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The conus medullaris ratio: A new way to identify tethered cord on MRI

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ABSTRACT

Purpose: Approximately 25% of patients with anorectal malformation have tethered cord. The traditional way of determining conus medullaris level on magnetic resonance imaging (MRI) relies on counting vertebrae, which may be challenging due to vertebral numeric variation, segmentation anomalies, as well as transitional vertebral body anatomy. The purpose of this study was to utilize more reliable anatomic landmarks (foramen magnum, conus termination, and the upper limit of the iliac crest) to establish a consistent ratio that may differentiate patients with normal and low-lying conus.
Methods: A single institution database search identified two groups of patients: 255 with normal and 85 with abnormal spinal MRI, who underwent tethered cord release. The conus medullaris ratio was calculated in both groups. The ratio was obtained by dividing the distance between the conus level and the iliac crest by the distance between the foramen magnum and the conus level (IRB # 16–2330).
Results: The mean ratio was significantly higher in the non-tethered group compared to the tethered patients (0.184 [sd 0.03] versus 0.118 [sd 0.09]; $P < .0001$). The ratio proved to be a good discriminator between normal and abnormal patients, with area under the curve (AUC) equal to 0.749, meaning that at random, there is a 75% chance that the tethered cord patient will have a lower ratio than the non-tethered cord patient.
Conclusion: "The Conus Medullaris Ratio" is a good predictor of low-lying conus level on MRI and offers an easy alternative to counting vertebral body levels, particularly in patients with variant or abnormal vertebral body anatomy.
Level of Evidence: II, Study of Diagnostic Test.

Approximately 25% of patients with anorectal malformation have tethered cord [1]. This condition has important clinical and prognostic implications and, therefore, must be diagnosed early on in childhood. These patients, however, may also have sacral abnormalities (hemi-sacrum, short sacrum with a sacral ratio <0.4) [2], and anomalous level of the rectum (i.e. recto-bladder neck fistula), both of which can result in a neurogenic bowel and bladder. This makes the diagnosis of tethered cord and justification for the treatment thereof, a controversial one [3–9].

Part of the diagnosis of tethered cord on imaging is often made by identifying a low-lying conus medullaris, which is defined as the conus medullaris terminating below the inferior endplate of second lumbar vertebrae (L2) [10]. Tethered cord syndrome refers to patients with either a low-lying conus medullaris and/or a known tethering lesion on magnetic resonance imaging (MRI) in the presence of signs and symptoms such as pain and or neurological, orthopedic deficits, neurogenic bladder and bowel, leg or foot length discrepancy, foot deformities, and gait abnormalities [11]. Imaging screening strategies for newborns with potential cutaneous markers of cord tethering aim to diagnose potential tethered cord prior to onset of symptoms, which are traditionally thought to be irreversible.

The traditional method of determining the level of the conus medullaris relies on counting segments superiorly from L5-S1 or inferiorly from C1. The task may be complicated by variations in the number of vertebrae, segmentation anomalies, or transitional vertebral anatomy. As such, the conus level may differ when counting from below versus counting from above.

Our goal was to utilize more reliable anatomic landmarks (foramen magnum, conus termination, and the upper limit of the iliac crest) to create a ratio to differentiate patients with normal and low-lying conus, obviating the need to count vertebral body levels in patients with non-classical anatomy.

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1. Methods

The study period was from January 1, 2009 until October 1, 2017. The study had two phases of data collection. During the first phase, single institution database search in radiology and neurosurgery identified 208 patients: 150 with normal and 58 with abnormal spinal MRI, who underwent tethered cord release. The Conus Medullaris Ratio was obtained by dividing the distance between the conus level and the iliac crest by the distance between the foramen magnum and the conus level. The conus medullaris ratio was calculated in a straight and curved fashion on all 208 patients (Figs. 1 and 2).

During the second phase, an additional 132 patients were enrolled, 105 with normal and 27 with abnormal spinal MRI. Because the conus medullaris straight and curved ratios were highly correlated in the initial phase, only the straight ratio was calculated for these additional patients (Fig. 2).

