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ORIGINAL ARTICLE

Feasibility of ^1H -MR Spectroscopy in evaluation of cervical spondylotic myelopathy

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Abstract *Purpose:* To assess the diagnostic value of magnetic resonance spectroscopy (MRS) in the evaluation of cervical spinal cord biochemical changes in patients with cervical spondylotic myelopathy (CSM).

Materials and methods: Twenty-four patients with cervical spondylotic myelopathy (patient group) and eleven age matched neurologically free volunteers (control group) underwent magnetic resonance imaging. MRS was assessed for the main metabolites including *N*-acetylaspartate (NAA), Choline (Cho), Creatine (Cr) and Lactate (Lac). The MRS findings of both groups were compared. *Results:* Significant reduction in NAA/Cr ratio of patients with CSM (mean = 1.34 ± 0.09) in comparison to controls (mean = 1.82 ± 0.08). No significant differences in Cho/Cr ratio between both groups. Lactate peak was detected in nine patients while it was not detected in any of the controls. The difference in NAA/Cr ratio between patients with Lac peak and those without Lac peak was insignificant.

Conclusion: MRS is a promising non invasive technique that can help to evaluate metabolic changes of the cervical cord in cervical spondylotic myelopathy even in normally looking-areas.

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1. Introduction

Myelopathy describes any neurological deficit related to the spinal cord, cervical myelopathy results from compression of

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the spinal cord usually due to congenital cervical canal stenosis, prolapsed inter-vertebral disc, impinging osteophyte, ossified posterior longitudinal ligament, hypertrophic ligamentum flavum and dynamic instability. Cervical spondylotic myelopathy (CSM) is the most common cause of spinal cord dysfunction in the older population [1–4].

Magnetic resonance imaging (MRI) provides the greatest range of information about osseous and soft tissue structures for cervical myelopathy, however macrostructure of the spinal cord was the focus of most of these studies [5–9]. Proton MR spectroscopy (^1H -MRS) is a non invasive technique that can provide biochemical information about metabolic changes in

Table 1 Significant Lac peak detection in patients and controls.

Lac peak	Patients (<i>n</i> = 24)	Control (<i>n</i> = 11)
Present	9	0
Absent	15	11
Total	24	11

tissues, so it can help to elucidate the underlying pathophysiology. ^1H -MRS is often used to measure *N*-acetyl-aspartate (NAA), total choline (Cho), and total creatine (Cr) [10–12].

Functional evaluation of the spinal cord using MRS had been used in more recent studies [13–18]. It showed to have the potential to add metabolic information to the spinal cord MRI and improve the clinical evaluation and research investigations of spinal cord diseases, such as multiple sclerosis (MS) and intraspinal tumors. However, extensive application is still limited because of its difficulty which can be attributed to magnetic field inhomogeneities, physiological movements, and the size of the anatomical region of interest (ROI) [16,18].

In the current study, we attempted to assess the diagnostic value of ^1H -MRS in evaluation of cervical spinal cord biochemical changes in patients with cervical spondylotic myelopathy.

2. Materials and methods

2.1. Patients

Our study comprised of 32 patients with clinical and radiographic evidence of cervical spondylotic myelopathy who had been referred to perform magnetic resonance imaging (MRI). First, we excluded any patient with a history of previous cervical disc surgery (*n* = 4), claustrophobia (*n* = 2), or those with MRI-incompatible implants (*n* = 2). Therefore, remaining 24 patients (patient group) underwent MRI examination. Eleven age-matched volunteers who were neurologically free were used as controls (control group). We choose normal volunteer as control rather than normal spinal cord regions on MRI in our patient as microscopic white matter lesion could exist and not appear on conventional MRI.

