Conservative Treatment of Chiari Malformation Type I Based on the Phase-Contrast Magnetic Resonance Imaging: A Retrospective Study

Anas Abdallah[1] and Usame Rakip[2]

■ BACKGROUND: **The use of phase-contrast magnetic resonance imaging is interestingly increased in the diagnosis and follow up of patients with Chiari type I malformation (CM1). The current study aimed to elaborate the benefits of conservative treatment by evaluating consecutively treated adult patients with CM1 who were selected on basis of phase-contrast magnetic resonance imaging.**

■ METHODS: **Medical records of patients diagnosed with CM1 were retrospectively reviewed at 2 neurosurgical centers spanning 8 years (2010–2017). Adult patients with CM1, who were treated conservatively and met study criteria, were selected to be the core sample for this study. Between-group (benefited vs. nonbenefited) comparisons were performed to understand the factors that may affect the outcomes.**

■ RESULTS: **Ninety adult patients (68 female and 22 male) received conservative treatment for CM1. The mean age was 40.6 years. Headaches and pinprick loss were the most commonly recorded symptoms and clinical findings, which were recorded in 58 (64.4%) and 31 (34.4%) patients, respectively. Eleven patients were presented with a syrinx. The mean aqueductal stroke volume (ASV) was 16.5 μL. Conservative treatment was ineffective in treating 5 (5.6%) patients, who underwent surgical intervention. The means of ASV in the benefited and nonbenefited groups were 16.7 and 13.2 μL, respectively ($P = 0.004$).**

■ CONCLUSIONS: **Conservative approaches (prescriptive medications, physical therapy, Pilates, and swimming) can improve the life quality of nonsurgical candidate adult patients with CM1. Conservative treatment can be useful in selected patients with variably CM1 (ASV = 16.7 μL). Heavy sleep apnea or/and functional symptoms were prognostic factors that affected the conservative treatment negatively.**

INTRODUCTION

Chiari malformation type I (CMI) is a puzzling clinicopathologic entity that remains a challenge for neurosurgeons.[1] The advent of magnetic resonance imaging (MRI) has led to an increase in patients who are diagnosed with CMI. CMI is a herniation of the cerebellar tonsils or medulla oblongata from the foramen magnum caudally down to the cervical spinal.[2-4] The presenting symptoms have a variable spectrum, from a mild headache to dysphagia and cognitive impairment. Clinical and functional symptoms in the symptomatic patients may appear due to the congestion of the posterior fossa and its critical neurovascular structures.[3,4]

The accurate etiology of CMI is unclear. Although it is believed to be present from birth (congenital) or may develop later in life (acquired), exact estimates are difficult to make. CMI-related syringomyelia can be developed as the consequence of several

Key words
- Chiari malformation type I
- Conservative treatment
- CSF flow MRI
- Phase-contrast MRI
- Prognosis
- Prognostic factor

Abbreviations and Acronyms
ASV: Aqueductal stroke volume
CM1: Chiari malformation type I
CSF: Cerebrospinal fluid
FOV: Field of view
mCCOS: modified Chicago Chiari outcome scale
MRI: Magnetic resonance imaging
PC-MRI: Phase-contrast magnetic resonance imaging
PTR: Physical therapy and rehabilitation

From the [1]Department of Neurosurgery, Istanbul Training and Research Hospital, Samatya—Istanbul; and [2]Department of Neurosurgery, Faculty of Medicine, Afyonkarahisar Health Sciences University, Afyonkarahisar—Afyon, Turkey

To whom correspondence should be addressed: Anas Abdallah, M.D.
[E-mail: abdallahanas@hotmail.com; dr.anasabdallah@gmail.com]

Anas Abdallah and Usame Rakip contributed equally to this work and are co—first authors.

Citation: World Neurosurg. (2022).
https://doi.org/10.1016/j.wneu.2022.03.126

Journal homepage: www.journals.elsevier.com/world-neurosurgery

Available online: www.sciencedirect.com

mechanisms such as compression at the craniocervical junction, impairment of cerebrospinal fluid (CSF) flow at the foramen magnum level, or the obstruction of the subarachnoid space at the level below the fourth ventricle.[3,5-7] Most studies have supposed that patients with CM1 have not the same surgical outcomes.[3,4] The critical factors necessary to obtain a favorable outcome are the patient selection and timing of the surgical intervention.[6] Many studies showed improvements in the presenting symptoms of most patients with CM1 after decompressive surgical intervention. However, some patients had worse neurologic deficits after receiving sufficient anatomic decompression.[1-4,6,8-11]

The management of asymptomatic patients with CM1 remains controversial. A few studies reported a comparison between the outcomes of surgical and conservative treatment in patients with CM1.[12,13] After conducting full physical and neurologic examinations, we also requested a whole craniospinal MRI (particularly the evaluation of the coronal sequences at the cervicomedullary junction) and phase-contrast (CSF flow) MRI (PC-MRI) before managing adult patients with CM1. This retrospective study aimed to elaborate the benefits of conservative approaches by evaluating consecutively treated adult patients with CM1 who were selected on basis of the PC-MRIs.

METHODS

Study Design, Patient Population, and Study Criteria

The ethical board of our institution (Bezmialem Vakif University [BVU], Istanbul, Turkey) approved this retrospective study on October 24, 2017, with decision number 54022451-050.05.04). Medical records of patients diagnosed with CM1 were retrospectively reviewed at 2 referral neurosurgical centers spanning 8 years (January 2010—December 2017). Consecutive adult patients with CM1 who were treated conservatively and met study criteria were selected to be the core sample for this study. We discussed presenting symptoms, radiologic MRI findings, neurologic functional assessment, and treatment outcomes.

Inclusion criteria are as follows: 1) patients who were diagnosed clinically with specific symptoms for CM1; 2) adults (age >18 years old); 3) received conservative treatment; 4) radiologic diagnosis was determined by sagittal, coronal, and axial sequences of MRI and PC-MRIs; 5) followed up for a minimum of 2 years, attended to all the control visits with control MRIs; and 6) consent for study and participation.

Exclusion criteria are as follows: 1) patients who underwent surgical intervention for CM1 without conservative treatment; 2) syndromic patients; 3) had cranial, spinal lesions, or received a ventriculoperitoneal shunt for coincident hydrocephalus; 4) contraindication for MRI or no pre- or posttreatment MRIs; 5) lost to follow-up for any reason; and 6) rejected participation. Thus, our core sample yielded 90 patients (Table 1).

Imaging Strategy

MRI scanning with a head coil on a 1.5 Tesla system (Avanto; Siemens, Germany) was performed. Using axial plane slices obtained from a 2-dimensional Q FLOW PC-MR angiography method, the CSF flow hydrodynamics quantitative assessment was achieved. Our neuroradiologists planned axial plane slices to pass through the ampulla of the aqueduct sylvii level, which is the widest and middle-third region of aqueduct sylvii.

