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Comparative Evaluation of Morphological Findings and Flow-Sensitive Magnetic Resonance Parameters in Patients with Chiari 1 Malformation Against Healthy Individuals

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ABSTRACT

Introduction: A better understanding of the cerebrospinal fluid (CSF) flow dynamics of Chiari 1 malformation (CM-1) may help to reach more specific parameters for indicating therapy and response to therapy. This study developed a parameter to better characterize CSF flow alterations in the cerebral aqueduct in patients presenting with CM-1.

Methods: We retrospectively scanned archives for CM-1 patients who underwent CSF flow analysis between January 2016 and December 2022. Eighty-eight CM-1 patients and 83 control cases were included in the study. The cerebellar tonsillar descensus was measured in all patients. In 11 cases with the syrinx cavity, the largest transverse diameter of the cavity was measured. Phase-contrast magnetic resonance imaging was performed using a 1.5 T scanner. Peak velocity (P-Vel) (cm/s), average velocity (A-Vel) (cm/s), forward flow volume (µL), reverse flow volume (µL), peak flow (P-Fl) (mL/s), and time to peak velocity (TP-Vel) (s) and cerebral aqueduct's stroke volume (µL) were calculated. Sixteen CM-1 patients underwent decompression surgery, and we examined postoperative CSF flow analyses.

Results: A-Vel and P-F1 were statistically significantly higher in CM-1 cases than in controls (p=0.006, p=0.037). There was a significant negative correlation between the diameter of the syrinx cavity and P-Vel and P-Fl, and a positive correlation between TP-Vel. We found no significant difference between the postoperative and preoperative CSF flow parameters of the CM-1 patients.

Conclusion: P-Fl differs between the patient and control groups and correlates with the syrinx diameter; therefore, it could be a useful parameter in CSF flow analysis in CM-1 cases. However, higher case numbers can achieve more effective results.

Keywords: Chiari 1 malformation, CSF flow, PC-MRI, peak flow

Introduction

Chiari malformations (CM) are defined as varying degrees of extension of the brainstem and cerebellar structures into the cervical spinal canal (1). CM-1 is a congenital anomaly in which the cerebellar tonsils extend caudally and is the most common group among CMs (2). CM-1 cases may be asymptomatic and occur incidentally in magnetic resonance imaging (MRI) examinations, which are increasing nowadays (3,4). Symptoms ranging from a mild headache to difficulty swallowing and an unsteady gait, may also occur. If symptomatic, patients present clinical signs of brain stem compression or syringomyelia in adulthood (5). However, the incidence of clinically significant CM-1 anomalies is quite low (1,3). Syrinx cavities, hydrocephalus, and skeletal anomalies may accompany CM-1 cases at different rates (6,7).

The main purpose of surgery in CM-1 malformations is to restore cerebrospinal fluid (CSF) flow at the level of the foramen magnum and around the brain stem. The applied decompression surgery removes a part of the occipital bone and posterior arch of the first cervical vertebra (C1). Thus, it reduces the pressure at the craniocervical junction level and the width of the syrinx cavity (1). It has been shown that CM-1 patients benefit from decompression surgery. However, not all patients may benefit equally from this treatment. Therefore, it is necessary to select suitable patients for the operation (8,9).

A better understanding of the effects of CM-1 pathophysiology on CSF flow dynamics may lead to the identification of diagnostic tools that can more specifically predict the indication for therapy and the response to therapy. Therefore, this study developed a parameter to better characterize CSF flow alterations in the cerebral aqueduct in patients presenting with

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CM-1. In the literature, different studies have been conducted on CSF flow changes at the level of the craniocervical junction in patients with CH-1 (10-12). However, because the intracranial space is a closed area, dynamic changes in the outlet of the CSF may also be reflected in the flow dynamics at proximal CSF distances and cause flow disturbances. Because the normal anatomy of the craniocervical junction will be disrupted after decompression surgery, it will be difficult to make quantitative measurements at this level. Furthermore, velocity aliasing artifacts from the vertebral arteries can complicate phase-contrast magnetic resonance imaging (PC-MRI) flow measurements at the craniocervical junction. For these reasons, we measured and evaluated the cerebral aqueduct level instead of the craniocervical junction. First, we compared the dynamic CSF flow parameters in the cerebral aqueduct between CM-1 and normal cases. We also compared the postoperative and preoperative values of CSF flow dynamics at the cerebral aqueduct level in CM-1 patients who underwent decompression surgery.

