Neurosurgical Review (2022) 45:263–273
https://doi.org/10.1007/s10143-021-01592-4

REVIEW

Is there a morphometric cause of Chiari malformation type I? Analysis of existing literature

William H. Shuman[1] · Aislyn DiRisio[1] · Alejandro Carrasquilla[1] · Colin D. Lamb[1] · Addison Quinones[1] · Aymeric Pionteck[2] · Yang Yang[3] · Mehmet Kurt[2] · Raj K. Shrivastava[1]

Received: 9 April 2021 / Revised: 10 June 2021 / Accepted: 17 June 2021 / Published online: 13 July 2021

Abstract

Although many etiologies have been proposed for Chiari malformation type I (CM-I), there currently is no singular known cause of CM-I pathogenesis. Advances in imaging have greatly progressed the study of CM-I. This study reviews the literature to determine if an anatomical cause for CM-I could be proposed from morphometric studies in adult CM-I patients. After conducting a literature search using relevant search terms, two authors screened abstracts for relevance. Full-length articles of primary morphometric studies published in peer-reviewed journals were included. Detailed information regarding methodology and symptomatology, craniocervical instability, syringomyelia, operative effects, and genetics were extracted. Forty-six studies met inclusion criteria, averaging 93.2 CM-I patients and 41.4 healthy controls in size. To obtain measurements, 40 studies utilized MRI and 10 utilized CT imaging, whereas 41 analyzed parameters within the posterior fossa and 20 analyzed parameters of the craniovertebral junction. The most commonly measured parameters included clivus length ($n=30$), tonsillar position or descent ($n=28$), McRae line length ($n=26$), and supraocciput length ($n=26$). While certain structural anomalies including reduced clivus length have been implicated in CM-I, there is a lack of consensus on how several other morphometric parameters may or may not contribute to its development. Heterogeneity in presentation with respect to the extent of tonsillar descent suggests alternate methods utilizing morphometric measurements that may help to identify CM-I patients and may benefit future research to better understand underlying pathophysiology and sequelae such as syringomyelia.

Keywords Chiari · Malformation · Type 1 · Radiography · Imaging · Morphometric · Morphometric Analysis · Anatomy · Symptomatology · Review

Introduction

Chiari malformations are a complex neurological condition representing a spectrum of presentations within four categories (types I–IV) [7]. The most commonly seen in clinical practice for adults is Chiari malformation type I (CM-I), with imaging prevalence studies estimating that 0.24–3.6% of the population are affected [26]. Despite the fact that many etiologies and presentations have been discussed, there currently is no unifying theme on pathogenesis and morphometric or anatomical determinants [33]. Traditionally accepted criteria for radiographic diagnosis of CM-I included cerebellar tonsillar herniation greater than 3–5 mm below the foramen magnum [32]. However, there has since been clear documentation of patients showing symptoms consistent with CM-I without severe herniation of the cerebellar tonsils [45, 49].

Radiographic imaging has also been employed in research efforts to outline the underlying cause of CM-I. Frequent co-occurrence with bony anomalies of the skull base and cervical spine such as occipital dysplasia, suboccipital dysplasia, and basilar impression inspired early research to investigate the relationship between bony anatomy morphology and the

✉ William H. Shuman
will.shuman@icahn.mssm.edu

[1] Department of Neurosurgery, Icahn School of Medicine At Mount Sinai, 1468 Madison Avenue, New York, NY 10029, USA

[2] Department of Mechanical Engineering, Stevens Institute of Technology, Hoboken, NJ, USA

[3] Department of Diagnostic, Molecular, and Interventional Radiology, Icahn School of Medicine At Mount Sinai, New York, NY, USA

presence of CM-I [31, 47, 58]. Early hypotheses attributed the cerebellar ectopia of CM-I to the disproportion between a posterior fossa reduced in size by hypoplasia of the chondrocranium and the relatively late spurt of the rapid growth of the cerebellum during embryonic development [34, 58]. Over the past three decades, several studies have investigated relationships between several morphometric parameters on radiographic imaging and the clinical presentations of CM-I.

Advances in imaging have greatly progressed the study of CM-I, and there has been no shortage of studies evaluating morphometric parameters. Despite this, a consensus has not been reached on which parameters are important, and the studies are heterogeneous and discordant. The purpose of this study was to review the literature to determine if an anatomical cause for CM-I could be proposed from morphometric studies in adult CM-I patients. This review also aims to describe the major aspects of their methodology, to present the most frequently utilized morphometric parameters, to characterize commonly reported findings, and to discuss areas that lack consensus for future research.

Materials and methods

Ethics committee and institutional review board approvals were waived as this study is a review and does not involve human or animal subjects.

Literature search

A PubMed literature search was conducted using the search terms "Chiari" and "morphometric." Abstracts were screened for inclusion by two authors. Selected articles were screened in full, and relevant references were screened for inclusion. The inclusion criteria for the resulting studies were morphometric studies in adult CM-I patients published in peer-reviewed journals. Manuscripts were excluded if they were not full-text primary research studies (literature reviews, case reports, abstracts), were written in a language other than English, analyzed animal subjects, primarily investigated cerebrospinal fluid dynamics, or studied solely other types of Chiari malformation or unaffected patient populations.

For included studies, several methodological factors were recorded, including the number of CM-I subjects and, if relevant, the number of healthy controls, quantitative vs. qualitative analysis performed, imaging modality utilized, anatomic regions of interest, and related subjects of interest. Detailed information from the included studies was extracted on general symptomatology, craniocervical instability, syringomyelia, operative effects, and genetics.

Commonly measured parameters

To assess which morphometric parameters are the most commonly used, parameters measured in each study were recorded and tabulated. The number of studies to measure each parameter was calculated, and parameters investigated in four or more studies were tabulated.

