Clinical Investigative Study

MRI-based Morphometric Analysis of Posterior Cranial Fossa in the Diagnosis of Chiari Malformation Type I

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ABSTRACT

BACKGROUND AND PURPOSE

The diagnosis of Chiari malformation type I (CMI) relies on MRI identification of a tonsillar descent (TD) through the foramen magnum, reflecting the overcrowding of an underdeveloped posterior cranial fossa (PCF). However, TD occurs in some patients with normal-sized PCF and, conversely, some patients with borderline or no TD have small PCF. We thus sought to identify a set of prototypic PCF measures for the diagnosis of CMI.

METHODS

We performed nineteen measurements of the PCF on sagittal MRI of 100 cases with cerebellar TD \geq 5 mm and 50 control individuals, compared the average values in both cohorts and used logistic regression to devise a probability model to predict CMI status.

RESULTS

Significant decrements were detected for several PCF-related measures in the patients' cohort. We developed a probability model that combined seven of these parameters to predict diagnosis with 93% sensitivity and 92% specificity.

CONCLUSIONS

The addition of simple morphometric measurements in the diagnostic work-up of patients with suspected CMI may facilitate radiological diagnosis. Moreover, identification of the subset of CMI that arise from basichondrocranium underdevelopment is important for both, selection of the most appropriate therapeutic approach as well as proper CMI categorization in research studies. **Keywords:** Chiari malformation type I, MRI, morphometry, ROC.

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Introduction

CMI is characterized by underdevelopment and overcrowding of the PCF and the associated neurological dysfunction secondary to hindbrain compression and hydrosyringomyelia. Since the advent of MRI, CMI has been defined by the chronic herniation of the cerebellar tonsils of at least 3 mm below the foramen magnum (FM).¹

The etiology of CMI is unclear and appears to be multifactorial. Pathogenic hypotheses invoking a primary neural defect²⁻⁴ gave way to the current notion that CMI is primarily a mesodermal developmental anomaly, based on experimental observations of vitamin A-induced occipital bone undergrowth and cerebellum displacement in rodents.^{5,6} Morphometric studies in CMI patients corroborated the overcrowding of a normally developed hindbrain within a hypoplastic PCF.⁷⁻¹⁶ "Acquired" CMI may differ mechanistically and encompass conditions such as cranial settling, growth hormone deficiency, cerebrospinal fluid (CSF) leaks, lumboperitoneal shunts and intracranial space-occupying lesions.^{14,17-19} In this work we will use the term "classical CMI" for referring to CMI produced by an underdeveloped PCF, as proposed by Milhorat et al.¹⁹

Since both age at presentation and symptoms show great variability in CMI, radiological diagnosis becomes paramount. However, some limitations are evident when using the standard definition of CMI based on tonsillar herniation. The prevalence of CMI is estimated to be in the range of 1 per 1,000 to 1 per 5,000 individuals²⁰ but TD may constitute an incidental finding.²¹⁻²³ Conversely, there is increasing evidence that many patients with an overcrowded PCF and typical CMI signs, such

as hydrosyring omyelia, do not show TD; many authors refer to these cases as Chiari malformation "type $0.^{\rm n10,24}$

A number of morphometric studies have provided evidence of occipital bone hypoplasia in CMI, lending support to the theory of paraaxial mesoderm insufficiency, as originally introduced by Marín-Padilla.⁶ These studies have demonstrated a selective shortness of the basioccipital^{8,10,13,25,26} the clivus^{7,9,12,14,16,19,26} or the basioccipital and the posterior supraoccipital-exoccipital.^{14,19,25,26} In contrast, volumetric PCF analyses have provided less consistent results and reduced,^{8,12} normal²⁵ or even increased¹¹ PCF volumes have been described.

In view of the limitations of solely using TD greater than 3^1 or 5 mm²⁷ to establish CMI diagnosis, the main goal of this study was to devise a mathematical model to help identifying, based on morphometric findings and irrespective of TD, symptomatic hypoplastic PCF.

