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Morphometric and volumetric comparison of 102 children with symptomatic and asymptomatic Chiari malformation Type I

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OBJECTIVE Chiari malformation Type I (CM-I) is typically defined on imaging by a cerebellar tonsil position ≥ 5 mm below the foramen magnum. Low cerebellar tonsil position is a frequent incidental finding on brain or cervical spine imaging, even in asymptomatic individuals. Nonspecific symptoms (e.g., headache and neck pain) are common in those with low tonsil position as well as in those with normal tonsil position, leading to uncertainty regarding appropriate management for many patients with low tonsil position and nonspecific symptoms. Because cerebellar tonsil position is not strictly correlated with the presence of typical CM-I symptoms, the authors sought to determine if other 2D morphometric or 3D volumetric measurements on MRI could distinguish between patients with asymptomatic and symptomatic CM-I.

METHODS The authors retrospectively analyzed records of 102 pediatric patients whose records were in the University of Michigan clinical CM-I database. All patients in this database had cerebellar tonsil position ≥ 5 mm below the foramen magnum. Fifty-one symptomatic and 51 asymptomatic patients were matched for age at diagnosis, sex, tonsil position, and tonsil morphology. National Institutes of Health ImageJ software was used to obtain six 2D anatomical MRI measurements, and a semiautomated segmentation tool was used to obtain four 3D volumetric measurements of the posterior fossa and CSF subvolumes on MRI.

RESULTS No significant differences were observed between patients with symptomatic and asymptomatic CM-I related to tentorium length (50.3 vs 51.0 mm; p = 0.537), supraoccipital length (39.4 vs 42.6 mm; p = 0.055), clivus-tentorium distance (52.0 vs 52.1 mm; p = 0.964), clivus-torcula distance (81.5 vs 83.3 mm; p = 0.257), total posterior fossa volume (PFV; 183.4 vs 190.6 ml; p = 0.250), caudal PFV (152.5 vs 159.8 ml; p = 0.256), fourth ventricle volume to caudal PFV ratio (0.0140 vs 0.0136; p = 0.649), or CSF volume to caudal PFV ratio (0.071 vs 0.061; p = 0.138).

CONCLUSIONS No clinically useful 2D or 3D measurements were identified that could reliably distinguish pediatric patients with symptoms attributable to CM-I from those with asymptomatic CM-I.

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KEY WORDS Chiari malformation Type I; morphometrics; syringomyelia; volumetrics

Chiari malformation Type I (CM-I) is typically defined on imaging by cerebellar tonsil position ≥ 5 mm below the foramen magnum.[1,6] Although the use of this measurement alone to establish the diagnosis of CM-I on imaging is widespread, there are clear limitations to this diagnostic criterion. Although low tonsil position may certainly influence the development of CM-I symptoms, tonsil position as an isolated variable is a poor predictor of the presence and/or severity of such symptoms.[12,15,16,20,24,28,37,41,44] Some individuals with tonsil posi-

ABBREVIATIONS CM-I = Chiari malformation Type I; PFV = posterior fossa volume.

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tion < 5 mm below the foramen magnum may present with typical CM-I symptoms or syringomyelia.[1,17,34] Conversely, many asymptomatic or minimally symptomatic individuals have low tonsil position.[7,24,28,29,35,37,43]

Because the number of cranial and cervical imaging studies have been increasing for decades, the incidental discovery of individuals with low tonsil position has become more common.[14,24,25,42] Using the tonsil position criterion, current estimates of CM-I prevalence among patients undergoing MRI range from 0.8% to 3.7% in children[2,24,35,37] and from 0.24% to 0.9% in adults.[25,35,42] Symptomatic CM-I seems to be much less prevalent.[2] This suggests that additional diagnostic imaging criteria beyond the standard measurement of tonsil position would be useful for determining the best candidates for surgical treatment.