Respectively, sagittal, coronal, T1-weighted images, semi-axial plane directional phase difference, the magnitude of complex difference, and "mean modulus" images perpendicular to the cerebral aqueduct in the sagittal plane were obtained. Our radiologists determined velocity encoding that measured the flow sensitivity as 20 cm/s. The used parameters for the 14—30 cardiac phase sections according to heart rate were: 3-mm slice thickness, field of view (FOV): 16 $\times$ 10 cm, number of signals average: 1, echo time: 8.06 milliseconds, repetition time: 31.25 milliseconds, matrix: 128 $\times$ 256, and flip angle 10° for axial plane images.

After achieving a PC-MRI that lasted approximately 5 minutes for each patient, sagittal T2-CISS (constructive interference in steady state) and T2-SPACE (sampling perfection with application-optimized contrasts by using different flip angle evolutions) sequences were obtained. The used parameters were: 1-mm slice thickness, echo time: 2.61 milliseconds , matrix: 290 $\times$ 320, repetition time: 6.06 milliseconds, FOV: 200 mm, and flip angle 70° for 3-dimensional T2-CISS images. The used parameters were: 1-mm slice thickness, echo time: 501, matrix: 231 $\times$ 256, repetition time: 2500, and FOV: 240 mm for 3D-T2-SPACE images. The neuroradiologists accepted forward (systolic) flow in the craniocaudal as a positive flow. Reverse (diastolic) flow in the caudocranial direction was accepted as a negative flow.[4]

Radiologic Analysis. During one cardiac cycle, the mean volume flow was calculated with the formula as follows: systolic volume + diastolic volume/range (0—680 milliseconds) $\times$ 60 mL/min. The aqueductal stroke volume (ASV) was calculated with the formula as follows: systolic volume + diastolic volume/2 (μL).[4]

The neuroradiologists used axial plane slices of PC-MRI to assess CSF flow hydrodynamics. In one cardiac cycle, flow contours were drawn by a region of interest that was copied over entirely axial phase slices. The sum and difference of systolic and diastolic times (milliseconds), and systolic time/diastolic time ratios were calculated.

Technical Details and Validity. ASV is heavily impacted by many factors, such as volume of the aqueductal area, ventricular volume, the production and absorption of CSF, pulsatility measure, arterial pulsation, respiration, and the presence of neurovascular disorders.[4,6,12] Therefore, the benefit of PC-MRI use in diagnosis and follow-up patients with CM1 remains debatable.

The restrictions of CSF flow in CM1 are on more than one level (aqueduct sylvii, the anterior, and posterior of the foramen magnum). Moreover, there is no consensus regarding the optimal method to measure an exact ASV. In this cohort, CSF movements were measured at only the aqueduct sylvii level. However, measuring CSF flow only done at one level may give insufficient or false results due to the partial volume effect on a selected plane of the image.[4,12]

Management of Adult Patients with CM1

Many management algorithms have been established for the treatment of CM1. The first used algorithms depended on the clinical symptoms and caudal herniation part (above 7 mm into the upper cervical canal).[1,4,6,11] In clinical practice, the authors

Table 1. Reviewed Patients Regarding the Centers and Treatment Approaches ($n = 331$)

	Center (A)	Center (B)	All Patients
Study period	January 2010 to July 2016	January 2012 to December 2017	January 2010 to December 2017
All patients diagnosed with CM1	210	121	331
Asymptomatic patients	41 (19.5%)	29 (24.0%)	70 (21.1%)
Symptomatic patients	169 (80.5%)	92 (76.0%)	261 (78.9%)
Observed patients without treatment	28 (16.6%)	15 (16.3%)	43 (16.5%)
Conservative with or without 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 patients (<18 years)	18 (20.5%)	7 (15.6%)	25 (18.8%)
Syndromic adult patients	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 PFD alone	2 (2.3%)	2 (4.4%)	4 (3.0%)
For recurrent CM1	1 (1.1%)	2 (4.4%)	3 (2.2%)
Lost to follow-up	4 (4.5%)	3 (6.7%)	7 (5.3%)
Patients received PFDD	47 (53.4%)	25 (55.6%)	72 (54.1%)*

No pre/PO adequate MRIs: if the patients lost comparative sagittal, coronal, or PC-MRIs; Additional pathologies: hydrocephalus, intracranial, or spinal lesions; Received PDF alone: no duraplasty or/and C1 laminectomy.

CM1: Chiari malformation type I; PTR, physical therapy and rehabilitation; pre, preoperative; PO, postoperative; PFD, posterior fossa decompression without a duraplasty; PFDD, posterior fossa decompression with a duraplasty; MRI, magnetic resonance imaging.

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

ought to use 4 critical aspects before managing CM1. The clinical symptoms, full neurologic examination, and radiologic investigations were the first 3 aspects. Radiologic investigations included routine craniospinal, coronal images of the craniocervical junction, and PC-MRIs. If these 3 critical aspects did not give sufficient data to decide regarding surgical intervention, the somatosensory-evoked potential was applied.[3,6]

Clinical and Neurologic Diagnosis. We divided the presenting symptoms into 4 categories. The first 3 categories are the same as in the study by Aliaga et al.,[11] comprising pain, neurologic nonpain, functional symptoms, and the fourth group was the sleep apnea category. Pain symptoms include high cervical or occipital and upper extremities pain or dysesthesia. A tussive headache that reproduces with a Valsalva maneuver, neck, spinal, chest, and arm pains were other types of CM1 patients' pain fashions. Neuropathic pain also was included in the pain group. Neurologic nonpain symptoms comprised dysphagia, vertigo, tinnitus, nystagmus, paresis, and myelopathy. Lower-extremity spasticity (ataxia), pinprick/temperature sensory disturbance, hyper- or hyporeflexia, fecal, or/and urine incontinence were included in this group. Since it is a symptom, we excluded syrinx from this category. Functional symptoms include the ability of the patients to attend to their jobs, school, and continue normal daily activities, syncope, hoarseness, cognitive impairments (such as fine motor skills impairments, navigation ability impairments, and memory impairment), and dysarthria as well as sleep apnea and similar symptoms such as severe snoring, hiccups, and recurrent aspiration. Nocturnal polysomnography, when indicated, can be useful to diagnose sleep apnea. Therefore, attention in taking the history for such symptoms and a full neurologic examination are essential to diagnose CM1 before requesting MRIs. Some neglected tests are critical for suspected CM1, such as the pharyngeal reflex (gag reflex). The absence of this reflex requires further investigation for incidentally diagnosed patients with CM1.[4]

Radiologic Studies and Follow-Up Protocol. After observing the suggestive symptoms of CM1, we requested the craniospinal MRI for all the patients. The patients with ectopic cerebellar tonsils into the upper cervical canal at more than 5 mm on sagittal and coronal sequences[1,3,4,6] (Figure 1) underwent PC-MRIs to evaluate the dynamics of CSF at the craniocervical junction (Figure 2). Hypodynamic flow was defined as an ASV <18 μL.[4,6,14,15] It was observed that the patients with an ASV <12 μL were invariably symptomatic. Therefore, such patients were selected to treat surgically.[4,6] Patients with ASVs of 18 ± 3 μL were classified as a risky group[4]; therefore, they were closely followed up once every 3 months.