Patients and Methods

Patients

This retrospective study was conducted on a prospective registry started in 1989 at our institution, which includes 307 patients admitted for surgical evaluation of CMI. From this cohort we selected 100 consecutive adult patients diagnosed with symptomatic CMI in the period 2004-2010. All patients received a complete clinical evaluation and a cranial and spinal MRI study and all displayed a cerebellar TD ≥ 5 mm on midsagittal T1W1 MRI. Sixty-two cases were female and the mean age was 42.6 ± 12.2 years (median 42, range 19-71 years). The most frequent signs and symptoms in the 100 cases that underwent the morphometric analysis are depicted in Table 1. Patients had been symptomatic for a median period of 36 months prior to diagnosis. The most common symptom in this cohort was headache (69%), which often featured neck irradiation (68% of those with headache). Other common symptoms were cough headaches (45%), upper limb paresthesia (39%) and dizziness (26%). Seven patients, presenting with papilledema in the absence of hydrocephalus, had intracranial hypertension when intracranial pressure was monitored. No patient displayed tethered cord. Other, less common signs and symptoms, as well as associated comorbidity were typical for CMI. Brain and spinal MRI documented hydrocephalus and syringomielia in 23% and 45% of cases, respectively. Hydrocephalus was defined as an Evans index, or the maximal frontal horn ventricular width divided by the transverse inner diameter of the skull $> .30.^{28}$ Associated findings were retrocurved odontoid in 12 patients, basilar invagination and platybasia in 5 and Klippel-Feil malformation in a single patient (Table1). Surgical PCF reconstruction was performed in 50% of patients.

As a control group, we included 50 individuals (31 female, mean age 35.6 ± 7.6 years) that underwent a brain MRI after presenting with a clinically isolated syndrome suggestive of multiple sclerosis, and who were presumed to reflect the normal population in terms of PCF morphology. All patients and control subjects gave informed consent to participate in the study, which was approved by the local Ethics Committee.

Table 1. Clinical Findings in 100 Patients with CMI

	CMI (TD \geq 5 mm)
Number of patients	100
Sex (M/F)	38/62
Age (y)	$45.5 \pm 12.2(20 - 71)$
Age at diagnosis	$35.7 \pm 12.12/88^*$
Hydrocephalus	23/100 (23%)
Hydrosyringomyelia	45/100 (45%)
Pseudotumor cerebri	7/100 (7%)
Complex craniocervical malformation	6/100 (6%)
Klippel-Feil malformation	1/100 (1%)
Retrocurved odontoid	12/89 (13.5%)
SIGNS AND SYMPTOMS	
Time elapsed from onset (mo)	$67.2 \pm 68.1/88$
Headaches	67/97 (69.1%)
Occipital headache/cervicalgia	46/97 (47.4%)
Cough headaches	44/96 (45.8%)
Dizziness	26/99 (26.3%)
Vertigo	8/99 (8%)
Visual alterations	9/99 (9%)
Nystagmus	11/63 (17.5%)
Kyphoscoliosis	12/66 (18.2%)
Fatigue	7/98 (7.1%)
Instability	20/98 (20.4%)
Sensory loss	23/98 (20.4%)
Motor weakness	23/99 (23.5%)
Dysphagia	19/99 (19.2%)
Dysphonia	10/99 (10.1%)
Gait disturbances	13/99 (13.1%)
Paresthesia/pain upper limbs	39/99 (39.4%)
Paresthesia/pain lower limbs	14/99 (14.1%)
Other symptoms:	
Anxiety	16/97 (16.5%)
Depression	14/98 (14.3%)
THERAPEUTIC PROCEDURES	
Surgical treatment	50/100 (50%)

*Except for sex ratios, the figure after the slash indicates, for each variable, the number of subjects for which information was available.

Morphometric Analysis of the PCF

Brain MRI Protocol

MR data were acquired using a 1.5 T scanner (MAGNETOM Symphony or MAGNETOM Vision, Siemens, Erlangen, Germany) equipped with a circular polarized receiver head array coil. In all patients sagittal, transverse and coronal conventional spin-echo T1-weighted sequences were obtained (repetition time [TR] /echo time [TE]/acquisitions 450-600 ms/12-20 ms/2). In addition and for clinical purposes transverse T2-weighted fast spin-echo (TR 4300 ms/TE 96 ms/acquisitions 1-2) and fast-FLAIR (TR 8500 ms/ TE 104 ms/ inversion time 2500 ms/acquisitions1) were also performed. All sequences were obtained with 4-5-mm section thickness and .1-.3 interslice gap, 144-256 \times 256-384 matrix, and 196 \times 230 mm field of view.