Results

Search results and study characteristics

A total of 85 studies resulted from the literature search. Of these, 39 studies failed to meet inclusion criteria and were excluded from further review. The remaining 46 studies were included for analysis and are displayed in Table 1 [1–5, 8, 10, 11, 13–17, 19–25, 27, 28, 30, 32, 35, 37–46, 49, 52–60, 62]. The earliest of these studies was published in 1990, and the most recent studies were published in 2020. Cohorts for CM-I subjects averaged 93.2 patients in size with a standard deviation of 119.2 patients and a range of 12–741. Control subject cohorts averaged 41.4 patients in size with a standard deviation of 44.5 and range of 0–155. Of the 46 studies, 40 (87.0%) utilized magnetic resonance imaging (MRI) and 10 (21.7%) utilized computed tomography (CT), with 4 (9.5%) using both MRI and CT imaging. In terms of anatomical regions of interest, 41 studies (89.1%) analyzed parameters in the posterior fossa, and 20 studies (43.5%) measured parameters of the craniovertebral junction. Notably, several studies investigated associations between morphometric parameters and related themes, including syringomyelia ($n=7$, 15.2%) [4, 13, 15, 16, 20, 41, 62], symptomatology ($n=10$, 21.7%) [11, 14, 16, 17, 19, 22, 24, 45, 49, 53], craniocervical stability ($n=5$, 10.9%) [17, 27, 38, 39, 59], genetics ($n=2$, 4.3%) [35, 57], and operative outcomes ($n=5$, 10.9%) [2, 19, 25, 30, 41].

Commonly measured parameters

Reported measurements included various distances, angles, two-dimensional areas, surface areas, volumes, and ratios of multiple measurements. Distances consisted of the lengths of structures (i.e., the clivus or foramen magnum) or distances between two predetermined points on different structures (i.e., the basion to the posterior axial line of the odontoid). Angles included commonly used diagnostic parameters (i.e., the basal or Wackenheim angles) and angles between two predetermined lines (i.e., the angle between the tentorium and Twining's line). Areas and volumes included those of structures (i.e., the

Table 1 Literature review sources

Source no.	PubMed ID	Author	Year	No. of patients	No. of controls	Imaging modality	Anatomical region of interest	Related themes
1	2086722	Vega[6]	1990	42	46	CT	SB/PCF	
2	1561334	Elster[10]	1992	68	0	MRI	SB/PCF	Syrinx; symptomatology
3	8988080	Nishikawa[11]	1997	30	50	MRI + CT	SB/PCF	
4	9805898	Yamazaki[12]	1998	22	0	MRI	SB/PCF	
5	10834643	Munshi[13]	2000	34	0	MRI	SB/PCF + CVJ	Syrinx; variability of operative techniques
6	11862517	Karagoz[14]	2002	22	21	MRI	SB/PCF	
7	16099255	Aydin[15]	2005	60	30	MRI	SB/PCF	
8	16359556	Sekula[4]	2005	22	0	MRI	SB/PCF	Symptomatology
9	18074684	Milhorat[16]	2007	169	55	CT	SB/PCF + CVJ	Stability
10	17260118	Takeuchi[17]	2007	86	86	MRI	CVJ	
11	19463049	Noudel[18]	2009	17	30	MRI	SB/PCF	
12	19559924	Milhorat[19]	2009	280	155	MRI	SB/PCF	
13	20440631	Milhorat[20]	2010	741	80	MRI + CT	SB/PCF	Stability
14	21515505	Dufton[21]	2011	81	107	MRI	SB/PCF	
15	21333437	Dagtekin[22]	2011	15	25	MRI	SB/PCF	
16	23437350	Urbizu[23]	2013	211	0	MRI	SB/PCF	Genetics
17	24379947	Hwang[24]	2013	12	24	MRI	SB/PCF	Variability of operative techniques
18	23324118	Urbizu[25]	2014	100	50	MRI	SB/PCF + CVJ	
19	24359474	Markunas[26]	2014	92	28	MRI	SB/PCF	Genetics
20	26713146	Alkoc[27]	2015	66	33	MRI	SB/PCF + CVJ	
21	25275579	Moncho[28]	2015	50	0	MRI	SB/PCF + CVJ	
22	26871424	Halvorson[29]	2016	34	0	MRI	SB/PCF	Pediatric; syrinx
23	28684453	Gad[30]	2017	108	0	MRI	SB/PCF + CVJ	Pediatric; syrinx
24	28498073	Thakar[31]	2017	25	25	MRI	SB/PCF + CVJ	Symptomatology
25	27153161	Urbizu[32]	2017	76	49	MRI	SB/PCF + oral cavity	
26	29403363	Eppelheimer[33]	2018	236	140	MRI	SB/PCF + CVJ	Syrinx
27	29587156	Basaran[34]	2018	141	91	MRI	SB/PCF + CVJ	Syrinx
28	29053075	Urbizu[35]	2018	105	50	MRI	SB/PCF	
29	28826656	Houston[36]	2018	162	140	MRI	SB/PCF + CVJ	
30	29066319	Grangeon[37]	2018	49	0	MRI	SB/PCF + CVJ	Symptomatology; variability of operative techniques
31	29803060	Gholampour[38]	2018	41	18	MRI	SB/PCF	Symptomatology; stability
32	30554565	Lawrence[2]	2018	23	10	MRI		
33	31187348	Nwotchuang[39]	2019	30	30	CT	SB/PCF + sphenoid sinus	
34	31103770	Karaaslan[40]	2019	25	93	MRI	CVJ	Stability
35	31210559	Houston[41]	2019	52	52	MRI	SB/PCF + CVJ	
36	30535814	Biswas[42]	2019	235	140	MRI	SB/PCF	
37	31094552	Houston[43]	2019	18	18	MRI	SB/PCF + CVJ	Symptomatology
38	31033761	Ocakoglu[44]	2019	20	20	MRI	Cerebellar shape	
39	30621833	Ferré[45]	2019	164	0	MRI + CT	SB/PCF + CVJ	Symptomatology
40	32969751	Wan[46]	2020	47	47	CT	CVJ	Stability

Table 1 (continued)

Source no.	PubMed ID	Author	Year	No. of patients	No. of controls	Imaging modality	Anatomical region of interest	Related themes
41	32791229	Wang[47]	2020	50	50	CT	SB/PCF + CVJ	
42	32985602	Gholampour[48]	2020	58	20	MRI	SB/PCF	Syrinx; symptomatology
43	33357109	Aslan[49]	2020	54	0	MRI + CT	SB/PCF + CVJ	Variability of operative techniques
44	32418026	Nwotchuang[5]	2020	210	90	MRI	SB/PCF	Symptomatology
45	32204299	Kirnaz[50]	2020	32	0	CT	SB/PCF	Variability of operative techniques
46	31996967	Huang[51]	2020	72	0	MRI	SB/PCF + CVJ	Symptomatology

Contractions: *MRI*, magnetic resonance imaging; *CT*, computed tomography; *SB/PCF*, skull base/posterior cranial fossa; *CVJ*, craniovertebral junction

cerebellar area on midsagittal imaging) and spaces (i.e., the posterior cranial fossa). The vast majority of studies obtained measurements from midsagittal or axial images. Commonly measured parameters and the number of times they are reported in the included studies are depicted in Table 2. The most commonly measured parameters included clivus length ($n = 30$), tonsillar position or descent ($n = 28$), McRae line length ($n = 26$), and supraocciput length ($n = 26$). Findings from recent studies comparing metrics of CM-I patients to those of controls are summarized in Table 3. Illustrative representations of relevant structures and parameters are depicted in Fig. 1.