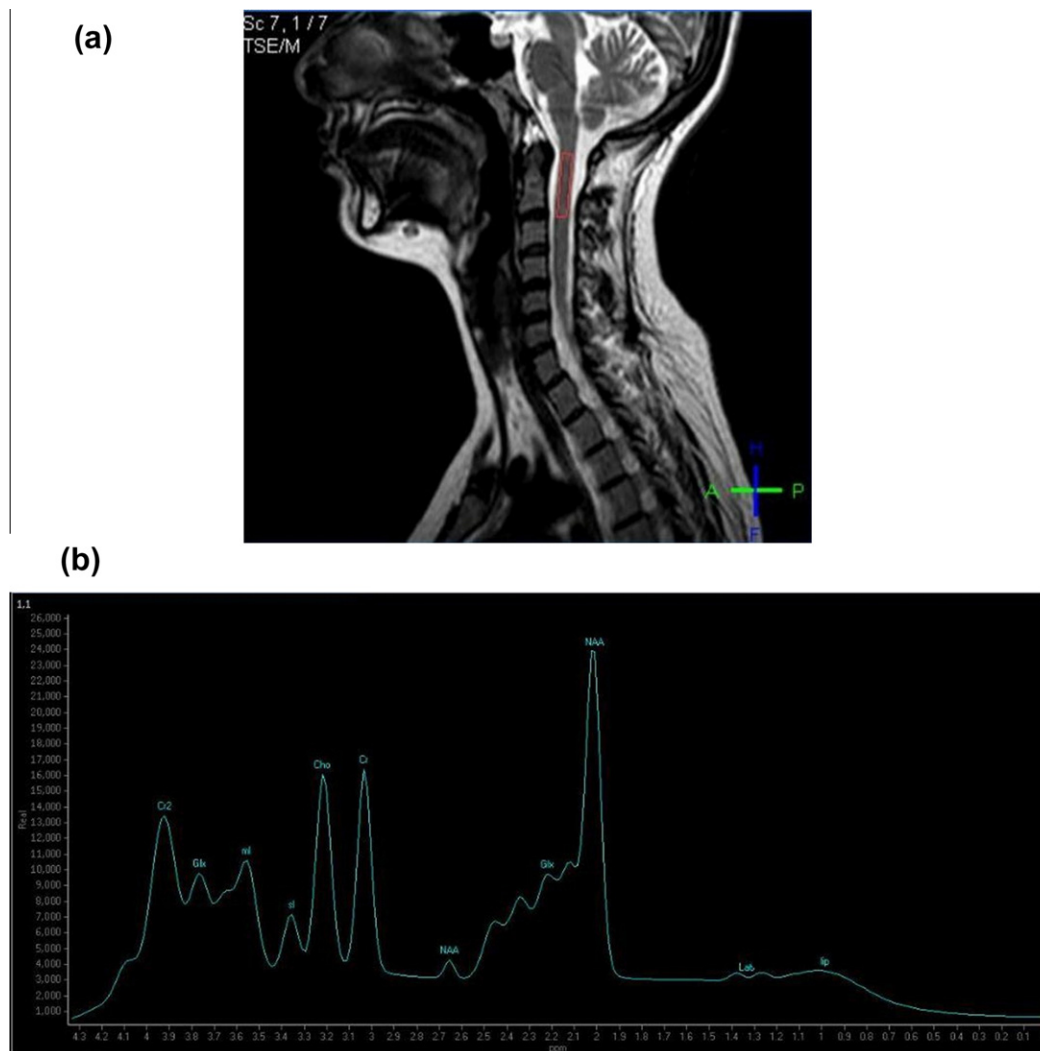


Fig. 1 Neurologically free volunteer (a) sagittal cervical spine MR with voxel box placed opposite to C2 level (b) MR spectra showing normal NAA/Cr ratio and no Lac peak.