Brain MRI of all patients and controls were analyzed using the digital picture archiving and communication system (PACS) on a NUMARIS/4 syngo[®] post-processing workstation, version MR 2004A, (Siemens AG, Erlangen, GE) and image J processing package version 1.41 (http://rsb.info.nih.gov/ij).



Fig 1. Morphometric measurements made on mid-sagittal T1WI of a CMI case (A,B,C) and a control subject (D). A) A number of measurements were taken in reference to the FM planum and assessed the shallowness of the PCF: FM (A), TD (B), basilar impression (C) and distance from fastigium, pons and corpus callosum to FM (D-E, respectively). B) Angular measurements were used to assess the degree of basicranium dysplasia and suboccipital shortening: tentorium angle (A), basal angulation (B), Wackenheim angle (C) and odontoid angle (D). C), D): Landmarks and linear measurements used to assess PCF dimensions and estimate areas: The height of PCF (K) was estimated by drawing the line from the upper tentorial end (E) to the basion (C)-opisthion (B) line. The anteroposterior diameter of PCF (L) was inferred from a line running from the internal occipital protuberance (A) to top of the dorsum sellae (D). The PCF area was estimated as the polygon delimited by (A) (B) (C) (D) and (E) and the osseus PCF area as the one delimited by (A) (B) (C) and (D). Length of tentorium (F), supraoccipital (G) and clusus (H), including the basioccipital (I) and basisphenoid (J) lengths when the spheno-occipital synchondrosis was discernible, were also measured.

Morphometric Methodology

The following measurements, including linear, surface and angular parameters were made in mid-sagittal T1WI from 100 patients with untreated, classical CMI and 50 control subjects (Fig 1):

Cerebellar TD

The degree of TD was measured as previously described.^{27,29,30} In summary, the line between the basion and opisthion (ie, McRae's line) was assumed to represent the planum of the FM. TD was then evaluated by measuring the distance to the most caudal aspect of the tonsils on a line running perpendicular to the opisthion-basion line. Tonsillar position above the FM was assigned a negative value.

Morphological Features of PCF

The PCF area was estimated from a single MRI sagittal slice and the surface delimited by the following boundaries: tentorium, supraoccipital portion of the occipital bone, FM and clivus. The area of the osseous PCF was estimated from a polygon bounded by the following edges: occipital bone (basioccipital portion of the clivus and supraoccipital portion of the occipital bone to the insertion of the tentorium), basisphenoid and a line from the upper basisphenoid to the internal occipital protuberance.³¹ All the edges of the PCF polygon were also measured: FM, the distance from basion to opisthion along the McRae's line,^{19,24} the length of supraoccipital^{8,19,25} and the clivus length.^{8,19,25} The height of PCF was calculated as a perpendicular line from the highest point of the fossa to the basion-opisthion line, and its anteroposterior diameter as a line from the highest point of the sella turcica to the internal occipital protuberance (ie, Twining's line).⁷

To Assess the Degree of PCF Overcrowding

We measured the length of three lines, which have proven to be reliable indicators of the presence of a cranioencephalic disproportion: the distance from corpus callosum to FM⁷, the distance from the fastigium to FM and the distance from the pons to the FM.

Odontoid Process

To assess the presence/absence of basilar impression, the distance from the tip of the odontoid process to the McRae's line was measured. Values can be negative (below McRae's line) or positive (above McRae's line). In addition, we measured the odontoid angle formed by a horizontal line along the base of C2 body and another bisecting the odontoid process.³²

Angular Measurements

Three measurements were taken: (1) the tentorium angle (formed by the tentorium and supraoccipital),^{8,33} (2) the angle formed by a line from the basion to the center of the sella turcica and a second line drawn from the center of the sella turcica to the nasion³³ and (3) the Wackenheim's angle, formed by a line drawn along the clivus prolonged downwards to meet a line tangential to the posterior aspect of the odontoid process.

