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Braden J. Lawrence, University of Washington
Mark Luciano, Johns Hopkins University
John Tew, University of Cincinnati
Richard G. Ellenbogen, University of Washington
John Oshinski, Emory University
Francis Loth, University of Akron
Amanda P. Culley, University of Idaho
Bryn A. Martin, University of Idaho

Journal Title: World Neurosurgery
Volume: Volume 116
Publisher: Elsevier: 12 months | 2018-08-01, Pages E298-E307
Type of Work: Article | Post-print: After Peer Review
Publisher DOI: 10.1016/j.wneu.2018.04.191
Permanent URL: https://pid.emory.edu/ark:/25593/v1d60

Final published version: http://dx.doi.org/10.1016/j.wneu.2018.04.191

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Accessed December 4, 2022 7:20 AM EST
Cardiac-related spinal cord tissue motion at the foramen magnum is elevated in Type I Chiari malformation patients and decreases post-decompression surgery

Braden J. Lawrence, BS, MBA1,4,8, Mark Luciano, MD, PhD2, John Tew, MD3, Richard G. Ellenbogen, MD4, John N. Oshinski, PhD5, Francis Loth, PhD6, Amanda P. Culley, BS, MS7, and Bryn A. Martin, PhD8

1School of Medicine, University of Washington, Seattle, Washington 2Department of Neurosurgery, Johns Hopkins University, Baltimore, Maryland 3Department of Neurosurgery, University of Cincinnati Neuroscience Institute and University of Cincinnati College of Medicine, and Mayfield Clinic, Cincinnati, Ohio 4Department of Neurological Surgery, University of Washington, Seattle, Washington 5Department of Radiology & Imaging Science and Biomedical Engineering, Emory University, Atlanta, Georgia 6Conquer Chiari Research Center, Department of Mechanical Engineering, University of Akron, Ohio 7Department of Statistical Science, University of Idaho, Moscow, Idaho 8Department of Biological Engineering, University of Idaho, Moscow, Idaho

Abstract

Objective—Type 1 Chiari malformation (CM-I) is a craniospinal disorder historically defined by cerebellar tonsillar position (TP) greater than 3-5mm below the foramen magnum (FM). This definition has come under question since quantitative measurements of cerebellar herniation do not always correspond with symptom severity. Researchers have proposed several additional radiographic diagnostic criteria based on dynamic motion of fluids and/or tissues. The present study objective was to determine if cardiac-related craniocaudal spinal cord tissue displacement is an accurate indicator of the presence of CM-I and if tissue displacement is altered with decompression.

Methods—A cohort of 20 symptomatic patients underwent decompression surgery. Fifteen healthy volunteers were recruited for comparison to the CM-I group. Axial phase-contrast magnetic resonance imaging (PC-MRI) measurements were collected pre- and post-surgery at the FM with cranial-caudal velocity encoding and 20 frames per cardiac cycle with retrospective...
reconstruction. Spinal cord motion (SCM) at the FM was quantified based on the peak-to-peak integral of average spinal cord velocity.

Results—Tissue motion for the pre-surgical group was significantly greater than controls (p=0.0009). Motion decreased following surgery (p=0.058) with an effect size of -0.151 mm and a standard error of 0.066 mm. Post-operatively, no statistical difference from controls in bulk displacement at the FM was found (p=0.200) after post hoc testing using Tukey’s adjustment for multiple comparisons.

Conclusions—These results support SCM measurement by PC-MRI as a possible non-invasive radiographic diagnostic for CM-I. Dynamic measurement of SCM provides unique diagnostic information about CM-I alongside static quantification of TP and other intracranial morphometrics.

Introduction

Type I Chari Malformation (CM-I) is the most prevalent of the Chiari malformation subgroups and is commonly associated with syringomyelia and hydrocephalus. CM-I is an afflictive craniospinal disorder that has historically been defined radiographically by caudal descent and herniation of the cerebellar tonsils into the spinal canal > 3-5mm beyond the basion-opisthion line (McRae's line), at the foramen magnum (FM). The result is crowding of the posterior fossa with reduced posterior fossa volume for the cerebellomedullary tissue that can lead to stenosis and aberrancies in cerebrospinal fluid (CSF) dynamics at the craniovertebral junction (CVJ). Clinical manifestations are a constellation of idiosyncratic and diverse symptomatology including, but not limited to a tussive headache, poor coordination and unsteady gait, severe head and neck pain, dizziness, vision and hearing problems.