Discussion

Common findings and themes

To date, no singular cause of CM-I has been determined [5, 16, 45, 46, 60]. Several studies have utilized morphometric analysis of the skull base and craniovertebral junction to investigate structural differences found in Chiari malformation to possibly explain causes of tonsillar descent, posterior fossa crowding, and the various presentations and symptoms of CM-I patients. A significant amount of initial analysis was performed in the pre-MRI area with CT imaging. With the advent of MRI and higher resolution imaging, there is a need and an opportunity for more detailed analysis. Such analyses would provide great assistance in diagnosing CM-I as there are several pathophysiologic mechanisms that may result in tonsillar herniation, and a radiologic diagnosis of herniation is not sufficient evidence for diagnosis of CM-I. Detailed analyses that identify anatomical associations with CM-I would thus provide great utility in identifying CM-I patients and differentiating such cases from other causes of benign tonsillar ectopia. This literature review is the first to describe morphometric studies of adult CM-I patients, as well as their methodology and commonly assessed parameters.

Common findings and themes are present across studies despite differing hypotheses and study designs. Compared to controls, CM-I patients are often reported to have a shorter clivus [1, 23, 25, 28, 39, 56, 58, 60], shorter posterior fossa height [3, 21, 23, 28, 63], and steeper tentorial angle [25, 28, 42]. These morphometric parameters have been used to develop predictive models to accurately detect symptomatic CM-I from imaging [14, 55]. Conversely, a few studies report no significant correlation between some of these parameters and CM-I [4, 43, 56]. For example, some studies have found that CM-I patients have a longer McRae line, defined as the anteroposterior diameter of the foramen magnum (FM) [10, 23], whereas other studies have found no significant difference between CM-I patients and controls [60]. Similarly, some studies chose to instead analyze the cross-sectional area of the foramen, and there are varying results with this parameter as well [4, 37].

Several theories have been developed from these various findings. A substantial number of studies report evidence that CM-I is classically due to underdevelopment of the para-axial mesoderm leading to hypoplasia of the skull base and a small crowded posterior fossa [3, 8, 10, 28, 41–43, 53, 57, 58, 60]. Certain studies place emphasis on the role that the hypoplasia of the basiocciput and the clivus play in Chiari symptomatology [44, 45, 58]. Genetic markers found to be associated with posterior fossa morphology support the theory that certain anomalous features of CM-I are heritable [35, 57]. Meanwhile, these same developmental anomalies have also been shown to result in alterations in the cervical spine, with changes in its ligaments, joints, and musculature leading to instability and neck pain [23, 27, 38, 53, 59]. Other theories suggest that instability of the cervical

Table 2 Commonly measured morphometric parameters

No.	Parameter	No. of reports	Reporting sources (see Table 1)
1	Clivus length	30	1,3,4,6–8,12–16,18–21,23,25–30,33,35,37,39,41,42,44,46
2	Tonsillar position	28	2,4,7,11,14–16,18–30,32,35–37,39,43,44,46
3	Supraocciput length	26	3,6–8,11–13,15–21,25–30,35,37,39,41,42,46
4	McRae line length	26	1,6–8,11–22,25,26,28–30,35,37,39,41,46
5	Basal angle	19	1,4,6,16,18–21,23,25,26,28–30,35,37,39,41,46
6	PCF diameter/Twining's line	16	6–8,16–18,20,25,26,28–30,25,37,41,42
7	Tentorium angle	15	6,11,15–20,26,28,29,35,37,39,41
8	PCF area	14	1,16,18,19,21,22,26,28,29,35–37,39,44
9	Wackenheim angle	13	16,18,20,21,25–30,25,37,39
10	Basilar impression	12	2,4,18,21,23,25,26,28,29,35,37,39
11	PCF height	11	7,17–19,25,26,28,29,35–37
12	PCF osseous area	11	16,18,21,25,26,28,29,35–37,39
13	Boogard angle	11	1,6,14,17,19,20,26,29,35,37,44
14	Fastigium height	11	18,21,25,26,28,29,35–37,39,44
15	Tentorium length	9	18,19,21,26,28,29,35,37,39
16	Pons height	9	18,21,25,26,28,29,35,37,39
17	PCF volume	9	1,3,12,20,22,27,30,31,42
18	Odontoid angle	8	18,21,23,26,29,37,39,46
19	Corpus callosum height	7	18,25,26,28,29,35,37
20	Length of the cerebellum	7	3,8,11,15,17,36,38
21	Length of brainstem	6	3,8,11,15,17,42
22	Tentorium–Twining's line angle	6	3,6,8,20,27,41
23	Length of basiocciput	6	3,8,11,15,17,18
24	AP diameter dura-opisthion	5	26,29,35,37,41
25	pB-C2 measurement	5	26,29,30,37,46
26	Basion-dens interval	5	9,26,29,35,37
27	Intracranial area	5	22,26,29,35,37
28	Length of basisphenoid	5	3,8,11,15,18
29	Transverse diameter of FM	5	1,12,13,39,42
30	Dural angle	4	26,29,35,37
31	Intracranial height	4	26,29,35,37
32	Intracranial diameter	4	26,29,35,37
33	Chamberlain's line	4	1,20,21,23

Abbreviations: *PCF*, posterior cranial fossa; *AP*, anteroposterior; *pB-C2*, basion to posterior aspect of C2 vertebrae

spine is the underlying cause of CM-I and its symptoms [18, 27]. The contribution of the cerebellum and hindbrain to CM-I pathology has also been investigated, with some studies suggesting that neural structures of the posterior fossa develop normally [8], while some other studies have found the larger size and altered shape of the cerebellum in CM-I [5, 46]. Lastly, some studies focus on a classic presentation of CM-I with a small posterior fossa and descending cerebellar tonsils, whereas others acknowledge a multifactorial etiopathology with various causal mechanisms and diverse presentations [1, 35, 37, 39, 57].

Multiple studies also acknowledge possible differences in morphology found between male and female patients [13, 21, 53]. Future prospective studies must take this into account in their study design, and as a result, multiple studies have analyzed all-female cohorts with age- and gender-matched controls to isolate possible confounders [13, 23, 45]. Additionally, although morphometric parameters may be predictive of CM-I presentations, measurements made by independent interpreters are open to subjectivity. For example, one study showed poor inter-operator reliability for measurements or tonsillar ectopia made by seven expert operators [32].

