Chiari Academy Video Transcription
Beyond Tonsillar Position – Static Measures of Chiari

0:00

[Music]

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In the Bootcamp course, we explored both the origins of the radiological, 5mm definition of

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Chiari and the limitations of this definition. Specifically, we learned that research has

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repeatedly shown that in Chiari the amount of tonsillar herniation is not strongly related

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to symptom severity. We also learned that only a fraction of people who meet the radiological

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definition of Chiari will ever experience symptoms. Then in the last module, we evaluated

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the 5mm test quantitatively as we would any other disease biomarker. In scientific terms, we found

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that tonsillar herniation is a necessary but not sufficient component of symptomatic Chiari.

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In this module, we will turn our attention to the

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efforts of researchers to go beyond tonsillar position in attempting to

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explain Chiari at a fundamental level and to improve diagnosis and treatment.

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Not surprisingly, a large portion of these efforts have entailed looking

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for other radiological markers that are indicative of Chiari. At the highest level,

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these markers can be classified as either static, meaning measures of basic anatomy, or dynamic,

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meaning a measure of an active process in the human body. We will start by looking at

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the static measures, commonly referred to as morphometrics. Morphometrics means the study

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of the dimensions and shapes of living organisms and their anatomy, so with Chiari morphometrics

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involves taking quantitative measurements of the skull, brain, and spine from imaging.

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Morphometrics is one of the most active fields of Chiari research and a quick literature

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search with the keywords 'Chiari morphometrics' returns well over 100 publications. In Chiari,

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morphometrics research includes many different types of studies

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that can be categorized according to their purpose, imaging technology, and subjects.

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For example, in terms of purpose, morphometrics has and can been used to:

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• Identify differences between Chiari patients and healthy controls

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• Identify differences between different groups of Chiari patients

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• Explore the causative mechanisms of specific symptoms, and

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• Identify predictors, both positive and negative, of surgical outcome

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Meanwhile, the imaging technology can include but is not limited to different types of MRI's, CT

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scans, and even X-rays; while the subjects can be pediatric Chiari, adult Chiari, healthy controls,

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and though harder to find people with tonsillar herniation but no symptoms. Any given study can be

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a mix and match of these components. For example, a study might look at morphometric predictors

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of syringomyelia in pediatric females using conventional MRIs. Another study might use CTs to

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look for differences in the cervical spine between adult Chiari patients and healthy controls.

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Because morphometrics has such a broad scope and includes so many published studies,

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for the purposes of this module we will focus primarily on the morphometric differences

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between Chiari patients and healthy controls. We will further refine our focus to mainly

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adults. From a research point of view, studying children is much more complex

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and therefore more data is available on adult patients than pediatric ones.

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The origins of this type of research in Chiari can be traced back to the neurosurgeon,

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Thomas Milhorat's, landmark publication in 1999 on 364 patients. While the study included detailed

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clinical records and genetic testing, it also included a quantitative analysis of the posterior

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fossa and CSF spaces of 50 Chiari patients compared to age and gender matched controls.

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Recall that the posterior fossa is the area in the back of the skull that houses the cerebellum

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and brainstem. Milhorat found that the average posterior fossa volume for Chiari patients was

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smaller than the healthy subjects, but that the brain volume was the same. From this he

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theorized that the posterior fossa region for Chiari patients doesn't develop to its

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full size and the normally growing brain herniates out of the skull in response.

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He also found that every Chiari patient had reduced CSF space around the herniated tonsils.

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His finding that CSF spaces are reduced in Chiari patients has been shown to be true repeatedly over

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the years, but the small posterior fossa finding and theory is not as cut and dried. Over time,

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not all studies have found this to be true, and it appears that not every Chiari patient

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has a small posterior fossa. In addition, studies of large hospital imaging databases

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have shown that tonsillar position is normally distributed in the population, much like height,

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with nearly 1% of adults and even more children having a tonsillar position of

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5mm or more below the foramen magnum. This calls into question the small posterior fossa theory,

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or at the very least indicates that something else is going on as well.