Treatment of CM-I is controversial given that the etiology of CM-I remains a mystery and that diagnostic criteria are dynamic and not uniformly agreed upon by all clinicians. Effective treatment options for symptomatic CM-I patients are limited to posterior fossa decompression surgery based on the clinical indications defined by each surgeon. Conservative therapy includes medical management of symptoms as well as serial follow-up with a non-invasive option for asymptomatic or mildly symptomatic patients. Most surgical interventions have two major goals. The goals are 1) a posterior fossa and upper cervical decompression reducing impedance to CSF flow at the FM and 2) improved volume for, and mobility of, tissue occupying the FM and nearby PCF. Some treatment options for CM-I include, but are not limited to variations of posterior fossa decompression surgery: PCF decompressive surgery, cerebellar tonsillectomy, suboccipital decompression and laminectomy, dural splitting decompression, duraplasty expansion, extradural decompression, and enlargement of the PCF.

Efficacy of treatment is often unreliable, with studies indicating 20-40% of operations failing to resolve CM-I symptoms. As previously stated, the traditional definition of CM-I is cerebellar tonsillar position (TP) of >3-5mm below the foramen magnum (FM). This measurement has come under question since herniation depth does not always correspond with symptom severity. And, the indications for surgery based on clinical
symptoms vary from institution to institution. Thus, there is a need for diagnostic markers that identify symptomatic CM-I and correspond to both specific symptoms and the severity of those symptoms. As an alternative to static morphometric analysis, dynamic MRI-based methods have been explored as a CM-I diagnostic such as phase-contrast MR imaging (PC-MRI) to quantify cerebrospinal fluid (CSF) velocities\(^\text{10,14,42-47}\) and cardiac related neural tissue motion.\(^\text{15,48-50}\)

Several imaging MR imaging modalities exist that allow users to quantify static and dynamic measurements in individuals. To date, only static measurements have fully translated to clinical use, but are often poorly correlated with clinical presentation and treatment outcome.\(^\text{4}\) A classic example of this static measurement is TP at McRae’s line. This linear 2D metric is reasonably easy to measure, however, it fails to account for 3D crowding and CSF flow within and around the PCF and CVJ. While Chiari-like TP may occur in 1 to 3 percent of the population\(^\text{51}\), symptoms may occur in only 0.06 percent.\(^\text{1}\)

The poor correlation between the extent of cerebellar crowding and symptoms has led medical scientists to seek other features beyond the static anatomical picture seen on static T1 or T2-weighted MRI to predict symptoms and guide surgical treatment.

Dynamic measurements aim for a better representation of clinical presentation by incorporating additional parameters such as neural tissue motion and CSF velocities. Many dynamic MRI methods have been used for evaluating CM-I such as cine MRI, CSF flowmetry, and cerebellar tonsillar motion using cine PC-MRI. Studies using those methodologies have produced variable results as reviewed previously by Shaffer et al.\(^\text{16}\) In specific, PC-MRI has found elevated and decreased CSF velocities in CM-I. A recent study by Leung, et al. demonstrated potential to help stratify Chiari and the impact of surgery by using cine MRI and motion tracking.\(^\text{52}\)

The goal of the present study was to quantify cranio-caudal spinal cord motion (SCM) in CM-I patients pre- and post-decompression surgery and compare findings to healthy controls. We hypothesized that: 1) SCM would be elevated in CM-I patients compared to controls, 2) that TP would positively correlate with SCM, and 3) that SCM would decrease post-decompression surgery. The rationale for examining spinal cord motion is that this data is often collected clinically to assess flow dynamics and this same scan can be used to assess the same or related parameters. This study particularly adds to previous studies by including the impact of surgery and relation to controls. While many dynamic MRI methods have not yet translated to clinical use, previous indices (static measurements) are unable to provide deeper understanding between anatomic and physiologic interplay.

**Materials and Methods**

**Patients**

This prospective study was approved by the University of Akron, Cleveland Clinic, University of Cincinnati and Emory University institutional review boards (UA IRB #20130226), and all subjects signed an informed written consent. 20 clinically diagnosed CM-I patients from 18-55 years of age with TP ≥3-5 mm were prospectively enrolled at Cleveland Clinic and Mayfield Clinic. Inclusion criteria for included subjects were those...
who met the diagnostic and clinical criteria. TP was used as an initial screening with further evaluation of Chiari crowding of the cisterna magna and restricted space at the CVJ. The clinical picture and diagnosis was confirmed by the treating surgeon based on all diagnostic information and patient presentation.

Patients were recruited from a pool of individuals scheduled to receive imaging or evaluation for CM-I. Controls were recruited from a random pool of individuals without a remarkable history or symptomatology. Patients were excluded if they presented with craniospinal deformity, Dandy-Walker malformation, Ehlers-Danlos syndrome, spinal fusion, previous decompression surgery, syringomyelia, or additional neurological disorders. All 20 CM-I patients received decompression surgery (19 female:1 male, age = 38 ± 10 years). 15 controls were included from 18-55 years of age with age controlled to the patient group (8 female:7 male, age = 36 ± 10 years). Controls with organ diseases, neurological conditions, and craniospinal deformity were excluded. Data obtained for all CM-I patients and controls took place from March 2011 to August 2014. A summary of CM-I patient clinical presentation is listed in Table 1.