A single observer, blinded to the clinical diagnosis, obtained the above-referred 19 measures from a midsagittal T1WI slice. In order to evaluate intraobserver agreement for each morphometric method and consistence of measurements between the two methods, we performed two-way mixed intraclass correlation coefficients (ICC) (95% confidence interval) on repeated measures for all measurements in 15 randomly selected cases. In both instances, high intraobserver reliability was found (ICC > .7, range .69-.99, P < .01).

Statistical Analysis

Data are presented as percentages for categorical variables and mean values with their standard deviations for continuous variables. Parametric (ANOVA) or nonparametric (Mann-Whitney U) tests were used to compare continuous variables between patient and control groups. Statistical significance, initially set at P < .05, was modified to P < .0025 after applying the Bonferroni correction for multiple comparisons. The statistical analyses were performed with JMP[®] 7.0.2 (SAS Institute Inc., Cary, NC) and SPSS Statistics 17.0 (SPSS Inc., Chicago, IL).

In order to identify the most robust measures to differentiate patients' from controls' PCF, a predictive model was developed using the *Screening* module of the JMP Software, which ranks the variable effects in a similar way to a forward stepwise regression. Next, a logistic regression model with the variables that maximized the classification properties (sensitivity and specificity) was fitted using the SPSS software. The corresponding ROC curve was calculated to determine the accuracy of the model and the cut-off value above which an individual can be predicted to suffer classical CMI malformation.

Results

MRI Morphometric Data

Table 2 shows the average values of the PCF measurements in both cohorts. Patients showed statistically significant differences (P < .0025) with respect to controls in several PCFrelated measurements. The most remarkable were observed

Table 2.	Morphometric PCF Analysis in Patients and Control Sub-
	jects. Average Values (mean \pm SD) are Indicated for the 19
	Performed Measurements

Variable	Patients (<i>n</i> = 100)	Controls (<i>n</i> = 50)	Р
Age (v)	42.6 ± 12.2	35.6 ± 7.6	
Sex (M/F)	38/62	19/31	
Measurements			
TD (mm)	$10.8~\pm~4.5$	-4.9 ± 3.7	4.97E-41
Tentorium (mm)	50.1 ± 5.5	53.1 ± 4.8	.001
Supraoccipital (mm)	41.3 ± 5.1	43.8 ± 5.1	.004
FM (mm)	$34.7~\pm~3.4$	35.4 ± 3.0	.229
Clivus (mm)	$42.2~\pm~4.0$	47.0 ± 3.3	2.17E-11
PCF area (cm^2)	33.7 ± 3.7	37.8 ± 3.5	1.56E-09
Osseous PCF area (cm ²)	20.3 ± 2.5	$23.7~\pm~2.8$	1.98E-12
Corpus callosum to FM (mm)	$56.0~\pm~4.2$	63.3 ± 3.2	2.4E-20
Height PCF (mm)	62.6 ± 6.1	$68.5~\pm~4.9$	1.84E-08
Width PCF (mm)	$85.5~\pm~5.0$	$85.7~\pm~4.2$.821
Fastigium to FM (mm)	26.1 ± 3.7	31.6 ± 2.2	5.69E-18
Pons to FM (mm)	$35.8~\pm~4.5$	43.2 ± 3.2	3.46E-20
Basal angulation (°)	133.7 ± 6.7	127.8 ± 4.2	3.36E-08
Tentorium angle (°)	$90.1~\pm~8.0$	$93.2~\pm~7.1$.022
Wackenheim angle (°)	153.5 ± 11.4	154.2 ± 7.2	.971
Basilar impression (mm)	-4.3 ± 2.3	-4.2 ± 2.2	.823
Odontoid angle (°)	67.3 ± 5.6	$66.9~\pm~5.0$.726
Clivus to basiesphenoid (mm)	11.5 ± 4.5	$14.0~\pm~6.7$.211
Clivus to basioccipital (mm)	$24.3~\pm~4.3$	$26.0~\pm~5.2$.315

in the parameters measuring the distance from several neural structures (corpus callosum, pons and fastigium) to the FM, which were considerably reduced and reflected the shallowness of the PCF. We also observed a marked reduction in PCF areas and a reduced length of the clivus. Patients showed significantly increased basal angle and reduced tentorium's length. In contrast, the average length of the supraoccipital, the anteroposterior diameter of the FM and the anteroposterior diameter of the PCF, as well as the tentorium, Wackenheim and odontoid angles showed no significant differences between the two groups (Fig 2). In the subgroups of 23 cases and 11 controls where we were able to discern basioccipital from basisphenoid, their mean length values showed no significant differences.