Methods

Subjects

After obtaining the Ethics Committee approval from University of Health Sciences Turkey, İstanbul Training and Research Hospital (approval number: 20, date: 27.01.2023), our medical records were retrospectively scanned for patients who underwent CSF flow analysis between January 2016 and December 2022. The diagnosis of CM-1 can be made if the cerebellar tonsils extend 5 mm or more from the level of the foramen magnum to the caudal in adults (13). The study did not include cases with cerebellar tonsils extending 5 mm or less. Cases with intracranial hypertension (secondary or idiopathic) and intracranial hypotension were excluded from the study. Only cases aged 18 years and over were included in the study because there may be changes in clinical management. Patients whose CSF flow examinations had artifacts and inappropriate images for measurement were also excluded from the study. Finally, 88 cases diagnosed with CM-1 after excluding differential diagnoses were included in the study. Sixteen patients were operated on for CM-1 and had postoperative CSF flow examination. These images were obtained for follow-up on an average 3 to 6 months after the operation. Eighty-three patients who underwent CSF flow examination with headache in a similar time interval and had a stress-related cluster-tension headache diagnosis were also included in the study as the control group.

Image Acquisition and Analyses

All MRI were performed with a 1.5 T-scanner (Siemens Healthcare, Aera Magnetom, Erlangen, Germany) equipped with an 8-channel head coil. First, each case was evaluated with conventional MR sequences, including 3D T2-SPACE sequences (slice thickness: 1 mm, FOV: 240 mm, matrix 231×256, TR: 2500, and TR: 501). CSF flow imaging was performed using the two-dimensional phase-contrast MRI technique in the axial and midsagittal planes. Axial views were planned perpendicular to the extent of the cerebral aqueduct on the midsagittal view of PC-MRI. Rephase, magnitude, and phase images were obtained in the axial and sagittal planes. Cardiac triggering was retrospectively used for an average of 15-20 cardiac phases according to the heart rate. Velocity encoding (Venc) was determined as 5, 10, and 20 cm/s for each patient. Flow in the caudocranial direction (diastolic) was coded as positive, and the craniocaudal direction (systolic) was coded as negative.

MRI of all patients were transferred to the Syngo Via® workstation (Siemens Medical Solutions) for measurement with appropriate software. All images were examined separately by a radiologist experienced in neuroradiology and CSF flow examination for five years (Direnç Özlem Aksoy). The distance of the caudal endpoint of the cerebellar tonsils from the plane of the foramen magnum (the line drawn from the opisthion to the basion) was measured in sagittal SPACE images of each case (Figure 1A). In addition, the 11 cases with a syrinx cavity were identified, and the widest mediolateral diameter of the syrinx cavity was measured on the axial SPACE image (Figure 1B). Axial PC-MRI images were used for CSF flow quantification. Measurements were made on the image acquired at the appropriate Venc setting with the brightest flow signal without aliasing artifacts. A manual region of interest (ROI) indicated flow boundaries observed in the cerebral aqueduct (Figure 2). The ROI was also copied into all previous and subsequent phase images acquired during a cardiac cycle to obtain the time-velocity curve. Peak velocity (P-Vel) (cm/s), average velocity (A-Vel) (cm/s), forward flow volume (FV) (µL), reverse flow volume (RV) (µL), peak flow (P-Fl) (ml/s), and time to peak velocity (TP-Vel) (s) were calculated from time-velocity curve data automatically by the software (Figure 1). We manually calculated the cerebral aqueduct stroke volume (SV) (µL) as the average of FV and RV.