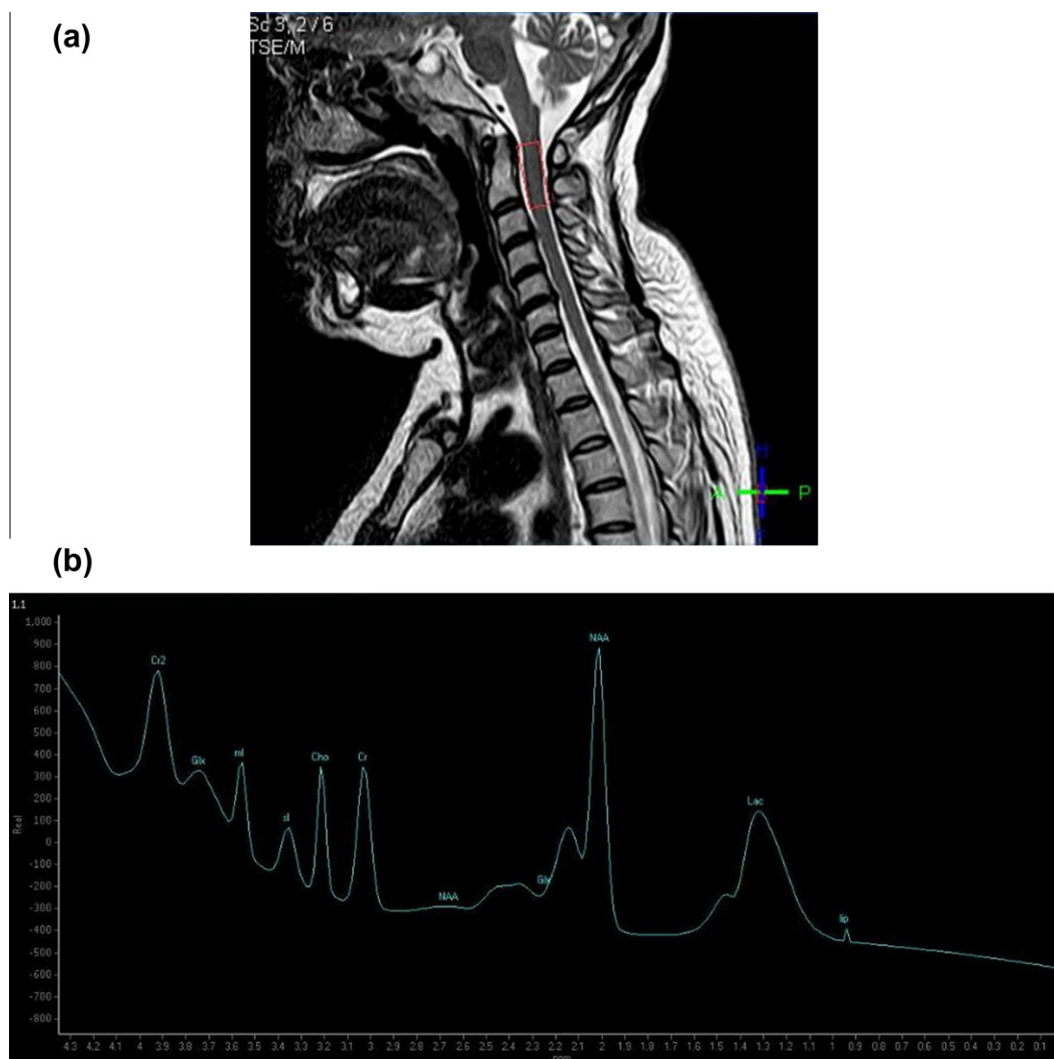


Fig. 2 Patient with cervical spondylotic myelopathy (a) sagittal cervical spine MR demonstrate cord compression, voxel box is placed at C-2 spinal cord level (b) MR spectra showing low NAA/Cr ratio with detected Lac peak.

Patients were 15 males and 9 females and the mean age was 53 ± 11.4 years. Institutional review board approval and informed consent were taken for all patients.

2.2. MR imaging protocol

MR imaging was performed using a 1.5-T MR (Achieva, Philips Medical Systems, Netherland B.V.) by using a neck circular polarization surface coil. Patients were positioned in the supine position and were informed to avoid movement during the examination. Scout scans were taken in axial, coronal and sagittal planes. Several sequences were done including sagittal and axial T1-weighted images [(500–600/8–9) repetition time msec/echo time msec] and axial and sagittal T2-weighted fast spin echo images (3000/100) with a section thickness of 3–4 mm, an intersection gap of 1 mm, a field of view (FOV) of 250 mm and flip angle of 90 degrees.

Magnetic resonance spectroscopy was performed for all patients and volunteers. Single voxel spectra were obtained by a point-resolved spectroscopy (PRESS) spin-echo sequence with the following parameters; repetition time (TR)/echo time (TE)

2000/36 ms, signal acquisition 64, spectral width 1000 Hz, number of points 512 with average scan time 4.54 min. A three-pulse chemical shift-selective (CHESS) saturation sequence was applied for water suppression. Very selective suppression pulses (VSS) saturation bands were placed contiguously to the volume of interest (VOI) to minimize fat contamination. Then the data are processed automatically. Pulse oximeter triggering was applied in MRS sequences to reduce the artifact attributed to spinal cord and CSF motion.

2.3. Image analysis and data interpretation

Conventional T1 and T2-weighted images were assessed for evaluation of the macroscopic pathological changes. In MRS, the voxel, measured $1 \times 1 \times 1.5$ –2 cm (antero-posterior, transverse and cranio-caudal respectively) was positioned at the C2 spinal cord level and carefully adjusted on the cord to exclude any surrounding structures. Spectra were analyzed for the presence of NAA (2.0 ppm), Cho (3.25 ppm), Cr (3.03 ppm) and Lac (1.32 ppm). NAA/Cr and Cho/Cr were recorded.

