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AREA MEASUREMENTS WITHIN THE FORAMEN MAGNUM: COMPARISON OF 171 PATIENTS WITH SYMPTOMATIC AND ASYMPTOMATIC CHIARI MALFORMATION TYPE 1

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ABSTRACT

Objective: In previous studies, different radiological measurement techniques could not reliably distinguish patients with symptomatic Chiari type 1 malformation (CMI) from those with asymptomatic CMI. We aimed to develop a new perspective to select patients with CMI for surgery by calculating the brainstem area (BA), cerebellar tonsillar area (CTA), foramen magnum area (FMA), and CTA/BA ratio in T2 MR axial imaging at the foramen magnum level.

Materials and Methods: Eighty six symptomatic and 85 asymptomatic patients evaluated by neurosurgeons were included in the study. The patients' BA, CTA, FMA, and CTA/BA ratios were calculated by two neuroradiologists. In addition, the measurements of the operated patients in the postoperative period were re-made, and the pre-operative and postoperative measurements were compared.

Results: The mean BA was 1.57 cm^2 and 1.76 cm^2 in symptomatic and asymptomatic patients, respectively ($p<0.05$). The cut-off value between symptomatic patients with BA and asymptomatic patients was 1.74 cm^2. The results of our study were found to be statistically significant in such a way that BA measurements can show the amount of compression on the brainstem. The mean postoperative BA (1.73±0.32) was higher than the mean pre-operative BA (1.58±0.35; $p<0.001$). There was no difference between the mean postoperative BA of symptomatic patients (1.73±0.33) and the mean BA of asymptomatic patients. Symptomatic patients' CTAs were wider than asymptomatic patients. In addition, FMA was different between symptomatic and asymptomatic patients ($p<0.001$).

Conclusion: BA and FMA may provide a new perspective on the distinction between symptomatic and asymptomatic CMI.

Keywords: Chiari type 1 malformation, brainstem, symptomatic, asymptomatic

INTRODUCTION

According to imaging-based prevalence studies, Chiari type 1 malformation (CMI) affects between 0.24% and 3.6% of the population[(1)]. This heterogeneous abnormality is characterized by impaired cerebrospinal fluid (CSF) circulation through the foramen magnum[(2)]. While cerebellar tonsillar herniation is part of CMI's definition, numerous studies indicate a weak correlation between the degree of cerebellar tonsil herniation and the manifestation of clinical symptoms such as syringomyelia[(3)]. Prior research has further demonstrated that patients with a lesser degree of tonsillar herniation could exhibit severe clinical symptoms, whereas those with a higher degree may remain asymptomatic[(4,5)].

Herniation of cerebellar tonsils within the foramen magnum impedes CSF flow, leading to Valsalva-induced headaches and syrinx formation[(6,7)]. Additionally, herniated cerebellar tonsils can compress the cervicomedullary junction and lower cranial nerves, potentially causing dysphagia, sleep apnea, and a loss of gag reflex[(8)]. Surgical indications for CMI are primarily driven by the patient's clinical symptoms[(9)]. Undoubtedly, a case of syringomyelia and CMI presenting with pyramidal signs necessitates surgical intervention[(3)]. However, the role of surgery in cases featuring only headaches or asymptomatic syringomyelia remains less clear. Extensive studies have explored the significance of radiological measurements of the foramen magnum in making surgical decisions for CMI patients[(4,9-12)]. Nevertheless, the symptoms of CMI are primarily caused by the compression of cerebellar tonsils on the brainstem and increased CSF pressure at the foramen magnum[(9)]. Headaches are more likely to occur due to dural stretch when the tonsils constrict the foramen magnum during Valsalva maneuvers[(13)]. Consequently, symptoms such as headaches from dural pressure and swallowing, respiratory distress, or sensory disorders due to brainstem pressure are often accompanied by an increase in pressure at the level of the foramen magnum in symptomatic cases.

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We hypothesize that measuring brainstem compression could serve as a reliable criterion for determining surgical indications in these patients. The objective of this study is to offer a new perspective for selecting CMI patients for surgical intervention. We aim to calculate the brainstem area (BA), cerebellar tonsillar area (CTA), foramen magnum area (FMA), and the ratio of cerebellar tonsil area to BA, using T2 axial imaging that passes through the McRae line at the foramen magnum (Figure 1).