Statistical Analysis

In the descriptive statistics of the data, mean, standard deviation, median, minimum, maximum, frequency, and ratio values were used. The distribution of variables was measured using the Kolmogorov-Smirnov test. Independent sample t-test and Mann-Whitney U test were

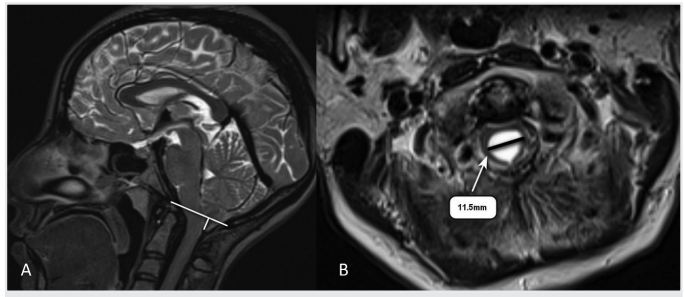

Figure 1. Measurement of the cerebellar tonsillar descensus in the sagittal SPACE image (A) and syrinx cavity in the axial SPACE image (B)

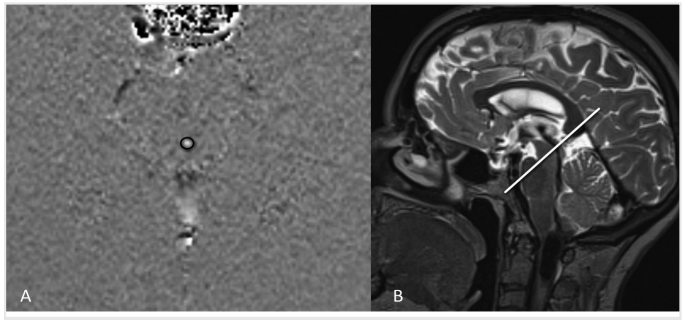

Figure 2. Aqueductal ROI placement in the axial phase image (A) and corresponding aqueduct level in the sagittal plane (B)

ROI: Region of interest

used to analyze independent quantitative data. Paired-sample t-test and Wilcoxon test were used to analyze dependent quantitative data. The chi-square test was used to analyze independent qualitative data, and the Fisher's exact test was used when the chi-square test conditions were not met. Spearman correlation analysis was used in the correlation analysis. SPSS 28.0 program was used in the analysis.

Results

There were 88-CM-1 cases and 83 control cases in our study. While the mean age was 47.3±18.5 in the control group, the mean age in CM-1 patients was 40.4±14.0 years. 65.1% (54) of the control group were female and 65.1% (29) were male. 76.1% (67) of CM-1 patients were female and 23.9% (21) were male. The results of the CSF flow measurements for CM-1 cases and the control group are summarized in Table 1. A-Vel and P-F1 were statistically significantly higher in CM-1 cases than controls (p=0.006, p=0.037). We found no significant difference between the patient and control groups in other parameters. The analysis we conducted to show the correlation of the distance of the caudal decensus of the cerebellar tonsils and the width of the syrinx cavity with the CSF flow parameters in CM-1 cases is also summarized in Table 2. There was no statistically significant correlation between the distance of the descensus and the flow parameters. There was a significant negative correlation between the diameter of the syrinx cavity and P-Vel and P-Fl, and a positive correlation between TP-Vel. We compared the postoperative CSF flow measurement parameters of 16 patients with CM-1 who underwent decompression surgery with their preoperative measurements (Table 3). We found no significant difference in the parameters between the two groups.

Table 1. CSF flow measurements for CM-1 and control group

	Control		CM-1		p	
	Mean ± SD/(n, %)	Median	Mean ± SD/(n, %)	Median		
P-Vel (cm/s)	-2.9±7.8	-6.0	-3.6±7.5	-6.6	0.471	[m]
A-Vel (cm/s)	0.13±0.27	0.13	0.20±0.18	0.20	**0.006**	[m]
TP-Vel (s)	592.3±188.7	608.8	597.1±193.2	624.7	0.667	[m]
FV (µL)	48.6±25.2	45.0	53.5±32.2	44.5	0.650	[m]
RV (µL)	41.0±23.9	35.0	40.7±28.0	34.5	0.524	[m]
SV (µL)	44.8±23.5	39.0	47.1±29.5	39.5	1.000	[m]
P-Fl (µL/s)	-26.3±243.7	-112.0	-100.2±240.4	-149.0	**0.037**	[m]

[m] Mann-Whitney U test. Bolded p-values are for statistically significant results (p<0.05). P-Vel: Peak velocity, A-Vel: Average velocity, TP-Vel: Time to peak velocity, FV: Forward volume, RV: Reverse volume, SV: Stroke volume, P-Fl: Peak flow, SD: Standard deviation, CSF: Cerebrospinal fluid, CM-1: Chiari 1 malformation