Surgical Technique

The goal of the surgical technique was removal of primary brain compression and the creation of a CSF space around brain tissue. Two CM-I decompression techniques were utilized in this study: bony decompression with duraplasty (BD) and bony decompression with tonsillectomy and duraplasty (BDT). All 20 patients underwent decompression of the CVJ under general anesthesia in the prone position with 3-point Mayfield fixation and elevation of the head. Surgical preparation, draping, and administration of antibiotics and local anesthesia was carried out in a standard fashion. An incision was made from the inion and extended downward just beyond the apex of the herniated tonsils, followed by subperiosteal dissection and suboccipital craniectomy. Intraoperative ultrasound was utilized immediately following PCF decompression as an indicator of adequate decompression, tonsillar pulsatility, and improved CSF velocities. Since all subjects enrolled in this study were prepared to undergo surgical treatment, intraoperative ultrasound was the only key variable on whether or not they underwent more conservative or aggressive decompression. 76% of CM-I patients required dural opening and tonsillectomy (BDT), 24% required dural opening with duraplasty alone (BD). Tonsillectomy was performed to achieve minimal shrinkage of tonsils and optimal CSF flow. Closure of the dura was performed in a multilayer fashion using autologous pericranium with absorbable sutures to ensure watertight closure. Need for duraplasty was made by the surgeon's subjective interpretation of ultrasonography findings. Surgical treatment took place at Cleveland Clinic and Mayfield Clinic.

Symptom Assessment

The presence of the following specific symptoms and clinical signs were recorded at the baseline and follow-up MRI exam for all subjects enrolled in the study. Assessment of surgical outcome was based on comparison post-operative follow-up results with a standardized pre-surgical screening. This method categorically assessed chief complaint for each patient and whether or not specific symptoms were present pre- and post-
decompression. We also noted other symptoms as reported by the patient that were not included in our initial screening assessment form. The patient's reported outcome was categorized as “Improved,” “Unchanged,” or “Worse” with respect to the patient's initial chief complaint. No surgical complications were noted for any patients. Clinical outcomes were categorized and scored by an external evaluator to eliminate operator bias.

**Neuroimaging Studies**

**In vivo PC-MRI**—An identical MRI protocol was obtained for all subjects enrolled in the study. Patients were scanned both pre- and post-operatively with a mean post-operative follow-up of 9 months. Transverse PC-MRI scans, with thru-plane (cranial-caudal) velocity encoding (VENC = 10 cm/s), slice thickness = 5 mm, were acquired at the FM level with imaging planes oriented perpendicular to the CSF flow direction and imaging parameters based on Martin et al (Video 1).

The minimum repetition time available was used to optimize temporal resolution, and the minimum echo time available was used to optimize signal-to-noise ratio and reduce intra-voxel phase dispersion. All scans were ECG triggered with ~20 phases retrospectively reconstructed. Scan time was approximately two minutes. All images were acquired using a 3-T MRI (Siemens Magnetom Trio TIM 3.0T syngo MR B17).

**PC-MRI Post-Processing of Spinal Cord Motion (SCM)**

SCM was quantified based on the integral of the average spinal cord velocities at the FM. The axial PC-MRI images were post-processed using an in-house code developed in MATLAB (Version R2013b, MathWorks, Natick, Ma). A region of interest (ROI) within the spinal cord was manually selected. Pixels near the spinal cord tissue edges bordering CSF were omitted. The average velocity of all pixels in the ROI was computed and numerically integrated to obtain unsteady spinal cord motion over the cardiac cycle (Figure 1). To achieve this, velocity at each time step was multiplied by the time increment to obtain displacement at each time step. Displacement was then integrated using trapezoidal rule with the trapz function in MATLAB (Version R2013b, MathWorks, Natick, Ma). Peak-to-peak magnitude of SCM was quantified as the difference between the maximum positive displacement and minimum negative displacement (Figure 1). Eddy current offsetting was applied to the ROI velocities within the spinal cord to assure zero average velocity within the spinal cord tissue over the cardiac cycle.