Table 3 Most recent (2018–2020) comparisons of CM-I patients against healthy controls

PMID	Author	Year	Summary of relevant findings
29403363	Eppelheimer	2018	Shorter McRae line in CM-I participants with SM compared to those without ($p < 0.002$) Larger TP and smaller clivus length, fastigium, and corpus callosum heights in CM-I compared to controls
29587156	Basaran	2018	Significant relation between SM and cerebellar descent length ($p = 0.042$), FMA ($p < 0.01$), FMA/ICV ($p < 0.01$), FMA/PFV ($p < 0.01$) CoC-SO ($p = 0.019$), and CM subtype ($p < 0.01$)
29053075	Urbizu	2018	Proposes a predictive model using 3 parameters of basion location to discern CM-I with 90% accuracy Suggests considering anterior alterations in the evaluation of surgical procedures and outcomes
28826656	Houston	2018	Eighteen parameters different between CM-I and controls ($p < 0.002$), each fitting into categories of PCF structures heights, clivus angulation, or odontoid process irregularity
29803060	Gholampour	2018	CSF volume reduced by 57% in CM-I alone, by < 9% in CM-I/OAAJI and CM-I/TCS. PCF volume reduced by 11.3%, 1.4%, and 1.7% for the same groups. PCF volume more favorable to assessing symptom intensity
31187348	Nwotchuang	2019	Clivus volume 31% smaller ($p < 0.001$) and sphenoid sinus volume 38% bigger ($p < 0.001$) in CMI subjects
31103770	Karaaslan	2019	CM-I patients had shorter transverse ($p = 0.027$) and alar (0.007) ligaments than controls. Differences in the CCJ ligaments could be the reason behind stability differences in CM-I
31210559	Houston	2019	Males with CM-I had shorter distances for McRae line to the corpus callosum ($p < 0.001$) and clivus length ($p < 0.001$), compared to females with CM-I
30535814	Biswas	2019	PCF area anterior to the brain stem was smaller in CM-I subjects ($p < 0.002$), which appears to be the major cause for the overall smaller PCF area and greater cerebellar crowding compared to controls
31094552	Houston	2019	CM-I patients presented seven morphometric differences of the PCF compared to healthy controls, including heights of the fastigium, pons, and corpus callosum, some of which were associated with self-reported pain and disability Group differences in tonsillar position were associated with self-reported pain, disability, and delayed memory
31033761	Ocakoglu	2019	Statistically significant cerebellum shape difference between CM-I patients and controls ($p < 0.001$) Cerebellum shape variability determined to be higher in patients than controls (0.149 vs. 0.133)
32969751	Wan	2020	Atlanto-occipital joints are flatter (smaller depth/length ratio) in CM-I compared to controls ($p < 0.01$)
32791229	Wang	2020	CM-I patients had smaller clivus ($p < 0.001$), supraocciput ($p < 0.001$), Klaus index ($p < 0.001$), axial length ($p < 0.001$), clivo-axial angle ($p < 0.001$), tentorial angle ($p < 0.05$), and bony PCF volume ($p < 0.001$) and larger clivus angle ($p < 0.001$), basal angle ($p < 0.001$), and distance Chamberlain line to dens axis ($p < 0.001$)
32985602	Gholampour	2020	Among volumetric parameters, PCF volume had the highest correlation with maximum CSF pressure PCF volume higher in CM-I/SM/scoliosis patients compared to other CM-I patients or controls ($p = 0.0022$)
32418026	Nwotchuang	2020	CM-I patients with TP < 5 mm differed from controls with normal TP for 4 morphometric features ($p < 0.05$) CM-I patients with TP < 5 mm differed from controls with low-lying TP for clivus length only ($p = 0.01$)

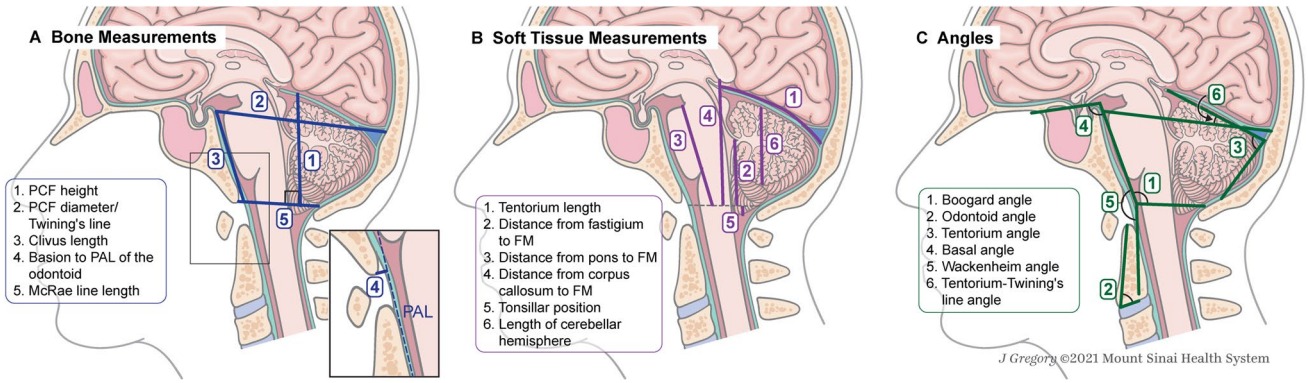

Fig. 1 Relevant morphometric parameters: commonly reported parameters of the posterior fossa and craniocervical junction

Genetics

Chiari malformations including CM-I were long considered sporadic conditions until several karyotyping studies revealed familial clusters of CM-I patients, suggesting a hereditary factor [29, 50, 51, 57]. Two early genetic studies have proposed possible genes involved in CM-I pathogenesis [35, 57]. Both of these studies correlated these

genes to several posterior fossa traits, including morphology of the basal angle, Wackenheim angle, and posterior fossa height. These findings further support theories that morphology of the basal components of the skull base are more centrally linked to CM-I development. Moreover, in a study by Urbizu et al. [57], two of the associated genes (ALDH1A2 and CDX1) were related to retinoic acid signaling during somitogenesis of para-axial mesoderm precursors. This finding supports the theory that para-axial underdevelopment leads to hypoplasia of the posterior fossa elements.

