200 × 239 × 176	164	90°
Phase contrast MR	15 ms	10 ms	1.5 × 1.5 × 5 mm	150 × 102 × 5	1	10 °

Results

Study population

The 15 patients (8 men and 7 women) were aged from 53 to 78 (68 ± 7.8) (mean ±SD). All patients had at least gait disorders, sometimes associated with other elements of the triad (cognitive impairment: 11/15 and urinary incontinence: 13/15). The preoperative MMSE ranged from 17 to 30 (25.7 ± 4.2), and the modified Larsson's score ranged from 1 to 11 (3.8 ± 2.7) (Fig. 2).

Preoperative MRI study

The mean Evans' index was 0.38 ± 0.04 and the mean ventricular area was 31.6 ± 9.1 cm^2. The mean third ventricle width was 1.54 cm ± 0.33. The mean callosal angle was 102.8° ± 20.8°. Concerning the velocimetric analysis, the aqueductal stroke volume (SVa) was less than 15 μL/R-R in 12 out of the 15 patients; in the three other cases, the obstruction was located at a distance from the middle part of the aqueduct (Fig. 1): one obstruction was located at the rostral part of the aqueduct and two obstructions were situated at the caudal part of the aqueduct or in the

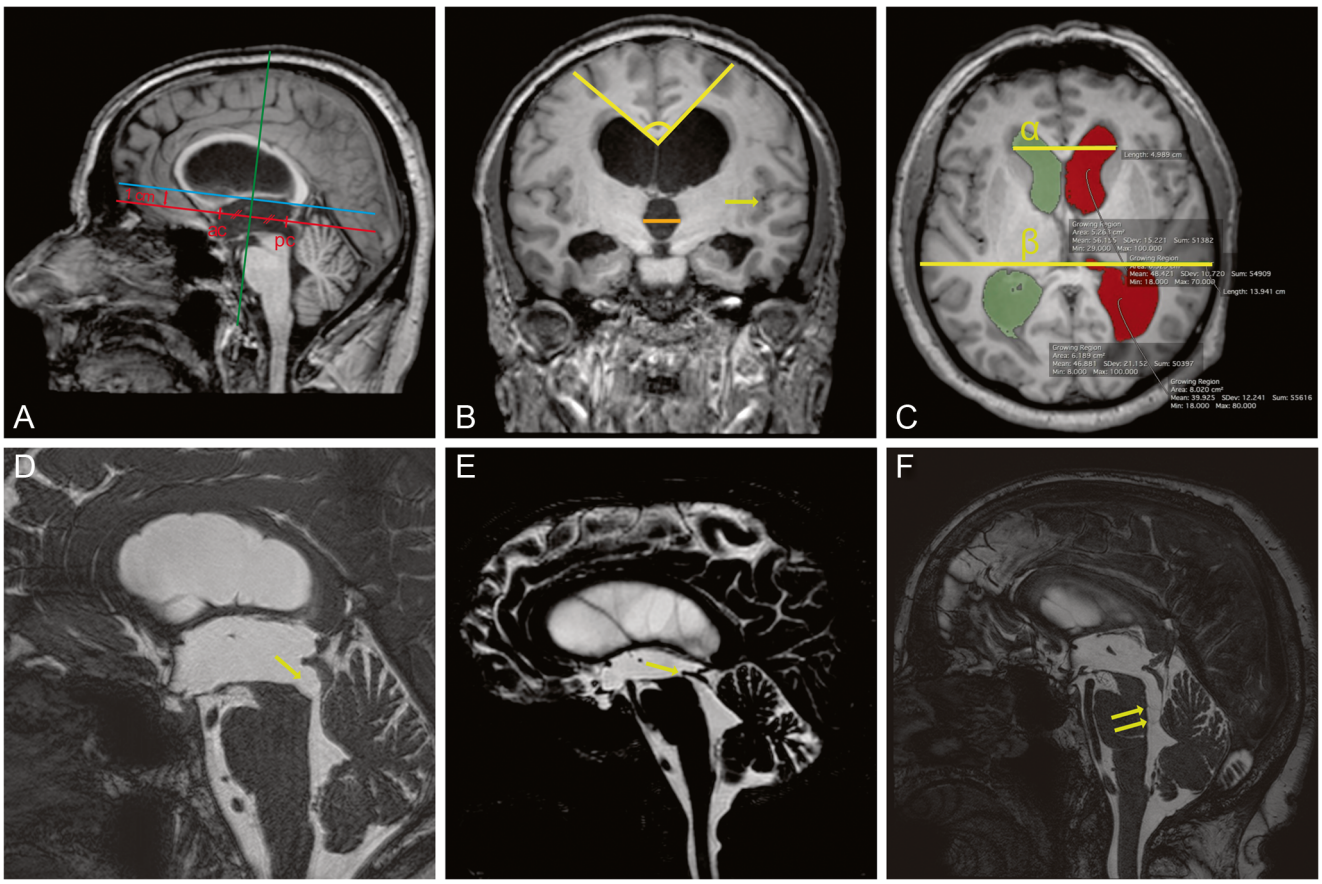

Fig. 1 Morphometric analysis. **a** Identification of the anterior (ac) and the posterior commissure (pc)—green line: coronal section perpendicular to the midline of the bi-commissural line (red line)—blue line: axial section situated 1 cm above the bi-commissural line. **b** Callosal angle and third ventricular width (orange line) measured on the bi-commissural line; we note the absence of dilation of the lateral sulcus (yellow arrow). **c** Evans' index (α/β) and ventricular surface (green: right lateral ventricle (LV); red: left LV. **d** Sagittal slice, T2 weighted with a clear membrane in the aqueduct and a dilatation of the rostral part of the aqueduct; the floor of the third ventricle is also lowered. **e** Sagittal section T2 weighted with rostral obstruction of the aqueduct and lowering of the third ventricle floor. **f** Sagittal section T2 weighted with distal and multiple obstruction of the aqueduct; note the large dilatation of the rostral part of the aqueduct

