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The factors affecting the outcomes of conservative and surgical treatment of chiari i adult patients: a comparative retrospective study

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ABSTRACT

Background: The prognosis of the Chiari malformation type 1 (CM1) demonstrates a variant spectrum that varies from full recovery to complicated worse neurological disability.
Objective: To investigate the factors affecting the outcomes of conservative and surgical treatment for CM1 by evaluating adult patients consecutively managed at our institutions.
Materials and methods: We retrospectively reviewed the medical records of patients diagnosed with CM1 at two reference neurosurgical centers for eight years (2010–2017). We selected all CM1 adult patients who managed conservatively or surgically as the core sample for this study. For clinical evaluation, we used a Chicago Chiari Outcome Scale (CCOS). For radiological assessment, we adopted both craniocervical and contrast-phase MRIs. We investigate factors such as age, sex, pretreatment symptoms, symptoms duration, and radiological findings in both groups.
Results: Ninety patients were treated conservatively. After a progression, five of them were treated surgically later and included in a total of 72 patients who underwent decompressive surgery. We successfully managed 85 patients (94.4%) of the conservative group and 64 patients (88.9%) of the surgical group. We found that patients with aqueductal stroke volume (ASV) of 12 μl are surgical candidates. We observed a strong positive correlation between clinical improvement and the increase in ASV values.
Conclusions: ASV≤12 μl is a significant predictor for surgical intervention. The presence of heavy sleep apnea or/and functional symptoms, tonsillar herniation >13.4 mm on coronal images, low ASV, long symptom durations, and a syrinx are the independent prognostic factors that affected outcomes negatively.

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Chiari malformation type i; conservative therapy; posterior fossa decompression with duraplasty; cp-mri; csf flow mri

Introduction

Chiari malformation type I (CM1) is a herniation of the cerebellar tonsils 5 mm below the foramen magnum[1]. In the last two decades, the number of diagnosed patients with CM1 interestingly has increased related to the advent of MRI. CM1 patients have a variant spectrum [1,2]. The responses for surgical intervention are not the same in CM1 adult patients. The necessary conditions to obtain an acceptable outcome include the patient selection and timing of the surgical intervention. Several authors have reported that applying a posterior fossa decompression with a duraplasty (PFDD) is sufficient surgery [3–5]. Other authors supposed that posterior fossa decompression (PFD) without a duraplasty is adequate[6]. However, some studies reported a progression of the syrinx and presenting symptoms after PFD [3,7]. There are no standardized guidelines to manage mild or moderate symptomatic CM1 adult patients [3,4].

Several studies have recommended contrast-phase MRI (CP-MRI) to diagnose and follow-up CM1 patients [8,9]. Several techniques were defined to measure the hydrodynamics of CSF [8–10]. However, no study reported the cut-off values to manage these patients. This retrospective comparative study primarily aimed to find the main criteria of surgical candidates of CM1 adult patients by defining the cut-off value of aqueductal stroke volume (ASV) on CP-MRI and to investigate the possible factors affecting the outcomes of conservative and surgical treatment for CM1. Secondarily, the study aimed to evaluate the patients managed conservatively and surgically at our institutions.

Materials and methods

Study design and inclusion criteria

The ethical committee of our institution approved this comparative study. We retrospectively reviewed the medical records of the diagnosed patients with

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Table 1. The adult CM1 patients diagnosed at both neurosurgical centers (n = 331).

	Center [A]	Center [B]	All pts
Study period	Jan 2010 – Jul 2016	Jan 2012 – Dec 2017	Jan 2010 – Dec 2017
All pts diagnosed w/ CM1	210	121	331
Asmptomatic pts	41 (19.5%)	29 (24.0%)	70 (21.1%)
Symptomatic pts	169 (80.5%)	92 (76.0%)	261 (78.9%)
– Observed pts w/o treatment	28 (16.6%)	15 (16.3%)	43 (16.5%)
– Conservative ± PTR	*53 (31.4%)*	*32 (34.8%)*	*85 (32.6%)*
– Surgically treated	*88 (52.0%)*	*45 (48.9%)*	*133 (50.9%)*
Surgically treated	**88 (52.0%)**	**45 (48.9%)**	**133 (50.9%)**
– Pediatric pts (< 18 years)	18 (20.5%)	7 (15.6%)	25 (18.8%)
– Syndromic adult pts	7 (8.0%)	2 (4.4%)	9 (6.8%)
– No adequate pre/PO MRIs	5 (5.7%)	3 (6.7%)	8 (6.0%)
– Additional pathologies (+)	4 (4.5%)	1 (2.2%)	5 (3.8%)
– Received PDF alone	2 (2.3%)	2 (4.4%)	4 (3.0%)
– For recurrent CM1	1 (1.1%)	2 (4.4%)	3 (2.2%)
– Lost follow-up	4 (4.5%)	3 (6.7%)	7 (5.3%)
– Pts received PFDD	47 (53.4%)	25 (55.6%)	*72* (54.1%)*

pts: patients; w/: with; CM1: Chiari malformation type I; w/o: without; PTR: Physical therapy and rehabilitation; Pre: Preoperative; PO: Postoperative; No pre/PO adequate MRIs: If the patients lost comparative sagittal, coronal or CSF flow MRIs; PDF alone no duraplasty or/and C1 laminectomy; additional pathologies: such as hydrocephalus, intracranial or spinal lesions. PFD: Posterior fossa decompression without a duraplasty; PFDD: Posterior fossa decompression with a duraplasty.

* Five of these patients, were firstly treated conservatively for ≥ 6 months before accepted to be surgical candidates.

CM1 at two neurosurgical centers. We included consecutive adult patients who managed conservatively or surgically treated and met our study criteria for eight years (2010–2017).

Inclusion criteria were: 1) CM1 adult patients (>18 years old) who were diagnosed after main symptoms and MRIs, 2) treating conservatively or underwent PFDD, 3) radiological diagnosing determined using sagittal, coronal, and CP-MRIs, 4) followed-up for a minimum of 2 years and attended to all the control visits and posttreatment MRIs, and 5) informed written consent obtained from the patients.

Exclusion criteria were: 1) undergoing surgical intervention for recurrent CM1 symptoms followed insufficient decompression, 2) undergoing PFD alone, 3) having syndromic diseases, cranial, spinal lesions, or receiving a ventriculoperitoneal shunt for coincident hydrocephalus, and 4) lost patients (Table 1).

The surgical group's patients consented to surgical procedures.

Clinical diagnosis

We divided the symptoms into four categories included pain, neurological non-pain, functional symptoms, and sleep apnea. The first three categories are the same as in Aliaga et al's study[3]. Pain symptoms include tussive headaches, high cervical or occipital, and upper extremities pain or dysesthesia. Neurological non-pain symptoms include myelopathy, dysphagia, dissociation sensory losses, vertigo, tinnitus, nystagmus, impaired reflexes, ataxia, fecal, and urine incontinence. The functional symptoms include syncope, hoarseness, cognitive impairments, and dysarthria. Sleep apnea, severe snoring, hiccups, and recurrent aspiration are the symptoms of the fourth category.