The straight ratios from all 340 patients (255 normal and 85 abnormal spinal MRI) were then used to test how well the ratio discriminated between normal and abnormal patients.

IRB approval was obtained for this study (# 16–2330).

1.1. Statistical methods

The Pearson's correlation coefficient (r) was used to test for correlation between the straight and curved ratio following the initial data collection phase. There was a high correlation between the straight and the curved ratio ($r = 0.995$) in the initial 208 patients, so it was decided that only the straight ratio would be used for the remainder of the study (Fig. 3). Age and gender were compared between the tethered cord and non-tethered cord groups with an independent two sample t-test and a chi-square test, respectively. Due to skewness, the straight ratio was summarized by median and interquartile range (IQR) and a Wilcoxon rank sum test was used to compare the ratio in tethered cord and non-tethered cord patients.

To assess how well the ratio discriminated between tethered cord and non-tethered cord patients, a receiver operating curve (ROC) was produced and the area under the curve (AUC) was calculated. There was no independent dataset available to perform external validation of the discriminatory ability of the ratio. Instead, internal validation was done by the "leave one out" methodology and the resulting AUC was reported. The sensitivity and specificity of each possible cut-off value of the ratio was calculated and taken into consideration when choosing a final cut-off.

The significance level and P value was set at 0.05 and SAS version 9.4 was used for all statistical analysis.

2. Results

The distribution of gender was similar within the abnormal and normal spinal MRI groups (Table 1). Those with abnormal spinal MRI were significantly older compared to those with normal spinal MRI (mean $\pm$ sd: 1.3 $\pm$ 1.6 years vs 0.6 $\pm$ 0.5).

Of the patients who underwent surgery, 74 of them had a fibrolipoma of the filum terminale.

There were 11 patients with more complex tethering lesions, these included 6 lipomyelomeningoceles, 3 dermal sinus tracts, 1 sacral teratoma, and 1 patient with an intraspinal tumor.

Patients with tethered cord had significantly lower ratios compared to patients without tethered cord (median (IQR): 0.14 (0.09, 0.18) vs. 0.18 (0.16, 0.21); $p < 0.0001$) (Fig. 4).

An ROC curve was produced to determine how well the ratio could discriminate between tethered and non-tethered patients. The area under the curve (AUC) was 0.75 (95% CI: 0.65–0.80). Cross-validation was performed using the "leave one out" methodology, and the AUC