**Anatomical MRI and Post-Processing Morphometric Quantification**

To define the brain and craniovertebral anatomy, a high-resolution T1-MPRAGE was acquired at a resolution of 1.1 × 1.1 × 1.1 mm voxels with whole brain coverage (176 slices sagittal slices, FOV 270 × 250 in-plane). Neck elements were left on. Scan time was six minutes. A high-resolution T2 3D-SPACE pulse sequence was also acquired at a resolution of 0.5 × 0.5 × 1.5 mm voxels with whole brain coverage (144 coronal slices, FOV 240 × 210 in-plane). Scan time was five minutes. The motion of the neural tissue was compared with the TP, as tonsillar position below the FM is a standard radiographic marker of CM-I. TP was measured with respect to McRae's line by a single operator using OsiriX software (Version 8, Geneva, Switzerland). A positive value of TP indicated TP caudal to the FM.
Since decompression surgery involved removal of part of the occiput, post-surgical TP was quantified with reference to the pre-surgical angle between the slope of the clivus and McRae's line.

**Statistical Analysis**

A total of 35 subjects were studied (Table 2). Descriptive comparisons were calculated for pre-decompression (n = 20), post-decompression (n = 18), and healthy controls (n = 15) expressed as mean ± standard deviation (Table 2 and Figure 3) using Microsoft Excel for Mac (Version 2016, Seattle, WA). To account for attrition and follow-up, multiple MR imaging sites, and a different number of individuals in surgical and control groups, we applied a linear mixed-effects (LME) model using Bates' approach. The LME model was used to determine the relationship between CM-I patient and control groups and SCM while controlling for sex, age, and procedure as a covariates. We used subject and imaging site as random effects and used surgical group, sex, age, and procedure as fixed-effects. Analysis of residual plots revealed no obvious deviations from homoscedasticity or normality. The LME model was assessed using a parametric bootstrap method, as outlined by Halekoh and Højsgaard, with one million sample iterations. SCM significance between the pre-op, post-op, and control groups was investigated with post-hoc Tukey contrasts with statistical correction for pairwise comparison of means. Linear correlation of TP to bulk axial SCM was quantified across all study groups using the Pearson product-moment correlation coefficient (Figure 4). Significance was assessed at a Type I error rate of α = 0.05 for all comparisons. All statistical analyses were performed using R (Version 3.4.0, Vienna, Austria), lme4 (Bates et al., 2015), and pbkrtest (Halekoh and Højsgaard, 2014).

**Results**

**Bulk Spinal Cord Motion (SCM) in CM-I Patients Compared to Healthy Volunteers**

The results for all subjects involved in the study are listed in Table 2, and overall motion differences for pre-op patients, post-op patients, and healthy controls are plotted in Figure 2. LME modelling demonstrated significance for the pre-op, post-op, and control group variable as assessed with a parametric bootstrap method set to one million simulations (p = 0.0024). SCM for the pre-surgical group (median = 0.45 mm, interquartile range (IQR) = 0.32 mm) was 231% greater than controls (median = 0.22 mm, IQR = 0.11 mm) and confirmed a statistically significant difference between pre-operative and control groups (p = 0.0009) after correcting for multiple comparisons. Motion at the FM decreased following surgery (median = 0.36 mm, IQR = 0.29 mm), but resulted in no statistically significant difference between the post-surgical and control groups at the 95% confidence level with correction for multiple comparison of groups (p = 0.20). Sex and age were controlled for as covariates in the LME model.

**Effect of Posterior Fossa Decompression (PFD) Surgery on Spinal Cord Motion (SCM) at the Foramen Magnum (FM)**

Results show that the mean bulk axial SC motion at the FM for pre-operative patients was greater than the post-operative group and decreased by 30% following surgical decompression (Table 2). Motion at the FM decreased following surgery (median = 0.38
mm, IQR = 0.29 mm), but failed to demonstrate a statistically significant difference between pre-surgical and post-surgical groups based on a significance level equal to 0.05 and correcting for multiple comparisons (p = 0.0578). The LME model demonstrated an estimated effect size of -0.1513 mm change in SCM with decompression surgery and a standard error of 0.0662 mm. A descriptive summary for all subjects involved in the study is listed in Table 2 with multiple comparison of means with Tukey contrast results listed in Table 3. Graphical comparison of overall motion differences for pre-operative, post-operative, and control groups are depicted in Figure 2.

Relationship of Spinal Cord Motion (SCM) at the Foramen Magnum (FM) with Tonsillar Position (TP)

Axial bulk SCM at the level of FM was plotted against cerebellar tonsillar position (TP) for each patient in the pre-op, post-op, and control groups as shown in Figure 3. Mean and standard deviation (mean ± SD) for tonsillar position measurements for symptomatic CM-I pre-op (n = 20), post-op (n = 18), control (n = 15) groups were 8.3 ± 4.9 mm, 4.9 ± 4.8 mm, and -0.41 ± 2.4 mm, respectively. Overall correlation (R² = 0.24) of bulk SCM at the FM with TP significantly lacked meaningful correlation when applying the Pearson correlation test across all subjects (p = 0.0003, 95% CI = 0.249 – 0.675).