Twenty-three CMI patients showed hydrocephalus. Because inclusion of patients with this complication could conceivably introduce a bias in our morphometric data, we compared, for all the parameters measured, the average values in the 23 cases with hydrocephalus and the 77 without hydrocephalus and found no significant differences (not shown). In addition, the distance from corpus callosum to FM, the fundamental variable for our probability model (see below), was significantly reduced in CMI cases as compared to controls irrespective of the presence ((P = 4,06E-14) or absence (P = 2,41E10-17) of hydrocephalus.

Development of a Probability Model

A logistic regression model with the variables that maximized the classification properties was fitted. The resulting model included up to seven variables that provided a high probability of accurate control/case classification according to the equation P (case) = $1/(1 + \exp(-z))$, where z = -1.533-2.666* corpus



Fig 2. Differences in PCF measurements between cases and controls. The boxplot denotes the ranges in seven illustrative measures, those included in the probability model. Significant differences were detected for osseous PCF area (OPCF), length of the clivus, distance corpus callosum to FM (CC_FM), distance from pons to FM and basal angulation, between the cases and the control groups. No significant differences were detected for the Wackenheim angle or basilar impression. Boxes indicate \pm 1 SD and include the mean value (thick line); whiskers indicate \pm 2 SD. Dots depict subjects with measurements greater than 2 SD. **P*<.0025.

callosum_FM - 3.785*pons_FM + .109*Wackenheim angle + .124*basal angle - .252*osseous PCF area + .813*McRae + 1.377*clivus.

This model revealed a sensitivity of 93% (95% CI, 86.3%-96.6%) and a specificity of 92%, (95% CI, 81.2%-96.8%) when applied to our cohorts using a cut-off point of P = .55. The area under the curve of the associated ROC was .955 (95% CI, .923-.988) (Fig 3).

Discussion

In this study we analyzed the PCF morphology of 100 adult CMI patients and 50 control subjects and used the data to generate a mathematical model that predicted, with high sensitivity and specificity, the diagnosis of CMI regardless of the degree of TD.

Evidences of Cranioencephalic Disproportion from Mesodermic Origin in CMI

The occurrence of hypoplastic PCF in CMI patients is widely accepted. Previous morphometric studies found small PCF both in children and adults with classical CMI.^{7-9,12,14,16,19,25,34} These observations led to the consensus that the radiological findings of overcrowded PCF along with demonstration of altered CSF dynamics, are highly suggestive of CMI, although patients without TD are actually referred to as Chiari malformation "type 0."²⁴ Some studies, however, acknowledge that a subset of CMI patients display low-lying cerebellar tonsils with normal-sized PCF.¹⁹ In addition, whether the label CMI should be applied to patients with TD resulting from intracranial masses or insertion of lumboperitonial shunts remains a matter of debate.

PCF morphometry in our patients further supports the role of hypoplastic PCF in CMI. Analyses revealed significant differences in 10 out of 19 selected measurements that, in the aggregate, indicated smaller PCF and osseous PCF in CMI. The

most significant differences between cases and controls were found in the height of the PCF, as measured by means of the distance from the McRae's line to three different anatomical landmarks (corpus callosum, fastigium and pons), as well as the clivus length, both being much shorter in the patients group. Previous morphometric studies showed underdeveloped bony parts of the PCF in both adult^{8,9,11,12,21,25,26} and pediatric patients.²⁴ Our results revealed that the underdevelopment of the bony structures of the PCF in the CMI group was only significant for the clivus, whereas the differences found for the supraoccipital did not reach statistical significance, in line with some studies^{7,10,13} but in contrast with others.^{7,8,10,13,14,19,25} Of note, we drew a curved line following the occipital squama to better measure the distance between the internal occipital protuberance and the opisthion. This differs from previous studies, which measured a straight line between these two landmarks, but it avoids the error derived from not considering the varying degrees of occipital bulging present in both patients and controls. The fact that we found differences in the length of the clivus but not in the chondrocranium-derived basioccipital might be due to the limited number of patients (n = 22) where a clear visualization of the spheno-occipital synchondrosis was possible. The length of the tentorium was also shorter in CMI patients, but no significant increments were found in the tentorial angle, at variance with other authors.^{8,10,13,16,25} Although we observed a smaller FM in our cases, the difference did not reach statistical significance, in contrast with studies conducted in classical CMI patients by Milhorat et al.^{7,19}

