Research in Developmental Disabilities 35 (2014) 215–222

Contents lists available at ScienceDirect

Research in Developmental Disabilities

Heterogeneity of muscle fat infiltration in children with spina bifida

Tishya A.L. Wren [a,*], Skorn Ponrartana [b], Alexander Van Speybroeck [c], Deirdre D. Ryan [d], Jonathan M. Chia [e], Houchun H. Hu [b]

[a] Children's Orthopaedic Center and Department of Radiology, Children's Hospital Los Angeles, United States
[b] Department of Radiology, Children's Hospital Los Angeles, United States
[c] Department of Pediatrics, Children's Hospital Los Angeles, United States
[d] Children's Orthopaedic Center, Children's Hospital Los Angeles, United States
[e] Philips Healthcare, United States

ARTICLE INFO

Article history:
Received 24 July 2013
Received in revised form 30 September 2013
Accepted 1 October 2013
Available online 26 October 2013

Keywords:
Spina bifida
Myelomeningocele
Muscle fat fraction
Water-fat MRI

ABSTRACT

Children with spina bifida have well recognized functional deficits of muscle, but little is known about the associated changes in muscle anatomy and composition. This study used water-fat magnetic resonance imaging (MRI) to measure fat infiltration in the lower extremity muscles of 11 children with myelomeningocele, the most severe form of spina bifida. MRI measurements of muscle fat fraction (FF) were compared against manual muscle test (MMT) scores for muscle strength. The FF measurements were objective and reliable with mean inter-rater differences of <2% and intraclass correlation coefficients > 0.98. There was a significant inverse relationship between muscle FF and MMT scores ($P \leq 0.001$). Surprisingly, however, muscles with negligible strength (MMT 0–1) exhibited a bimodal distribution of FF with one group having FF > 70% and another group having FF < 20%. The MRI also revealed striking heterogeneity amongst individual muscles in the same muscle group (e.g., 4% fat in one participant's lateral gastrocnemius vs. 88% in her medial gastrocnemius), as well as significant asymmetry in FF in one participant with asymmetric strength and sensation. These results suggest that quantitative water-fat MRI may serve as a biomarker for muscle degeneration which may reveal subclinical changes useful for predicting functional potential and prognosis.

Spina bifida is a congenital disorder caused when the neural tube fails to close properly in utero. Myelomeningocele is the most severe type of spina bifida. In myelomeningocele, part of the spinal cord protrudes outside the spinal column in a fluid-filled sac, resulting in spinal cord damage and paralysis or weakness in muscles of the lower limbs. The current standard for clinical evaluation of lower extremity muscle function in spina bifida is manual muscle testing (MMT). However, MMT provides only a semi-quantitative assessment that can be dependent on the individual performing the evaluation and the effort exerted by the person being tested. Physical assessment also has only limited ability to predict future function. Despite the well-recognized functional deficits of muscle in children with myelomeningocele, there is a lack of literature describing the associated changes in muscle anatomy and composition.

Magnetic resonance imaging (MRI) may be able to provide more quantitative and objective measurements of muscle integrity and detect subclinical changes that may be suggestive of future changes in function. MRI is non-invasive, does not

* Corresponding author at: Children's Hospital Los Angles, 4650 Sunset Boulevard, MS #69, Los Angeles, CA 90027, United States. Tel.: +1 323 361 4120; fax: +1 323 361 1310.
E-mail address: twren@chla.usc.edu (Tishya A.L. Wren).

0891-4222/$ – see front matter
http://dx.doi.org/10.1016/j.ridd.2013.10.002

involve ionizing radiation, and can provide rapid three-dimensional visualization of all muscles in the upper and lower legs, allowing for investigation of individual muscles. It is a recognized tool for quantifying muscle volume, fatty infiltration, and edema (Hollingsworth, de Sousa, Straub, & Carlier, 2012). In particular, recent developments in water-fat MRI techniques have advanced the accurate and precise quantification of fatty infiltration in skeletal muscles (Alizai et al., 2012; Bley, Wieben, Francois, Brittain, & Reeder, 2010; Karampinos, Yu, Shimakawa, Link, & Majumdar, 2011), and application of water-fat MRI in studies of Duchenne muscular dystrophy over the past decade has established a relationship between muscle fat fractions and disease progression (Kinali et al., 2011; Wokke et al., 2013; Wren, Bluml, Tseng-Ong, & Gilsanz, 2008). In addition to skeletal muscle, the utility of water-fat MRI in assessing fatty infiltration has been rigorously validated in abdominal organs, including the liver, heart, and pancreas, as well as in bone marrow (Alizai et al., 2012; Bley et al., 2010; Hu, Kim, Nayak, & Goran, 2010; Karampinos et al., 2011, 2013; Kellman et al., 2009; Reeder, Cruite, Hamilton, & Sirlin, 2011; Wokke et al., 2013).