Clinical Picture and Post-Operative Outcomes

Clinical presentation for the CM-I patient group is listed in Table 1 with long-term surgical outcomes summarized in Table 4. Notably, 100% of CM-I patients experienced tussive headaches, and 35% experienced dizziness. Categories for outcome assessment were simplified to account for all symptoms associated with each patient and include the patient's perspective on surgical outcome. Improved is defined as a reduction in some or all of CM-I symptoms. Out of the 18 patients in the post-operative group, 13 patients reported an overall improvement in symptoms, four reported no improvements, and one reported worsening in symptoms. Two patients from the pre-operative group did not follow-up post-surgery. The mid-sagittal MRI anatomy pre- and post-decompression surgery is shown in Figure 4 for several subjects.

Discussion

This study represents the first quantitative assessment of cardiac-related SCM using PC-MRI applied to CM-I patients pre- and post-decompression surgery. SCM was found to be significantly greater in CM-I patients than controls and decompression surgery reduced SCM. These results support the possible importance of SCM as a dynamic MRI diagnostic alongside static morphometrics to help characterize CM-I disease state.

Pathophysiological Importance of Tissue Motion

Several theories and explanations have been proposed for the pathophysiology of CM-I symptoms and related disorders. Two primary theories help explain the progression of CM-I and related symptoms: the “hydrodynamic theory” proposed by Gardner and colleagues in 1958 and “cranial-spinal pressure dissociation hypothesis” later proposed by Williams in 1969. The ball-valve or ball-in-cone “valve” theory proposed by Williams
and further elucidated by Oldfield et al.\textsuperscript{12} helps to explain the CSF and disturbances that occur when cerebellar tonsils descend and obstruct CSF around the craniocervical junction. Under stress or strain, such as Valsalva maneuver, tissue blockade at the CVJ leads to CSF flow cranially but not caudally, thereby leading to craniospinal pressure dissociations, and ultimately, tissue deformation.\textsuperscript{13,60,61}

\textit{In vivo} measurement of craniospinal pressure dissociation by invasive placement of pressure transducers has been found to be an indicator of CM pathophysiology and symptoms.\textsuperscript{59,62,63} Our findings confirm increased SCM at the FM in CM-I patients in comparison to healthy controls and support the application of dynamic PC-MRI methods to clinical imaging methods. However, these results obtained at the FM indicate that while the SCM differences are significant, this measurement alone would not be sufficient to distinguish CM-I (Figure 2). These results reaffirm the notion that tonsillar bulk motion acts as a dynamic ball-in-cone “valve” leading to increased pressure dissociation.\textsuperscript{12,59,62-64} We found a lack of correlation of SCM and TP (Figure 4). This can be expected since TP does not consistently correlate with symptom severity or definitively imply causation of bulk tissue motion.\textsuperscript{3,39-41} TP is a static 1-dimensional simplification of the 3D dynamic problem of CM-I. Future studies could be conducted to determine if symptom severity and/or surgical outcome correlates with SCM.

\textbf{Comparison of Results to Previous Studies}

Neural tissue deformation in terms of bulk motion has been assessed in CM patients in a number of studies using a variety of MRI techniques (Table 5). The results presented in this paper are consistent with the previous studies in Table 5 and also confirm Leung’s findings of diminished motion in post-operative CM-I patients compared to pre-operative CM-I patients.\textsuperscript{52} The present results also agree with Alperin’s (2014) finding of elevated SCM in CM-I patients compared to controls using PC-MRI collected at the C2-C3 level.\textsuperscript{10} Hofmann et al. and Pujol et al. used PC-MRI to quantify bulk cord and tonsil motion in terms of a motion index, and found that the motion index was significantly elevated in CM.\textsuperscript{19,25} Alperin et al. (2005), and Cousins et al. assessed spinal cord and tonsil bulk motion and both found that motion was greater on average in CM patients than controls but not statistically different.\textsuperscript{39,44} Similarly, Yiallouro et al. found elevated 2D tonsillar displacement in four CM patients compared to three controls.\textsuperscript{48} Terae et al. used bolus tracking MRI measurements and visually interpreted greater motion of the spinal cord in CM patients.\textsuperscript{55} Leung analyzed tissue motion using a cine MRI-based motion tracking algorithm and reported similar findings to the current study in pre-op, post-op, and control groups.\textsuperscript{52} While their study reports similar trends in tissue motion, the study used cine balanced fast-field echo (bFFE) MRI for quantifying tissue motion via motion tracking algorithms, which is a uniquely different method than used in the present study. The study was also retrospective in nature with selection of patients from a clinical database. In collection, these studies indicate that SCM could be a useful tool to help quantify CM-I. It should be noted that the TP for pre-operative CM-I patients in this study was relatively mild on average (8.3 ± 4.9 mm) with a wide range of values. We found a relatively weak positive correlation of TP and SCM (Figure 3, $R^2 = 0.24$).
Relation of Neural Tissue Deformation and Damage