We did not attempt to measure the PCF volume, despite its potential to better define the actual dimensions of the PCF compartment. A volumetric analysis would not have been possible in this retrospective study, since not all the sequences were obtained with the same slice thickness and interslice gap, preventing volume estimation using the Cavalieri principle.³⁵

Thus, our data add to the accumulating evidences that CMI is a disorder of the paraxial mesoderm characterized by the



Fig 3. ROC curve illustrating high sensitivity and specificity of the application of the morphometry-based CMI probability model to case and control cohorts. Using the cutoff point of P = .55, the area under the curve was .955 (95%, CI [.923-.988]).

underdevelopment and overcrowding of the PCF. Of note, the statistical power of our study was enhanced by using a sample bigger than those in previous reports, with the exception of the recent work of Milhorat et al.¹⁹ Furthermore, we excluded patients younger than 18 years to minimize age-related changes in the size of skull and brain structures and used case and control cohorts with identical male/female ratio.

Proposed Criteria for Diagnosis of CMI: Identification of Cranioencephalic Disproportion

The current gold standard for the diagnosis of CMI is the observation of TD on a sagittal MRI. However, it has become progressively evident that TD may result from an array of disorders^{14,36-40} that very often do not entail occipital underdevelopment, for which the label CMI might not be appropriate. Following a pathophysiological approach, Milhorat et al classified patients with Chiari malformations as possibly caused by five distinct mechanisms of cerebellar tonsil herniation and compared their respective PCF morphology, including occipital bone size, PCF volume and FM dimensions.¹⁹ Only patients with Chiari malformation of the classical type or those associated with craniosynostosis, displayed occipital bone hypoplasia and reduced PCF volume and FM. Patients with TD associated with tethered cord syndrome, cranial settling, intracranial space-occupying lesions or lumboperitoneal shunts showed normal occipital bone size, PCF volume and FM or even enlarged FM in the former case. Our view is that the term CMI should be reserved for those cases arising from occipital bone undergrowth, that is, those designated "classical" in the study by Milhorat et al.¹⁹ Such distinction will prove fundamental in future research addressing the genetic basis of the

Chiari malformations. In this regard, a limitation of our study resided in the patient sample composition: use of the standard TD criteria for selection of cases, which were used to model the CMI prototypic PCF, inevitably resulted in the inclusion of a few patients without underdeveloped PCF.

Our data show that a combination of seven straightforward PCF measures, regardless of TD, correctly predicts the probability of an affected CMI status with a 93% probability. We propose that this logistic regression model, based on reliable markers of the characteristic CMI craniocephalic disproportion, may prove useful for diagnosis of symptomatic borderline CMI or Chiari malformation "type 0" patients, thus reducing the uncertainty associated with the application of the current, somewhat restrictive radiological criteria. Inclusion of additional measures assessing CSF flow or CSF spaces could potentially lead to a further improvement in the detection of patients with classical CMI. Since disappearance of retrocerebellar CSF spaces is a constant radiological finding in CMI,^{13,19} the analysis of cardiac-gated phase-contrast cine-MRI sequences should be considered an important aid in early diagnosis of CMI-related CSF flow abnormalities.^{10,41}

Conclusion

Definition of CMI based uniquely on tonsillar ectopia has limitations. In the absence of other specific biomarkers, such as genetic tests or complex functional studies, our results suggest that the use of standard PCF measures may facilitate MRI diagnosis of CMI.