Table 2. Correlation analysis of CSF flow parameters with descensus distance and syrinx width in CM-1 cases

	Descensus (mm)		Syrinx (mm)	
	r	p	r	p
P-Vel (cm/s)	-0.029	0.786	-0.706	**0.015**
A-Vel (cm/s)	-0.010	0.927	-0.296	0.377
TP-Vel (s)	-0.048	0.660	0.606	**0.048**
FV (µL)	-0.006	0.954	0.524	0.098
RV (µL)	0.034	0.756	0.571	0.067
SV (µL)	0.025	0.818	0.524	0.098
P-Fl (µL/s)	-0.036	0.736	-0.715	**0.013**

Spearman correlation. Bolded p-values are for statistically significant results (p<0.05). P-Vel: Peak velocity, A-Vel: Average velocity, TP-Vel: Time to peak velocity, FV: Forward volume, RV: Reverse volume, SV: Stroke volume, P-Fl: Peak flow, CSF: Cerebrospinal fluid, CM-1: Chiari 1 malformation

Table 3. Postoperative and preoperative CSF flow measurement parameters of CM-1 patients undergoing decompression surgery

	Preoperative		Postoperative		p	
	Mean ± SD	Median	Mean ± SD	Median		
P-Vel (cm/s)	-3.7±8.0	-7.2	-5.8±6.5	-7.3	0.163	[w]
A-Vel (cm/s)	0.28±0.19	0.27	0.26±0.22	0.23	0.753	[p]
TP-Vel (s)	635.6±176.7	682.8	650.5±202.8	674.6	0.569	[w]
FV (µL)	65.3±28.7	73.0	57.2±30.9	47.0	0.326	[w]
RV (µL)	44.1±24.8	43.0	43.1±22.0	35.5	0.791	[p]
SV (µL)	54.7±25.3	56.0	50.1±26.0	40.5	0.386	[p]
P-Fl (µL/s)	-99.3±271.1	-181.0	-82.5±238.3	-157.0	0.469	[w]

[p]: Paired sample t-test, [w]: Wilcoxon test. Bolded p-values are for statistically significant results (p<0.05). P-Vel: Peak velocity, A-Vel: Average velocity, TP-Vel: Time to peak velocity, FV: Forward volume, RV: Reverse volume, SV: Stroke volume, P-Fl: Peak flow, CSF: Cerebrospinal fluid, CM-1: Chiari 1 malformation, SD: Standard deviation

Discussion

There is a cyclic flow of CSF in the craniocaudal direction in the systole phase of the cardiac cycle and the caudocranial direction in the diastole phase (14). On PC-MRI, the cephalad flow of CSF during diastole is positively coded above the flow time curve. The caudal flow of CSF, on the other hand, is negatively coded under the flow time curve during systole (15,16). PC-MRI is the only non-invasive method to assess the direction and amount of this biphasic CSF flow (17,18). Therefore, many studies have been conducted using PC-MRI in normal cases and diseases expected to make differences in CSF flow dynamics, such as normal pressure hydrocephaly, idiopathic intracranial hypertension, hydrocephaly, atrophy, and CM-1 (19-21).

As a result of obliteration at the level of the foramen magnum due to herniation of the cerebellar tonsils, CSF flow may be restricted, and higher velocities and turbulence may be produced in CM-1 (22). It has been argued that changes in CSF P-Vel values in the aqueduct of Sylvius are sensitive to detect changes caused by increased intracranial pressure (18). In our study, P-Vel and P-Fl in the caudal direction in the cerebral aqueduct were higher in CM-1 cases than in the control group. Although we could not find a statistically significant difference in P-Vel (p=0.471), our difference in P-Fl (p=0.037) was significant. In addition, A-Vel was significantly higher in CM-1 cases (p=0.006). Bapuraj et al. (23), in their study on a pediatric case group, found the mean velocity amplitude and P-Vel amplitude at the level of the cerebral aqueduct to be higher in patients with CM-1 malformation compared to the control group. Wang et al. (15), in their study comparing the caudal and cephalad flow separately, found that the P-Vel of the cephalad flow of the aqueduct in CM-1 patients was significantly lower than the control (p=0.022). The PV of the caudal flow was higher than that of healthy controls (p=0.004) (15). Ahmad et al. (21), in their study on different diseases, found that peak diastolic velocity (p=0.03) and peak systolic velocity (p=0.003) significantly higher in CM-1 cases than in the control group. In the study of Liu et al. (24), maximum velocity was found to be higher in both caudal (p=0.018) and cranial (p=0.007) directions in the patient group when compared to the control group. However, we did not detect any were significant difference in SV (p=1.000). In our study, SV values at the cerebral aqueduct level in CM-1 cases were slightly higher compared with the control group, but it was not statistically significant (p=1.000). Slightly high results for SV at the cerebral aqueduct of CM-1 patients were obtained in the literature, which was not statistically significant and similar to our results (p=0.06) (21).