We compared various morphometric parameters of the posterior cranial fossa between symptomatic and asymptomatic children, all of whom fulfilled diagnostic criteria for CM-I by tonsil position. The purpose of this comparison was to identify other measures on imaging that might differentiate patients who are symptomatic. The morphometric parameters used in our comparison of symptomatic versus asymptomatic CM-I included 3D volumetric analyses of the posterior fossa and CSF spaces, in addition to a number of 2D morphometric measurements.

In a preliminary, hypothesis-generating study of a smaller database, we assessed the capabilities of 19 different anatomical measurements of posterior fossa anatomy. We selected the most promising of these measures for assessment in this larger study and added a semiautomated technique for assessing posterior fossa volumes (PFVs). Because our primary goal was to identify any radiographic measures that might readily differentiate between patients with symptomatic versus asymptomatic CM-I, we assessed their behavior in 2 cohorts of clearly symptomatic and clearly asymptomatic patients, as assessed clinically. Although this limited the ability of the study to determine the usefulness of these parameters in a sample of less clear-cut patients, any value not found to discriminate in such a diagnostically clear setting would be very unlikely to perform well in a broader context.

Methodologically, a case-control format was selected. Symptomatic and asymptomatic pediatric patients were matched for age and sex to account for these variables that are known to independently influence cranial morphology, as well as for tonsil position and morphology, because these are already accepted (albeit imperfect) predictors of CM-I symptomatology.

Methods

Patient Selection

After approval by the University of Michigan institutional review board, patients were selected for this study via retrospective chart and MR image review of the University of Michigan clinical database. All patients in this data set were younger than 18 years at the time of initial diagnosis and had cerebellar tonsil position ≥ 5 mm below the foramen magnum. For this study, we identified patients in the data set who we considered either definitely asymptomatic (no neurological symptoms attributable to CM-I) or definitely symptomatic (classic CM-I symptoms). Symptoms considered attributable to CM-I were Valsalva-induced occipital headaches and neck pain, central sleep apnea, extremity numbness or paresthesias, dysphagia, poor fine motor skills, and unsteady gait. Patients with nonspecific symptoms or unclear symptomatic status were not included.

We identified 51 patients with symptomatic CM-I and matched this group to 51 patients with asymptomatic CM-I according to age at diagnosis, sex, tonsil position (within a 2-mm difference), and tonsil morphology (rounded vs pointed). All patients considered to be symptomatic had Chiari decompression surgery. None of the asymptomatic patients had Chiari decompression surgery. For surgically treated patients, all measurements were made from the initial preoperative MR image. Because the objective of this study was to identify morphometric and volumetric differences between symptomatic and asymptomatic patients, we did not match for any features other than those mentioned above.

2D and 3D Morphometric Measurements

In this study, we examined 2D morphometric measurements (tonsil position, basilar impression, tentorium length, supraoccipital length, clivus-tentorium distance, and clivus-torcula distance)[40] in addition to 3D volumetric measurements (total PFV, caudal PFV, and total CSF/cisternal space to PFV ratio). All measurements were made by a single observer (N.G.) who was blinded to the symptomatic or asymptomatic status of the patient at the time of measurement.

The presence or absence of a syrinx was noted for each patient, although not used to define the groups. Syrinx was defined as a central spinal fluid collection with a diameter > 3 mm, whereas a diameter ≤ 3 mm was considered a dilated central canal. This definition was used to avoid the inclusion of thin spinal fluid collections that are less likely to be clinically significant or causally associated with CM-I.[36]

For the 2D measurements, sagittal T1-weighted MR images were manually reviewed to obtain six 2D measurements (Fig. 1). The following measurements were obtained based on a single manually selected slice, without multiplanar reconstruction: tonsil position with respect to the foramen magnum (for use in the matching process), tentorium length, supraoccipital length, clivus-tentorium distance, and clivus-torcula distance. These 2D morphometric measurements were made using National Institutes of Health ImageJ software.[30]

The 3D volumetric measurements were made on axial T2-weighted MR images using a custom semiautomated volume and CSF segmentation tool described previously.[19] Voxel size for these scans ranged from 0.2 to 1.3 mm in plane resolution and 4.0- to 7.7-mm slice thickness. Volumes were calculated by determining the number of voxels within the posterior cranial fossa via Canny edge detection, then multiplying the number of voxels by the 3 dimensions of pixel spacing embedded within the MRI DICOM file. The CSF volume was determined by isolating connected voxels with a minimum intensity corresponding to CSF on T2-weighted imaging.