MATERIALS AND METHODS

Method and Data Collection

We conducted a retrospective analysis of all patients diagnosed with CMI at our clinic between January 2011 and January 2021. Within this period, a total of 171 patients (86 symptomatic and 85 asymptomatic) who underwent evaluations by neurosurgeons at our facility were included in the study. Those who underwent surgical intervention for CMI were classified as symptomatic. A comprehensive search was conducted for all MR images of the brain and cervical spine in our institution's imaging report database, using the keywords "Chiari", "syringomyelia", and "syrinx". This search was intentionally broad to minimize the risk of overlooking relevant records. The initial search results were manually reviewed, and patients were excluded if their records showed a tonsillar herniation of less than 5 mm or the presence of other pathologies.

Patients were classified as clinically asymptomatic if they met the following criteria:

- No observable signs or symptoms of tonsillar herniation. Symptoms associated with CMI include Valsalva-induced occipital headaches, neck pain, central sleep apnea, extremity numbness or paresthesias, dysphagia, impaired fine motor skills, and gait disturbances.
- Lack of symptoms related to CMI as confirmed by two neurologists at our hospital.

For all qualifying patients, a supplementary review of all hospital documents, including admission notes, surgical notes, and radiological and imaging studies, was conducted to ensure no exclusion criteria were missed. Patients who met all criteria were deemed clinically asymptomatic.

After exclusions, two groups were formed: A symptomatic group of 86 patients and an asymptomatic group of 85 patients. Radiographic CMI was defined as cerebellar tonsillar herniation extending at least 5 mm below the foramen magnum in all subjects. Patients with intracranial mass lesions or a history of cranial or spinal surgery were excluded from the study.

Magnetic resonance imaging (MRI) scans were performed using 1.5-T (Magnetom Aera, Siemens, Erlangen, Germany) and 3-T (Magnetom Skyra, Siemens, Erlangen, Germany) scanners. Intravenous gadolinium was not routinely administered. Both T2-weighted sagittal and axial images and T1-weighted sagittal images were obtained.

All images were stored in a separate offline workstation (Syngo via Version VB30A, Siemens). Measurements were independently conducted by two neuroradiologists who were blinded to the patients' treatment status. The cerebellum, brainstem, and FMA at the level of the foramen magnum were measured using T2 axial imaging that passed through the McRae line at the foramen magnum (Figure 1). The CTA/BA ratio was also calculated. The extent of tonsillar herniation was determined based on T2-weighted MRI in the sagittal plane, marked by drawing a vertical line from the McRae line to the tip of the lower cerebellar tonsil.

This study was conducted with the approval of the Ethics Committee of Selçuk University Faculty of Medicine (decision no: 2021/189, date: 07.04.2021).

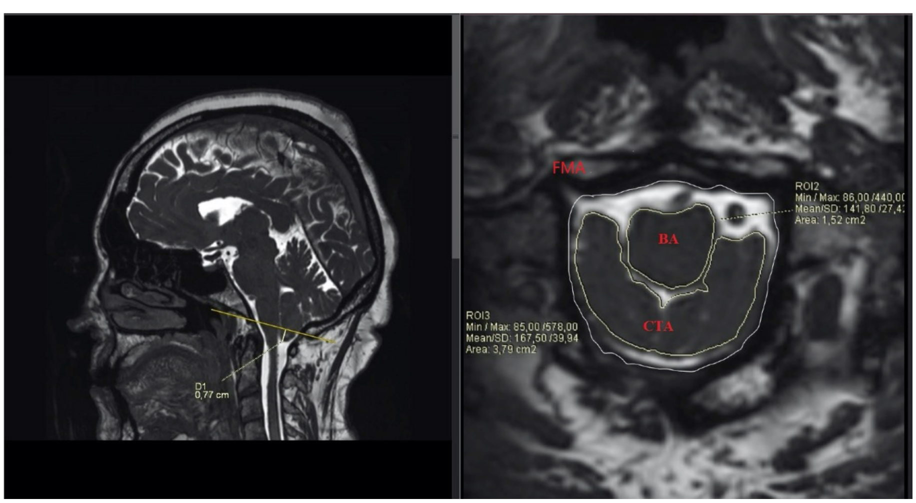

Figure 1. Measurements at the level of the foramen magnum
The brainstem area (BA), cerebellar tonsillar area (CTA), and foramen magnum area (FMA) are delineated. BA represents the area of the brainstem, and CTA represents the area of the cerebellar tonsils, both measured at the level of the foramen magnum. FMA indicates the overall area of the foramen magnum

Statistical Analysis

All data were evaluated using the Statistical Package for the Social Sciences (SPSS) 22.0 statistical package and presented as numbers, percentages, means, and standard deviations. Kurtosis and skewness values were assumed to be normal variances between -1.5 and +1.5[14]. Using multivariate statistics (Boston, Pearson), an intergroup chi-squared test was performed on categorical data frequency distribution. Student's t-test was used to compare the measurements of two distinct groups for a particular variable. A paired sample t-test was used to compare the mean values of a group or sample for a variable at two different times. Receiver operating curve analysis was performed to determine the cutoff value for all parameters. The highest sum of sensitivity and specificity values was used as the optimum cutoff value. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 171 patients were included in the study, with a mean age of 39.85±13.49 years, ranging from 18 to 71 years. The patient population comprised two groups: 50.3% (n=86) were symptomatic, and 49.7% (n=85) were asymptomatic. Gender distribution was 29.8% male (n=51) and 70.2% female (n=120), with no statistically significant differences between the symptomatic and asymptomatic groups (p=0.376).