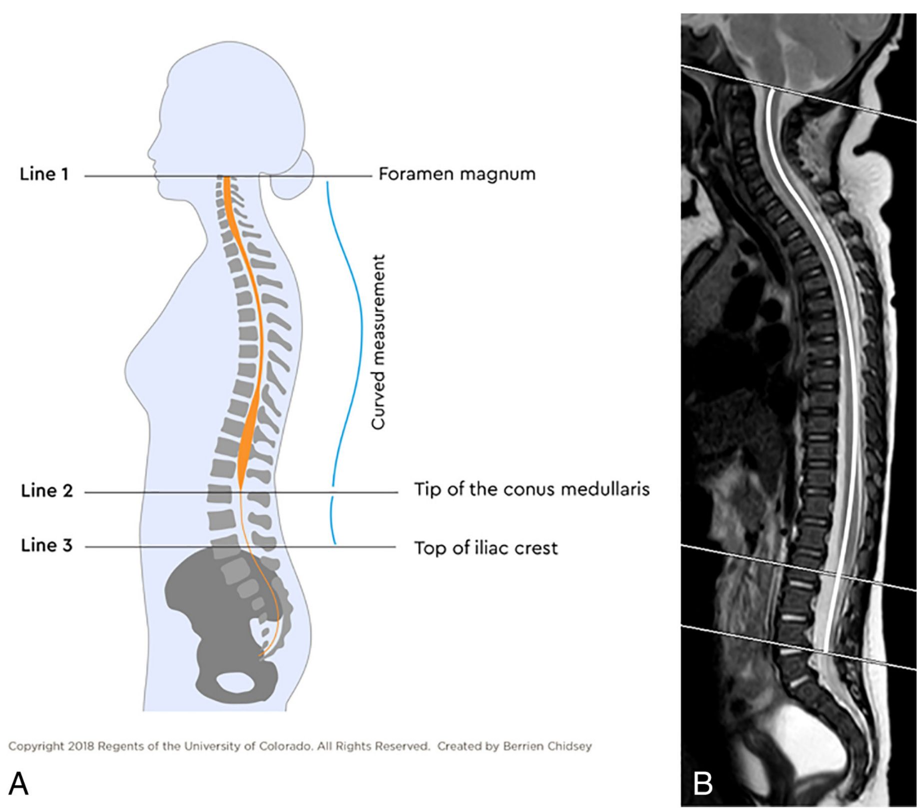

Fig. 1. The Conus Medullaris Ratio. A, Diagram showing how the curved measurement is obtained following the spine curvature, at the selected anatomic landmarks. The ratio is calculated by dividing the distance between lines 2 and 3, divided by the distance between lines 1 and 2. B, MRI showing the curved measurement.

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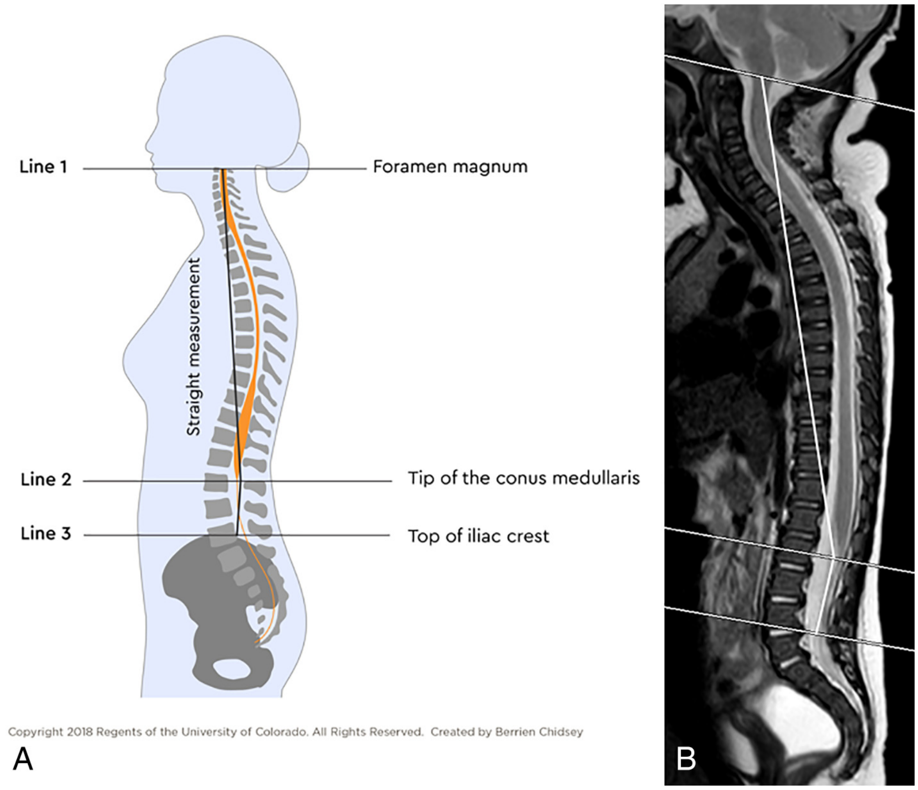

Fig. 2. The Conus Medullaris Ratio. A, Diagram showing how the straight measurement is obtained by drawing a straight line from the selected anatomic landmarks. The ratio is calculated by dividing the distance between lines 2 and 3, divided by the distance between lines 1 and 2. B, MRI showing the straight measurement.

was 0.72 (95% CI: 0.68–0.82), which did not decrease much from the original AUC.

A cut-off was chosen based on the sensitivity and specificity of all possible ratio values. Based on the obtained ratio values, patients with ratios of 0.10 or lower all had low-lying conus, and patients with a ratio of 0.29 and above all had normal conus level (Fig. 4). By choosing a cut-off between 0.11 and 0.28, some patients will be misdiagnosed. The study team decided on a cut-off by weighing the importance of sensitivity and specificity. The cut-off 0.15 was selected for a 0.79 sensitivity and 0.81 specificity to detect low lying conus.