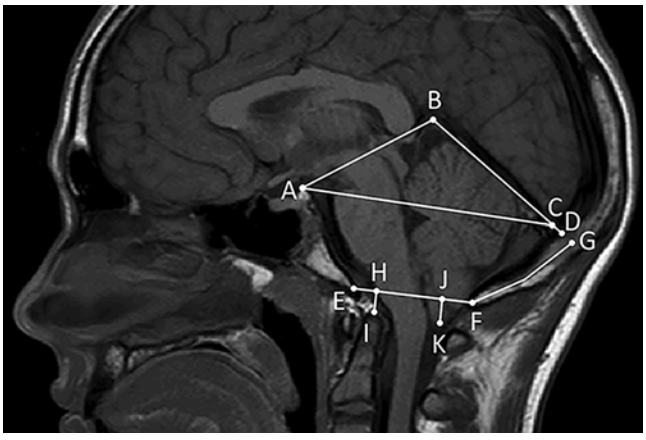

FIG. 1. Sagittal MR image indicating morphometric landmarks and lines. Clivus-tentorium distance (AB), tentorium length (BD), clivus-torcula line (AC), McRae's line (EF), supraoccipital length (FG), basilar impression (HI), and tonsil position (JK).

The total PFV was defined as the volume posterior to a plane passing through the tips of the clivus and tentorium (line AB of Fig. 1), inferior to the tentorium, anterior to the occipital bone, and superior to the foramen magnum. The caudal PFV was the portion of the PFV inferior to a plane extending between the tip of the clivus and torcula (line AC of Fig. 1). The CSF/caudal PFV ratios (Fig. 2) were assessed as a measure of posterior fossa crowding. A smaller CSF/caudal PFV ratio indicates a more significant degree of crowding within the posterior fossa due to displacement of CSF.

All 102 patients with CM-I (51 asymptomatic and 51 symptomatic) underwent measurement and comparison of basilar impression, tentorium length, supraoccipital length, and clivus-tentorium distance. Seventy-eight patients underwent volumetric analysis for total PFV (12 pairs were excluded from volumetric analysis due to poor axial image quality preventing edge detection, lack of axial T2-weighted images, and incomplete sets of axial images that excluded the foramen magnum). Seventy-four patients underwent subvolume analysis for CSF volume, clivus-torcula distance, and caudal PFV (2 additional pairs were excluded due to the presence of a large arachnoid cyst that was expected to confound CSF volume analysis and an anomalous gantry that interfered with clivus-torcula distance measurement). Hypothesis testing was completed using the paired t-test. A p value < 0.05 was considered statistically significant.

Results

By design, the symptomatic and asymptomatic groups were closely matched for age, sex, tonsil position, and morphology (Table 1). The mean (± SD) ages for the symptomatic group (8.0 ± 5.3 years) and the asymptomatic group (7.9 ± 5.3 years) were similar ($p = 0.23$). The mean (± SD) tonsil position was 11.4 ± 4.7 mm below the foramen magnum in symptomatic patients and 10.9 ± 4.1 mm in individuals without symptoms ($p = 0.11$). There were 25 boys and 26 girls in each group. Among the 51 symptomatic patients, 21 had a syrinx, 21 had a dilated central canal, and 9 had no syrinx. Among the 51 asymptomatic patients, 6 had a syrinx, 24 had a dilated central canal, and 21 had no syrinx.