Several features of CM-I remain to be explained in a genetic context. Markunas et al. [35] reported that clivus length was not found to be heritable. This finding may have been confounded by a close association between clivus length and age or by the clivus being composed of two bony components, the basiocciput and basisphenoid. This same study likewise found that degree of cerebellar tonsil herniation was almost entirely dependent on environmental factors, with little hereditary association. This may further support the primary role of morphologic factors in the pathogenesis of CM-I with tonsillar herniation occurring secondary to such changes. However, tonsillar herniation is currently often used as a gold-standard diagnostic parameter both clinically and for inclusion in CM-I research studies. It is known that the degree of the tonsillar herniation does not correlate well with the degree of symptoms and that it may not be necessary to cause the disease [35], so these findings may not be generalizable to all presentations of CM-I. Both studies also employed measures to reduce heterogeneity such as subgroup analysis of patients with smaller posterior fossa [57] or stratified linkage analysis based on clinical criteria [35]. Overall, these studies' findings emphasize the inherited nature of several features in classically presenting CM-I, as well as the utility of morphometric analysis to identify CM-I patients who may not fit classic criteria due to heterogeneous presentations.

Symptomatology

Of the studies investigating relationships between morphometric parameters and symptomatology in CM-I, the most commonly studied parameter is tonsillar position (TP) [11, 19, 22, 24, 45]. Multiple studies found that tonsillar descent of at least 12 or 14 mm below the foramen magnum was predictive of worsened headache and symptoms of brainstem compression [11, 24]. Greater tonsillar descent has also been shown to be associated with worsened memory, anxiety, weakness, and hypermobility [22, 45]. On the contrary, conflicting studies found that tonsillar descent was not associated with patient-reported symptoms of pain, weakness, numbness, dizziness, double vision, or sensitivity to light [45], and one study reported that TP was not associated with improvement in headaches following the surgical intervention [19]. While radiographic cutoffs of 3–5 mm are often used clinically to establish CM-I diagnosis, two studies independently found these cutoffs to be too restrictive, given that many patients with a smaller degree of tonsillar descent still had symptom profiles indistinguishable from patients meeting radiographic criteria [45, 49]. Furthermore, many asymptomatic individuals have tonsillar descent meeting radiographic criteria for CM-I, classified as asymptomatic tonsillar ectopia [11, 45]. These findings have more recently challenged the traditional diagnostic criterion of tonsillar descent in CM-I.

Clivus length has also been found to correlate with CM-I symptoms [24, 45, 49]. Specifically, Nwotchouang et al. [45] reported that reduced clivus length was the only studied radiographic parameter that could reliably differentiate between patients with symptoms of CM-1 and those without symptoms of CM-1, including asymptomatic individuals with low-lying tonsils. Sekula et al. [49] showed that symptomatic patients not only had reduced clivus length but also reduced basisphenoid and supraocciput lengths and increased tentorial angle. In another study of adults with CM-1, increased clivus length was shown to be associated with respiratory dysfunction during sleep [14]. Despite this evidence in support of clivus length as a predictor of various CM-I-related symptoms, one study found no relationship between clivus length and cough-associated headache (CAH) in CM-I patients [24].

Phase-contrast (PC) MRI was used in two studies to evaluate the relationship between CSF dynamics and symptom burden in CM-I patients [16, 17]. In these studies, smaller PCF volume correlated with symptom severity, especially for headaches, whereas maximum CSF pressure and CSF volume were not associated with symptomatology in these patients. This stands in contrast to two 2-dimensional imaging studies that found no relationship between PCF area and symptoms [22, 45].

Lastly, one study radiographically assessed the relationship between paraspinal musculature (PSM) and neck pain in adults with CM-I. They found that symptom severity was associated with atrophy of the deep extensor and flexor PSM, which was quantified as the ratio of muscular cross-sectional area (CSA) to bony CSA [53].

A number of other morphometric measurements have not shown any relationship across the included studies. These include supraocciput length, McRae's line length, Twining's line length, odontoid retroversion angle, fastigium height, brainstem height, cerebellar hemisphere length, angle of the clivus–cervical canal, basal angle, obex position, pB-C2 line, and Boogard angle [17, 19, 22, 24, 45, 49].

Craniocervical instability

Several studies support a theory that instability of the upper cervical spine or the craniocervical junction contributes to the pathogenesis of CM-I or may serve as an alternative mechanism of CM-I development for patients who do not have classic CM-I morphometry [27, 38, 39, 59]. One study reported that patients with both CM-I and occipitoatlantoaxial joint instability had normal posterior fossa volume and occipital bone size, compared to reductions in classical CM-I patients [39].

Meanwhile, morphometric variations within the craniocervical junction have been reported for CM-I patients, including shortened lengths of the alar and transverse ligaments of the odontoid and flatter atlanto-occipital joints compared to healthy controls [27, 59]. These structural differences are said to lead to craniocervical instability and hypermobility, resulting in variable presentations such as cranial settling of the basion onto the odontoid, posterior gliding of the occipital condyles, altered morphology of several skull base angles, and retro-odontoid pannus formation [38]. CM-I is also frequently associated with basilar impression and basilar invagination [42, 60]. Studies investigating associations with these features have found that basilar invagination may lead to more severe herniation of the tonsils and that instability and hypermobility contribute to symptoms referable to basilar impression [38, 42].

Syringomyelia

A wide range of prevalence rates of syringomyelia (SM) in CM-I patients has been reported from 30 to 70% [13, 20, 41]. Despite its common presentation, the pathogenesis of SM in the context of CM-I is incompletely understood [48]. Several studies have investigated morphometric parameter alterations in the context of SM, although findings between studies are often inconsistent. One early study by Yamazaki et al. [62] found that CM-I patients with SM have significantly less cerebellar descent compared to CM-I patients without SM, and another study by Basaran et al. [4] also reported a negative association between the extent of cerebellar descent and the presence of SM. However, the third study by Halvorson et al. [20] found that patients with SM had significantly greater cerebellar descent, nearly 4 mm longer on average.

Similarly, while Basaran et al. [4] found no significant correlation between foramen magnum diameter and the presence of SM, a study by Eppelheimer et al. [13] found multiple significant associations between SM and the length of the McRae line. Most noteworthy, they reported that patients with CM-I and SM have significantly shorter measurements of the McRae line compared to CM-I patients without SM. Conversely, the study by Basaran et al. [4] evaluated the area of the FM in relation to SM and found that SM was less common in patients with narrower FM. Whereas inconsistent findings have been reported using dimensions of the FM itself, a recent study by Davis et al. [9] similarly investigated associations between the presence of syringomyelia and the area of CSF at the level of the FM. They reported that less CSF space was associated with the presence of SM and that SM resolution following surgery was associated with increased subarachnoid space. They therefore postulated that syrinx development in CM-I is correlated with the degree to which subarachnoid CSF spaces at the FM are diminished.