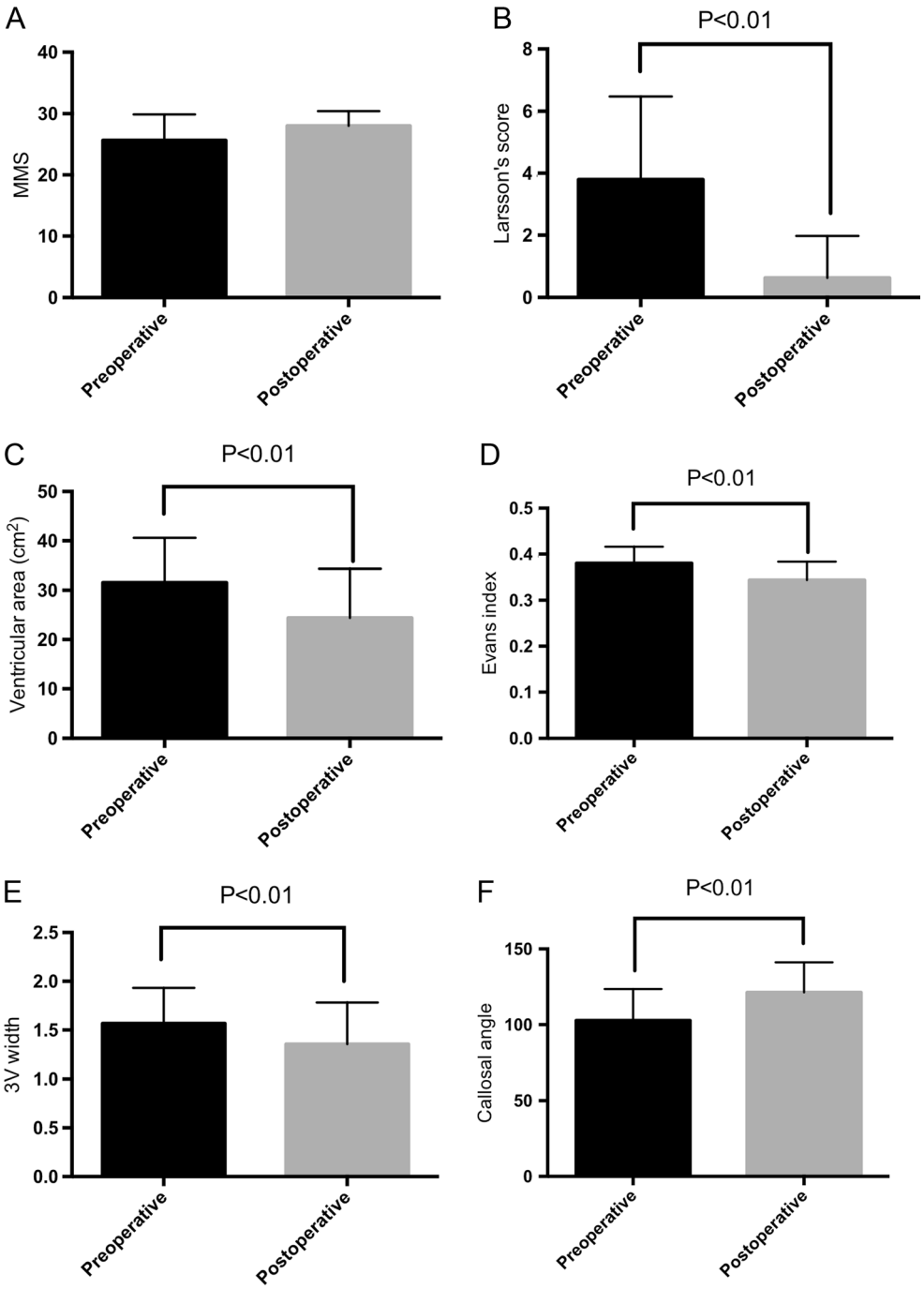

Fig. 2 Evolution between pre and postoperative clinical scores (MMSE (**a**) and modified Larsson's score (**b**)) and morphometric MRI parameters (ventricular area (**c**), Evans index (**d**), third ventricle width (**e**), and callosal angle (**f**))

fourth ventricle. Indirect signs of obstructive hydrocephalus (lowering of the floor of the third ventricle) were visible in all patients.

Postoperative findings

The mean follow-up lasted 17.9 months ± 14. No postoperative complications were noted. The postoperative MRI was realized 9.1 months ± 6 after the ETV.

Fourteen out of 13 patients were significantly improved. Mean MMSE increased from 25.7 to 28 ± 2.4 ($P = .084$) and mean Larsson's score decreased from 3.8 to 0.6 ± 1.3 ($P \leq 0.01$). We did not observe any secondary clinical deterioration. The only patient considered unimproved had mild preoperative walking disorders (Larsson 1) that improved postoperatively (Larsson 0); unfortunately, neurocognitive impairment worsened, with a decrease from 29 to 21 in the MMSE score.

Evans' index, ventricular area, and third ventricle width decreased postoperatively (from 0.38 to 0.34 ± 0.04, $P \leq 0.01$; from 31.6 to 24.4 ± 10, $P \leq 0.01$; and from 1.54 to 1.34 ± 0.41, $P \leq 0.01$ respectively) and the callosal angle increased (from 91.3 to 110.2, $P \leq 0.01$) (Figs. 2 and 3). A flow void at the site of cisternostomy was visible in all patients.

Discussion

Among the 15 patients operated on by ETV for obstructive chronic hydrocephalus, 14 were significantly improved: mean Larsson's score decreased and mean MMSE increased. Evans' index, third ventricle width, and ventricular area decreased postoperatively and the callosal angle increased.

The radiological diagnosis of chronic hydrocephalus in adults is usually difficult; ventriculomegaly is a necessary but not sufficient condition for the diagnosis. Kojoukhova et al. found that visually evaluated disproportion between suprasylvian and sylvian subarachnoid spaces was significantly associated with communicating hydrocephalus [19] and we previously showed the interest of measuring the ventricular surface and the callosal angle in the diagnosis of chronic hydrocephalus [3]. However, it is sometimes possible to find direct or indirect signs of obstructive hydrocephalus. The aqueduct is the most common site of