Results of the comparison of 2D morphometric and 3D volumetric measurements are shown in Table 1. Independent groups t-tests were used to compare group means. After matching for age at diagnosis, tonsil position within a 2-mm difference, tonsil morphology (rounded vs pointed), and sex, no significant differences were observed between patients with symptomatic and asymptomatic CM-I with respect to tentorium length (50.3 vs 51.0 mm; $p = 0.537$), supraoccipital length (39.4 vs 42.6 mm; $p = 0.055$), clivus-tentorium distance (52.0 vs 52.1 mm; $p = 0.964$), clivus-torcula distance (81.5 vs 83.3 mm; $p = 0.257$), total PFV (183.4 vs 190.6 ml; $p = 0.250$), caudal PFV (152.5 vs 159.8 ml; $p = 0.256$), fourth ventricle volume to caudal PFV ratio (0.0140 vs 0.0136; $p = 0.649$), and CSF volume to caudal PFV ratio (0.071 vs 0.061; $p = 0.138$). There was a 1.1-mm mean difference between groups in basilar impression, which did achieve statistical significance (5.9 vs

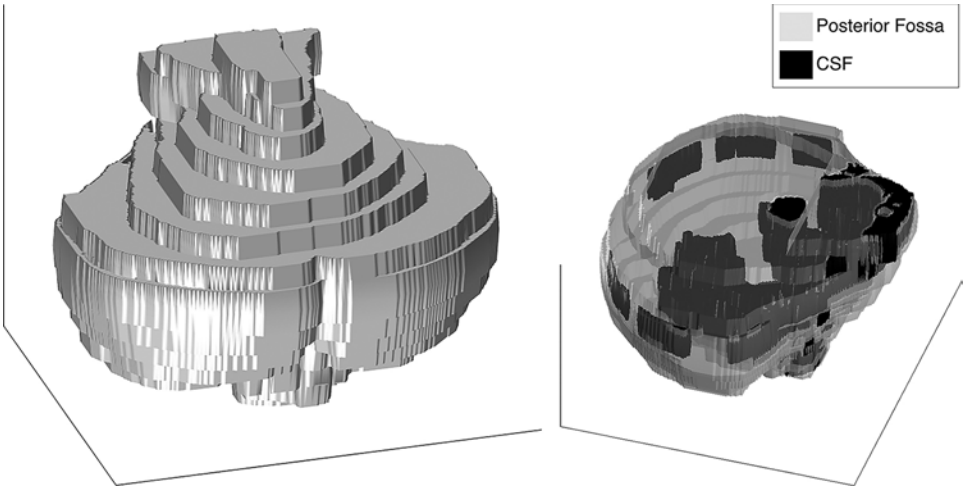

FIG. 2. 3D illustration. **Left:** Total PFV. **Right:** Caudal PFV (*gray*) and CSF volume (*black*).

TABLE 1. Comparison of morphometric data between matched symptomatic and asymptomatic patients with CM-I