Though conflicting findings have been reported from these studies, some similarities are found behind their hypotheses for syrinx pathogenesis. All of them appreciate some form of cord compression or blockage of CSF flow, whether it is by osseous elements at the foramen magnum, herniation of neural structures into the spinal canal, or crowding within the craniocervical junction [4, 9, 20, 62]. Further studies with large patient cohorts are needed to verify these findings and associations with several other morphometric parameters that have yet to be externally validated, such as the size of the basal, Boogard, Wackenheim, and odontoid angles [13].

Variability of operative techniques

Recent studies have begun to investigate relationships between morphometric parameters and surgical parameters including patient symptomatic outcomes, postoperative morphometric changes, and operative planning. To assess changes in skull base and CSF properties during and after surgery, studies have employed intraoperative doppler ultrasonography and MRI as well as postoperative imaging to compare against preoperative measurements [2, 6, 12, 36, 41]. Postoperative morphometrics reveal that decompression surgery results in greater posterior fossa volume, increased CSF space around the cerebellum, and decreased severity of syringomyelia and hydrocephalus as well as other changes in morphology, such as the craniocervical angle [2, 12, 41]. However, no preoperative morphometric parameters have been identified that accurately predict symptom improvement, such as with headache resolution [19].

When planning for posterior fossa decompression (PFD), there are several factors to consider, including the extent of decompression, the employment of duraplasty, and the need for occipitocervical fusion. Hwang et al. [25] argue that because the posterior fossa shape in CM-I resembles that of a "narrow funnel," cephalocaudal extension of the posterior fossa has more decompressive effect than extension in any other direction. To this end, standard practice of PFD for Chiari malformations includes suboccipital craniectomy and C1 laminectomy for cephalocaudal extension and decompression, whereas the decision of whether to employ

duraplasty after bony decompression is subject to surgeon preference [41]. In an early study, Munshi et al. [41] reported that PFD with duraplasty leads to a more reliable reduction in hydromyelia but that there also exists a population of patients who improve from decompression alone when a postoperative increase in posterior fossa volume is demonstrated. A later study comparing several preoperative and postoperative morphometric parameters by Aslan et al. [2] found that PFD with superficial durotomy achieved equal decompression as surgery with duraplasty while reducing accompanying complications. They thus supported the use of minimally invasive surgical methods to avoid major complications associated with Chiari surgery. A few studies have employed intraoperative ultrasonography or MRI to tailor the surgery to the patient [6, 36], although they have reported limitations such as changes in morphology and CSF flow dynamics from simple positioning of the patient for surgery.

In addition to decompression, CM-I patients with concomitant occipitocervical instability often require fusion of the occipitocervical junction. However, certain surgical techniques such as posterior onlay bone grafts have had inadequate results, and new techniques using rigid internal fixation with screws and rods are often technically challenging due to the altered shape of the bony anatomy in CM-I patients [30, 61]. The role of occipitocervical instability as an etiology of CM-I and of surgical fusion as a treatment has not yet been fully described and requires further study.

Limitations

Like all literature reviews, this study has limitations and is subject to its indexed search terms and the search engine on which the query is performed. Additionally, the resulting included studies were variable in terms of the size of their cohorts and also their composition. Several of the studies included all-female cohorts or populations from one institution or country, which may limit the generalizability of their findings. Furthermore, heterogeneity in the included studies, including the metrics used to quantify morphometric features and the span of variables studied, limits our ability to perform quantitative meta-analysis. Also, inherent in any population analysis is variability in demographics, which may associate with access to care. Lastly, the patient populations of the included studies are likely to consist of patients with moderate to severe symptoms, as these patients are most likely to seek medical attention. Patients with mild symptoms or no symptoms are not likely to be included in clinical studies, leading to sampling bias of study populations. Despite this, we think that this study addresses an important gap in the literature regarding morphometric parameters for CM-I. Further research is needed to better understand these metrics in order to improve our understanding of CM-I and associated radiographic criteria.

Conclusions

In summary, while several structural anomalies have been implicated in the development of CM-I, there is a lack of consensus on how several other morphometric parameters may or may not contribute to the presentation of the malformation, to the best methods for its diagnosis, or to its treatment. Heterogeneity of its presentation in the literature, especially with respect to the extent of tonsillar descent, suggests alternate methods or additional parameters that may help to identify CM-I patients. Multiple studies have found clivus length to be a promising metric associated with symptoms, and while similar correlations have been found with PCF volume, this has not yet been replicated on 2-dimensional imaging. Enlarging the posterior fossa is accepted as the primary effective treatment, yet the extent of intervention, from purely extradural to intradural techniques, to best achieve adequate decompression is debated. Several morphometric parameters have been examined in the literature. Future use of such parameters can allow for more sensitive identification of CM-I patients in clinical contexts and may be utilized in research to better understand the pathophysiology of the malformation and sequelae such as syringomyelia.

Author contribution All authors contributed to the study conception and design. Study conception was developed by Raj Shrivastava and Mehmet Kurt. Material preparation, literature search, data extraction, and analysis were performed by William Shuman, Colin Lamb, Addison Quinones, and Alejandro Carrasquilla. The first draft of the manuscript was written by William Shuman and Aislyn DiRisio, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data availability Not applicable.

Code availability Not applicable.

Declarations

Ethics approval Institutional Review Board approval was waived for this review because it does not involve human or animal subjects.

Consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

References

1. Alkoç OA et al (2015) "Stereological and morphometric analysis of MRI Chiari malformation type-1", (in eng). J Korean Neurosurg Soc 58(5):454–461
2. Aslan A et al (2020) "Posterior fossa decompression and superficial durotomy rather than complete durotomy and duraplasty in the management of Chiari 1," (in eng). Neurol Res 1–7
3. Aydin S, Hanimoglu H, Tanriverdi T, Yentur E, Kaynar MY (2005) "Chiari type I malformations in adults: a morphometric analysis of the posterior cranial fossa," (in eng). Surg Neurol 64(3):237–41; discussion 241
4. Basaran R, Efendioglu M, Senol M, Ozdogan S, Isik N (2018) "Morphometric analysis of posterior fossa and craniovertebral junction in subtypes of Chiari malformation", (in eng). Clin Neurol Neurosurg 169:1–11
5. Biswas D et al (2019) "Quantification of cerebellar crowding in type I Chiari malformation", (in eng). Ann Biomed Eng 47(3):731–743
6. Bond AE, Jane JA, Liu KC, Oldfield EH (2015) "Changes in cerebrospinal fluid flow assessed using intraoperative MRI during posterior fossa decompression for Chiari malformation", (in English). Journal of Neurosurgery JNS 122(5):1068–1075
7. Bordes S, Jenkins S, Tubbs RS (2019) "Defining, diagnosing, clarifying, and classifying the Chiari I malformations", (in eng). Childs Nerv Syst 35(10):1785–1792
8. Dagtekin A et al (2011) "Posterior cranial fossa morphometry in symptomatic adult Chiari I malformation patients: comparative clinical and anatomical study", (in eng). Clin Neurol Neurosurg 113(5):399–403
9. Davis GT et al (2020) "Cerebrospinal fluid area and syringogenesis in Chiari malformation type I," (in English). J Neurosurg JNS 1–6
10. Dufton JA, Habeeb SY, Heran MK, Mikulis DJ, Islam O (2011) "Posterior fossa measurements in patients with and without Chiari I malformation", (in eng). Can J Neurol Sci 38(3):452–455
11. Elster AD, Chen MY (1992) "Chiari I malformations: clinical and radiologic reappraisal", (in eng). Radiology 183(2):347–353
12. Eppelheimer MS et al (2019) "Quantification of changes in brain morphology following posterior fossa decompression surgery in women treated for Chiari malformation type 1", (in eng). Neuroradiology 61(9):1011–1022
13. Eppelheimer MS et al (2018) "A retrospective 2D morphometric analysis of adult female Chiari type I patients with commonly reported and related conditions", (in eng). Front Neuroanat 12:2
14. Ferré Á et al (2019) "A conditional inference tree model for predicting sleep-related breathing disorders in patients with Chiari malformation type 1: description and external validation", (in eng). J Clin Sleep Med 15(1):89–99
15. Gad KA, Yousem DM (2017) "Syringohydromyelia in patients with Chiari I malformation: a retrospective analysis", (in eng). AJNR Am J Neuroradiol 38(9):1833–1838
16. Gholampour S, Gholampour H (2020) "Correlation of a new hydrodynamic index with other effective indexes in Chiari I malformation patients with different associations", (in eng). Sci Rep 10(1):15907
17. Gholampour S, Taher M (2018) "Relationship of morphologic changes in the brain and spinal cord and disease symptoms with cerebrospinal fluid hydrodynamic changes in patients with Chiari malformation type I", (in eng). World Neurosurg 116:e830–e839
18. Goel A (2015) "Is atlantoaxial instability the cause of Chiari malformation? Outcome analysis of 65 patients treated by atlantoaxial fixation", (in eng). J Neurosurg Spine 22(2):116–127
19. Grangeon L et al (2018) "Predictive factors of headache resolution after Chiari type 1 Malformation Surgery", (in eng). World Neurosurg 110:e60–e66
20. Halvorson KG, Kellogg RT, Keachie KN, Grant GA, Muh CR, Waldau B (2016) "Morphometric analysis of predictors of cervical syrinx formation in the setting of Chiari I malformation", (in eng). Pediatr Neurosurg 51(3):137–141
21. Houston JR et al (2019) "Evidence for sex differences in morphological abnormalities in type I Chiari malformation", (in eng). Neuroradiol J 32(6):458–466
22. Houston JR et al (2019) "Type I Chiari malformation, RBANS performance, and brain morphology: connecting the dots on cognition and macrolevel brain structure", (in eng). Neuropsychology 33(5):725–738
23. Houston JR et al (2018) "A morphometric assessment of type I Chiari malformation above the McRae line: a retrospective case-control study in 302 adult female subjects", (in eng). J Neuroradiol 45(1):23–31
24. Huang CWC, Chang YM, Brook A, Bezuidenhout AF, Bhadelia RA (2020) "Clinical utility of 2-D anatomic measurements in predicting cough-associated headache in Chiari I malformation", (in eng). Neuroradiology 62(5):593–599
25. Hwang HS, Moon JG, Kim CH, Oh SM, Song JH, Jeong JH (2013) "The comparative morphometric study of the posterior cranial fossa: what is effective approaches to the treatment of Chiari malformation type 1?" (in eng). J Korean Neurosurg Soc 54(5):405–410
26. Kahn EN, Muraszko KM, Maher CO (2015) "Prevalence of Chiari I Malformation and syringomyelia", (in eng). Neurosurg Clin N Am 26(4):501–507
27. Karaaslan B, Börcek A, Uçar M, Aykol Ş (2019) "Can the etiopathogenesis of Chiari malformation be craniocervical junction stabilization difference? Morphometric analysis of craniocervical junction ligaments", (in eng). World Neurosurg 128:e1096–e1101
28. Karagöz F, Izgi N, Kapíjcíjoğlu Sencer S (2002) "Morphometric measurements of the cranium in patients with Chiari type I malformation and comparison with the normal population," (in eng). Acta Neurochir (Wien) 144(no. 2): 165–71; discussion 171
29. Keser N, Kuskucu A, Is M, Celikoglu E (2019) Familial Chiari type 1: a molecular karyotyping study in a Turkish family and review of the literature. World Neurosurgery 121: e852-e857, 2019/01/01/ 2019
30. Kirnaz S, Gerges MM, Rumalla K, Bernardo A, Baaj AA, Greenfield JP (2020) "Occipital condyle screw placement in patients with Chiari malformation: a radiographic feasibility analysis and cadaveric demonstration", (in eng). World Neurosurg 136:470–478
31. Kruyff E, Jeffs R (1966) Skull Abnormalities associated with the Arnold Chiari malformation". Acta Radiologica. Diagnosis 5(P1):9–24
32. Lawrence BJ et al (2018) "Cerebellar tonsil ectopia measurement in type I Chiari malformation patients show poor inter-operator reliability", (in eng). Fluids Barriers CNS 15(1):33
33. Mancarella C, Delfini R, Landi A (2019) "Chiari malformations", (in eng). Acta Neurochir Suppl 125:89–95
34. Marin-Padilla M, Marin-Padilla TM (1981) "Morphogenesis of experimentally induced Arnold—Chiari malformation", (in eng). J Neurol Sci 50(1):29–55
35. Markunas CA et al (2014) "Genetic evaluation and application of posterior cranial fossa traits as endophenotypes for Chiari type I malformation", (in eng). Ann Hum Genet 78(1):1–12
36. Milhorat TH, Bolognese PA (2003) Tailored operative technique for Chiari type I malformation using intraoperative color doppler ultrasonography. Neurosurgery 53(4):899–906