Radiological diagnosis

We performed MRI scanning via a head coil on a 1.5 Tesla system (Avanto; Siemens, Germany). The CSF flow hydrodynamics quantitative assessment was achieved with axial plane slices obtained from a 2-dimensional CP-MRI. We obtained sagittal, coronal, T1-WI, and T2W1 images. We accepted herniated cerebellar tonsils >5 mm on sagittal [11] or coronal images [12] (Figure 1). We used CP-MRI to evaluate the dynamics of CSF [8–10] (Figure 2). Measuring the CSF flow on CP-MRI precisely can be variable from one institution to another [2,9]. However, the CSF velocities vary significantly by levels of aqueduct sylvii, the foramen magnum, and the upper cervical region[2]. Hypodynamic flow was defined as an ASV <18 μl.[13-15][13]. The radiologists used axial plane slices of CP-MRI with the widest flow-related signal through aqueduct sylvii to assess CSF flow hydrodynamics [2,9]. The ASV was calculated as (Systolic Volume+Diastolic Volume)/2.

On coronal and mid-sagittal images, we measured the differences between pre-and postoperative tonsillar herniation and ASVs. For syrinx cases, on mid-sagittal images, we calculated the differences between pre-and post-treatment maximal syrinx length, and on axial images, the differences between the ratio of the maximal anteroposterior diameters of both syrinx and spinal cord (S/C) [11] (Figure 3).

Two neuroradiologists separately evaluated pre-and postoperative MRIs. They were blinded to the groups. The inter-observer agreement was seen in 93.0% and 96.5% of the surgical and conservative groups, respectively. To solve the differences they argued and adopted the final decision after the consensus.

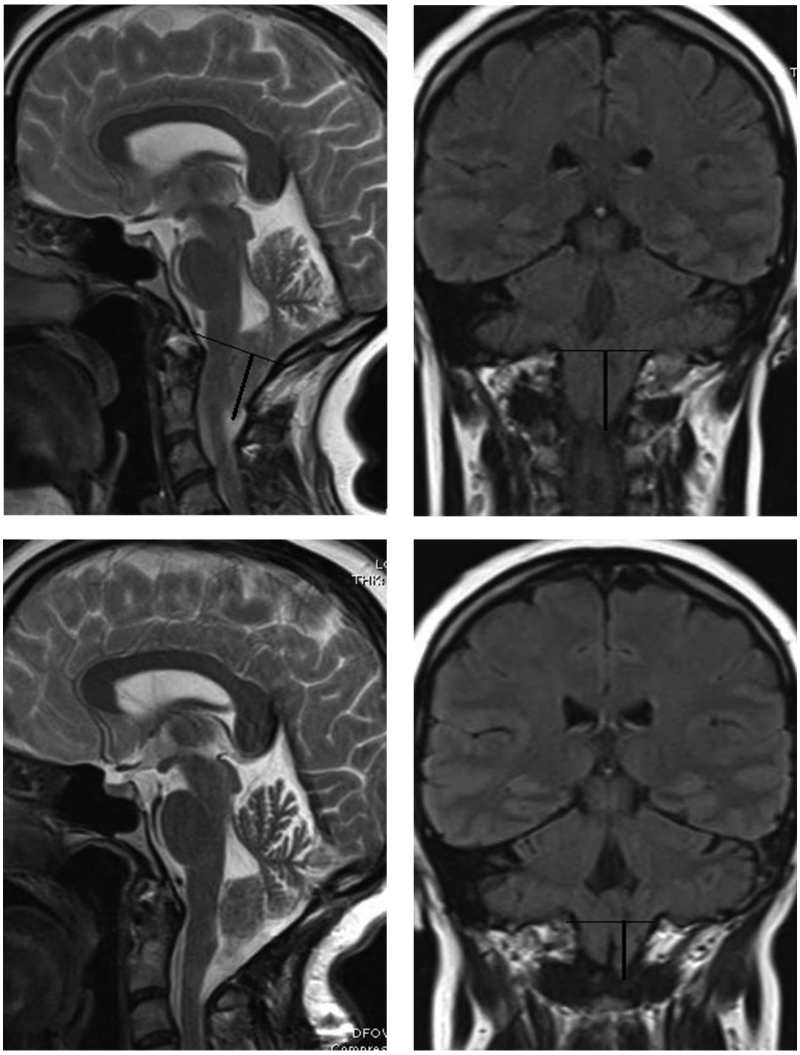

Figure 1. Pre-and postoperative MRI of a male patient aged 42 diagnosed with CM1. **[A, B]**: A caudal descent of the tonsillar ectopia on the preoperative mid-sagittal and coronal images was 16.1 mm and 14.0 mm, respectively. **[C, D]**: On the postoperative mid-sagittal and coronal images, the tonsillar ectopia decreased to 7.6 mm and 9.0 mm, respectively. A significant fourth ventricle enlargement was noticed on the postoperative coronal image **[D]** when compared to the preoperative coronal image **[B].**

Our management approach

The clinical symptoms, neurological findings on examination, and identifier radiological findings consisting of ASV on CP-MRIs and coronal images of the craniocervical junction were the main aspects that we used to evaluate our patients. The fourth aspect was neurophysiological tests such as SSEP that were used in the discrepancy between the aspects[4].

We divided our CM1 patients into three groups: asymptomatic, variably symptomatic, and invariably symptomatic patients. The asymptomatic group included patients with incidental radiological findings and/or nonspecific presenting symptoms. Variably symptomatic patients included the patients with typical symptoms without identifier radiological findings (hypodynamic SCF flow ≤12 μl and syrinx cavity). Invariably symptomatic patients included the patients with typical presenting symptoms that radiologically reflected on CSF hydrodynamics. We observed that invariably symptomatic patients had at least three functional symptoms, sleep apnea symptoms, or identifier radiological findings[11].

To reduce possible permanent neurological deficits, we directly operated on the third group's patients after completing all investigations, while we preferred to manage other groups' patients conservatively with close follow-up once every three months for the second group's patients and once every six months for asymptomatic patients.

Conservative treatment

If the patient did not meet our criteria for surgical intervention, we treated the patient conservatively. We divided our conservative therapy modalities into four lines. We started with analgesics, myorelaxants,