The extent from the McRae's line (i.e., the declined line was drawn between 2 anatomical landmarks; opisthion and basion points) to the lowest point of ectopic tonsils through the upper

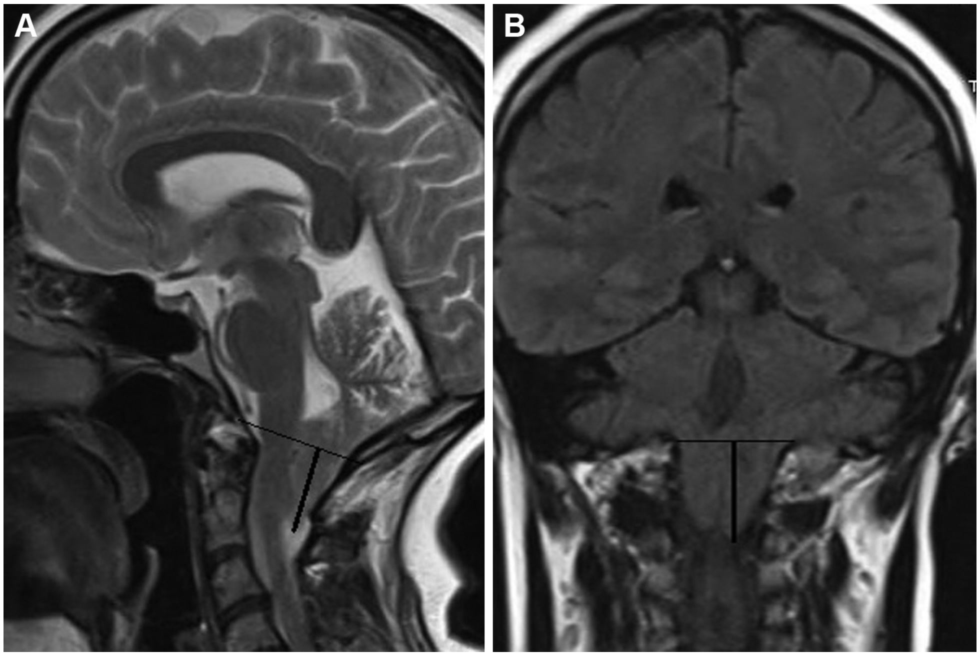

Figure 1. A 40-year-old female patient diagnosed with Chiari malformation type I. The pretreating midsagittal (**A**) and coronal (**B**) sequences showed a caudal descent of the cerebellar tonsils of 15.6 mm and 13.7 mm, respectively.

cervical canal was measured on sagittal sequences. The extent between a horizontal line drawn at the 2 lowest points of the foramen magnum and the lowest point seen of ectopic tonsils was measured on coronal images.[16] Two group-blinded senior neuroradiologists with experience of >20 years evaluated all MRIs. The interobserver agreement seen in 85 of the 90 (94.4%) studied patients was acceptable with Cohen's Kappa coefficient of 0.86. In disagreement cases, neuroradiologists adopted the consensus after arguing.

Management Protocol for Adult Patients with CM1

In our practice, after investigating, the adult patients with CM1 were classified into 3 main groups regarding their symptoms and imaging scans: 1) asymptomatic group: incidentally diagnosed patients without permanent clinical symptoms; 2) variably symptomatic group: patients were presented with typical symptoms without definite radiologic findings (i.e., hypodynamic CSF flow or/and the syrinx); and 3) invariably symptomatic group: patients were presented with at least 3 typical symptoms from different 3 categories (see clinical and neurologic diagnosis previously) with radiologic proven reflected on CSF hydrodynamics. Patients from the latter group are surgical candidates. The prognosis of CM1 in these patients is poor and they do not benefit from the conservative treatment. To avoid advanced neurologic deficits, the authors recommended surgery for this group. In this study, our target groups are the first 2 groups. The authors managed both groups conservatively with close follow-up for the second group.

Outcome Variables

As part of our standard care, patients with CM1 received a routine clinical assessment monthly. If neurologic impairment occurred, new cervical and PC-MRIs with coronal, sagittal, and axial sequences were requested. The patient was re-evaluated after conservative therapy. For clinical evaluation of the treatment benefit, the sixth posttreatment month modified Chicago Chiari Outcome Scale (mCCOS) scores were calculated and recorded (Table 2).[6] For assessment of the radiologic progression and improvement, the differences in ASV values between the pretreatment and the sixth-month posttreatment MRIs were measured. For the follow-up, the patients were examined and a yearly MRI was requested.

Statistical Analysis

All the data were expressed thereafter as the mean $\pm$ standard deviation with the ranges. A receiver operating curve (ROC) analysis was achieved using the Youden index to identify the cutoff value of ASV that related to recovery and improvement outcomes (CCOS $\geq$13) in operated patients. Univariate analysis was conducted to examine the association between clinical and radiologic variables. Pearson (for normally distributed data) or Spearman (for ordinal data) correlation analysis was used to evaluate the correlations between the scales and variables. For categorical data such as the comparison between the presence of syrinx and improvement, the authors used an independent samples t test. With the SPSS 24.0 statistical package software (IBM Corp., Armonk, New York, USA), the authors assessed the