Variable	No. of Patients	Mean (SD)	Mean Paired Difference (SD)	95% CI	p Value (2-tailed)
Age at diagnosis, yrs			0.08 (0.50)	−0.06 to 0.23	0.225
Symptomatic	51	8.0 (5.3)			
Asymptomatic	51	7.9 (5.3)			
Tonsil position, mm			0.58 (2.51)	−0.13 to 1.29	0.105
Symptomatic	51	11.4 (4.7)			
Asymptomatic	51	10.9 (4.1)			
Basilar impression, mm			1.09 (3.40)	0.14 to 2.05	0.026
Symptomatic	51	−5.9 (3.0)			
Asymptomatic	51	−7.0 (3.1)			
Tentorium length, mm			−0.71 (8.14)	−3 to 1.58	0.537
Symptomatic	51	50.3 (5.8)			
Asymptomatic	51	51.0 (6.6)			
Supraoccipital length, mm			−3.2 (11.7)	−6.53 to 0.07	0.055
Symptomatic	51	39.4 (7.4)			
Asymptomatic	51	42.6 (7.0)			
Clivus-tentorium distance, mm			−0.07 (8.90)	−2.95 to 2.82	0.964
Symptomatic	51	52.0 (6.1)			
Asymptomatic	51	52.1 (7.9)			
Clivus-torcula distance, mm			−1.8 (9.3)	−4.86 to 1.34	0.257
Symptomatic	37	81.5 (7.0)			
Asymptomatic	37	83.3 (7.2)			
Total PFV, ml			−7.2 (38.6)	−19.7 to 5.3	0.250
Symptomatic	39	183.4 (27.2)			
Asymptomatic	39	190.6 (29.9)			
Caudal PFV, ml			−7.2 (38.2)	−19.97 to 5.48	0.256
Symptomatic	37	152.5 (25.7)			
Asymptomatic	37	159.8 (31.1)			
CSF/caudal PFV ratio			0.01 (0.04)	−0.003 to 0.022	0.138
Symptomatic	37	0.071 (0.032)			
Asymptomatic	37	0.061 (0.030)			
4th ventricle/caudal PFV ratio			0.0004 (0.0051)	−0.0013 to 0.0021	0.649
Symptomatic	37	0.0140 (0.0045)			
Asymptomatic	37	0.0136 (0.0046)			

7.0 mm; p = 0.026). The 3D volume comparison is also illustrated in Fig. 3, which reveals no significant difference between symptomatic and asymptomatic patients.

A secondary analysis was performed, with all patients with a syrinx included in the symptomatic group. As was the case with our primary analysis, in which groups were divided only by symptom status, no significant differences in any of the 2D or 3D metrics were observed between the symptomatic and asymptomatic groups with this secondary analysis.

Discussion

Cerebellar tonsil position is the most frequently used measurement on imaging for evaluating the presence of CM-I. Unfortunately, this measurement alone does not reliably identify the presence and severity of CM-I symptoms across a group of patients with CM-I by the traditional radiographic criterion of a tonsil ≥ 5 mm below the foramen magnum. Although lower tonsil position does predict an increased likelihood of presenting with typical CM-I symptoms in general,[37] many asymptomatic individuals also have low cerebellar tonsil position.[12,15,16,20,28,41,44] In addition, symptoms of CM-I or syringomyelia may occur in patients with normal tonsil position in some cases.[3,9,31,39]

Asymptomatic or minimally symptomatic patients with CM-I incidentally discovered on imaging have become an increasingly common reason for referral to neurosurgeons.[14,24,25,42] The clinical decision making is relatively clear for patients who are completely asymptomatic and for those with severe symptoms and syringomyelia that are considered clearly attributable to CM-I. However, many patients with CM-I have symptoms that may be attributed to either CM-I or other causes.[34] It is important to

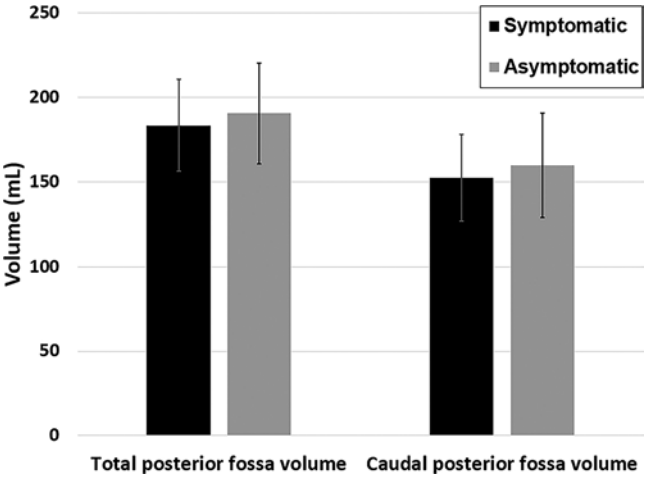

FIG. 3. Graph comparing mean total PFV (*left*) and caudal PFV (*right*) between symptomatic (*black*) and asymptomatic (*gray*) patients. *Error bars* equal standard deviation.