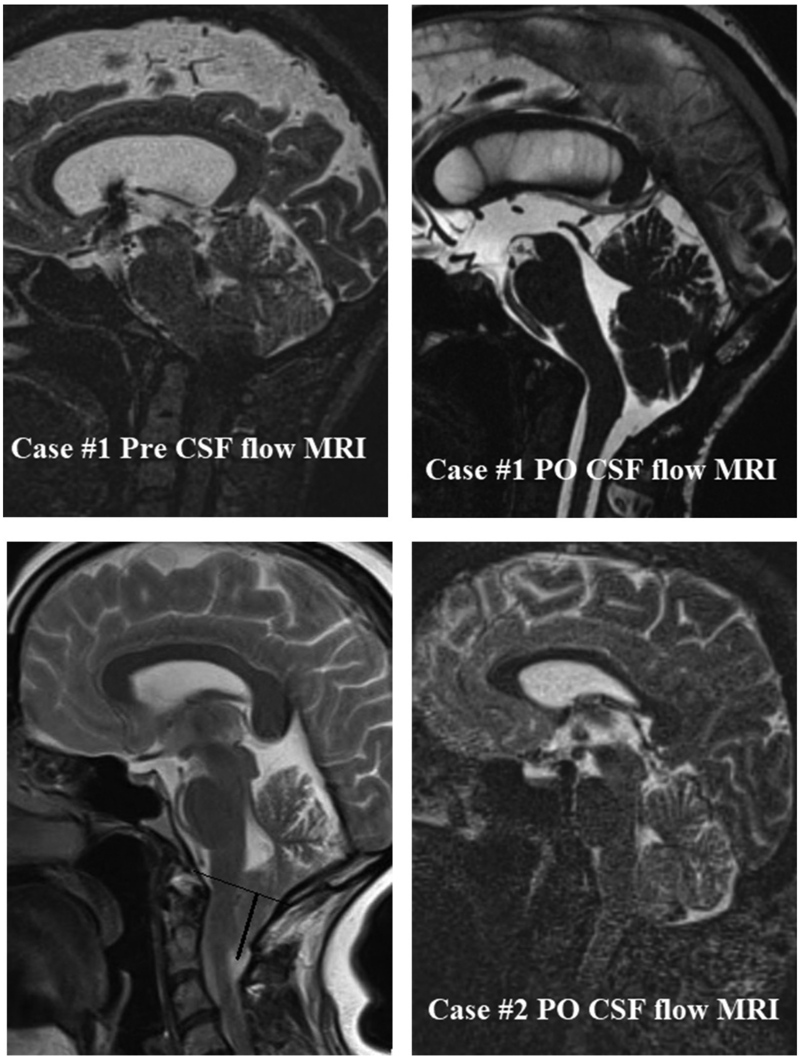

Figure 2. Two cases of surgically treated CM1 patients are demonstrating the differences between the preoperative and the 6th-month postoperative CP-MRIs. **[A, C]**: Preoperative CP-MRIs showed that tonsillar ectopia displaced into the upper spinal canal causes impairment of CSF flow (hypodynamic, i.e, the ASVs were ≤15 μl) related to the cerebellar and hindbrain compression at the cervicomedullary junction. **[B, D]**: Postoperative CP-MRIs showed the adequate decompressions were performed in all three cases. All CSF hydrodynamics were normalized the biphasic CSF motion and improved CSF flow to >18 μl. **[A, B]**: Case 1 is a female patient aged 41 diagnosed with CM1. After decompressing, ASV increased from 15 μl to 38 μl. **[C, D]**: Case 2 is a male patient aged 31 diagnosed with CM1. After decompressing, ASV increased from 12 μl to 19 μl. However, the posterior CSF flow in Case 2 was still partially restricted. Note that the minimal restriction reflected the increase of the postoperative ASV value.

multivitamins, and weekly swimming (the first line). After one month or in any clinical progression, we reevaluate the patient. If the response was unsatisfactory, we prescribed the second line that included Pregabalin 1–1.5 mg/kg daily and weekly pilates exercises. In case of the presence of a tolerance problem or unsatisfied response, we passed to the third line that included the physical therapy and rehabilitation (PTR) 15–30 séances/six months besides dramatically increasing a Pregabalin dose up 4 mg/kg. In unsatisfied or recurrent cases, the fourth line, which included a high Pregabalin dose up 5–6 mg/kg besides PTR with swimming or pilates exercise, was adopted. There is no fixed rule stated.

Surgical procedure

In the prone position with a midline incision below the inion to the C2 level, we performed a standard craniectomy and a C1 laminectomy with the high-speed drill and bone rongeurs. We then removed the anterior constricting bands of the C1 vertebra and opened the dura in a Y-shaped fashion under a white-lighted microscope. If it was indicated, we inspected the foramen of Magendie gently with appreciating the posterior inferior cerebral artery. In suspicion of the presence of the webs, adhesions, or obstacles, the 4th ventricle was exposed[11]. After the hemostasis, a tight closure duraplasty using an autograft patch or synthetic graft was performed. To

Figure 3. Pre-and postoperative MRI of a 36-year-old female CM1 patient. **[A]**: On the preoperative mid-sagittal image, a mild cervical kyphosis was noticed, besides the tonsillar ectopia and the syrinx length measuring 17.6 mm and 102 mm, respectively. **[B]**: On the postoperative mid-sagittal image, the tonsillar ectopia decreased to 1.8 mm, the syrinx had regressed, and kyphosis was corrected without additional surgeries.

avoid adhesions, we kept the operative field clean. Multilayer closure was done appropriately with the anatomy.

Clinical and radiological follow-up and outcome variables

CM1 patients postoperatively received routine clinical assessments and early postoperative computerized tomography. For evaluation of the clinical improvement, we used a Chicago Chiari Outcome Scale (CCOS) for the surgical group and a modified CCOS (mCCOS) for the conservative group (Table 2).

We calculated the differences between pre-and post-treatment 6, 12, 24, 36 months ASVs to assess the radiological response. In the syrinx cases, the regression of both the syrinx' length and S/C on coronal, midsagittal, and axial images were evaluated postoperatively. A new clinical symptom or progression developed within the first 30 postoperative days was considered a surgery-related complication.

Statistical analysis

We gave the data as the mean±SD and the ranges in parenthesis. To understand the association between the radiological and the clinical variables, univariate analyses were conducted. We used a paired t-test to assess the statistical differences between mean values of pre-and post-treatment variables using the statistical package software SPSS 24.0 (Microsoft Co., Chicago, IL, USA). All tests were two-tailed. The significance level was accepted when the p-value <0.05. Spearman's (for ordinal data) or Pearson's (for normally distributed data) correlation analysis was used to investigate the correlations between the variables and scales. We utilized an independent samples t-test for categorical data.

We applied a Receiver Operating Curve (ROC) analysis using the Youden Index to determine the cut-off value of ASV that associated with the improvement and/or recovery outcomes (CCOS≥13) in the operated patients.

Results

A total of 157 patients were diagnosed with symptomatic CM1 and met the study's criteria. Ninety (68 females and 22 males) of these 157 adult patients were managed conservatively. Five were treated surgically later and included in a total of seventy-two (52 females and 20 males) patients who received PFDD (Table 1). The mean age was 40.6 ± 15.2 (range; 18–74) and 38.0 ± 11.7 (range; 16–68), respectively. The most

Table 2. Modified Chicago Chiari Outcome Scale for conservatively treated patients

Pain intensity	S	Non-pain	S	Functionality	S	Outcome	TS
Worse	1	Worse	1	Unable to attend to daily activities	1	Incapacitated	3–5
Unchanged or no response to treatment	2	Unchanged or improved w/ impairment	2	Moderate impairment (< 50%)	2	Impaired	6–8
Improved or controlled w/ treatment	3	Improved w/o impairment	3	Mild impairment (> 50%)	3	Functional	9–11
Resolved	4	Resolved	4	Fully functional	4	Excellent	12

S: Score; TS: total score.

commonly seen symptom was a headache. The baseline demographic and clinical characteristics of the studied patients were shown in Table 3. The most common clinical finding in neurological examinations was pinprick loss (Table 4).