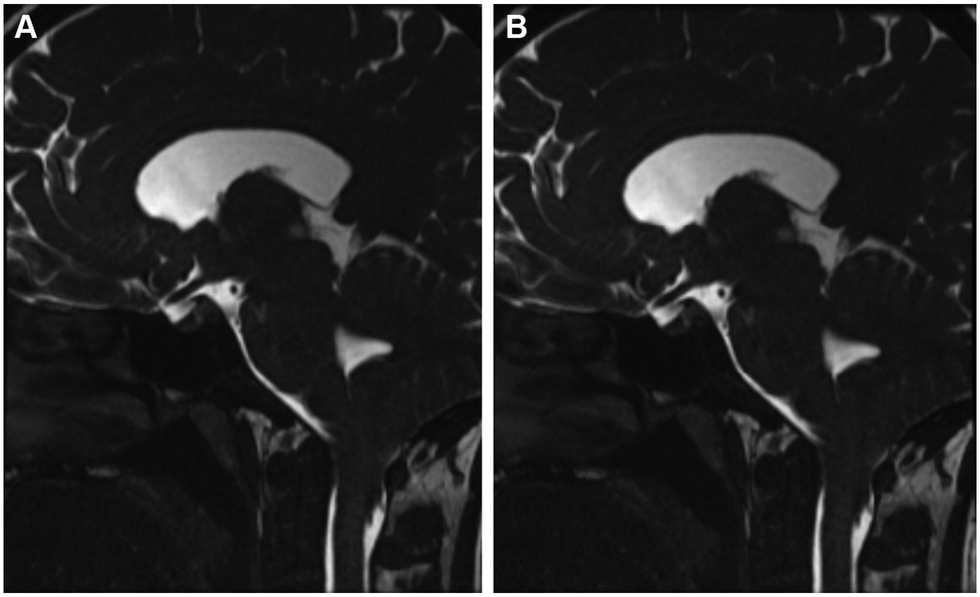

Figure 2. The pre- and the sixth post-treating phase-contrast magnetic resonance imaging (PC-MRI) was obtained from a 37-year-old-female patient who was treated conservatively with a daily dose of pregabalin of 1–1.5 mg/kg and weekly 1-hour swimming. (**A**) The pretreating sagittal 3D fast imaging employing steady-state acquisition with phase cycling (FIESTA-C) PC-MRI sequence demonstrated that cerebellar tonsils were displaced into the cervical canal with compression of the cerebellum at the cervicomedullary junction that caused impairment of cerebrospinal fluid flow, making it a mild hypodynmanic. The aqueductal stroke volume (ASV) value was measured to be 16 µL. (**B**) The sixth post-treating sagittal 3D FIESTA-C PC-MRI sequence demonstrated that the ASV value was improved to 19 µL, which was associated with improvement of clinical and functional outcome (modified Chicago Chiari outcome scale = 11).

statistical differences between mean values of pre- and posttreatment measurements in the same patients by a paired t-test. Significance was determined using a *P* value of < 0.05. All tests were 2-tailed.

RESULTS

A total of 331 patients were diagnosed with symptomatic CM1 in the first (A) institution from January 2010 to July 2016 or the second (B) institution from January 2012 to December 2017. Among these patients, 90 (68 female and 22 male) adult patients received conservative treatment for CM1 who met the study criteria (Table 1). The mean age was 40.6 ± 15.2 years (range, 18–74 years). The most commonly seen symptom was a headache, which was observed in 58 (64.4%) patients. The most common clinical finding in neurologic examinations was the pinprick loss, seen in 31 (34.4%) patients. Radiologically, 11 patients (12.2%) presented with a syrinx. The mean tonsillar herniation on midsagittal and coronal sequences was 8.8 ± 2.2 mm (range, 3–16 mm) and 9.3 ± 2.1 mm (range, 4–18 mm), respectively. The mean ASV was 16.5 ± 1.8 µL (range, 12–25 µL) (Table 3).

The applied conservative treatment modalities were divided into 4 lines. The first line included analgesics, myorelaxants, multivitamins, and weekly swimming that was successful in 22 (24.4%)

Table 2. Modified Chicago Chiari Outcome Scale for Conservatively Treated Patients[6]

Pain Intensity	S	Nonpain	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.

Table 3. Demographics, Clinical Characteristics, and Radiologic Findings

	Center (A)	Center (B)	All Patients
Number of patients	56 (62.2%)	34 (37.8%)	90 (100%)
Sex (F/M)	40/16 (71.4%)	28/6 (82.4%)	68/22 (75.6%)
Mean age, years	41.2 ± 16.4 (18–74)	39.7 ± 14.8 (24–72)	40.6 ± 15.2 (18–74)
Presenting symptoms			
Pain and dysesthesia	49 patients (87.5%)	29 patients (85.3%)	78 patients (86.7%)
Headache*	37 (66.1%)	21 (61.8%)	58 (64.4%)
Neuropathic pain	9 (16.1%)	5 (14.7%)	14 (15.6%)
Neck pain	10 (17.9%)	3 (8.8%)	13 (14.4%)
Upper extremity pain	8 (14.3%)	2 (5.9%)	10 (11.1%)
Back with or without low back pain	3 (5.4%)	1 (2.9%)	4 (4.4%)
Chest pain	2 (3.6%)	1 (2.9%)	3 (3.3%)
Neurologic nonpain	12 patients (21.4%)	7 patients (20.6%)	19 patients (21.1%)
Dissociated sensory loss	10 (17.9%)	4 (11.8%)	14 (15.6%)
Vertigo/dizziness	8 (14.3%)	5 (14.7%)	13 (14.4%)
Impaired reflexes	7 (12.5%)	5 (14.7%)	12 (13.3%)
Nystagmus	5 (8.9%)	3 (8.8%)	8 (8.9%)
Tinnitus	3 (5.4%)	2 (5.9%)	5 (5.6%)
Ataxia	2 (3.6%)	1 (2.9%)	3 (3.3%)
Disequilibrium	2 (3.6%)	1 (2.9%)	3 (3.3%)
Dysphagia	1 (1.8%)	1 (2.9%)	2 (2.2%)
Urge incontinence	1 (1.8%)	1 (2.9%)	2 (2.2%)
Functional symptoms	7 patients (12.5%)	6 patients (17.6%)	13 patients (14.4%)
Fatigue	5 (8.9%)	4 (11.8%)	9 (10.0%)
Cognitive impairment	2 (3.6%)	2 (5.9%)	4 (4.4%)
Dysarthria	2 (3.6%)	1 (2.9%)	3 (3.3%)
Syncope	2 (3.6%)	1 (2.9%)	3 (3.3%)
Hoarseness	1 (1.8%)	0	1 (1.1%)
Sleep apnea category	4 patients (7.1%)	3 patients (8.8%)	7 patients (7.8%)
Sleep apnea	2 (3.6%)	2 (5.9%)	4 (4.4%)
Severe snoring	2 (3.6%)	1 (2.9%)	3 (3.3%)
Recurrent aspiration	1 (1.8%)	1 (2.9%)	2 (2.2%)
Hiccups	0	1 (2.9%)	1 (1.1%)
Symptom duration, months	19.2 ± 14.6 (4–48)	17.6 ± 7.7 (3–30)	18.6 ± 12.4 (3–48)
Follow-up period, months	92.0 ± 26.2 (43–121)	58.5 ± 22.8 (26–97)	80.4 ± 23.6 (26–121)
Clinical findings			
Headache with Valsalva	23 (41.1%)	13 (38.2%)	36 (40.0%)
Pinprick loss	19 (33.9%)	12 (35.3%)	31 (34.4%)
Sensation disturbance	12 (21.4%)	6 (17.6%)	18 (20.0%)
Vertigo test (+)	8 (14.3%)	5 (14.7%)	13 (14.4%)
Impaired DTRs	7 (12.5%)	5 (14.7%)	12 (13.3%)