Because of the significant difference between the two groups in terms of age, a sensitivity analysis was performed to see if age significantly influenced the results. We subsetted the data to include only patients who were 0–2 years of age, as the majority of patients from the original analysis fell within this age range. This left 255 in the normal and 69 in the abnormal spinal MRI group. Age was no longer significantly different between groups (0.64 ± 0.52 vs. 0.67 ± 0.51; p = 0.64). After following the same procedure as outlined above for the full dataset, the AUC for the 0–2 year subset was 0.77. The cross-validated AUC was 0.75.

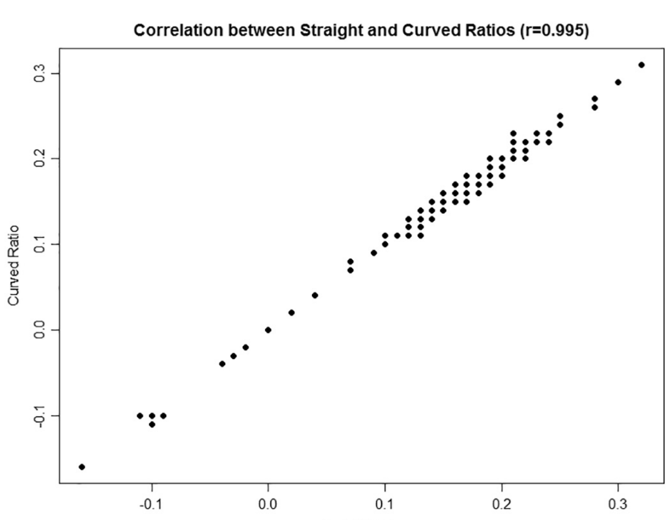

Fig. 3. Correlation between straight and curved ratios (r = 0.99).

3. Discussion

Clinicians caring for patients with anorectal malformations have long struggled with the diagnosis and management of tethered cord. Patients and parents frequently request the pediatric surgeon's opinion when agonizing between the decision to operate without clear symptoms of tethered cord syndrome vs. contemplating the condition and risking being late with irreversible changes. Many of these patients already have neurogenic bowel and bladder as a result of their primary malformation, and the quality of their sacrum; raising a serious question on the clinical implications of tethered cord as well as the clear benefit of a prophylactic de-tethering in this group of patients.

A "tethered cord effort group" including neurosurgery, neuroradiology, pediatric surgery, and urology was created at Children's Hospital Colorado in an attempt to better answer these questions. During the first meetings, it became clear the need for a more standardized approach

Table 1
Demographics.

Demographic variable	Tethered cord (TC)	Non-tethered cord (non-TC)	p Value
Sex			
Male *n* (%)	140 (55%)	40 (47%)	0.26
Female *n* (%)	116 (45%)	45 (53%)	
Age (*mean* ± *SD*)	1.3 ± 1.6 years	0.6 ± 0.5 years	<0.0001

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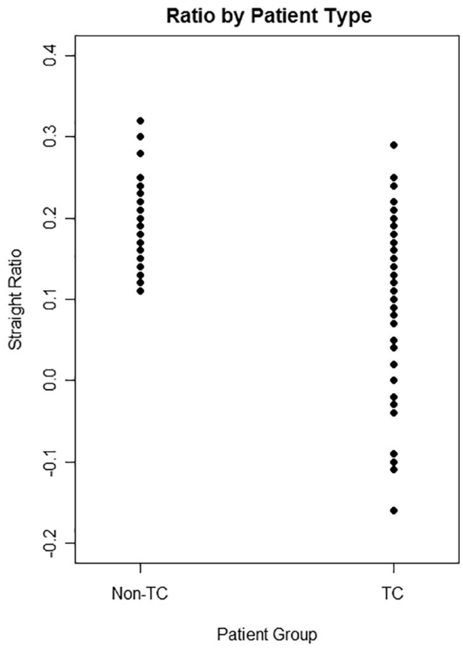

Fig. 4. Ratio by patient type.

for the diagnosis of low-lying conus on MRI to help to better categorize those patients, since the clinical diagnosis relies heavily on imaging. The idea was to have values that would aid on the diagnosis and be able to discriminate the severity of the condition. It would be important that the numeric value identified could be used at different ages, instead of a simple newborn measurement, because in our clinical practice, patients are first seen and imaged at a variety of ages. A ratio seemed to be an ideal way to account for differences in patient size.