The delicate intracranial tissues absorb energy from ∼30 million heartbeats per year. Each heartbeat acts on the tissues with large arterial pressure oscillations of ∼40 mmHg. Under healthy conditions, the cerebrospinal fluid (CSF) acts to help absorb each pulsation by moving freely out of the intracranial space into the spine. However, in CM, CSF motion is constricted at the skull base due to cerebellar tonsil herniation that acts as a dynamic “valve.” This constriction causes CSF pressure dissociation and abnormal repetitive tissue stress that leads to tissue deformation, damage and symptoms. Although SCM is not a direct measure of tissue damage, SCM is likely correlated with tissue-level stress that leads to damage. This concept is supported by recent studies show cellular mechanosensitivity of central nervous system tissues to low level magnitude strains and also corresponding microstructural alterations in CM-I patient brain tissue using diffusion tensor imaging.

Need for Additional CM-I Diagnostics

Despite being first described over 100 years ago, there is confusion regarding the validity of the historical definition, etiology, diagnostic criteria and standard of treatment for CM-I, which have a negative impact on CM-I patient experiences and outcomes. There is concern in the medical community that there will be unnecessary operations unless better CM-I diagnostic criteria are developed. The current clinical definition for CM-I is based on a static MRI measurement of tonsillar descent > 3-5 mm below the skull, but is considered inadequate to diagnose CM-I. An increasing number of asymptomatic, minimally symptomatic, and doubtfully symptomatic patients are being diagnosed. Widespread use of MRI has shown that 1-3% of the U.S. population has radiographic indication of CM-I. However, less than ∼1 in 30 of these people are regarded as true CM-I patients. If left untreated, CM-I can progress to result in permanent CNS damage. The leading CM-I treatment is a highly invasive brain surgery with little consensus for operative techniques. The AANS estimated that approximately 11,000 CM-I patients received surgical treatment in 2007 and 20-40% of these surgeries do not resolve symptoms. The importance of improved diagnostic testing for CM-I was recognized by a 2010 congressional mandate to encourage aggressive development of an objective CM-I test. Ideally, an adequate CM-I diagnostic would elucidate the following: a) stratify CM-I from related diseases, b) initial surgical decision, c) assessment of post-operative anatomical success in context of residual symptoms and d) decision for redo of decompression surgery. Our study results support that SCM may be investigated alongside other static and dynamic MRI-based diagnostics to understand their potential clinical utility.

Limitations

There are several limitations that need to be taken into account when interpreting the results of this study: 1) sex distribution in CM-I patient and control groups, 2) CM-I patient imaging follow-up, 3) asymptomatic CM-I patients, 4) PC-MRI post-processing method, 5) study size, and 6) correlation of motion changes with symptoms.

This study demonstrated significant differences in SCM in one out of three comparisons at a 95% confidence level. To validate results of SCM between groups, we accounted for sex.
distribution as a covariate when running an all-inclusive LME model. Since the pre- and post-surgery results were paired, we would not expect male/female group differences to have a significant impact. The principal factor affecting sex distribution in CM-I groups is the two female patients that failed to follow up after surgery, however this was accounted for in the LME model.

Furthermore, while the degree of change of SCM between pre-op and post-op groups was borderline significant, we integrated statistical corrections for multiple groups using the Tukey's adjustment for multiple comparisons, which conservatively increased final comparison p-values. Similar corrections for multiple groups and comparisons were not performed in other papers except Leung's. Failing to account for multiple testing error would certainly yield apparent significance between surgical groups. It should also be noted that the standard error was rather large relative to the overall effect size. The results after corrections can be expected in part due to the inherent variability of CM-I and decompression surgery, and heterogeneous nature of the study population in terms of TP and SCM. Applying the same methods in this paper to a larger sample size would help to give a more accurate report of surgical effect.

This study only analyzed symptomatic CM-I patients and did not include asymptomatic individuals who meet the diagnostic criteria for CM-I. Future studies should include asymptomatic CM-I patients, as this is an important group in the diagnostic problem. Post-processing of phase-contrast MR images was also only analyzed SCM at one axial level. Similar to CSF flow, tissue motion occurs in 3D. It is possible that the exact location of maximum motion magnitude was missed in some subjects due to slice placement. It should also be noted that the increased motion of the cerebral tonsils in CM-I may be a result of increased CSF flow at the CVJ as demonstrated previously by cine PC-MRI. Future improvements on this method may include mid-sagittal velocity measurements as well as quantifying strain and tissue deformation.