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Over the ensuing years , morphometric analysis of Chiari has expanded to include many measures

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and evolved to use sophisticated software. Since Chiari does involve the cerebellar tonsils, most

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morphometric analysis is focused on the posterior fossa, skull base, and cranio-vertebral junction.

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In general, morphometrics research has identified five major areas where adult

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Chiari patients tend to have abnormal anatomy:

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• The height of posterior fossa structures • The size and angle of

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the clivus bone • The amount of space

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available for cerebrospinal fluid • The odontoid process, and

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• Stabilization of the atlanto-occipital and atlanto-axial joints

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If we look at a mid-sagittal MRI, which is essentially the head cut in half from

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nose to back, the posterior fossa is a 5 sided shape defined by the clivus bone on the left,

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the foramen magnum or McRae line at the bottom, the occipital bone on the right,

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the tentorium – which separates the cerebellum and the cerebrum – across the top,

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and finally a non-anatomical line connecting the top of the clivus and the tentorium. From this,

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researchers have looked at the length of the individual posterior fossa components,

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such as the clivus bone length, McRae line length, and occipital bone length,

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and of course the posterior fossa height, width, and area.

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Several studies have noted that in adult Chiari patients the clivus bone is significantly shorter

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and the McRae line length is significantly larger compared to healthy controls. Specifically,

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a large Conquer Chiari Research Center study of over 300 adult female Chiari patients and

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controls found that the clivus bone was about 3mm shorter and the McRae line 1mm

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longer on average with Chiari. For the occipital bone, results have been mixed,

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some studies have found it to be shorter in Chiari patients, but other studies have not

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found a difference. For the posterior fossa, the Conquer Chiari study found that while the height

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was significantly shorter in Chiari patients, the overall area was not significantly different.

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As we learned earlier, the McRae line is used as a reference to measure tonsillar position.

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The Conquer Chiari study went further and used the McRae line as a reference to measure the

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distance to three locations above the line, rather than below. Namely the fastigium which

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is a point where the fourth ventricle meets the cerebellum and is easy to see on an MRI;

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the pons, which is part of the brainstem; and the corpus callosum, which connects the right and left

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hemispheres of the brain. Much like the clivus bone, in Chiari patients, these distances are

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reduced on average by about 3mm, meaning that the entire hindbrain sags or sits lower, not just the

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cerebellar tonsils. Interestingly, one study found that these posterior fossa height reductions are

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even more pronounced among Chiari men, even though among adults Chiari predominantly affects women.

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The clivus bone has been the focus of several morphometrics studies.

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The clivus is part of the skull base which slopes up and backwards from the foramen magnum in the

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middle of the skull. In fact, clivus means “slope” in Latin. The pons, which is part of

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the brainstem, essentially sits on the clivus and the pituitary gland is located above the

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top of the clivus. Research has shown that in addition to being shorter in Chiari patients,

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the clivus bone can be angled differently. The clivo-axial angle is a widely used clinical

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measure which shows the angle of the clivus bone relative to the top vertebra. Studies

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have shown that the average clivo-axial angle among healthy adults is around 150 degrees and

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that a value of less than 135 degrees can indicate brainstem compression. Changes in

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the clivo-axial angle as the head tips forward and back can also indicate cervical instability.

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The clivus angle can also be measured relative to the McRae line;

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this is known as the Boogard angle . The average Boogard angle in healthy

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people is 126 degrees, and the medical consensus is that a Boogard angle of

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136 degrees or more indicates flattening of the skull base, also known as platybasia.

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With both angles, the average among Chiari patients is significantly different than

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healthy controls, but it is not beyond the radiological cut-offs mentioned above. However,

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there is tremendous variability in these angles among Chiari patients, and a subgroup of patients

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clearly do have abnormal clivus angles. In fact, data from the Chiari1000 indicates that out of

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474 adult female Chiari patients, a little more than 7% have a clivo-axial angle of 135 degrees or

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less and a similar percentage have a Boogard angle of 136 degrees or more. In addition,

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more than 10% are within 5 degrees of these somewhat arbitrary thresholds.