37. Milhorat TH et al (2009) "Association of Chiari malformation type I and tethered cord syndrome: preliminary results of sectioning filum terminale", (in eng). Surg Neurol 72(1):20–35
38. Milhorat TH, Bolognese PA, Nishikawa M, McDonnell NB, Francomano CA (2007) "Syndrome of occipitoatlantoaxial hypermobility, cranial settling, and chiari malformation type I in patients with hereditary disorders of connective tissue", (in eng). J Neurosurg Spine 7(6):601–609
39. Milhorat TH, Nishikawa M, Kula RW, Dlugacz YD (2010) "Mechanisms of cerebellar tonsil herniation in patients with Chiari malformations as guide to clinical management", (in eng). Acta Neurochir (Wien) 152(7):1117–1127
40. Moncho D, Poca MA, Minoves T, Ferré A, Rahnama K, Sahuquillo J (2015) "Brainstem auditory and somatosensory evoked potentials in relation to clinical and neuroimaging findings in Chiari type 1 malformation", (in eng). J Clin Neurophysiol 32(2):130–138
41. Munshi I, Frim D, Stine-Reyes R, Weir BK, Hekmatpanah J, Brown F (2000) "Effects of posterior fossa decompression with and without duraplasty on Chiari malformation-associated hydromyelia," (in eng). Neurosurgery 46 (6): 1384–9; discussion 1389–90
42. Nishikawa M, Sakamoto H, Hakuba A, Nakanishi N, Inoue Y (1997) "Pathogenesis of Chiari malformation: a morphometric study of the posterior cranial fossa", (in eng). J Neurosurg 86(1):40–47
43. Noudel R, Jovenin N, Eap C, Scherpereel B, Pierot L, Rousseaux P (2009) "Incidence of basioccipital hypoplasia in Chiari malformation type I: comparative morphometric study of the posterior cranial fossa. Clinical article", (in eng). J Neurosurg 111(5):1046–52
44. Nwotchouang BST et al (2019) "Three-dimensional CT morphometric image analysis of the clivus and sphenoid sinus in Chiari malformation type I", (in eng). Ann Biomed Eng 47(11):2284–2295
45. Nwotchouang BST et al (2020) "Clivus length distinguishes between asymptomatic healthy controls and symptomatic adult women with Chiari malformation type I", (in eng). Neuroradiology 62(11):1389–1400
46. Ocakoglu G, Baykal D, Altunyuva O, Taskapilioglu MO, Yilmazlar S (2019) "Statistical shape analysis of cerebellum in patients with Chiari malformation I", (in eng). J Craniofac Surg 30(6):1683–1685
47. Schady W, Metcalfe RA, Butler P (1987) The incidence of craniocervical bony anomalies in the adult Chiari malformation. Journal of the Neurological Sciences 82(1):193–203
48. Sekula RF, Arnone GD Jr, Crocker C, Aziz KM, Alperin N (2011) "The pathogenesis of Chiari I malformation and syringomyelia", (in eng). Neurol Res 33(3):232–239
49. Sekula RF, Jannetta PJ Jr, Casey KF, Marchan EM, Sekula LK, McCrady CS (2005) "Dimensions of the posterior fossa in patients symptomatic for Chiari I malformation but without cerebellar tonsillar descent", (in eng). Cerebrospinal Fluid Res 2:11
50. Speer MC et al (2003) "Review article: Chiari type I malformation with or without syringomyelia: prevalence and genetics", (in eng). J Genet Couns 12(4):297–311
51. Speer MC, George TM, Enterline DS, Franklin A, Wolpert CM, Milhorat TH (2000) "A genetic hypothesis for Chiari I malformation with or without syringomyelia", (in eng). Neurosurg Focus 8(3):E12
52. Takeuchi K, Yokoyama T, Ito J, Wada K, Itabashi T, Toh S (2007) "Tonsillar herniation and the cervical spine: a morphometric study of 172 patients", (in eng). J Orthop Sci 12(1):55–60
53. Thakar S, KurudiSiddappa A, Aryan S, Mohan D, Sai Kiran NA, Hegde AS (2017) "Does the mesodermal derangement in Chiari type I malformation extend to the cervical spine? Evidence from an analytical morphometric study on cervical paraspinal muscles", (in eng). J Neurosurg Spine 27(4):421–427
54. Urbizu A et al (2017) "Cephalometric oropharynx and oral cavity analysis in Chiari malformation type I: a retrospective case-control study", (in eng). J Neurosurg 126(2):626–633
55. Urbizu A et al (2018) "Machine learning applied to neuroimaging for diagnosis of adult classic Chiari malformation: role of the basion as a key morphometric indicator", (in eng). J Neurosurg 129(3):779–791
56. Urbizu A, Poca MA, Vidal X, Rovira A, Sahuquillo J, Macaya A (2014) "MRI-based morphometric analysis of posterior cranial fossa in the diagnosis of chiari malformation type I", (in eng). J Neuroimaging 24(3):250–6
57. Urbizu A et al (2013) "Chiari malformation type I: a case-control association study of 58 developmental genes", (in eng). PLoS One 8(2):e57241
58. Vega A, Quintana F, Berciano J (1990) "Basichondrocranium anomalies in adult Chiari type I malformation: a morphometric study", (in eng). J Neurol Sci 99(2–3):137–145
59. Wan M, Zong R, Tong HY, Zhang ZZ, Zhao B, Yu XG (2020) "A morphometric study of the atlanto-occipital joint in adult patients with Chiari malformation type I," (in eng), Br J Neurosurg 1–4
60. Wang S et al (2020) "Chiari malformations type I without basilar invagination in adults: morphometric and volumetric analysis", (in eng). World Neurosurg 143:e640–e647
61. Wertheim SB, Bohlman HH (1987) "Occipitocervical fusion. Indications, technique, and long-term results in thirteen patients", (in eng). J Bone Joint Surg Am 69(6):833–6
62. Yamazaki Y, Tachibana S, Takano M, Fujii K (1998) "Clinical and neuroimaging features of Chiari type I malformations with and without associated syringomyelia," (in eng). Neurol Med Chir (Tokyo) 38(9): 541–6; discussion 546–7
63. Yan H et al (2016) "Morphometric features of posterior cranial fossa are different between Chiari I malformation with and without syringomyelia", (in eng). Eur Spine J 25(7):2202–2209