While study size was sufficient to observe a significant difference across surgical and control groups, it would be beneficial to expand further the number of CM-I patients included in future studies. We were not able to enroll additional subjects in the study due to limited grant funding to support MR imaging session that was not in the normal clinical routine for patients and controls. The relatively few pre- and post-surgical CM-I patients enrolled in the study and coarse measure of clinical outcome (Improved, Unchanged, Worse), did not allow statistical analysis of relationship of SCM and clinical outcome. Additional outcome metrics such as the Chicago Chiari Outcome Scale were not applied since such instruments were not developed prior to conception of this prospective study. Also, retrospective construction of clinical outcomes would not accurately score patient symptoms and surgical outcomes.

Conclusions

The study objective was to determine if cardiac-related craniocaudal spinal cord tissue displacement is an accurate indicator of the presence of CM-I and if tissue displacement is altered due to decompression surgery. These results support further exploration of SCM as a possible dynamic MRI based-parameter to help assess CM-I. Axial bulk SC displacement at
the FM was elevated in pre-operative CM-I patients relative to controls and was observed to decrease following posterior fossa decompression surgery. There was no significant difference between pre-surgical and post-surgical, or post-surgical and control groups. Dynamic measurement of SCM provides unique diagnostic information about CM-I alongside static quantification of TP and other intracranial morphometrics.

**Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

**Acknowledgments**

The authors thank Michael Majcher, Nicholas Shaffer, Jennifer Chisko, Daniel McQuaide and Kyla Lowenkamp for assistance with data processing on this project.

Funding: This work was supported by NIH NINDS grant 1R15NS071455-01 and NIH NIGMS grants P20GM103408 and 4U54GM104944-04, Conquer Chiari; and the University of Washington School of Medicine Medical Student Research Training Program (MSRTP).

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**Abbreviations**

- **BD**: bony decompression
- **BDT**: bony decompression and tonsillectomy
- **bFFE**: balanced fast-field echo
- **CM**: Chiari malformation
- **CM-I**: Chiari malformation Type I
- **CSF**: cerebrospinal fluid
- **CV**: coefficient of variation
- **CVJ**: craniovertebral junction
FM foramen magnum
FOV field of view
IQR interquartile range
LME linear mixed-effects
MPRAGE magnetization-prepared rapid acquisition with gradient echo
PCF posterior cranial fossa
PC-MRI phase-contrast magnetic resonance imaging
ROI region of interest
SC spinal cord
SCM spinal cord motion
SPACE sampling perfection with application optimized contrasts using different flip angle evolution
TP tonsillar position
VENC velocity encoding
Highlights

- Spinal cord motion is an indicator of the presence of type 1 Chiari malformation.
- Tissue motion for the pre-surgical group was significantly greater than controls.
- Spinal cord tissue displacement is decreased with decompression surgery.
Figure 1.
A) Representative CM-I patient showing spinal cord ROI selection. B) Spinal cord displacement waveform with depiction of magnitude of spinal cord motion (SCM).
Figure 2.
Comparison of the magnitude of spinal cord motion (SCM) at the Foramen Magnum (FM) for healthy control (white), CM-I preoperative (light gray), and CM-I post-operative (dark gray) groups. Asterisks indicate *p < 0.10 and **p < 0.001 according to linear mixed effects model analysis with post-hoc Tukey contrast.
Figure 3.
Linear correlation of cerebellar tonsillar position (TP) and magnitude of axial spinal cord motion (SCM) at the foramen magnum (FM) for all subjects (R² = 0.24). TP greater than zero represents tonsillar position caudal to the FM.
Figure 4.
Sagittal T2-weighted MR image of symptomatic CM-I patients one through five. A - pre-op scan, B - post-op scan for same patient.
Table 1
Summary of Clinical Presentation Symptoms in 20 CM-I Patients.

