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Standardization and validation of a novel and simple method to assess lumbar dural sac size

M.L.A. Daniels [a,*], J.R. Lowe [a], P. Roy [b], M.V. Patrone [a], J.M. Conyers [a], J.P. Fine [b], M.R. Knowles [a], K.R. Birchard [c]

[a] Department of Medicine, UNC School of Medicine, Chapel Hill, NC 27599, USA
[b] Department of Biostatistics, UNC at Chapel Hill, Chapel Hill, NC 27599, USA
[c] Department of Radiology, UNC School of Medicine, Chapel Hill, NC 27599, USA

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AIM: To develop and validate a simple, reproducible method to assess dural sac size using standard imaging technology.

MATERIALS AND METHODS: This study was institutional review board-approved. Two readers, blinded to the diagnoses, measured anterior–posterior (AP) and transverse (TR) dural sac diameter (DSD), and AP vertebral body diameter (VBD) of the lumbar vertebrae using MRI images from 53 control patients with pre-existing MRI examinations, 19 prospectively MRI-imaged healthy controls, and 24 patients with Marfan syndrome with prior MRI or CT lumbar spine imaging. Statistical analysis utilized linear and logistic regression, Pearson correlation, and receiver operating characteristic (ROC) curves.

RESULTS: AP-DSD and TR-DSD measurements were reproducible between two readers ($r = 0.91$ and 0.87, respectively). DSD (L1–L5) was not different between male and female controls in the AP or TR plane ($p = 0.43$; $p = 0.40$, respectively), and did not vary by age ($p = 0.62$; $p = 0.25$) or height ($p = 0.64$; $p = 0.32$). AP-VBD was greater in males versus females ($p = 1.5 \times 10^{-8}$), resulting in a smaller dural sac ratio (DSR) (DSD/VBD) in males ($p = 5.8 \times 10^{-6}$). Marfan patients had larger AP-DSDs and TR-DSDs than controls ($p = 5.9 \times 10^{-9}$; $p = 6.5 \times 10^{-9}$, respectively). Compared to DSR, AP-DSD and TR-DSD better discriminate Marfan from control subjects based on area under the curve (AUC) values from unadjusted ROCs (AP-DSD $p < 0.01$; TR-DSD $p = 0.04$).

CONCLUSION: Individual vertebrae and L1–L5 (average) AP-DSD and TR-DSD measurements are simple, reliable, and reproducible for quantitating dural sac size without needing to control for gender, age, or height.

Introduction

Patients with heritable connective tissues disorders (HCTD), such as Marfan syndrome, Ehlers–Danlos syndrome (EDS), and Loeys–Dietz syndrome (LDS), show diverse manifestations of disorganized connective tissue matrices, particularly in the cardiovascular and skeletal systems. Lung disease in Marfan patients includes apical blebs and spontaneous pneumothorax, and is included in the systemic score of the Ghent criteria for Marfan syndrome.[1] These patients also have an increased frequency of pneumonia and bronchiectasis.[2–8] Although dural ectasia, dilation of the dural sac surrounding the spinal cord, is

* Guarantor and correspondent: M.L.A. Daniels, 7019 Thurston-Bowles Bldg, CB 7248, Chapel Hill, NC 27599, USA. Tel.: +1 919 966 6780; fax: +1 919 966 7524.
E-mail address: Leighanne_Daniels@med.unc.edu (M.L.A. Daniels).

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sensitive for the diagnosis of Marfan syndrome,[9–11] it is not specific and can be seen in LDS and variant EDS.[1,12–14] Data regarding the presence of both dural ectasia and lung abnormalities in HCTD patients is limited. In one study, ~10% of 138 Marfan patients had apical blebs or spontaneous pneumothorax, even though ~50% had dural ectasia; however, it is unclear how many patients had both lung disease and dural ectasia.[15] In another study of 33 patients with Marfan-like features without mutations in *FBN1*, *TGFβR1*, or *TGFβR2*, two patients had spontaneous pneumothorax and dural ectasia.[16]