The purpose of this preliminary study was to extend the application of water-fat MRI to a cohort of children with myelomeningocele. To the best of our knowledge, quantitative MRI assessment of skeletal muscle fat infiltration has not been reported in this population. First, we aimed to characterize and quantify the distribution of fat infiltration in multiple lower extremity muscles. Second, we examined the relationship between MRI-derived percent fat content in individual muscles and MMT-assessed functional strength. Finally, we evaluated the inter-rater reliability of measuring muscle fat content with water-fat MRI.

1. Materials and methods

Eleven children with myelomeningocele participated in this study after providing written assent and parental consent following institutional review board approval. There were 7 boys and 4 girls, all Hispanic whites, ages 7.1–15.8 years (Table 1). An experienced pediatric physical therapist performed a comprehensive physical examination including MMT to measure lower extremity muscle strength. Strength was graded on the standard 0–5 scale: 0 (no palpable contraction), 1 (trace contraction, no joint movement), 2 (poor, completes range of motion (ROM) with gravity eliminated), 3 (fair, completes ROM against gravity without resistance), 4 (good, completes ROM against gravity with moderate resistance), 5 (normal, completes ROM against gravity with maximal resistance; Kendall, Kendall, & Wadsworth, 1971). The muscles examined included the ankle dorsiflexors and plantarflexors, knee extensors and flexors, and hip adductors. Functional neurologic level was determined based on the MMT results following the International Myelodysplasia Study Group (IMSG) criteria (Wright, 2001). Muscles were also grouped in terms of strength: Negligible Strength Group = MMT of 0 or 1; High Strength Group = MMT score of 5 for the hamstrings and 4 or 5 for all other muscles; Intermediate Strength Group = all values in between, i.e., 2–4 for the hamstrings and 2–3 for all other muscles. A different cutoff was used for the hamstrings based on visual inspection of the data which may reflect differences in the recording of MMT scores for different muscle groups.

MRI examinations of the thighs and lower legs were performed on a 3T whole-body system (Achieva R3.2, Philips Healthcare, Cleveland, OH). A research version of the vendor's mDIXON water-fat pulse sequence was used (Eggers, Brendel, Duijndam, & Herigault, 2011). Participant setup and scan parameters for the 3D spoiled-gradient-echo sequence were: supine, feet first, axial acquisition, TR = 10 ms, first TE = 1.48 ms, ΔTE = 1.2 ms, 6 echoes, bipolar readouts, 1 mm voxels with 2 mm overlapping slices, flip angle = 3°, bandwidth = 1.3 kHz/pixel, and two-fold anterior-posterior parallel acceleration. Scan time was ~2 min for 125–170 contiguous slices. Four separate scans were performed in each child, one each for the right lower leg, the left lower leg, the right thigh, and the left thigh. The patient was repositioned as needed to obtain sufficient coverage of the desired anatomy. A 16-channel torso array was used. We were not able to obtain four scans in 3 children due to time constraints (one left lower leg, one right thigh, one left and right thigh); the analysis included data from all of the scans that were obtained. The subsequent image reconstruction of the water-fat MRI pulse sequence employed a seven-peak spectral model of fat based on previous spectroscopy data in bone marrow and subcutaneous adipose tissue (Ren, Dimitrov, Sherry, & Malloy, 2008) to generate voxel-wise muscle fat fraction (FF) maps. Such protocol has been shown

Table 1
Participant characteristics.

Characteristic	Category/statistic	Count/value
Sex	Male	7
	Female	4
Age (years)	Mean ± SD (range)	12.5 ± 2.8 (7.1, 15.8)
Race	White Hispanic	11
IMSG level[a]	Sacral	5
	Low lumbar	1
	Mid lumbar	3
	High lumbar	1
	Thoracic	1

[a] IMSG, International Myelodysplasia Study Group classification of functional level (Wright, 2001). Sacral level is the highest functioning with decreasing function to thoracic level, which is usually non-ambulatory.