Continues

Table 3. Continued

	Center (A)	Center (B)	All Patients
Gag reflex (−)	5 (8.9%)	2 (5.9%)	7 (7.8%)
Positive Romberg sign (+)	2 (3.6%)	1 (2.9%)	3 (3.3%)
Radiologic findings			
Mean tonsil hernia (mid-sagittal), mm	8.7 ± 2.3 (5—15)	8.9 ± 3.0 (3—16)	8.8 ± 2.6 (3—16)
Mean tonsil hernia (coronal), mm	9.2 ± 1.9 (4—16)	9.5 ± 2.4 (5—18)	9.3 ± 2.1 (4—18)
Mean ASV value, µL	17.1 ± 2.4 (14—21)	15.6 ± 3.0 (12—25)	16.5 ± 2.7 (12—25)
Presence of syrinx +/−	7/49	4/30	11/79

Neuropathic pain: dysesthesia, paresthesia, and hyperesthesia; dissociated sensory loss: loss of pin-prick and temperature sensation.
F, female; M, male; CM1, Chiari malformation type I; DTRs, deep tendon reflexes.
*Headaches contain both typical and atypical headaches; typical headache for CM1 included occipital, Valsalva-induced, tussive and exertional headache, whereas atypical headache included poorly localized frontal temporal or nonspecific headache.

patients. The second line included pregabalin 1—1.5 mg/kg daily and weekly Pilates exercises that were successful in 42 (46.7%) patients. The third line included the physical therapy and rehabilitation (PTR) 15—30 sessions/6 months besides dramatically increasing a Pregabalin dose up 4 mg/kg that was successful in 19 (21.1%) patients. The fourth line included a high pregabalin dose up 5—6 mg/kg besides PTR with swimming or Pilates exercise that was applied in 7 (7.8%) patients. Five of these patients were treated surgically after the unsatisfied response to conservative therapy. Improvements and outcomes of the patients regarding the presenting symptoms are given in Table 4. The mean value of mCCOS after 6 months of conservative treatment was 10.4 ± 1.5 (range, 5—12) that can consider as a functional outcome (Table 5). The median of the pregabalin usage period was 5.5 years (range, 3—121 months).

The comparison between (benefited) and those (non-benefited) patients is shown in Table 6. A strong positive correlation was observed between clinical improvement and high ASV values (>16.7 µL) ($r = 0.4$, $P = 0.004$). Negative correlations were noticed between clinical improvement and all of the long symptom durations (symptoms >31.6 months), presenting symptoms (≥2 sleep apnea or/and functional symptoms), presence of the syrinx, and the herniated ectopia on coronal sequences (>13.4 mm) $r = -0.32$, $P = 0.01$, $r = -0.41$, $P < 0.001$, $r = -0.28$, $P = 0.012$, and $r = -0.38$, $P < 0.001$, respectively. The Youden index of ROC showed that the cut-off value was 12 µL (Figure 3).

DISCUSSION

The Importance of the Current Study

Our findings demonstrated that conservative approaches such as prescriptive medications, physical therapy, Pilates, and swimming can improve the life quality of nonsurgical candidate adult patients with CM1. To the best of our knowledge, our study is the first study that discusses conservative treatment modalities and clinical outcomes. It demonstrates that conservative treatment can be useful in selected adult patients with variably CM1 (ASV = 16.7 µL). Moreover, the findings show that the presence of heavy sleep apnea or/and functional symptoms are prognostic factors that affected the conservative treatment negatively. Previously published articles regarding CM1 focus on personal experiences, surgical outcomes, how to measure the herniation, or postoperative evaluation of operated patients.[1,3,4,6,10-13,16] A few studies discussed the conservative treatment for CM1. 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.[13,17] Another study was a systematic review study.[18]

In comparison with this cohort, our cohort was larger, performed in 2 institutions, and conducted on adult patients only without pooling syndromic and child patients. We used a quantifiable scale (mCCOS) to evaluate the clinical improvement and objective scanning images to assess the radiologic improvements whereas the previously mentioned 2 studies did not use such tools. The main difference between both publications was the former compared between conservatively managed and surgical treated groups,[13] but the latter investigated conservative treatment in the nonoperative group.[17] The authors concluded that the presence of cough headache and/or enlarging syrinx cavities are valid surgical indications for patients with CM1. These findings were in line with ours. In addition to these negative prognostic factors, our findings showed that the presence of more than 2 sleep apnea or/and functional symptoms, tonsillar herniation >13.4 mm on coronal sequences, ASV<13.2 µL, and long symptom durations >31.6 months are other factors that were affected prognosis negatively. Although the systematic review duplicated these publications, it concluded for observation of a patient with CM1 with mild symptomatic symptoms, even in the presence of significant tonsillar herniation or syrinx cavities.[18]

The Usefulness of PC-MRI

ASV is heavily impacted by many factors, such as the volume of the aqueductal area, ventricular volume, the production and absorption of CSF, pulsatility measure, arterial pulsation, respiration, and the presence of neurovascular disorders.[4,6,12] Therefore, the benefit of PC-MRI use in diagnosis and follow-up patients with

Table 4. Improvements and Outcomes of the Pretreatment Symptoms

Symptoms and Findings	**Outcomes (*n* = 90)**				
Pretreatment symptoms*	T	R	I	U	W
Pain and dysesthesia	73	28	42	2	1
Typical headache for CM1	31	8	21	1	1
Atypical headache	27	12	13	2	0
Neuropathic pain	10	6	3	1	0
Neck pain	12	7	4	1	0
Upper extremities pain	8	5	2	1	0
Spinal pain	3	2	1	0	0
Chest pain	2	1	1	0	0
Neurologic nonpain	16	4	7	3	2
Dissociated sensory loss	12	3	4	3	2
Vertigo/dizziness	10	2	6	1	1
Ataxia	2	0	0	2	0
Tinnitus	5	1	1	2	1
Impaired reflexes	10	1	5	3	1
Nystagmus	8	2	3	3	0
Dysphagia	1	0	1	0	0
Disequilibrium	1	0	1	0	0
Paresis	0	0	0	0	0
Fecal and/or urine incontinence	2*	0	0	2	0
Myelopathy	0	0	0	0	0
Functional symptoms	10	1	6	2	1
Fatigue	8	1	5	2	0
Syncope	2	0	1	0	1
Cognitive impairment	2	0	1	1	0
Dysarthria	2	0	1	1	0
Hoarseness	1	0	0	1	0
Sleep apnea	5	0	2	2	1
Sleep apnea	2	0	1	1	0
Severe snoring	2	0	1	1	0
Recurrent aspiration	1	0	0	0	1
Hiccups	1	0	1	0	0
Syrinx (+)	8/85 (9.4%)				
Fully regressed	1/8 (12.5%)				
Markedly regressed	2/8 (25.0%)				
Unchanged	5/8 (62.5%)				
Required SP shunt	0				

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 was worsened or impaired the patient from the daily activities); CM1, Chiari malformation type I; SP, syringopleural.