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References

- Barkovich AJ, Wippold FJ, Sherman JL, et al. Significance of cerebellar tonsillar position on MR. *AJNR Am J Neuroradiol* 1986;7(5):795-799.
- Barry A, Patten BM, Stewart BH. Possible factors in the development of the Arnold-Chiari malformation. J Neurosurg 1957;14(3):285-301.
- Gardner WJ, Goodall RJ. The surgical treatment of Arnold-Chiari malformation in adults: an explanation of its mechanism and importance of encephalography in diagnosis. *J Neurosurg* 1950;7(3):199-206.
- McLone DG, Knepper PA. The cause of Chiari II malformation: a unified theory. *Pediatr Neurosci* 1989;15(1):1-12.
- Marin-Padilla M. Notochordal-basichondrocranium relationships: abnormalities in experimental axial skeletal (dysraphic) disorders. *J Embryol Exp Morphol* 1979;53:15-38.
- Marin-Padilla M, Marin-Padilla TM. Morphogenesis of experimentally induced Arnold–Chiari malformation. J Neurol Sci 1981;50(1):29-55.
- Aydin S, Hanimoglu H, Tanriverdi T, et al. Chiari type I malformations in adults: a morphometric analysis of the posterior cranial fossa. *Surg Neurol* 2005;64(3):237-241.
- Milhorat TH, Chou MW, Trinidad EM, et al. Chiari I malformation redefined: clinical and radiographic findings for 364 symptomatic patients. *Neurosurgery* 1999;44(5):1005-1017.
- Schady W, Metcalfe RA, Butler P. The incidence of craniocervical bony anomalies in the adult Chiari malformation. *J Neurol Sci* 1987;82(1-3):193-203.
- Sekula RF, Jr., Jannetta PJ, Casey KF, et al. Dimensions of the posterior fossa in patients symptomatic for Chiari I malformation but without cerebellar tonsillar descent. *Cerebrospinal Fluid Res* 2005;2:11.
- Stovner LJ, Bergan U, Nilsen G, et al. Posterior cranial fossa dimensions in the Chiari I malformation: relation to pathogenesis and clinical presentation. *Neuroradiology* 1993;35(2):113-118.
- Vega A, Quintana F, Berciano J. Basichondrocranium anomalies in adult Chiari type I malformation: a morphometric study. *J Neurol Sci* 1990;99(2-3):137-145.
- Noudel R, Jovenin N, Eap C, et al. Incidence of basioccipital hypoplasia in Chiari malformation type I: comparative morphometric study of the posterior cranial fossa. Clinical article. *J Neurosurg* 2009;111(5):1046-1052.
- Milhorat TH, Bolognese PA, Nishikawa M, et al. Association of Chiari malformation type I and tethered cord syndrome: preliminary results of sectioning filum terminale. *Surg Neurol* 2009;72(1):20-35.
- Nyland H, Krogness KG. Size of posterior fossa in Chiari type 1 malformation in adults. *Acta Neurochir (Wien)* 1978;40(3-4):233-242.
- Karagoz F, Izgi N, Kapijcijoglu Sencer S. Morphometric measurements of the cranium in patients with Chiari type I malformation and comparison with the normal population. *Acta Neurochir (Wien)* 2002;144(2):165-171.
- Atkinson JL, Weinshenker BG, Miller GM, et al. Acquired Chiari I malformation secondary to spontaneous spinal cerebrospinal fluid leakage and chronic intracranial hypotension syndrome in seven cases. J Neurosurg 1998;88(2):237-242.
- Murphy RL, Tubbs RS, Grabb PA, et al. Chiari I malformation and idiopathic growth hormone deficiency in siblings: report of three cases. *Childs Nerv Syst* 2007;23(10):1221-1223.
- Milhorat TH, Nishikawa M, Kula RW, et al. Mechanisms of cerebellar tonsil herniation in patients with Chiari malformations as guide to clinical management. *Acta Neurochir (Wien)* 2010;152(7):1117-1127.
- Speer MC, George TM, Enterline DS, et al. A genetic hypothesis for Chiari I malformation with or without syringomyelia. *Neurosurg Focus* 2000;8(3):1-4.