In the conservative group, the mean tonsillar herniation on midsagittal and coronal images was 8.8 ± 2.6 (3–16) mm and 9.3 ± 2.1 (4–18) mm, respectively. The mean ASV was 16.5 ± 2.7 (range; 12–25) µl (Table 4). The first line was successful in treating 22 patients (24.4%). The second line was successful in treating 42 patients (46.7%). The third line was successful in treating 19 patients (21.1%). We applied the fourth line to 7 patients (7.8%). We operated on five of these seven patients after the unsatisfied response of conservative therapy. The five patients experienced a neurological progression (except for the patient who experienced recurrent aspiration, the other four patients all experienced at least two new symptoms from the second and third categories). In these five patients, the ASVs were ≤15 (10–15) µl. The mean value of mCCOS after six months of conservative treatment was 10.4 ± 1.5 (range; 5–12). The median of the Pregabalin usage period was 5.5 years (range; 3–121 months). The comparison of treatment outcomes between both groups regarding the pretreatment symptoms was given in Table 5. Although the comparison led to bias, the surgical treatment was significantly effective to treat the dissociated sensory loss ($p = 0.032$), ataxia ($p = 0.032$), and a syrinx ($p = 0.013$). In the surgical group, the recovered patients were significantly higher ($p > 0.0001$). The comparison between (conservative treatment benefited) and (conservative treatment failed) patients was shown in Table 6. In the conservative group, strong positive correlations were noticed between high ASVs (>16.7 µl) and clinical improvement and between the increase in ASVs and clinical improvement ($p = 0.004$, rs = 0.4) and ($p < 0.001$, rs = 0.61), respectively.

Table 3. Baseline demographic and clinical characteristics of 157 investigated patients.

	Conservative G.	Surgical G.	p-values	All patients
Number of the patients	85 (54.1%)	72* (45.9%)	-	157 (100%)
Sex (F/M)	64/21 (75.3%)	52/20 (72.2%)	0.72	116/41 (73.9%)
Mean age (years)	40.6 ± 15.2 (18–74)	38.0 ± 11.7 (18–68)	0.24	39.4 ± 13.9 (18–74)
Pretreatment Symptoms:**				
1) Pain and dysesthesia C.	**73 pts** (85.9%)	**64 pts** (88.9%)	0.64	**137 pts** (87.3%)
– Typical headache for CM1	31 (42.4%)	46 (63.9%)	***< 0.001***	82 (52.2%)
– Atypical headache	27 (25.9%)	10 (13.7%)	***0.013***	32 (20.4%)
– Neuropathic pain	10 (11.8%)	29 (40.3%)	***< 0.0001***	39 (24.8%)
– Neck pain	12 (14.1%)	23 (31.9%)	***0.01***	35 (22.3%)
– Upper extremities pain	8 (9.4%)	8 (11.1%)	0.8	16 (10.2%)
– Spinal pain	3 (3.2%)	6 (8.3%)	0.3	9 (5.7%)
– Chest pain	2 (2.4%)	2 (2.8%)	1.0	4 (2.5%)
2) Neurological non-pain C.	**16 pts** (18.8%)	**47 pts** (65.3%)	***< 0.0001***	**63 pts** (40.1%)
– Dissociated sensory loss	12 (14.1%)	36 (50.0%)	***<***	48 (30.6%)
– Vertigo/dizziness	10 (11.8%)	25 (34.7%)	***0.0001***	35 (22.3%)
– Ataxia	2 (2.4%)	20 (27.8%)	***< 0.001***	22 (14.0%)
– Tinnitus	5 (5.9%)	14 (19.4%)	***< 0.001***	19 (12.1%)
– Impaired reflexes	10 (11.8%)	7 (9.7%)	***0.013***	17 (10.8%)
– Nystagmus	8 (9.4%)	8 (11.1%)	0.8	16 (10.2%)
– Dysphagia	1 (1.2%)	15 (20.8%)	0.8	16 (10.2%)
– Disequilibrium	1 (1.2%)	9 (12.5%)	***< 0.0001***	10 (6.4%)
– Paresis	0	8 (11.1%)	***0.005***	8 (5.1%)
– Fecal ± Urine incontinence	2*** (2.4%)	4 (5.6%)	***0.002***	6 (3.8%)
– Myelopathy	0	5 (6.9%)	0.41	5 (3.2%)
3) Functional symptoms C.	**10 pts** (11.8%)	**34 pts** (47.2%)	***0.02***	**44 pts** (28.0%)
– Fatigue	8 (9.4%)	29 (40.3%)	***< 0.0001***	37 (23.6%)
– Syncope	2 (2.4%)	8 (11.1%)	***< 0.0001***	10 (6.4%)
– Cognitive impairment	2 (2.4%)	5 (6.9%)	***0.044***	7 (4.5%)
– Dysarthria	2 (2.4%)	5 (6.9%)	0.25	7 (4.5%)
– Hoarseness	1 (1.2%)	4 (5.6%)	0.25	5 (3.2%)
4) Sleep apnea C.	**5 pts** (5.9%)	**19 pts** (26.4%)	0.18	**24 pts** (15.3%)
– Sleep apnea	2 (2.4%)	11 (15.3%)	***< 0.001***	13 (8.3%)
– Severe snoring	2 (2.4%)	8 (11.1%)	***0.004***	10 (6.4%)
– Recurrent aspiration	1 (1.2%)	7 (9.7%)	***0.044***	8 (5.1%)
– Hiccoughs	1 (1.2%)	3 (4.2%)	***0.024***	4 (2.5%)
			0.33	
Symptom duration (months)	18.6 ± 12.4 (3–48)	20.2 ± 14.4 (3–60)	0.75	19.3 ± 13.8 (3–60)
Follow-up period (months)	78.8 ± 21.9 (26–121)	80.4 ± 23.6 (26–121)	0.44	79.5 ± 23 (26–121)
Mean LOS (days)	-	3.2 ± 2.1 (1–28)	-	-
Mean IP blood loss (ccs)	-	167.0 ± 54.5 (50–250)	-	-

$p < 0.05$ is statistically significant. G.: Group; F: Female; M: Male; C.: Category; Typical headache for CM1: occipital, Valsalva induced, tussive and exertional headache; Atypical headache: Poorly localized frontal temporal or nonspecific headache; Neuropathic pain: dysesthesia, paresthesia, and hyperesthesia; Dissociated sensory loss: loss of pin-prick and temperature sensation; LOS: length of hospital stay; IP: Intraoperative. To compare findings between both groups, an independent samples t-test was used.

* Five of these patients were first treated conservatively for 6 months before being accepted as surgical candidates.

** The numbers (1, 2, 3, and 4) are the categories' numbers as our classification.

*** These patients suffered from urge incontinence.

Table 4. Comparison between the pretreatment clinical findings in neurological examinations and the pretreatment radiological findings between the surgical and conservative groups.