*These patients suffered from urge incontinence.

Table 5. Conservative Treatment Modalities and Clinical Outcomes

	Center (A) (n = 56)	Center (B) (n = 34)	All Patients (n = 90)
Conservative modalities			
Success of the first-line treatment	14 (25.0%)	8 (23.5%)	22 (24.4%)
Success of the second-line treatment	26 (46.4%)	16 (47.1%)	42 (46.7%)
Success of the third-line treatment	12 (21.4%)	7 (20.6%)	19 (21.1%)
Applied fourth-line treatment	4 (7.2%)	3 (8.8%)	7 (7.8%)
Mean mCCOS value*	10.3 ± 1.7 (5–12)	10.6 ± 1.4 (6–12)	10.4 ± 1.5 (5–12)
Final overall outcome			
Recovered (excellent)	14 (25.0%)	7 (20.6%)	21 (23.4%)
Improved (functional)	39 (69.6%)	25 (73.6%)	64 (71.1%)
Unchanged (Impaired)†	2 (3.6%)	1 (2.9%)	3 (3.3%)
Worsened (progressed) †	1 (1.8%)	1 (2.9%)	2 (2.2%)

First-line treatments included analgesics, myorelaxants, multivitamins, and weekly swimming; second-line treatments included pregabalin 1–1.5 mg/kg daily and weekly Pilates exercises; third-line treatments included the physical therapy and rehabilitation 15–30 sessions/6 months besides dramatically increasing in a pregabalin dose up 4 mg/kg; and fourth-line treatments included a high pregabalin dose up 5–6 mg/kg in addition to PTR with swimming or Pilates exercise.

mCCOS, modified Chicago Chiari outcome scale; Recovered, relieved all major symptoms; Improved, continuing at least 1 major symptom with obvious neurologic improvement in other major symptoms; Unchanged, continuing all major symptoms without any improvement; Worsened, worsening at least 1 major symptom or appearing at least one new neurologic deficit).

*All mCCOS scores were calculated after 6 months of conservative therapy.

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

Table 6. Comparison Between Benefited and Nonbenefited Patients

Prognostic Factors	Mean	n	SD	t	P Value	r
Benefited patient's sex (F/M)	—	64/21	—	—	1.0	χ^2 test was used.
Non-benefited patient's sex (F/M)	—	4/1	—			
Benefited patient's age, years	40.3	85	16.2	0.65	0.52	−0.21
Nonbenefited patient's age, years	45.2	5	16.1			
Benefited patient's symptom duration, months	17.8	85	11.6	2.32	0.01	−0.32
Nonbenefited patient's symptom duration, months	31.6	5	12.5			
Benefited patients with ≥2 functional and sleep apnea symptoms (+/−)	—	6/79	—	3.48	<0.001	χ^2 test was used.
Nonbenefited patients with ≥2 functional and sleep apnea symptoms (+/-)	—	4/1	—			
Benefited patients with herniated ectopia on midsagittal images, mm	8.55	85	2.4	1.50	0.069	−0.22
Nonbenefited patients with herniated ectopia on midsagittal images, mm	10.6	5	3.6			
Benefited patients with herniated ectopia on coronal images, mm	8.5	85	2.3	4.32	<0.001	−0.38
Nonbenefited patients with herniated ectopia on coronal images, mm	13.4	5	2.4			
Benefited patients' ASV, µL	16.7	85	2.6	2.74	0.004	0.40
Nonbenefited patients' ASV, µL	13.2	5	1.1			
Benefited patients who presented with syrinx (+/−)	—	8/77	—	2.3	0.012	χ^2 test was used.
Nonbenefited patients who presented with syrinx (+/−)	—	3/2	—			

$P < 0.05$ was regarded as statistically significant.

R, correlation coefficient.SD, standard deviation; M, male; F, female; ASV, aqueductal stroke volume value; −, absence; +, presence.