- Meadows J, Kraut M, Guarnieri M, et al. Asymptomatic Chiari Type I malformations identified on magnetic resonance imaging. J *Neurosurg* 2000;92(6):920-926.
- 22. Vernooij MW, Ikram MA, Tanghe HL, et al. Incidental findings on brain MRI in the general population. *N Engl J Med* 2007;357(18):1821-1828.
- 23. Morris Z, Whiteley WN, Longstreth WT, Jr., et al. Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis. *BMJ* 2009;339:b3016.
- Tubbs RS, Elton S, Grabb P, et al. Analysis of the posterior fossa in children with the Chiari 0 malformation. *Neurosurgery* 2001;48(5):1050-1054.
- Nishikawa M, Sakamoto H, Hakuba A, et al. Pathogenesis of Chiari malformation: a morphometric study of the posterior cranial fossa. *J Neurosurg* 1997;86(1):40-47.
- Dagtekin A, Avci E, Kara E, et al. Posterior cranial fossa morphometry in symptomatic adult Chiari I malformation patients: comparative clinical and anatomical study. *Clin Neurol Neurosurg* 2011;113(5):399-403.
- Aboulezz AO, Sartor K, Geyer CA, et al. Position of cerebellar tonsils in the normal population and in patients with Chiari malformation: a quantitative approach with MR imaging. J Comput Assist Tomogr 1985;9(6):1033-1036.
- Evans WAJ. An encephalographic ratio for estimating ventricular enlargement and cerebral atrophy. *Arch Neurol Psychiatry* 1942;47(6):931-937.
- Mikulis DJ, Diaz O, Egglin TK, et al. Variance of the position of the cerebellar tonsils with age: preliminary report. *Radiology* 1992;183(3):725-728.
- O'Connor S, du Boulay G, Logue V. The normal position of the cerebellar tonsils as demonstrated by myelography. *J Neurosurg* 1973;39(3):387-389.
- Tubbs RS, Hill M, Loukas M, et al. Volumetric analysis of the posterior cranial fossa in a family with four generations of the Chiari malformation Type I. *J Neurosurg Pediatr* 2008;1(1):21-24.
- Tubbs RS, Wellons JC, Blount JP, et al. Inclination of the odontoid process in the pediatric Chiari I malformation. 3rd ed. *J Neurosurg* 2003;98(1 Suppl):43-49.
- 33. Boyles AL, Enterline DS, Hammock PH, et al. Phenotypic definition of Chiari type I malformation coupled with high-density SNP genome screen shows significant evidence for linkage to regions on chromosomes 9 and 15. *Am J Med Genet A* 2006;140(24):2776-2785.
- Trigylidas T, Baronia B, Vassilyadi M, et al. Posterior fossa dimension and volume estimates in pediatric patients with Chiari I malformations. *Childs Nerv Syst* 2008;24(3):329-336.
- Mayhew TM, Olsen DR. Magnetic resonance imaging (MRI) and model-free estimates of brain volume determined using the Cavalieri principle. *J Anat* 1991;178:133-144.
- 36. Milhorat TH, Bolognese PA, Nishikawa M, et al. Syndrome of occipitoatlantoaxial hypermobility, cranial settling, and chiari malformation type I in patients with hereditary disorders of connective tissue. J Neurosurg Spine 2007;7(6):601-609.
- Cinalli G, Spennato P, Sainte-Rose C et al. Chiari malformation in craniosynostosis. *Childs Nerv Syst* 2005;21(10):889-901.
- Lemar HJ, Jr., Perloff JJ, Merenich JA. Symptomatic Chiari-I malformation in a patient with acromegaly. *South MedJ* 1994;87(2):284-285.
- Richards PS, Bargiota A, Corrall RJ. Paget's disease causing an Arnold-Chiari Type 1 malformation: radiographic findings. AJR AmJ Roentgenol 2001;176(3):816-817.
- Chumas PD, Armstrong DC, Drake JM, et al. Tonsillar herniation: the rule rather than the exception after lumboperitoneal shunting in the pediatric population. *J Neurosurg* 1993;78(4):568-573.
- Armonda RA, Citrin CM, Foley KT, et al. Quantitative cine-mode magnetic resonance imaging of Chiari I malformations: an analysis of cerebrospinal fluid dynamics. *Neurosurgery* 1994;35(2):214-223.