correctly diagnose asymptomatic CM-I to prevent unnecessary and ineffective surgery, as well as to avoid delayed diagnosis and treatment in truly symptomatic cases.[4,11]

Several morphometric studies have been published in recent years comparing radiographic posterior cranial fossa parameters between patients with CM-I and control subjects in the general population.[5,10,13,18,26,27,32,38] A combination of several parameters has been suggested as an alternative diagnostic criterion to tonsil position.[40] In this study, we investigated other imaging criteria that we thought could potentially distinguish symptomatic from asymptomatic CM-I. After matching for age at diagnosis, tonsil position within a 2-mm difference, tonsil morphology (rounded vs pointed), and sex, there were no clinically useful and statistically significant radiographic differences between patients with symptomatic and asymptomatic CM-I in the anatomical measures we made.

Although the 1.1-mm difference in basilar impression between our groups was statistically significant, we do not consider the magnitude of this difference clinically useful as a means of differentiating between the groups. None of the other measures were different between the groups. Our results are at odds with a number of the studies cited above. For example, Sgouros et al.,[32] using segmentation techniques similar to ours, found that children with CM-I and a syrinx had a smaller PFV than both healthy children and children with CM-I without a syrinx. Patients with asymptomatic CM-I who were not surgical candidates were not included in that analysis.

We did not define our groups on the presence or absence of a syrinx; however, 42% of symptomatic patients had syringes versus only 12% of those in the asymptomatic group. Despite this, we did not detect a difference in PFV between the groups. In addition, no differences between groups were identified even in a secondary analysis that included the asymptomatic patients with syringes in the symptomatic group.

Additional diagnostic methods and criteria will be needed to accurately diagnose symptomatic CM-I to guide prognosis and management. These methods include dynamic measurement of CSF motion using 4D flow MRI,[8] longitudinal impedance to CSF flow at the foramen magnum measured using computational fluid dynamics,[22] neural tissue motion quantification[23] and/or volumetric displacement[45] quantification over the cardiac cycle, and other techniques.

In particular, Shaffer et al.[33] quantified resistance to CSF flow at the foramen magnum using computational fluid dynamics modeling in healthy subjects (n = 8) and in patients with symptomatic (n = 10) and asymptomatic (n = 5) CM-I. Impedance to CSF flow showed a trend of lower values in the asymptomatic group compared with the symptomatic group. However, the limited number of subjects did not provide adequate power for statistical relevance.

There are several important limitations to this analysis. Most importantly, the assignment of patients to groups according to symptom status is necessarily subjective. We attempted to limit the subjective nature of these decisions by only examining patients with either classic CM-I symptoms or no neurological symptoms. In future studies, symptoms may be measured more objectively by prospectively recording validated health-related quality-of-life indices, such as the Chiari Health Index for Pediatrics.[21]

The necessity of closely matching symptomatic and asymptomatic patients limited the number who could be included in the analysis. Our study group included pediatric CM-I patients only. A study should be conducted in adults with CM-I to confirm the findings among adult CM-I patients. In addition, the retrospective study design did not allow control of the MRI protocols used to assess each patient. Thus, many parameters varied between scans that could have affected the results, such as scan pixel size and imaging parameters that lead to different pixel intensities for fluids versus solids. Finally, all measurements were made by a single observer.

Conclusions

No significant differences were observed in 2D morphometric and 3D volumetric measurements between the asymptomatic and symptomatic pediatric CM-I groups, for which tonsil position and morphology were matched. None of the additional measurements could predict symptom status after accounting for the matched variables. Further study will be necessary to establish if any imaging test can reliably distinguish symptomatic from asymptomatic pediatric CM-I.

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Disclosures

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Author Contributions

Conception and design: Maher, Martin, Strahle, Loth. Acquisition of data: Maher, Khalsa, Geh, Strahle. Analysis and interpretation of data: all authors. Drafting the article: Maher, Khalsa, Geh. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Statistical analysis: Khalsa. Study supervision: Maher.

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