Findings	Conservative G.	Surgical G.	p-values	All pts
Clinical:	31 (36.5%)	46 (63.9%)	***< 0.001***	77 (49.0%)
– Headache w/ Valsalva	28 (32.9%)	36 (50.0%)	***0.001***	64 (40.8%)
– Pinprick loss	14 (16.5%)	29 (40.3%)	***0.035***	43 (27.4%)
– Sensation disturbance	10 (11.8%)	25 (34.7%)	***< 0.001***	35 (22.3%)
– Vertigo test (+)	4 (4.7%)	23 (31.9%)	***<0.0001***	27 (17.2%)
– GAG reflex (-)	10 (11.8%)	14 (19.4%)	0.27	24 (15.3%)
– Impaired DTRs	3 (3.5%)	13 (18.1%)	***0.003***	16 (10.2%)
– Romberg sign (+)	0	8 (11.1%)	***0.02***	8 (5.1%)
– Paresis	2** (2.4%)	4 (5.6%)	0.41	6 (3.8%)
– Urine incontinence ± Sphincter laxity	0	5 (6.9%)	***0.02***	5 (3.2%)
– Musculature atrophy				
Radiological:	8.8 ± 2.6 (3–16) mm	13.1 ± 3.1 (3–18) mm	0.27	10.8 ± 2.7 (3–18)
– Mean tonsil hernia (midsag.)#	(n = 85)	(n = 72)		mm (n = 157)
– Mean tonsil hernia (coronal)#	9.3 ± 2.1 (4–18) mm (n = 24)	13.9 ± 2.4 (3.8–17) mm (n = 53)	0.12	11.3 ± 2.2 (3.8–17) mm (n = 77)
– Mean ASVs (µl) (n = 157) #	16.5 ± 2.7 (12–25)	12.3 ± 1.1 (9–15)	0.17	14.7 ± 2.5 (9–25)
– Syrinx (±)	8/77 (9.4%)	23/49 (31.9%)	***< 0.001***	31/126 (19.7%)
– Mild scoliosis (±) ***	4/81 (4.7%)	10/62 (13.9%)	0.053	14/143 (8.9%)
– Mid kyphosis (±) ***	1/84 (1.2%)	3/69 (4.2%)	0.33	4/153 (2.5%)

$p < 0.05$ is statistically significant. G.: Group, Headache w/ Valsalva: Valsalva induced, tussive and exertional headache; (+): the presence; (-): the absence; DTRs: Deep tendon reflexes; midsag.: Midsagittal; n: the number of the patients; ASVs: Aqueductal stroke volume values; w/: with. To compare findings between both groups, an independent samples t-test was used.
* Five of these patients, were firstly treated conservatively for 6 months before accepted to be surgical candidates.
** These patients suffered from urge incontinence.
*** The number of these patients was relatively small since we excluded the pathologies required additional surgeries for different pathologies. The pathologies in these patients were mild that did not require additional treatments.
#These values are the averages of the mean values which were obtained from the patients over the study period at all control visits except for postoperative values in operated patients.

In the surgical group, 64 (88.9%) patients were improved. The mean of the 6th-postoperative CCOS was 14.1 ± 2.1 (the functional outcome). At their last follow-up, 59 (82.0%) patients were fully recovered (i.e. their main presenting symptoms relieved). On mid-sagittal and coronal images, the mean regression in tonsillar ectopia was 9.4 ± 1.9 mm and 8.4 ± 1.5 mm, respectively ($p < 0.001$). The mean difference between the pre-and postoperative ASV was 12.6 ± 2.2 µl, $p < 0.001$. The comparisons between pre-and post-operative radiological and clinical variables in the surgical group were shown in Tables 7 and 8.

ROC analysis showed that the cut-off ASV value to identify surgical candidates of adult CM1 with an area under curve standard error of 0.99 (0.005) ($p < 0.001$). The patients with ASV <12 µl showed 88.2% sensitivity and 82.4% specificity to obtain positive outcomes after decompressive surgery (Figure 4). In the surgical group, CSF-related complications were observed in three patients (4.2%). One patient received a syringopleural shunt insertion for the aggression of the syrinx. Two other patients received a ventriculoperitoneal shunt in their postoperative 3rd and 5th years. One patient who had meningitis after CSF fistula had a worse neurological outcome.

Discussion

The only non-invasive imaging method that assesses the quantified CSF hydrodynamics is CP-MRI. It is a 2-dimensional scan that demonstrates only the selected plane in an image and rarely gives false or insufficient results due to the partial volume effect. CP-MRI has another disadvantage as the presence of turbulent-complex flow may lead to misinterpreting. Considering the measurement level of CSF hydrodynamics at only the aqueduct sylvii that we adopted, our CP-MRI has another limitation as the restrictions of CSF hydrodynamics are also observed at the level of the foramen magnum in CM1 patients. [8–11] To reduce the interobserver disagreement and standardize the obtained findings, we preferred this technique. In CM1 patients, the circulation of CSF is hypodynamic[14]. The herniated tonsils fill into the foramen magnum in the setting of CM1 through the systole. It is followed by reducing the CSF flow at the craniocervical junction. It imposes a compensatory pulsatile descent of tonsils. The ASV started to decrease over time after the failure of compensatory mechanisms [13–15]. Like other published studies [2,8,9,11,13–15], we used CP-MRI as a tool to decide if the CM1 patient deserves surgical intervention or not. We believed that two main criteria can guide surgeons to decide how to manage the CM1 patients. Both criteria are related one each other. The first is the pretreatment symptoms and the second one is ASVs. For CM1 patients with moderate symptoms, we requested CP-MRI. In the case with ASV >15 µl without any clinical deterioration, the patient was kept on the same conservative treatment. In cases with ASV >12 – ≤15 µl, close clinical and radiological follow-up was recommended. ASV ≤12 µl with progression, we recommended decompressive surgery.

Table 5. Comparison of outcomes between both groups regarding the pretreatment symptoms.