<table>
<thead>
<tr>
<th>Clinically Reported Symptoms</th>
<th>No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>100%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>35%</td>
</tr>
<tr>
<td>Neck Pain</td>
<td>30%</td>
</tr>
<tr>
<td>Gait Disturbance</td>
<td>30%</td>
</tr>
<tr>
<td>Weakness</td>
<td>30%</td>
</tr>
<tr>
<td>Hearing Loss</td>
<td>25%</td>
</tr>
<tr>
<td>Swallowing Difficulty</td>
<td>25%</td>
</tr>
<tr>
<td>Fatigue, Lethargy</td>
<td>15%</td>
</tr>
<tr>
<td>Memory Loss</td>
<td>15%</td>
</tr>
<tr>
<td>Vertigo</td>
<td>15%</td>
</tr>
<tr>
<td>Extremity Pain</td>
<td>10%</td>
</tr>
<tr>
<td>Sleep Apnea</td>
<td>5%</td>
</tr>
<tr>
<td>Extremity Numbness</td>
<td>5%</td>
</tr>
<tr>
<td>Variable</td>
<td>Pre-Op (n=20)</td>
</tr>
<tr>
<td>----------</td>
<td>--------------</td>
</tr>
<tr>
<td>Age</td>
<td>37.76 ± 9.97</td>
</tr>
<tr>
<td>TP</td>
<td>8.31 ± 4.93</td>
</tr>
<tr>
<td>SCM</td>
<td>0.53 ± 0.30</td>
</tr>
</tbody>
</table>

SCM = spinal cord motion; TP = tonsillar position
### Table 3
Summary of Linear Mixed-Effects (LME) Model Results with Post-Hoc Tukey Contrasts

<table>
<thead>
<tr>
<th>Object</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LME Model</td>
<td>0.0024</td>
</tr>
<tr>
<td>Pre-Op vs. Control</td>
<td>0.0009</td>
</tr>
<tr>
<td>Pre-Op vs. Post-Op</td>
<td>0.0578</td>
</tr>
<tr>
<td>Post-Op vs. Control</td>
<td>0.2000</td>
</tr>
</tbody>
</table>

LME = linear mixed-effects
Table 4
Long-Term Outcome for 18 CM-I Patients

<table>
<thead>
<tr>
<th>Chief Complaint</th>
<th>No. of Patients</th>
<th>No. of Patients (%)</th>
<th>SCM % Change</th>
<th>TP % Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved</td>
<td>13</td>
<td>72.2%</td>
<td>-26.0%</td>
<td>-44.1%</td>
</tr>
<tr>
<td>Unchanged</td>
<td>4</td>
<td>22.2%</td>
<td>0.9%</td>
<td>-18.4%</td>
</tr>
<tr>
<td>Worse</td>
<td>1</td>
<td>5.6%</td>
<td>-4.6%</td>
<td>11.0%</td>
</tr>
</tbody>
</table>

SCM = spinal cord motion; TP = tonsilar position
Table 5
Previous Studies on Neural Tissue Motion Quantification in Chiari

<table>
<thead>
<tr>
<th>Study</th>
<th>MRI Method</th>
<th>Location</th>
<th>Healthy</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alperin et al., 2005</td>
<td>PC-MRI</td>
<td>C2 Spinal Cord</td>
<td>0.33 ± 0.13 mm</td>
<td>0.39 ± 0.17 mm</td>
</tr>
<tr>
<td>Alperin et al., 2014</td>
<td>PC-MRI</td>
<td>C2 Spinal Cord</td>
<td>0.174 ± 0.047 mm</td>
<td>0.373 ± 0.198 mm *</td>
</tr>
<tr>
<td>Leung et al., 2016</td>
<td>Cine bFFE</td>
<td>Sagittal Tonsil (SI)</td>
<td>0.30 ± 0.10 mm *</td>
<td>0.79 ± 0.45 mm *</td>
</tr>
<tr>
<td>Cousins et al., 2009</td>
<td>T2 as cine loop</td>
<td>Sagittal Tonsil</td>
<td>0.43 ± 0.06 mm</td>
<td>0.57 ± 0.04 mm</td>
</tr>
<tr>
<td>Hoffman et al., 2000</td>
<td>PC-MRI</td>
<td>C2 Spinal Cord</td>
<td>0.7 mL/s</td>
<td>1.3 mL/s *</td>
</tr>
<tr>
<td>Lawrence et al., 2017</td>
<td>PC-MRI</td>
<td>FM Spinal Cord</td>
<td>0.23 ± 0.08 mm</td>
<td>0.53 ± 0.30 mm *</td>
</tr>
<tr>
<td>Pujol et al., 1995</td>
<td>PC-MRI</td>
<td>Sagittal Tonsil</td>
<td>16 ± 7 index</td>
<td>46 ± 25 index *</td>
</tr>
<tr>
<td>Terae et al., 1994</td>
<td>Bolus tracking</td>
<td>Spinal Cord</td>
<td>None</td>
<td>&gt; Healthy</td>
</tr>
<tr>
<td>Yiallourou et al., 2012</td>
<td>Balanced TFE</td>
<td>Sagittal Tonsil</td>
<td>None</td>
<td>&gt; Healthy</td>
</tr>
</tbody>
</table>

* Significant difference in tissue motion found for patients versus controls (p < 0.05).