For the purpose of this study, the definition of tethered cord was any patient who underwent tethered cord release and had a pre-operative MRI available for review. To that end, the MRI required a sequence of the entire spine, to identify the prescribed landmarks for the ratio. At our institution, a large field of view sequence is obtained in all "tethered cord" lumbar spine MRI, to assist with vertebral body counting. Patients with more complex surgery or other surgical indications were excluded, limiting the available number of patients that could be included in the study. We have not intentionally tried to make groups similar on age and gender, as our priority was to meet the inclusion criteria. This is a limitation of our study, and will grant further investigation to validate our results at different age groups. However, the sensitivity analysis that limited the age range to 0–2 years old demonstrated that our results may have underestimated how well the ratio discriminates between tethered cord and healthy children. We plan to enroll more patients from a wider age range to validate these results in the future.

We initially believed that the variation in spinal curvature in different patients would introduce additional error or uncertainty into measurements. For this reason, the ratio was initially calculated using a traditional straight line measuring the distance between the selected anatomic landmarks, and using a curved measurement following the spinal curvature. Straight and curved measurements can easily be obtained in PACS (picture archiving and communication system). After the initial data was collected, the similarities between the straight and curved ratios were striking and the impression that there was no difference was confirmed by a high correlation coefficient. This was fortunate, since the curved measurement is more challenging to perform than the straight one.

The area under the curve of 0.749 can be interpreted as: "if you were to choose a tethered cord patient and a non-tethered cord patient at random, there is an 75% chance that the tethered-cord patient will have a lower straight ratio than the non-tethered cord patient". An AUC of 0.75 is considered good [12], and we hope the AUC will increase when we consider more patients from a wider age range.

Finding a more standardized way to diagnose low-lying conus on MRI is the beginning of several future studies that our group aims to address properly and find answers to a very controversial subject such as tethered cord in patients with anorectal malformations.

In conclusion, we believe that the "Conus Medullaris Ratio" is a good predictor of low lying conus level on MRI and offers an easy alternative to avoid the need for vertebral counting, especially in patients with nonstandard vertebral anatomy.

Appendix A. Discussion

Presenter: Andrea Bischoff

Q: **(Identity Uncertain)** I may have missed the point a little bit, but what was the gold standard for defining what is a tethered cord?

A: Bischoff (Denver, Colorado) The defined gold standard is that the conus extends below L2, but the problem is that not all patients have the same amount of vertebra. The way the radiologists do it, is to count the vertebra from above or from below. Sometimes they are not sure if the conus level is normal or abnormal, since there is a difference between the above and below counts. Although I thought that there was indeed a standard, working on this paper with a neuroradiologist and a neurosurgeon, I was surprised to find out that it is not that easy for them to determine where the conus level is.

Q: (same unknown) But the measure you are using for the tethered cord is still L2?

A: Bischoff Yes

Q: (same unknown) So is it tethered at surgery?

A: Bischoff Well for the "tethered cord" group we included those who had the conus below L2 and had undergone release.

Q: Abraham Cherian, Great Ormond Street Hospital, London What is the current practice of neurosurgeons in your center with regard to finding an anomaly. Do they wait for symptoms or do they release the tethered cord prophylactically?

A: Bischoff As you know tethered cord is one of the most controversial issues on earth and I think I am going to dedicate my future career to try and clarify that! In the USA, because our practice is so concerned about future lawsuits if they find tethered cord or if the report says below L2 they will normally offer a prophylactic de-tethering procedure. Indeed I am not even sure of how effective this is as even if it is indicated we have seen patients that get worse, patients where it makes no difference and only some patients get better. So I think we have to clarify the indication. In my population of patients with anorectal malformations that have sacral anomalies and other reasons to have neurogenic bladder and bowel, I think it is even more controversial.

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