Outcome variables	Conservative G. (n = 90)					Surgical G. (n = 72) ##					p-values#
Pretreatment symptoms:*	T	R	I	U	W	T	R	I	U	W	**1.0**
1) Pain and dysesthesia C.	**73**	**28**	**42**	**2**	**1**	**65**	**57**	**5**	**2**	**1**	0.16
- Typical headache for CM1	31	8	21	1	1	46	42	4	0	0	0.56
- Atypical headache	27	12	13	2	0	10	3	5	2	0	1.0
- Neuropathic pain	10	6	3	1	0	29	23	4	1	1	1.0
- Neck pain	12	7	4	1	0	23	17	4	1	1	1.0
- Upper extremities pain	8	5	2	1	0	8	6	2	0	0	1.0
- Spinal pain	3	2	1	0	0	6	4	2	0	0	1.0
- Chest pain	2	1	1	0	0	2	1	1	0	0	**0.13**
2) Neurological non-pain C.	**16**	**4**	**7**	**3**	**2**	**47**	**37**	**4**	**5**	**1**	***0.032***
- Dissociated sensory loss	12	3	4	3	2	36	28	4	4	0	1.0
- Vertigo/dizziness	10	2	6	1	1	25	15	4	5	1	***0.043***
- Ataxia	2	0	0	2	0	20	14	3	3	0	0.26
- Tinnitus	5	1	1	2	1	14	8	3	2	1	1.0
- Impaired reflexes	10	1	5	3	1	7	2	3	2	0	0.57
- Nystagmus	8	2	3	3	0	8	5	2	1	0	1.0
- Dysphagia	1	0	1	0	0	15	9	2	4	0	1.0
- Disequilibrium	1	0	1	0	0	9	5	2	2	0	–
- Paresis	0	0	0	0	0	8	5	2	0	1	0.4-
- Fecal ± Urine incontinence	2**	0	0	2	0	4	1	2	1	0	**0.35**
- Myelopathy	0	0	0	0	0	5	0	0	5	0	0.56
3) Functional symptoms C.	**10**	**1**	**6**	**2**	**1**	**34**	**25**	**4**	**4**	**1**	1.0
- Fatigue	8	1	5	2	0	29	23	3	3	0	1.0
- Syncope	2	0	1	0	1	8	2	3	3	0	1.0
- Cognitive impairment	2	0	1	1	0	5	2	1	2	0	1.0
- Dysarthria	2	0	1	1	0	5	1	2	2	0	**0.33**
- Hoarseness	1	0	0	1	0	4	1	2	1	0	1.0
4) Sleep apnea C.	**5**	**0**	**2**	**2**	**1**	**19**	**8**	**5**	**6**	**0**	1.0
- Sleep apnea	2	0	1	1	0	11	6	2	3	0	0.25
- Severe snoring	2	0	1	1	0	8	5	1	2	0	1.0
- Recurrent aspiration	1	0	0	0	1	7	4	2	1	0	
- Hiccoughs	1	0	1	0	0	3	1	1	1	0	
Syrinx (+)	8/85 (9.4%)					23/72 (31.5%)					***0.013***
- Fully regressed	1/8 (12.5%)					12/23 (52.2%)					
- Markedly regressed	2/8 (25.0%)					8/23 (34.8%)					
- Unchanged	5/8 (62.5%)					3/23 (13.0%)					
- Required SP shunt	0					1/23 (4.3%)***					
Mean mCCOS/CCOS value	10.4 ± 1.5 (5–12)					14.1 ± 2.8 (4–16)					-
Final overall outcome:	N = 90					N = 72					< *0.0001* (for recovered patients)
- Recovered (Excellent)	21 (23.4%)					59 (82.0%)					
- Improved (Functional)	64 (71.1%)					5 (6.9%)					
- Unchanged (Impaired)	3 (3.3%)##					7 (9.7%)					
- Worsen (Progressed)	2 (2.2%)##					1 (1.4%)					

$p < 0.05$ is statistically significant. G.: Group; C.: Category; T: Total patients; R: (Recovered): Relieved the symptom; I: (Improved): Continuing the symptom with an obvious neurological improvement that did not affect daily activity; U: (Unchanged): Continuing the symptom without any improvement; W: (Worsened): The patients felt that the symptom is worsened or impaired the patient from the daily activities); SP: Syringopleural; mCCOS: modified Chicago Chiari outcome scale; N: The number of the patients.

* The numbers (1, 2, 3, and 4) are the categories' numbers as our classification.

** These patients suffered from urge incontinence.

*** This patient had unchanged syrinx posttreatment.

#The comparison was performed between improved patients (recovered and improved) and others (unchanged and worsened patients).

##Conservative treatment was not useful in a total of 5 CM1 patients who were surgically treated later.

Previously published articles regarding CM1 focus on personal experiences, surgical outcomes, or postoperative evaluation of operated patients [3–5,7,12,16]. A few studies discussed the conservative treatment for CM1 adult patients. Two studies investigated the same 68 conservatively managed patients. Both publications reported the same patients' numbers, performed in the same period (2000–2011), the same authors' names, and the same institution [17,18]. Another study was a systematic review study[19]. In comparison to this cohort, our cohort was larger, performed in two institutions, conducted on adult patients only without pooling syndromic and child patients. The authors concluded that the presence of cough headache or/and enlarging syrinx cavities are valid surgical indications for CM1 patients. These findings were in line with ours. Furthermore, we find that the presence of more than two sleep apnea or/and functional symptoms, tonsillar herniation >13.4 mm on coronal images, ASV<13.2 µl (cut-off value = 12), and long symptom durations >31.6 months were other prognostic factors affected negatively.

Although CM1 patients demonstrate the same symptoms, not all of them are invariably symptomatic. We believe that the selection criteria of the surgical candidates should precisely select to get good surgical results. Most studies that discussed conservative treatment in CM1 considered observation as a treatment [17–19]. For us, observation of the patients is not the same as the conservative treatment. In the observation approach, the physician observes the patients without medications. Several studies reported strong indicators for the surgical

Table 6. Comparison between (conservative treatment benefited) and (conservative treatment failed) patients.

Prognostic factors	Mean	n	SD	t	p	rs
Benefited pts sex (F/M)	-	64/21	-	-	1.0	An independent samples t-test was used.
Treatment failed pts sex (F/M)	-	4/1	-			
Benefited pts age (years)	40.3	85	16.2	0.65	0.52	− 0.21
Treatment failed pts age (years)	45.2	5	16.1			
Benefited pts symptom duration (months)	17.8	85	11.6	2.32	***0.01***	− 0.32
Treatment failed pts symptom duration (months)	31.6	5	12.5			
Benefited pts w/ ≥ 2 symptoms from 3rd and 4th categories (±)	-	6/79	-	3.48	***< 0.001***	An independent samples t-test was used.
Treatment failed pts w/ ≥ 2 symptoms from 3rd and 4th categories (±)	-	4/1	-			
Benefited pts herniated ectopia on midsag images (mm)*	8.55	85	2.4	1.50	0.069	− 0.22
Treatment failed pts herniated ectopia on midsag images (mm)*	10.6	5	3.6			
Benefited pts herniated ectopia on coronal images (mm)*	8.5	85	2.3	4.32	***< 0.001***	− 0.882
Treatment failed pts herniated ectopia on coronal images (mm)*	13.4	5	2.4			
Benefited pts ASV (μl)*	16.7	85	2.6	2.74	***0.004***	0.40
Treatment failed pts ASV (μl)*	13.2	5	1.1			
Benefited pts presented w/ syrinx (±)	-	8/77	-	2.3	***0.012***	An independent samples t-test was used.
Treatment failed pts presented w/ syrinx (±)	-	3/2	-			

p < 0.05: statistically significant; pts: patients; midsag.: Midsagittal; ASV: Aqueductal stroke volume value; w/: with; +: presence; -: absence; rs: Correlation coefficient.

* These values are the averages of the mean values which were obtained from the patients over the study period at all control visits except for postoperative values in operated patients.

Table 7. Comparison between the pre- and postoperative radiological variables in the surgical group.