The present authors have studied dural ectasia in patients with HCTD and idiopathic bronchiectasis because of the physical morphological similarities in idiopathic bronchiectasis and Marfan patients. However, there is currently no preferred method for quantification of dural sac size in the literature,[10] and a method that has been validated in normal and diseased subjects is needed. Published methods of quantitating dural ectasia do not routinely account for the effects of gender, height, or age. The most widely used approaches are those published by Oosterhof,[17] Habermann,[18] Lundby,[19] and Ahn.[20] The Oosterhof, Habermann, and Lundby methods rely on a dural sac "ratio" (DSR), calculated by dividing the lumbar anterior–posterior (AP) dural sac diameter (DSD) by the AP vertebral body diameter (VBD), as determined via MRI or CT imaging. All of these methods also focus on S1 measurements (either DSD or DSR). Conceptually, S1 should demonstrate robust dural ectasia in Marfan syndrome, as it is the most caudal and has the greatest cerebrospinal fluid (CSF) pressures in an upright position. However, the S1 vertebra is structurally different compared with the lumbar vertebrae in several ways, which may confound measurements. The five sacral vertebrae fuse to form the sacrum,[21] and the sacral base is pitched forward, creating the sacrovertebral angle,[22] which progressively increases from 20° at birth to 70° by adulthood. Although the sacrum is larger in men,[23] none of the published assessments of DSR account for potential differences in size of dural sac or vertebral body due to gender, height, age, or race. This is despite recognition that the AP diameters, TR diameters, and volumes of all the lumbar vertebral bodies are smaller in women as compared to men, even when matched for age, height, and weight.[24] Cross-sectional vertebral area is also significantly smaller in women as compared to age-matched men.[25,26]

The aim of the present study was to develop and validate a simple, reproducible, standardized method of quantitating dural sac size, and assess for the effects of gender, height, age, and race by using measurements from a large healthy control population. Measurements were also performed in a smaller group of Marfan syndrome patients for comparison.

Materials and methods

The local institutional review board approved the present study. Informed consent was waived for evaluation of pre-existing MRI images; informed consent and MRI safety screening forms were completed in prospective subjects. All data were recorded in a Health Insurance Portability and Accountability Act (HIPAA)-compliant protected database.

Patients

Normal adult (>18 years of age) control subjects ($n = 53$) who had normal pre-existing MRI examinations of the lumbo-sacral spine, obtained for clinical purposes, were used in a retrospective fashion. Normality was determined by a consensus of the MRI examination report, and re-review by a radiologist with >10 years of experience. Clinical information from medical records was used to exclude patients with definite or possible HCTD, lung disease, or any spinal disease not recognized on the MRI examination. Measurements were not made on imaging from these excluded individuals. Subsequently, healthy adult controls ($n = 19$), matched by age and gender to the retrospective control group, were prospectively enrolled for lumbo-sacral MRI examinations (Supplementary Material Fig S1). Exclusion criteria for all subjects included severe thoracic or lumbar scoliosis, thoracic or lumbar spine surgery, spinal stenosis, or spine injury. Exclusion criteria for the prospectively enrolled healthy controls included: presence of lung disease; bone or connective tissue disease (including hypermobility); history of malignancy; endocrine disorder requiring medication; atopy; chronic or recurrent systemic steroids; ≤50 years of age taking prescription medications; and >50 years of age taking prescription medication except for hypertension or hyperlipidaemia. An additional 24 subjects carrying a genetic or clinical diagnosis of Marfan syndrome and had a pre-existing MRI or CT examination of the lumbo-sacral spine available for measurement were included for comparison.

Imaging protocol

Both pre-existing and prospective lumbar MRI examinations were performed using a Siemens (Iselin, NJ, USA) 1.5 T Avanto or 3 T Biograph MRI machine. Pre-existing spine MRI images were generated using a clinical unenhanced protocol; T2-weighted 5 mm axial and sagittal images were viewed on an Agfa (Mortsel, Belgium) PACS workstation using standard Agfa measuring tools and were amenable to 3D manipulation with the Agfa PACS tools. Prospective scans were performed using a single unenhanced 7 min MRI sequence [T2-weighted 3-dimensional (3D) turbo spin echo without fat suppression], which yielded a single 3D-dataset. From this dataset, 1.5 mm images in the axial, sagittal, and coronal planes were reconstructed at the scanner workstation and evaluated on the same Agfa PACS station.

Image analysis

All examinations were reviewed by a board-certified radiologist with >10 years of experience (reader 1) and a second-year medical student (reader 2), both of whom were blinded to diagnosis. Reader 2 was trained on measurement techniques by the radiologist, and completed several practice cases under supervision before measuring study cases.