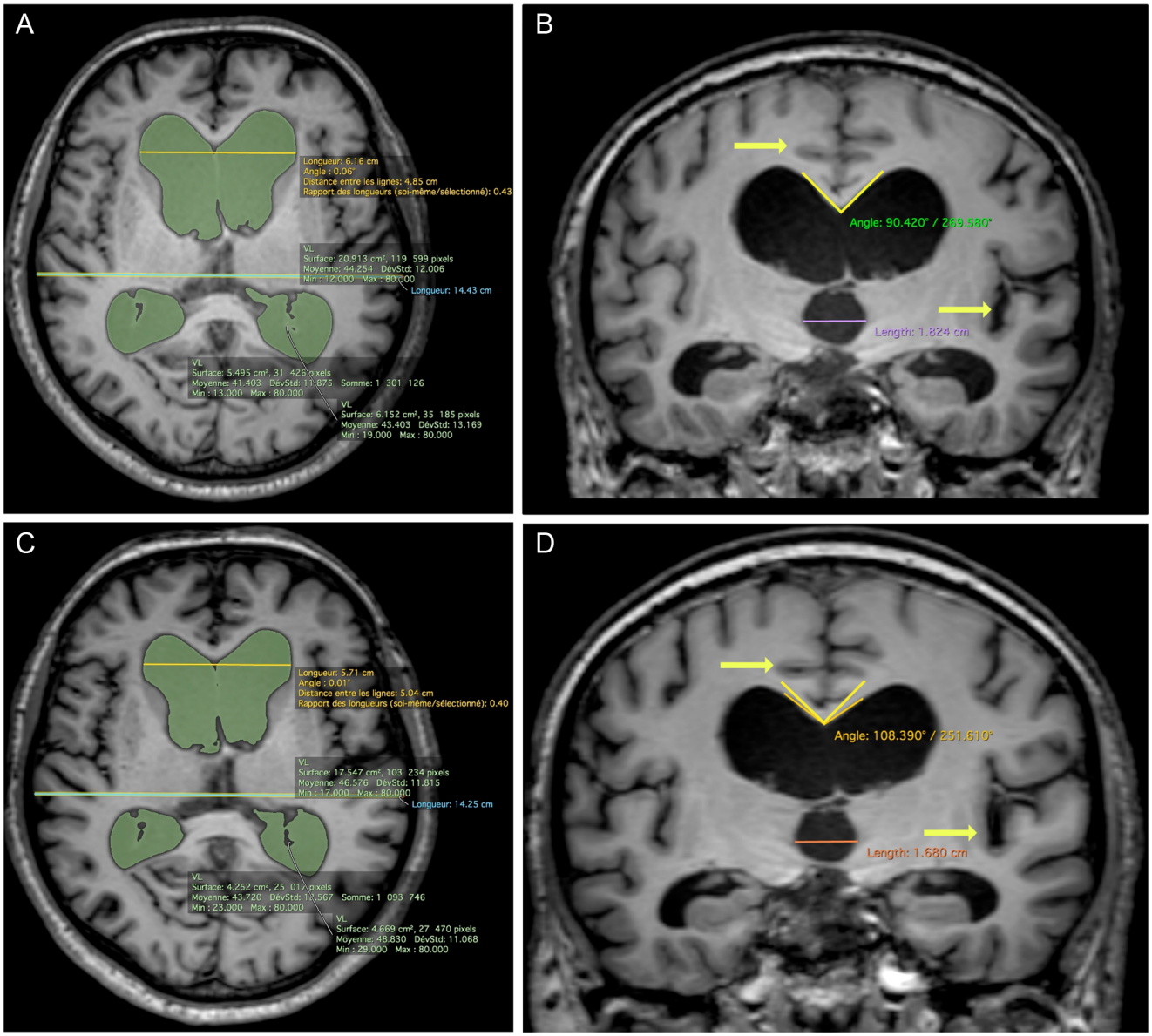

Fig. 3 Illustrative case of a 76-year-old patient: preoperative axial (**a**) and coronal (**b**) T1-weigthed MRI. On postoperative axial (**c**) and coronal (**d**) MRI, Evans' index, and ventricular area decrease (from 0.43 to 0.40 and from 32.5 to 26.5 cm^2 respectively) and callosal angle increases (from 90° to 108°). Note the re-expansion of subarachnoid spaces (yellow arrows) in the vertex and the lateral sulcus

intraventricular blockade of CSF flow [17] where membranes can be highlighted, particularly on high-resolution T2-weighted sequences. Indirect signs are in relation with a pressure gradient between the third and fourth ventricles inducing typical anatomical deformations of the third ventricle (enlargement of suprapineal, lamina terminalis, and infundibular recesses and formation of atrial diverticula) or a decrease in the subarachnoid spaces of the convexity and the lateral sulcus (ref. Kuchcinski et al., *in press paper in Neurosurgery*). A null or very low SVa can also be found. Stroke volume is defined as the average of the volume of CSF moving craniocaudally during cardiac cycle and could be regarded as expression of the compliance of the system [4]. If it is less than 15 μL/R-R, special attention should be given to the anatomy of the third ventricle and the aqueduct.

Our patients presented with a typical clinical picture of chronic adult hydrocephalus; this entity is to be distinguished from LOVA [24] (longstanding overt ventriculomegaly in adults) because our patients do not have severe ventriculomegaly, no macrocephaly, or destruction of the sella turcica. It must also be distinguished from subacute obstructive hydrocephalus where the clinical signs are different (headaches and papillary edema are usual). Consequently, high-volume (> 40 mL) lumbar puncture is not contraindicated because there is usually a large posterior cerebellomedullary cistern without prolapse of the cerebellar tonsils [13].