Variables	Mean	N	SD	t	p
Pre ectopia on midsagittal images (mm)	13.1	72	3.1	22.13	< 0.001
PO ectopia on midsagittal images (mm)	4.0	72	1.6		
Pre ectopia on coronal images (mm)	13.9	53	2.4	22.68	< 0.001
PO ectopia on coronal images (mm)	5.8	53	1.0		
Pre ASV (μl)	12.3	72	1.1	43.12	< 0.001
PO ASV (μl)	24.8	72	2.2		
Pre S/C ratio	0.81	23	0.1	5.49	< 0.001
PO S/C ratio	0.53	11	0.2		
Pre length of the syrinx (mm)	61.6	23	71.1	1.16	0.25
Pre length of the syrinx (mm)	33.6	11	51.4		

Pre: Preoperative; PO: Postoperative; max: maximum; ASVs: Aqueductal stroke volume values; S: Syrinx; C: spinal cord; S/C: the ratio of syrinx to the spinal cord on axial images; (+): presence.

Table 8. Comparison between the clinical improvement and the duration of preoperative symptoms, postoperative persistence of the syrinx, and the 6th postoperative MRIs in the surgical group.

Correlation Coefficient r/p	Clinical improvement
Long preoperative course	rs = −0.47 p < 0.001
PO absence of the syrinx**	- p = 0.005
Increasing of ASV values in the PO 6th month MRIs	rs = 0.61 p < 0.001
Regression of herniated cerebellar tonsils on coronal images	rs = −0.26 p = 0.014
Regression of herniated cerebellar tonsils on midsagittal images	rs = −0.16 p = 0.086

** An independent samples t-test was used.

intervention of CM1 patients as the presence of a syrinx, sleep apnea, recurrent aspiration, drop attacks, and dysphagia [6,16,17,20,2122].

We observed that the surgical treatment had superiority in improving the dissociated sensory loss, ataxia, and syrinx cavities than conservative modalities; however, such comparisons are confusing and led to statistical bias. The selection criteria and ASVs are not the same in both groups. To avoid irreversible neurological deficits, we suggested surgical intervention for CM1 patients with paresis and myelopathy. We managed CM1 patients with moderate or mild symptoms conservatively. Chavez and colleagues study [17] reported that surgical decompression was effective in improving cough headaches, paresthesias, and ataxia than conservative treatment.

Etiological factors that lead to abnormal CSF hydrodynamics can cause clinical symptoms as typical occipital Valsalva-type headaches, changes in neuropsychological and cognitive functions, the lower cranial nerve involvements, and myelopathy [1,11,16]. The association of CM1 with myelopathy is not a common phenomenon[22]. In our studied patients, five of them were presented with myelopathy and other advanced symptoms. After requesting an MRI, all of these patients were operated on to reduce irreversible neurological deficits. Obstruction of the 4th ventricular level can result in changes in craniospinal pressure that have been advocated in the genesis of syringomyelia. However, the exact relationship

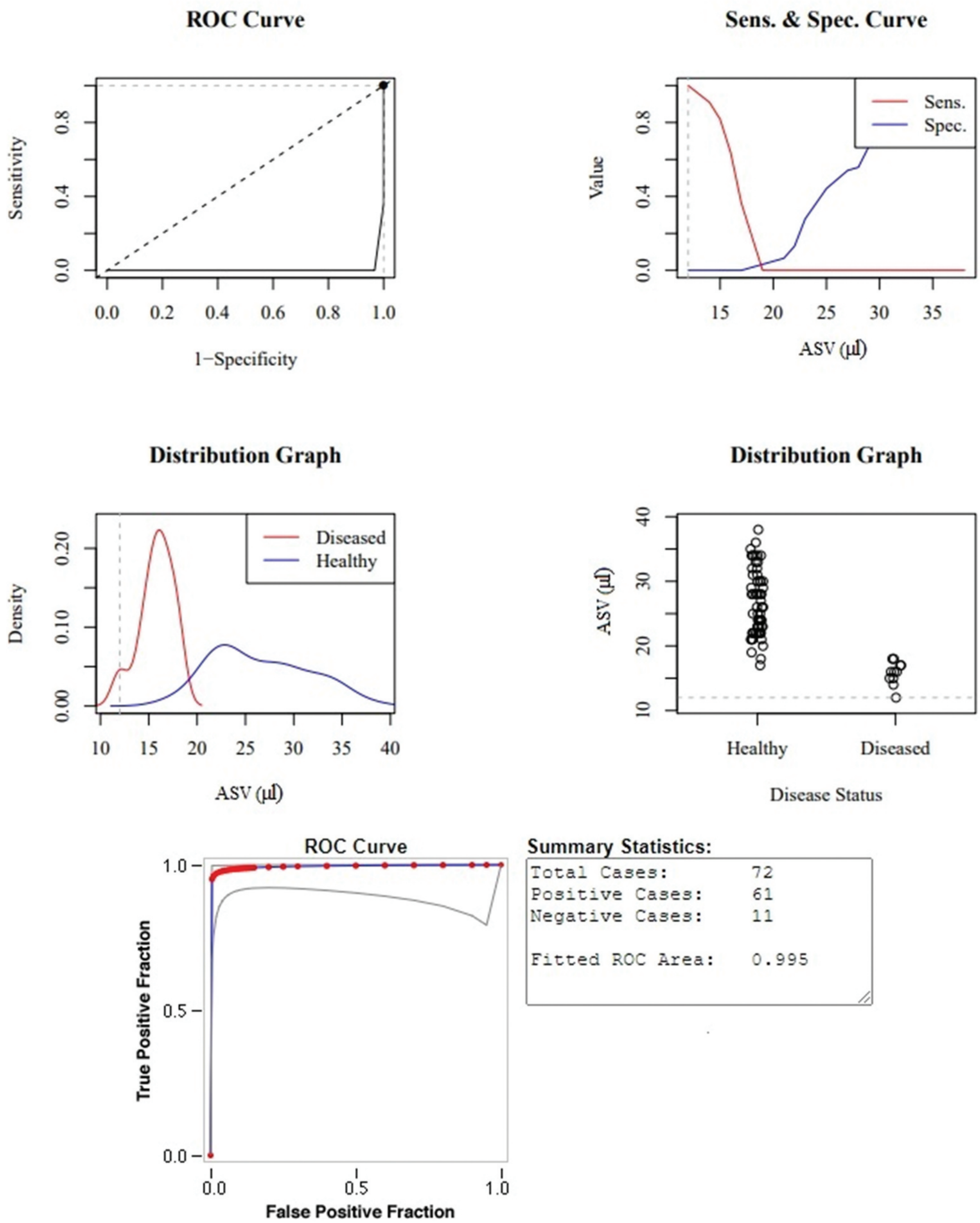

Figure 4. The Youden Index demonstrated ROC analysis of the cut-off value of the ASV was 12 µl. ASV: Aqueductal stroke volume; ROC: Receiver Operating Curve; Sens: Sensitivity; Spec: Specificity.

between syringomyelia and arachnoid veils is not yet completely identified [1,16]. Several studies suggested that the selection criteria for surgery should depend mainly on the degree of CSF flow obstruction rather than herniation degree and mild presenting symptoms. These studies supposed that CSF flow is an effective and better alternative parameter to assess treatment outcome [8,9,11]. In our clinical practice, we noticed that invariably symptomatic patients generally presented with ASV<15 µl. To obtain an acceptable outcome, we directly recommend surgical treatment for such cases.