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While these MRI based findings are significant, a Conquer Chiari study of the clivus bone using CT's

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revealed even more dramatic differences. Bones can be difficult to measure on MRI, but CT's,

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which are a fast series of X-rays controlled by a computer, allow for very precise measurements

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of bones. This study compared the clivus bones of 30 adult female Chiari patients to 30 age and BMI

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matched controls. The study found that the overall clivus volume of the Chiari group was 31% smaller

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on average than the control group. This difference can be readily seen in these side by side images

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of a Chiari clivus and a healthy control clivus . The same study also looked at the sphenoid sinus

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which is the sinus cavity directly opposite the brainstem on the other side of the clivus and

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found that the sphenoid sinus was 38% larger in the Chiari group. Finally, the study looked at

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the area of the sella turcica which is a saddle like structure at the top of the clivus where the

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pituitary sits. In the Chiari group, this area was reduced by 27%. It is not clear what effect this

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reduced area has on the function of the pituitary in Chiari patients, if any, but it is interesting

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to note that the average BMI of Chiari patients is significantly higher than the national average.

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Interestingly, a short clivus bone seems to be one of the only morphometric measures

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consistent across Chiari patients with different comorbidities, or related conditions. A 2018 study

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used data from the Chiari1000 to compare 28 morphometric measures of over 200 adult female

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patients to healthy controls. Additionally, the Chiari patients were grouped by several

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related conditions, including: syringomyelia, EDS, intracranial hypertension, scoliosis,

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and cervical instability. Interestingly, only 4 measures were consistently different from

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controls across the different related condition groups, with a short clivus being one of them.

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Finally, a 2020 Conquer Chiari study found that a short clivus may distinguish healthy

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adults with low lying tonsils from symptomatic Chiari patients. This

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study evaluated seven morphometrics measures on 210 adult females with

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symptomatic Chiari and 90 female controls. The subjects were divided into 4 groups:

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• Healthy controls with a normal tonsillar position above the McRae Line

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• Controls with low-lying tonsils, defined as a tonsillar position of 1-5mm below the McRae Line

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• Chiari patients with a tonsillar position of 1-5 mm, and finally

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• Chiari patients with a tonsillar position of 6-13mm

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All seven morphometric measures were significantly different between the Chiari group with severe

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tonsillar descent and both control groups. The Chiari group with tonsillar position between

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1-5mm had 4 measures that were significantly different from the Control group with normal

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tonsillar position; however, between the Chiari and Control group with similar tonsillar position,

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meaning 1-5mm, clivus length was the only measure that was different.

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While these studies seem to indicate that the clivus bone may play an important role

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in symptomatic Chiari, the details of this connection remain a mystery. For example,

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it is not clear if the loss of clivus volume is from the bone not developing properly during

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childhood and this then somehow contributes to symptoms, or if the abnormal CSF pressure

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environment that exists with Chiari interferes with the natural growth and resorption of the

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clivus bone and the loss of volume is a biomarker of altered pressure environment.

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Speaking of CSF, next let's turn our attention to the CSF system, and specifically the spaces

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around the craniovertebral junction. Recall that CSF stands for cerebrospinal fluid,

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which is a clear liquid that circulates under the dura, bathing, protecting, and nourishing

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the brain and spinal cord. In a healthy adult, there is a fairly large collection of CSF just

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below the foramen magnum, on both sides of the spinal cord. On a mid-sagittal MRI these spaces

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can be referred to as the posterior, meaning behind, and anterior CSF spaces. In Chiari,

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the herniated tonsils reduce the amount of space available for CSF in the posterior region. In some

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patients, this reduction is minimal, while in others the available space is completely

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occupied by the herniated tonsils. If we measure the area of the posterior CSF space between

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the foramen magnum and the bottom of the second vertebra, on average there is a 25% reduction in

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adult female Chiari patients compared to healthy controls. Restoring this space is a major goal

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of Chiari surgery and why some surgeons choose to remove part of the tonsils during the procedure.

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Interestingly, in adult female Chiari patients, the anterior CSF space is also reduced by an

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average of 20%. What causes the anterior reduction is not clear, and there is also evidence that this

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reduction occurs primarily in adult women, not adult men, or children with Chiari.

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Before we discuss the final two areas where Chiari patients tend

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to have altered morphometrics, we need to take a moment to review some anatomy

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around where the skull meets the spine. Head movement involves two main joints,

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the atlanto-occipital joint, and the atlanto-axial joint.