The mean BA were 1.57 cm^2, 1.76 cm^2 in symptomatic patients, in asymptomatic patients, respectively ($p<0.05$). The cut-off value for BA between the two groups was determined to be 1.74 cm^2 ($p<0.05$). CTA showed mean values of 4.23 cm^2 in symptomatic patients and 4.62 cm^2 in asymptomatic patients ($p<0.05$). No statistically significant difference was observed in the ratio of CTA to BA between the two groups (Table 1 and Figure 2). FMA showed mean values of 7.45 cm^2 and 11.03 cm^2 in symptomatic and asymptomatic patients, respectively ($p<0.001$).

The mean postoperative BA (1.73±0.32) was higher than the mean pre-operative BA (1.58±0.35; $p<0.001$). There was no difference between the mean postoperative BA of symptomatic patients (1.73±0.33) and the mean BA of asymptomatic patients (1.76±0.466; p=0.602; Table 2).

Among males, the mean BA were 1.67 cm^2, 1.89 cm^2 in symptomatic patients, in asymptomatic patients, respectively ($p<0.05$). The mean CTA were 4.28 cm^2, 4.89 cm^2 in symptomatic patients, in asymptomatic patients, respectively ($p>0.05$; Table 3). Among females, the mean BA were 1.54 cm^2, 1.69 cm^2 in

Table 1. Comparison of BA, CTA, CTA/BA, FMA between symptomatic and asymptomatic patients

Area (cm^2)	Patient	n	Mean	SD	p
BA	Symptomatic	86	1.57	0.35	**0.004**
	Asymptomatic	85	1.76	0.46	
CTA	Symptomatic	86	4.24	1.1	**0.028**
	Asymptomatic	85	4.62	0.18	
CTA/BA	Symptomatic	86	2.79	0.92	0.85
	Asymptomatic	85	2.76	0.9	
FMA	Symptomatic	86	7.45	1.28	**<0.001**
	Asymptomatic	85	11.03	1.59	

BA: Brainstem area, CTA: Cerebellar tonsillar area, FMA: Foramen magnum area, SD: Standard deviation

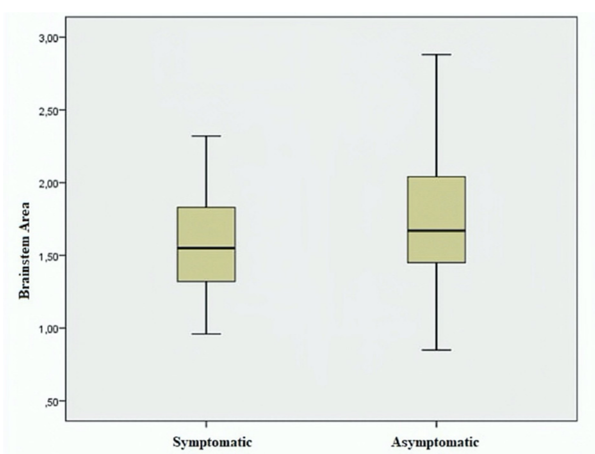

Figure 2. Comparison of BA between symptomatic and asymptomatic patients
BA: Brainstem area

Table 2. Comparison of BA of pre-operative and post-operative patients and post-operative and asymptomatic patients

Area (cm^2)	Mean	n	SD	p
Pre-op BA	1.58	86	0.35	**<0.001**
Post-op BA	1.73	86	0.32	
Area (cm^2)	Mean	n	SD	p
Post-op BA	1.73	86	0.32	0.6
Asymptomatic BA	1.76	85	0.46	

BA: Brainstem area, SD: Standard deviation symptomatic patients, in asymptomatic patients, respectively ($p<0.05$). The mean CTA were 4.22 cm^2, 4.48 cm^2 in symptomatic patients, in asymptomatic patients, respectively ($p>0.05$). In this study, the ratio of the CTA to the BA was not statistically significant between the two groups (Table 3).