According to our findings, the main poor prognostic factors affecting the treatment prognosis are long symptoms' duration and postoperative persistence of herniated tonsils on the coronal images and syrinx cavities. On the other hand, we didn't find any relationship between the surgical outcomes and the regression of tonsillar ectopia on midsagittal images. One study reported that in CM1 patients, mid-sagittal images of MRI alone led to the misdiagnosis of tonsillar ectopia degrees[12].

The study has a few limitations that are the relatively small sample size, the retrospective nature of the study, and the restricted conservative modalities. Other institutions may use different conservative modalities. In the CM1 disorder, the restrictions of CSF hydrodynamics occurred mainly at the aqueduct sylvii and the foramen magnum levels; however, our method measures the CSF hydrodynamics at one level only (the aqueduct sylvii) on CP-MRI. This is the main limitation of the current study. To support our findings, further randomized prospective studies with a long follow-up period and a large sample are mandatory.

Conclusions

ASV≤12 μl is a significant predictor for surgical intervention. The clinical improvement was correlated positively with the increase in post-treatment ASV values. The presence of heavy sleep apnea or/and functional symptoms, tonsillar herniation >13.4 mm on coronal images, low ASV, long symptom durations, and a syrinx are the independent prognostic factors that affected outcomes negatively.

This retrospective study was approved under decision number: (19/265) by the medical ethics committee of Bezmialem Vakif University in Istanbul-Turkey.

Name of the Departments and Institutions in which the work was done: Department of Neurosurgery – Bezmialem Vakif University (Center B) and Department of Neurosurgery – Bakırköy Research and Training Hospital for Neurology Neurosurgery, and Psychiatry (Center A).

statement of Authorship

AA: Conceptualization, Methodology, Software, Supervision, Formal analysis, Statistical analysis, Literature review, Visualization, Investigation, Writing – Original draft, and Writing – Review; **İÇ**: Conceptualization, Methodology, Supervision, Formal analysis, Literature review, Visualization, Investigation, Writing – Original draft, and Writing – Review; **MGP**: Conceptualization, Methodology, Literature review, Writing – Reviewing; **BGA**: Methodology, Literature review, Writing – Draft, Investigation, **ÖES**: Validation; **EE**: Supervision.

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References

[1] Rogers JM, Savage G, Stoodley MA. A Systematic. Review of Cognition in Chiari I Malformation. Neuropsychol Rev. 2018;28(2):176–187.

[2] Shah S, Haughton V, del Río AM. CSF flow through the upper cervical spinal canal in Chiari I malformation. Am J Neuroradiol. 2011;32 (6):1149–1153.

[3] Aliaga L, Hekman KE, Yassari R, et al. A novel scoring system for assessing Chiari malformation type I treatment outcomes. Neurosurgery. 2012;70 (3):656–664.

[4] Moncho D, Poca MA, Minoves T, et al. Are evoked potentials clinically useful in the study of patients with Chiari malformation Type I? J Neurosurg. 2017;126(2):606–619.

[5] Alzate JC, Kothbauer KF, Jallo GI, et al. Treatment of Chiari I malformation in patients with and without syringomyelia: a consecutive series of 66 cases. Neurosurg Focus. 2001;11:E3.

[6] Lin W, Duan G, Xie J, et al. Comparison of Results Between Posterior Fossa Decompression with and without Duraplasty for the Surgical Treatment of Chiari Malformation Type I: a Systematic Review and Meta-Analysis. World Neurosurg. 2018;110:460–474.

[7] Hekman KE, Aliaga L, Straus D, et al. Positive and negative predictors for good outcome after decompressive surgery for Chiari malformation type 1 as scored on the Chicago Chiari outcome scale. 2012;34 (7):694–700.

[8] McGirt MJ, Nimjee SM, Fuchs HE, et al. Relationship of cine phase-contrast MRI to outcome after decompression for Chiari I malformation. Neurosurgery. 2006;59:140–146.

[9] Wang CS, Wang X, Fu CH, et al. Analysis of cerebrospinal fluid flow dynamics and morphology in Chiari I malformation with cine phase-contrast magnetic resonance imaging. Acta Neurochir (Wien). 2014;156(4):707–713.

[10] Yılmaz TF, Aralasmak A, Toprak H, et al. Evaluation of CSF flow metrics in patients with communicating hydrocephalus and idiopathic intracranial hypertension. Radiol Med. 2019;124 (5):382–391.

[11] Papaker MG, Abdallah A, Cesme DH, et al. Clinical and radiological evaluation of treated Chiari I adult patients: retrospective study from two neurosurgical centers. Neurosurg Rev. 2020 Oct 14. DOI:10.1007/s10143-020-01414-z. [Published online].

[12] Tubbs RS, Yan H, Demerdash A, et al. Sagittal MRI often overestimates the degree of cerebellar tonsillar ectopia: a potential for misdiagnosis of the Chiari I malformation. Childs Nerv Syst. 2016;32:1245–1248.

[13] Luetmer PH, Huston J, Friedman JA, et al. Measurement of cerebrospinal fluid flow at the cerebral aqueduct by use of phase-contrast magnetic resonance imaging: technique validation and utility in diagnosing idiopathic normal pressure hydrocephalus. Neurosurgery. 2002;50:534–543.

[14] Battal B, Kocaoglu M, Bulakbasi N, et al. Cerebrospinal fluid flow imaging by using phase-contrast MR technique. Br J Radiol. 2011;84 (1004):758-765.

[15] Korbecki A, Zimny A, Podgórski P, et al. Imaging of cerebrospinal fluid flow: fundamentals, techniques, and clinical applications of phase-contrast magnetic resonance imaging. Pol J Radiol. 2019;84:e240-e250.
[16] Ciappetta P, Signorelli F, Visocchi M. The Role of Arachnoid Veils in Chiari Malformation Associated with Syringomyelia. Acta Neurochir Suppl. 2019;125:97–99.
[17] Chavez A, Roguski, M, Killeen, A, Heilman C, Hwang S. Comparison of operative and non-operative outcomes based on surgical selection criteria for patients with Chiari I malformations. J Clin Neurosci. 2014;21 (12):2201–2206.
[18] Killeen A, Roguski M, Chavez A, Heilman C, Hwang S. Non-operative outcomes in Chiari I malformation patients. J Clin Neurosci. 2015;22(1):133–138.
[19] Langridge B, Phillips E, Choi D. Chiari Malformation Type 1: a Systematic Review of Natural History and Conservative Management. World Neurosurg. 2017;104:213–219.
[20] Alden TD, Ojemann JG, Park TS. Surgical treatment of Chiari I malformation: indications and approaches. Neurosurg Focus. 2001;11(1):E2.
[21] Chiari SA. I malformation: clinical presentation and management. J Neurosci Nurs. 2001;33 (2):90–104.
[22] Perrini P, Gambacciani C, Martini C, Montemurro N, Lepori P. Anterior cervical corpectomy for cervical spondylotic myelopathy: Reconstruction with expandable cylindrical cage versus iliac crest autograft. A retrospective study. Clin Neurol Neurosurg. 2015;139:258–263.