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The atlanto-occipital joint is where the skull, or cranium, rests on the first cervical vertebra,

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also known as the atlas. Basically, the cranium has two protuberances,

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one on each side, called condyles that sit into depressions on each

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side of the atlas. This enables the head to move forward and backward.

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The atlanto-axial joint is the connection between the top spinal vertebra, the atlas,

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and the second vertebra, known as the axis. The axis has a bony projection called the

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odontoid process that passes through the atlas and enables rotational movement of the head.

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The two joints and their associated movements

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are controlled and stabilized by the cervical paraspinal muscles,

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the suboccipital muscles, and a series of ligaments and other connective tissues.

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Starting with the odontoid, in Chiari patients, or more accurately a subset of Chiari patients,

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the odontoid process can push too high into the skull base in what is called basilar invagination.

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It can also be angled in towards the spinal canal and brainstem in what is called retroflexion. This

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can cause compression of the brainstem from the front side and can lead to the brainstem bending,

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or kinking, around the odontoid. This subset of patients, which some clinicians

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call Complex Chiari, may also experience cervical instability, and often require additional surgical

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procedures to relieve the pressure caused by the odontoid and to stabilize the cervical spine.

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In general, the morphometric measures that have developed around the odontoid process

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are more clinical in nature as opposed to having a research focus. As such,

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they tend to have specific cut-off values which are suggestive of basilar invagination,

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brainstem compression, or instability. In general,

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they are used to help surgeons decide when additional procedures are necessary.

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For example, with basilar invagination, several measures have been suggested that involve where

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the top of the odontoid is located relative to a horizontal line on a mid-sagittal image,

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such as the McRae line. If the top of the odontoid is above one of these reference lines

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by a specific amount, then it is suggestive of basilar invagination. A large German study of over

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300 adult, surgical Chiari patients found that 14% met one of the most common imaging definitions of

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basilar invagination. However, it is important to note that this was surgical cases only,

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so if non-surgical cases were included the percentage would likely be much lower.

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For ventral brainstem compression, meaning from the front, Grabb-Oakes is one of the

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most used measures. Grabb-Oakes is a distance that assesses how far the tip of the odontoid

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pushes into the spinal canal and a value of more than 9mm is considered suspicious

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for brainstem compression. Data from the Chiari1000 indicates that about

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11% of adult female Chiari patients have a Grabb-Oakes measure of 9mm or more. However,

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the same data reveals that the average Grabb-Oakes distance for the Chiari group is not significantly

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different than for healthy controls and is well below the clinical cut-off value. So much like

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with the small posterior fossa, not every Chiari patient has odontoid irregularities.

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Instability of the atlanto-axial joint is a recognized issue among a subset of

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Chiari patients but does not have a widely accepted morphometric definition. Certain

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static measures can be suggestive of cervical instability, but the research is mixed in how

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useful these measures are. If cervical instability is suspected, some surgeons will order dynamic

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MRIs which are a series of scans taken with the head and neck in different positions. But again,

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there are no widely accepted criteria for when a dynamic MRI should be used or how to

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interpret the results. The role that cervical instability may play in symptomatic Chiari

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will be discussed more in a later module when we are reviewing Chiari theories,

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but currently, it is not clear if odontoid and cervical instability issues are limited

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to a small subset of Chiari patients or if small anatomical variations in this

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region are important and thus involve more Chiari patients than initially suspected.

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There is research that indicates Chiari patients in general may

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have subtle instability issues around the atlanto-occipital and atlanto-axial joints.

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For example, the paraspinal muscles are the groups of muscles that surround the spine,

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enabling movement and providing stability. One small study found that the cervical

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paraspinal muscles were smaller on average in Chiari patients than in healthy controls. The

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study also found that the reduced muscle mass was more pronounced in patients with

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neck pain than in those without neck pain. However, it is not clear if the reduced size,

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and presumably strength, occurs developmentally and is part of Chiari anatomy, or if it is a

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result of nerve damage due to the herniated tonsils and altered CSF pressure environment.