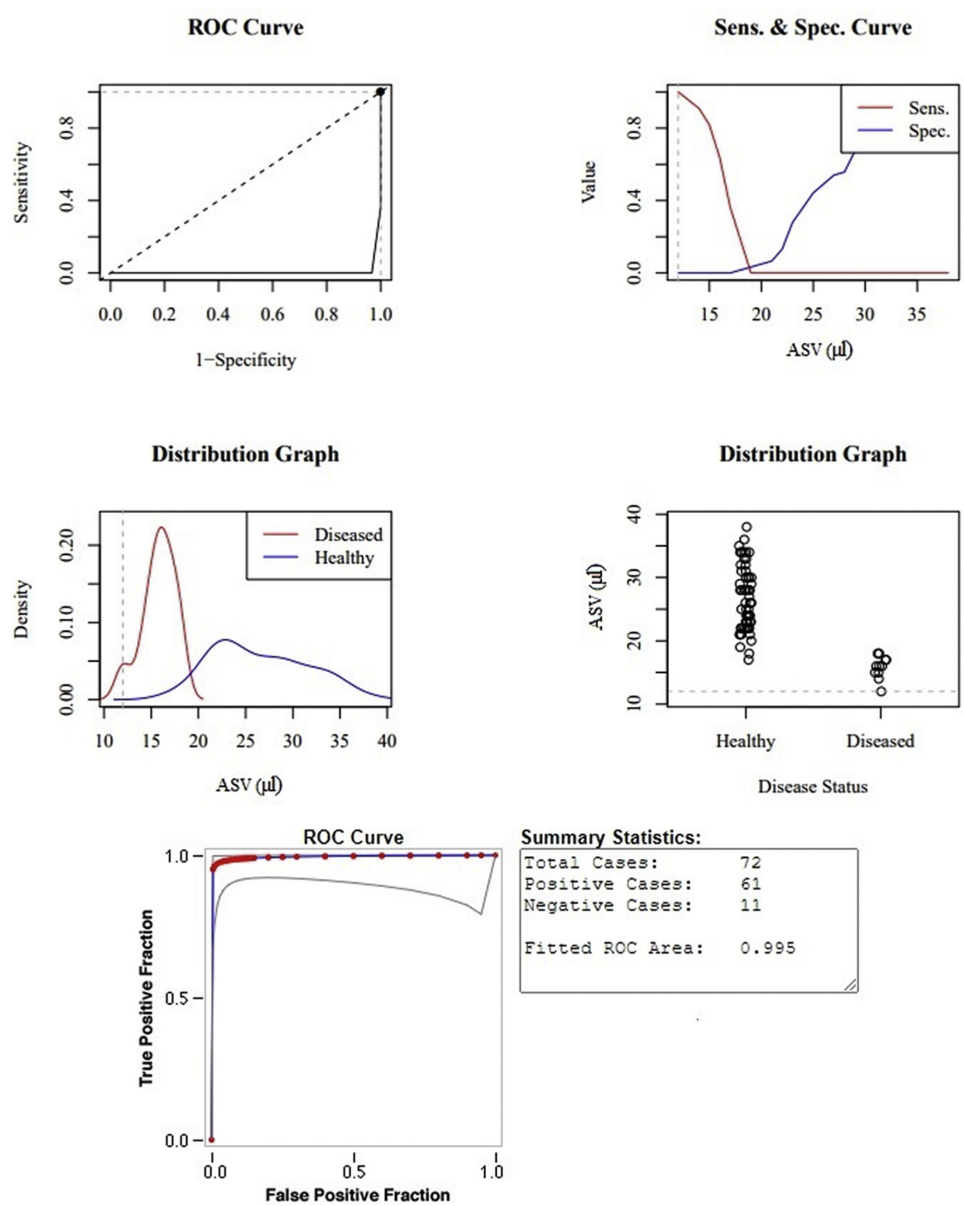

Figure 3. ROC analysis using the Youden index showed that the cut-off value of the aqueductal stroke volume (ASV) was 12 µL. ROC, receiver operating curve; Sens, sensitivity; Spec, specificity.

CM1 remains debatable. PC-MRI is the only noninvasive imaging that can be used to measure the CSF hydrodynamics, but it shows only a selected plane in a 2-dimensional image and misinterprets the values in the cases of turbulent-complex flow. The restrictions of CSF flow in CM1 are on more than one level (i.e., aqueduct sylvii and the foramen magnum). Moreover, there is no consensus regarding the optimal method to measure an exact ASV. Each institution has its approach to measuring ASV. Therefore, the values vary from one institution to another.[4,6,12] To reduce the interobserver disagreement among radiologists, minimize these disadvantages, and standardize the findings, the authors in this cohort measured the hydrodynamics of CSF flow at only the aqueduct sylvii level. However, measuring CSF flow only done at the aqueduct sylvii level may provide insufficient or false results due to the partial volume effect on a selected plane of the image.[4,12]

The usefulness of the PC-MRI in the assessment of several diseases such as CM1 and idiopathic normal pressure hydrocephalus has been discussed previously.[4,6,12,19,20] However, several studies have shown that ASV is heavily dependent on the volume of ventricles and aqueductal area, and respiration. The complex changes in aqueduct flow occur in physiological and pathological processes and can affect the redistribution of CSF flow by the compensatory mechanisms.[19-21] Therefore, ASV values obtained in short periods can be false or nonsufficient to provide exact values. It may reflect the compensated ASV values. This is true for short periods. Over time, the compensatory mechanisms will fail to compensate ASV values and the caudal and rostral peak aqueduct CSF flow decreases significantly in patients with CM1 (hypodynamic flow).[4,6,12] Therefore, we recommended evaluating PC-MRI with the sagittal and coronal sequences of upper cervical spine MRI with correlation to clinical presentation. The tonsillar ectopia fills the foramen magnum in the setting of CM1, followed by reducing the CSF flow at the craniocervical junction, and a compensatory pulsatile descent of tonsils is observed during the systole. After the compensatory mechanisms failed over time, the ASV started to decrease.[14,22] Thus, having a hypodynamic CSF flow can be better to select in patients with CM1 for management and follow up. Abdallah et al. observed that adult patients with ASV <12 μL were invariably symptomatic and that they deserve surgical intervention.[6,12]

Conservative Approaches for CM1

Although adult patients with CM1 demonstrate the same symptoms, not all of them are invariably symptomatic. In our approach, if the patient did not meet our criteria for surgical intervention, the patient was treated conservatively. First, medications such as analgesics, myorelaxants, multivitamins, and weekly swimming were recommended. After 1 month or in any clinical progression, the patient was reevaluated. If the response was unsatisfactory, the second-line treatment (pregabalin 1—1.5 mg/kg daily and weekly Pilates exercises) was applied. In case of the presence of a tolerance problem or unsatisfied response, the neurosurgeon can pass to the third-line treatment (PTR 15—30 sessions/6 months besides dramatically increasing a pregabalin dose up 5—6 mg/kg). There is no fixed rule stated. The neurosurgeons can use different lines in the same patient according to the resolution and progression in the patient's symptoms.

Conservative (nonsurgical) treatment modalities for adult patients with CM1 include anti-inflammatory agents,[6,12,23] myorelaxants, analgesia, multivitamins,[6,12] PTR, nonpharmacologic management (i.e., spinal or peripheral electrical stimulation),[23] Pilates,[4,6] swimming,[4,12] craniosacral osteopathy,[23] speech therapy,[23] and psychological supports.[6,12,23] The purpose of conservative modalities is to relieve pain and numbness, minimize symptoms, and improve the quality of life of the patient. There are 2 basic principles from these modalities: 1) form an integrated functional unit whose components influence and interact with each other in the musculoskeletal system and 2) integrate spinal biomechanics and normalize the biodynamics of connective tissue as a whole.[23]

In CM1, neuropathic pain is a total disruption of nerve conduction caused by the compression of junctional structures between the pons and the cerebellum, and the medulla spinalis. Pregabalin can benefit patients with refractory epilepsy, neuropathic pains, and minor depression.[6,24] It has shown antihyperalgesic properties and may have a minimal opioid-sparing effect.[24,25] In 2001, this medication was used for acute pain treatment.[25] However, it has the risk of serious adverse effects such as nausea, vomiting, sedation, dizziness, headache, and visual disturbances.[24,25] In our practice, we observed that a low dose of pregabalin with multivitamins can relieve the major nonspecific complaints in adult patients with CM1.

Study Limitations

The retrospective design, a small number of patients, and the possible selection bias in which patients were treated surgically versus those managed conservatively are all limitations of our study. The small size number restricted the investigation of presenting symptoms subgroups. The CSF flow measurement approach was only done at the aqueduct sylvii level, which may provide insufficient or false results due to the partial volume effect on a selected plane of the image. Further randomized prospective studies with a large sample and longer follow-up are mandatory to support the findings yielded from this study.