Once the diagnosis of obstructive hydrocephalus is made, treatment with endoscopic third ventriculostomy (ETV) should be considered, even if the late decompensation of an obstruction may suggest the association with a CSF resorption disorder. Indeed, aqueductal stenosis should not be considered as a stable condition even if it is well tolerated for years. Different hypotheses have been proposed to explain late decompensation (head traumas, subarachnoid hemorrhages, or viral infections [21]). In these different pathologies, one can fear associated resorption disorders. Yet, in our series of patients, the anamnesis did not find any particular neurological antecedents. When the obstruction is identified and without arguments for associated resorption disorders, the indication of ETC in the first intention should be proposed rather than shunt. In fact, the placement of an extracranial shunting device entails significant, rare but serious short-term intraventricular hemorrhage risk [27] and long-term risk of infection and malfunction.

This study is of course not the first to examine the results of an ETV, but most of the previous studies mixed pediatric and adult population [12, 28], mixed several etiologies (stenosis of the aqueduct, intraventricular tumors) [9], primary or secondary ETV (failed ventriculoperitoneal shunt) [16, 29, 30], or mixed acute and chronic hydrocephalus [23]. Pediatric and adult populations can hardly be compared since it is known that the risk of obstruction of ETV is greater in children under 1 year of age [8]. Our clinical results (with 12 improved patients out of 13) are in line with those of the literature showing 77 to 87% of clinical improvement or remission [9, 12]. In sharp contrast, ETV in cases of chronic communicating hydrocephalus without visible obstruction did not yield significant results [25, 27].

Besides clinical follow-up, carrying radiological monitoring seems important. To our knowledge, apart from checking the permeability of the stoma, the evolution of ventricular size after ETV has not been assessed in the literature. A standard radiological analysis usually concludes with the persistence of a large ventricular size. The use of simple tools such as the reproductible Evans' index, the third ventricle width, and especially the ventricular surface and the callosal angle demonstrate on the contrary that there is a discrete but certain decrease in ventricular size. The ventricular area is strongly correlated to the ventricular volume, but it was much easier to calculate. We agree with Holodny et al. who consider that volumetric analysis is time-consuming, is difficult to perform, and requires special equipment, making it impractical to perform in routine clinical practice [15]. The calculation of ventricular area is a good compromise. The callosal angle, first described for many years [5], is also a marker of ventricular size; moreover, we had previously highlighted a correlation between the callosal angle and ventricular area [3]. Finally, the re-expansion of the subarachnoid spaces of the convexity and the lateral sulcus is an indirect radiological sign of a favorable evolution in patient follow-up.

Our study suffers from some limits: (i) the median follow-up of our patients remains rather short (18 months), but it has been shown that the obstruction of ETV occurs preferentially in the year following the operation [12]; (ii) the neuropsychological assessment was succinct compared to other studies [20]. Nevertheless, the MMSE score is simple and reproductible. It could be an interesting tool for cognitive monitoring when considering cost-effectiveness [18].

Conclusion

ETV has a relatively high success rate in patients with non-communicating chronic hydrocephalus, with a low rate of complications. On preoperative MRI of a chronic hydrocephalus assessment, a low or null aqueductal stroke volume should make us consider a stenosis of the aqueduct. During radiological monitoring, a morphometric MRI evaluation shows a small decrease in ventricular size, an increase in the callosal angle, and a re-expansion of the subarachnoid spaces of convexity.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (ethics committee of the Amiens University Hospital where the full study protocol can be accessed: n° ID RCB: 2011-A01633-38) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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Comments

The authors report on 15 adult patients with chronic obstructive hydrocephalus who underwent endoscopic third ventriculostomy (ETV). Over a mean follow up period of almost 18 months, 14 showed significant improvement in gait and cognition, as assessed by the Larsson's score and MMSE respectively. There was also an improvement in radiological parameters, including the size of the third ventricle. Interestingly, over the follow up period, the authors did not see any deterioration. This is different from the commoner NPH cohort, where an early improvement following CSF diversion is often followed by a late deterioration. The authors conclude that the distinction between normal pressure hydrocephalus and chronic obstructive hydrocephalus is important; it mandates careful MR examination prior to treatment and allows the consideration of ETV rather than shunt.

Although this is not a new concept, the authors have treated these patients consistently and followed them up assiduously. The follow-up is relatively short for a chronic condition, and this remains a limitation of the study, which the authors acknowledge.

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