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In this study there was a modest correlation between duration of symptoms and reduced muscle

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size suggesting that it could be due to loss of nerve function in the affected muscles.

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Research has also found altered stabilizing ligaments and membranes in Chiari patients.

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The transverse ligament spans across the top vertebra, the atlas, and is the main

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source of support for the odontoid process. The alar ligaments connect each side of the

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foramen magnum to the odontoid process. One study found that the transverse ligament is

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about 7% shorter and the alar ligaments are 18% shorter in Chiari patients compared to

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healthy controls. Meanwhile, the posterior atlanto-occipital membrane is a broad

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membrane that connects the back of the skull to the back of the top vertebra.

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It is routinely removed during Chiari surgery and a microscopic analysis of removed samples found

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the connective tissue fibers that comprise the membrane were disorganized in Chiari patients,

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meaning oriented in different directions rather than parallel, and that the membrane

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had a higher fat content than normal. The cause and effects of these ligament

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and membrane alterations in Chiari need to be researched further.

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Finally, a Chinese study found that the atlanto-occipital joints, meaning where

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the occipital condyles fit into the depressions on the atlas, are nearly 40% more shallow in

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Chiari patients than healthy controls. This suggests that many Chiari patients may have

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subtle instability in this joint, and unlike the muscle and ligament alterations, this bony

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abnormality is more likely to be a contributing factor of symptomatic Chiari than an effect of it.

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In most of the studies discussed so far Chiari patients were compared to healthy

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control subjects, but to look beyond tonsillar position it would be beneficial to look at people

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with tonsillar herniation greater than 5mm but without symptoms. Some studies have used

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hospital records to identify such cases, but then the question becomes if they are in the

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hospital are they truly asymptomatic, or did a doctor just decide the symptoms were not due to

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Chiari? Conquer Chiari researchers found a way around this dilemma by leveraging the federal

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Adolescent Brain Cognitive Development study. The ABCD study as it is called involves over

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10,000 adolescents recruited through schools throughout the US who undergo MRIs every two

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years and are evaluated for a broad range of physical, mental, and behavioral issues.

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Using this massive database, the Conquer Chiari researchers identified 106 adolescents

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with tonsillar position greater than 5mm. They then pulled 106 controls from the same

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database who were matched individually by age, sex, BMI, race, and ethnicity.

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None of the subjects with tonsillar herniation displayed any symptoms or were different in any

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way from the controls in terms of health and behavior. However, morphometric analysis found

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that their anatomies were strikingly like what is seen in adult Chiari, with short clivus bones,

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reduced CSF spaces, etc.; indicating that a Chiari like anatomy, even beyond tonsillar position,

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does not always cause symptoms. In fact, researchers have struggled to connect

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morphometrics measures to specific symptoms, overall symptom severity, and surgical outcomes.

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While research has identified many anatomical differences in Chiari patients,

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a lot of these differences are small in absolute terms. So even though they may be significantly

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different in a statistical sense, that does necessarily equate to a meaningful difference.

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It’s also important to keep in mind that Chiari patients are a varied group. So,

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while some may have small posterior fossas, and others may have odontoid irregularities,

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for pretty much every morphometric measure, there are patients who are within the normal

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range for that anatomical feature. For example, a Conquer Chiari study of over 400 adults found

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that while the average clivus length is significantly shorter for Chiari patients,

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more than 60% of the same Chiari patients had a clivus length well within the normal range.

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Overall, it appears that an altered anatomy in the craniovertebral region,

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like tonsillar herniation, is only part of the story when it comes to Chiari. That is why some

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researchers have begun to look at dynamic processes in Chiari patients to understand

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how and why people become symptomatic, which is the subject of the next module.

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Key Points:

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• Many Chiari patients have anatomical differences compared to healthy people that

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extend beyond the herniated cerebellar tonsils. • Significant findings in static morphometric

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studies include reduced posterior fossa volume,

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clivus bone anomalies, alterations in CSF spaces, and abnormalities in

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the odontoid process and atlanto-axial joints. • However, it has been difficult to link these

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differences to specific symptoms or outcomes. • Further research is needed to better

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understand the implications of morphometric differences in Chiari.