CONCLUSIONS

Conservative approaches (i.e., prescriptive medications, physical therapy, Pilates, and swimming) can improve the life quality of nonsurgical candidate adult patients with CM1. Conservative treatment can be useful in selected patients with variable CM1 (ASV = 16.7 μL). The presence of heavy sleep apnea or/and functional symptoms, tonsillar herniation >13.4 mm on coronal sequences, low ASV (<13.2 μL), long symptom durations (>31 months), and the syrinx cavities were prognostic factors that affected the conservative treatment negatively. Thus, PC-MRI can play a role in the management of adult patients with CM1 before considering them for surgical intervention. Herniated cerebellar tonsils were evaluated more reliably on coronal sequences and PC-MRIs. A positive correlation between clinical improvement and the increase in ASV values was observed.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Anas Abdallah: Conceptualization, Methodology, Software, Supervision, Formal analysis, Statistical analysis, Literature review, Visualization, Investigation, Writing — original draft, Writing — review & editing, Validation. **Usame Rakip:** Validation, Writing — review & editing.

REFERENCES

1. Abdallah A, Çınar İ, Güler Abdallah B. Long-term surgical outcome of Chiari type-I malformation-related syringomyelia: an experience of tertiary referral hospital. *Neurol Res*. 2022;44:299-310.

2. Chiari H. Secondary changes in the cerebellum, pons and medulla oblongata associated with congenital hydrocephalus [Über Veränderungen des Kleinhirns, des Pons und der Medulla oblongata in Folge von congenitaler Hydrocephalie des Grosshirns]. *Dtsch Med Wochenschr*. 1891;17:1172-1175.

3. Aslan A, Rakip U, Boyacı MG, et al. Posterior fossa decompression and superficial durotomy rather than complete durotomy and duraplasty in

the management of Chiari 1. *Neurol Res*. 2021;43:440-446.

4. Gündağ Papaker M, Abdallah A, Cesme DH, et al. Clinical and radiological evaluation of treated Chiari I adult patients: retrospective study from two neurosurgical centers. *Neurosurg Rev*. 2021;44:2261-2276.

5. Rogers JM, Savage G, Stoodley MA. A systematic review of cognition in Chiari I malformation. *Neuropsychol Rev*. 2018;28:176-187.

6. Abdallah A, Çınar İ, Papaker MG, Abdallah BG, Sofuoğlu ÖE, Emel E. The factors affecting the outcomes of conservative and surgical treatment of Chiari I adult patients: a comparative retrospective study. *Neurol Res*. 2022;44:165-176.

7. Shah S, Haughton V, del Río AM. CSF flow through the upper cervical spinal canal in Chiari I malformation. *Am J Neuroradiol*. 2011;32:1149-1153.

8. Alzate JC, Kothbauer KF, Jallo GI, Epstein FJ. Treatment of Chiari I malformation in patients with and without syringomyelia: a consecutive series of 66 cases. *Neurosurg Focus*. 2001;11:E3.

9. Lin W, Duan G, Xie J, Shao J, Wang Z, Jiao B. 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.

10. 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. *Neurol Res*. 2012;34:694-700.

11. Aliaga L, Hekman KE, Yassari R, et al. A novel scoring system for assessing Chiari malformation type I treatment outcomes. *Neurosurgery*. 2012;70:656-664.

12. Abdallah A, Çınar İ, Papaker MG, Abdallah BG, Emel E. Management of Chiari I adult patients based on CSF flow magnetic resonance imaging: experience of two neurosurgical centers. *J Neurol Surg A Cent Eur Neurosurg*; 2022. https://doi.org/10.1055/s-0042-1745845. Accessed April 20, 2022.

13. 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;21:2201-2206.

14. Battal B, Kocaoglu M, Bulakbasi N, Husmen G, Tuba Sanal H, Tayfun C. Cerebrospinal fluid flow imaging by using phase-contrast MR technique. *Br J Radiol*. 2011;84:758-765.

15. Korbecki A, Zimny A, Podgórski P, Sąsiadek M, Bladowska J. Imaging of cerebrospinal fluid flow: fundamentals, techniques, and clinical applications of phase-contrast magnetic resonance imaging. *Pol J Radiol*. 2019;84:e240-e250.

16. 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.

17. Killeen A, Roguski M, Chavez A, Heilman C, Hwang S. Non-operative outcomes in Chiari I malformation patients. *J Clin Neurosci*. 2015;22:133-138.

18. 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.

19. Ringstad G, Emblem KE, Geier O, Alperin N, Eide PK. Aqueductal stroke volume: comparisons with intracranial pressure scores in idiopathic normal pressure hydrocephalus. *AJNR Am J Neuroradiol*. 2015;36:1623-1630.

20. Frič R, Lindstrøm EK, Ringstad GA, Mardal KA, Eide PK. The association between the pulse pressure gradient at the cranio-cervical junction derived from phase-contrast magnetic resonance imaging and invasively measured pulsatile intracranial pressure in symptomatic patients with Chiari malformation type 1. *Acta Neurochir (Wien)*. 2016;158:2295-2304.

21. Lindstrøm EK, Ringstad G, Mardal KA, Eide PK. Cerebrospinal fluid volumetric net flow rate and direction in idiopathic normal pressure hydrocephalus. *Neuroimage Clin*. 2018;20:731-741.

22. McGirt MJ, Nimjee SM, Fuchs HE, George TM. Relationship of cine phase-contrast MRI to outcome after decompression for Chiari I malformation. *Neurosurgery*. 2006;59:140-146.

23. Avellaneda Fernández A, Isla Guerrero A, Izquierdo Martínez M, et al. Malformations of the craniocervical junction (Chiari type I and syringomyelia: classification, diagnosis and treatment). *BMC Musculoskelet Disord*. 2009;10:S1.

24. Tassone DM, Boyce E, Guyer J, Nuzum D. Pregabalin: a novel gamma-aminobutyric acid analogue in the treatment of neuropathic pain, partial-onset seizures, and anxiety disorders. *Clin Ther*. 2007;29:26-48.

25. Fabritius ML, Strøm C, Koyuncu S, et al. Benefit and harm of pregabalin in acute pain treatment: a systematic review with meta-analyses and trial sequential analyses. *Br J Anaesth*. 2017;119:775-791.

Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Name of the departments and institutions in which the work was done: Department of Neurosurgerys—Aile, BVU, and Bakırköy Research and Training Hospital for Neurology Neurosurgery.

Received 14 February 2022; accepted 28 March 2022

Citation: World Neurosurg. (2022). https://doi.org/10.1016/j.wneu.2022.03.126

Journal homepage: ***www.journals.elsevier.com/world-neurosurgery***

Available online: ***www.sciencedirect.com***