The mean BA were 1.79 cm^2, 1.61 cm^2 in male, in female, respectively. The BA was statistically significantly higher in male patients than in female patients ($p=0.01$; Table 4). When asymptomatic patients were considered as a separate group, the BAs of males were larger than those of females ($p<0.05$) (Table 4).

DISCUSSION

Clinical Symptoms and Signs

CMI is known to induce an array of symptoms and radiological findings due to the herniation of cerebellar tonsils through the foramen magnum[15]. While the headaches experienced by patients are generally a result of dural stretching, other symptoms like respiratory distress and sensory issues often arise from brainstem compression[16,17]. However, existing literature has indicated a weak relationship between tonsillar herniation and these symptoms[3-5].

Our study introduces a new perspective concerning the tolerability of the brainstem to mechanical forces. The extent to which the brainstem can tolerate compression may be a pivotal factor in the onset of clinical symptoms. When this tolerance is exceeded, complications such as a decrease in interstitial fluid and thinning of the brainstem could manifest.

The Role of Radiological Findings in Clinical Decision-Making

Here, the relevance of radiological findings in the clinical decision-making process deserves exploration. Soft tissue density can be calculated by adding the areas of the brainstem and cerebellar tonsils and proportioning this sum to the FMA, as done by Fuell et al.[9]. However, this method does

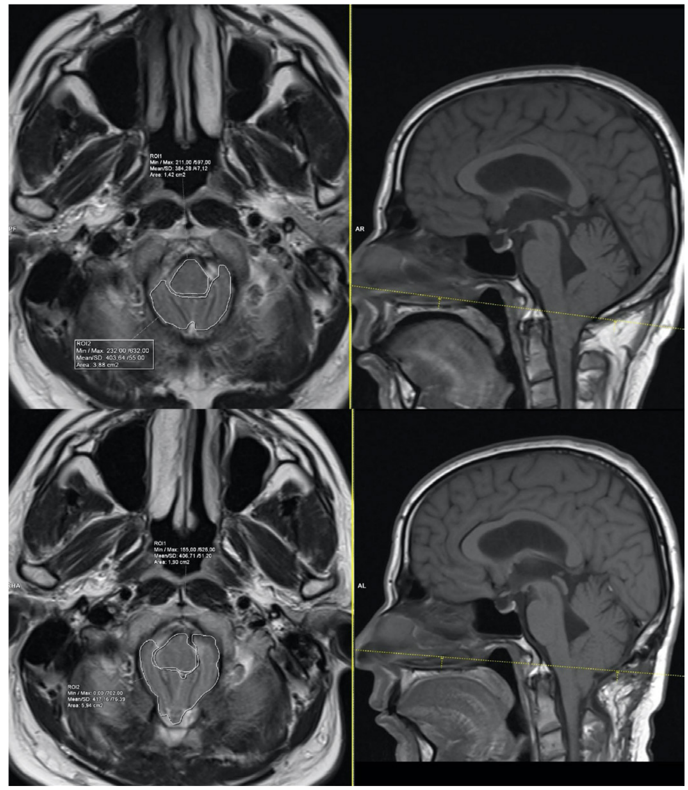

Figure 3. Preoperative and postoperative measurements changes

In a patient diagnosed with Chiari malformation type I (CMI), BA and CTA measurements were observed in pre-operative and post-operative MRI scans. In the pre-operative MRI, the BA was measured to be 1.42 cm², while the post-operative BA increased to 1.90 cm². Similarly, the pre-operative CTA was 3.88 cm² and expanded to 5.94 cm² in the post-operative MRI. Importantly, these measurements were taken at a consistent axial section level and angle in both pre-operative and post-operative scans

BA: Brainstem area, MRI: Magnetic resonance imaging, CTA: Cerebellar tonsillar area

Table 3. Comparison of symptomatic and asymptomatic patients according to gender groups BA, CTA, CTA/BA

	Area (cm^2)	Patient	n	Mean	SD	p
Male	BA	Symptomatic	23	1.67	0.35	**0.046**
		Asymptomatic	28	1.9	0.43	
	CTA	Symptomatic	23	4.28	1.17	0.11
		Asymptomatic	28	4.9	1.49	
	CTA/BA	Symptomatic	23	2.6	0.67	0.76
		Asymptomatic	28	2.69	1	
Female	BA	Symptomatic	63	1.55	0.34	**0.045**
		Asymptomatic	57	1.7	0.46	
	CTA	Symptomatic	63	4.22	1.07	0.16
		Asymptomatic	57	4.49	0.98	
	CTA/BA	Symptomatic	63	2.85	1	0.74
		Asymptomatic	57	2.8	0.84	