This increase in CSF flow velocities could represent an etiologic factor for syrinx formation (22). CSF must flow to the caudal from the foramen magnum to regulate the intracranial pressure that rises with blood inflow to the brain during the systole phase of the cardiac cycle (25). Our study also evaluated whether tonsillar decensus and syrinx cavity width correlated with flow parameters. According to the data we obtained, we did not detect a significant correlation between the caudal descensus distance of the cerebellar tonsils and the flow data. However, in our comparison with the width of the syrinx cavity, we found a significant negative correlation between the syrinx cavity width and P-Vel (p=0.015) and P-Fl (p=0.013). In addition, as the diameter of the syrinx cavity increased, TP-Vel also increased (p=0.048). Apart from that, we did not find any significant relationship between syrinx and SV. Capel et al. (26) also found no significant difference (p=0.13) in SV in the cerebral aqueduct when they compared patients with and without syringomyelia in CM-1 patients, which was also correlated with our results.

We also compared the preoperative and postoperative CSF flow parameters of CM-1 cases. However, we could not find a statistically significant difference. Capel et al. (26) also did not detect a statistically significant difference in the SV of the aqueduct after surgery (p=0.36). In the study of Wang et al. (15), the P-Vel of the cephalad flow of the aqueduct in CM-1 patients increased after surgery (p=0.003), while the P-Vel of the caudal flow decreased (0.012) (15). On the other hand, Bapuraj et al. (23) detected a statistically significant decrease in the amplitude of mean velocity in postoperative cases. However, there was no significant change in the amplitude of peak velocity (23).

Study Limitations

Our study has some limitations. The retrospective nature and small number of patients are the main limitations. A single radiologist made the measurements, so the interobserver and intraobserver agreement was not evaluated. Since we did not consider which cases were clinically symptomatic and which were not, we could not make an evaluation and comparison in this direction. We did not categorize surgical procedures and could not evaluate whether the difference in surgical approach affected postoperative results. In addition, we could not evaluate the relationship between preoperative flow parameters and surgical outcomes.

Conclusion

MRI plays an important role in the diagnosis and follow-up of CM-1 cases. In addition, because it will not be possible to detect changes in CSF flow with conventional methods, methods that are more sensitive to dynamic changes, such as PC-MRI, can be used. Therefore, we studied the CSF flow changes that we can detect with PC-MRI in CM-1 cases. We found a significant difference in A-Vel (cm/s) (p=0.006) and P-Fl (µL/s) (p=0.037) in CM-1 cases compared with the control group. We also found a statistically significant correlation between syrinx cavity diameter and P-Vel (cm/s) (p=0.015), TP-Vel (s) (p=0.048), and P-Fl (µL/s) (p=0.013). Since P-Fl differs between the patient and control groups and correlates with the syrinx diameter, it could be a useful parameter in CSF flow analysis in CM-1 cases. Although no significant difference was found in postoperative cases in this parameter, higher case numbers can achieve more effective results.

Ethics Committee Approval: The study was approved by the University of Health Sciences Turkey, İstanbul Training and Research Hospital Ethics Committee (approval number: 20, date: 27.01.2023).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept - V.G., A.S.M.; Design - D.Ö.A., S.K.G.; Data Collection or Processing - İ.Y., Y.K.; Analysis or Interpretation - D.Ö.A.; Literature Search - D.Ö.A., İ.Y., Y.K.; Writing - D.Ö.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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