BA: Brainstem area, CTA: Cerebellar tonsillar area, SD: Standard deviation

Table 4a. Comparison of BA, CTA, CTA/BA between gender in all patients

Area (cm^2)	Gender	n	Mean	SD	p
BA	Male	51	1.8	0.41	**0.01**
	Female	120	1.61	0.41	
CTA	Male	51	4.62	1.39	0.161
	Female	120	4.35	1.03	
CTA/BA	Male	51	2.65	0.86	0.28
	Female	120	2.82	0.92	

BA: Brainstem area, CTA: Cerebellar tonsillar area, SD: Standard deviation

Table 4b. Comparison of BA, CTA, CTA/BA between gender in asymptomatic patients

Area (cm^2)	Gender	n	Mean	SD	p
BA	Male	28	1.9	0.43	**0.049**
	Female	57	1.7	0.46	
CTA	Male	28	2.69	1	0.63
	Female	57	2.79	0.84	
CTA/BA	Male	28	4.9	1.49	0.13
	Female	57	4.5	0.98	

BA: Brainstem area, CTA: Cerebellar tonsillar area, SD: Standard deviation

not account for the subarachnoid space. The significance of the subarachnoid space for potential complications like syringomyelia has been shown by Taylor et al.[10]. Nonetheless, this approach is not appropriate for patients who have not yet developed syrinx.

Comprehensive Methodological Approaches and Findings

In our study, we focused on three primary scenarios regarding the pressure exerted on the brainstem:

- Radiological differences in the brainstem between symptomatic and asymptomatic patients with CMI,
- Changes in the brainstem following foramen magnum decompression in symptomatic patients with CMI,
- Measurable radiological differences in the FMA between symptomatic and asymptomatic patients with CMI.

Under these scenarios, measurements of BA could indicate the amount of compression exerted on the brainstem. Specifically, we found that the BA was significantly smaller in symptomatic patients (p=0.004) and observed a significant increase in BA postoperatively (p<0.001). This result has been reported for the first time in the literature. After reviewing the pathophysiology, the cerebellar tonsil, which should not be normally present at the foramen magnum level in patients with CMI, begins to cover a specific area in patients with CMI. When cerebellar tonsil herniation worsens, the pressure increases and the volume of interstitial fluid in the brainstem reduces to tolerate the increased pressure[18,19]. Because there are connections between CSF and interstitial fluid and they work together on management of intracranial pressure[10,19,20]. The interstitial fluid is withdrawn by moving to the cranial and caudal sides. For all abovementioned reasons, we believe that interstitial fluid loss in the brainstem at the foramen magnum level may be one of the causes of BA thinning. The scarcity of studies on this topic in the literature is also notable. These data suggest that the tolerability of the brainstem to compression is a crucial factor in symptom development and surgical decision-making.

In the present study, FMA was higher in asymptomatic patients than in symptomatic patients (p<0.001). We believe that this explains why cerebellar tonsillar herniation length is not important in terms of symptoms or surgical decision making. Because of the larger FMA, the cerebellar tonsils do not put pressure on the brainstem and do not obstruct CSF circulation. As a result, they do not cause any symptoms[21].

A previous study identified no clinically useful 2D or 3D measurements that could reliably distinguish patients with symptoms attributable to CMI from patients with asymptomatic CMI[22]. However, area measurements were not performed in this study. Our study showed that BA and FMA measurements are very important in CMI. As in other recent studies, we state the necessity of area measurement studies at the level of the foramen magnum in CMI[9,10].

Age and Gender Factors

Previous studies have shown that the tolerability of brain tissue to mechanical forces can vary with age[21]. This could lead to the establishment of percentiles by measuring BAs in different age and gender groups. For example, we observed significant gender-based differences in BA (p<0.05) (Table 4).

Study Limitations

The main limitation of our study is the small sample size and retrospective design.

CONCLUSION

In summary, our study indicates that measurements of BA and FMA are critical in the diagnosis and treatment of CMI. However, future studies should validate these findings using more comprehensive methodologies. Specifically, more exhaustive methods that take into account the subarachnoid space and interstitial fluid dynamics should be developed.

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Ethics

Ethics Committee Approval: This study was conducted with the approval of the Ethics Committee of Selçuk University Faculty of Medicine (decision no: 2021/189, date: 07.04.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.G., H.K., Concept: D.K.G., Design: D.K.G., Data Collection or Processing: B.G., H.C., Ö.F.T., Analysis or Interpretation: Ö.F.T., H.K., Literature Search: B.G., D.K.G., H.K., Writing: B.G., H.K.

Conflict of Interest: The authors have no conflicts of interest to declare.

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