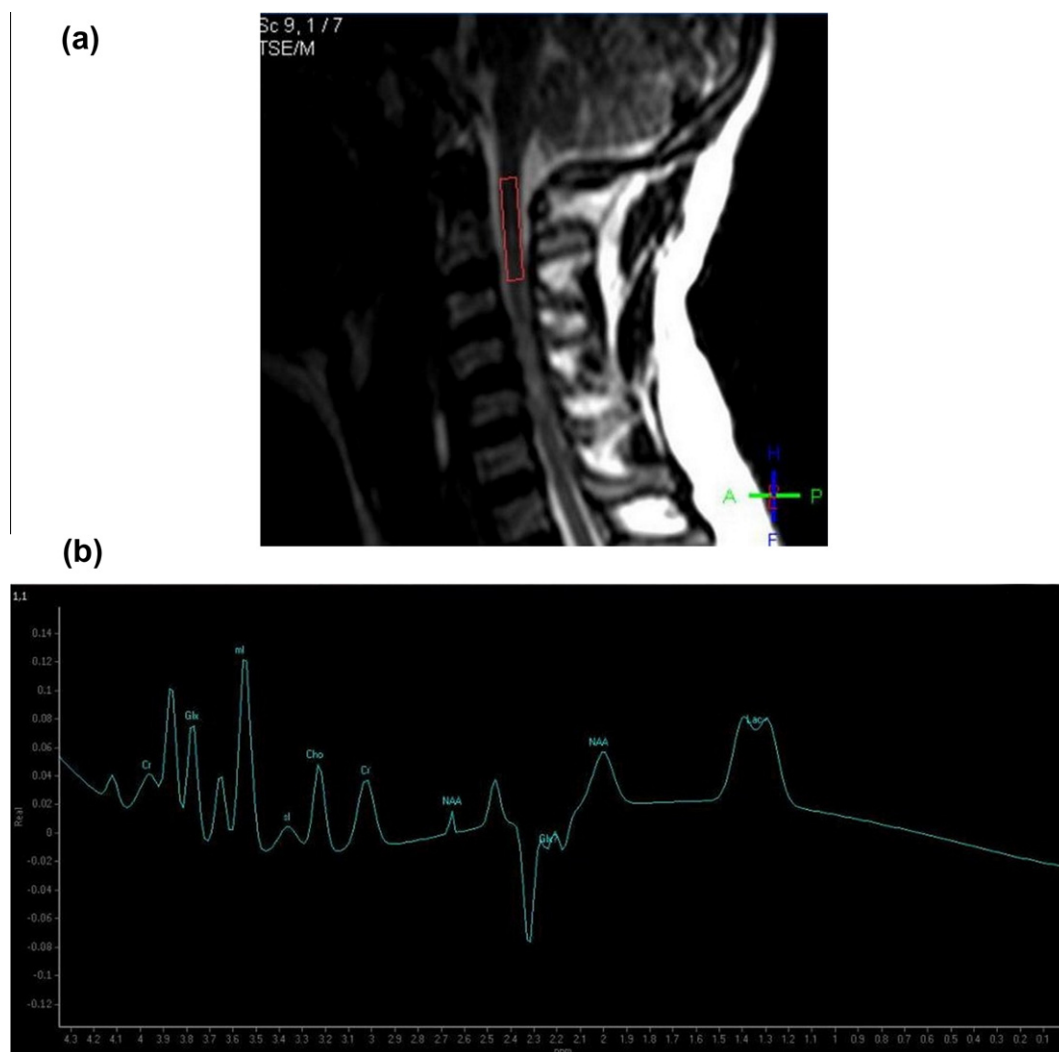


Fig. 3 Patient with cervical spondylotic myelopathy (a) sagittal cervical spine MR showing cord compression, voxel box is placed opposite C-2 spinal cord level (b) MR spectra showing damped NAA/Cr ratio with evident Lac peak.

2.4. Statistical analysis

The subjects were divided into two groups (patients and controls). Statistical analysis was done using SPSS version 10. The mean and standard deviation for NAA/Cho and Cho/Cr were calculated for patients and controls and the differences were assessed by *t*-test. The findings were regarded as significant if *p* value < 0.05.

3. Results

This study included 2 groups:

Patient group: 24 patients with cervical myelopathy (15 males, 9 females; mean age 53 ± 11.4 years).

Control group: 11 age-matched neurologically free volunteers.

A significant Lactate peak was detected in 9 patients while it was not detected in any of the controls (Table 1).

NAA/Cr ratio in the patient group (mean = 1.34 ± 0.09) was significantly less than that in the control group (mean = 1.82 ± 0.08), (*t*-test = 15.17, *p* < 0.0001) (Fig. 1). NAA/Cr ratio in patients with Lac peak (mean = 1.31 ± 0.10) (Figs. 2 and 3) was less than that of patients without Lac peak (mean = 1.36 ± 0.09) (Fig. 4), however this difference was statistically insignificant (*t*-test = 1.32, *p* = 0.20) (Fig. 5).

Cho/Cr ratio in the patient group (mean = 0.82 ± 0.12) showed no significant difference compared to control (mean = 0.75 ± 0.14) (*t*-test = 1.74, *p* = 0.09), also no detected significant differences in the Cho/Cr ratio between patients with Lac peak (mean = 0.80 ± 0.13) and that of patients without Lac peak (mean 0.84 ± 0.11) (*t*-test = 0.74, *p* = 0.47). (Tables 2 and 3) (Fig. 6).

4. Discussion

Several radiological classification systems have been developed to quantify the changes in signal intensity of the spinal cord in cervical myelopathy [9,19]. However, controversy exists in the interpretation of signal changes in the spinal cord [8,20]. This

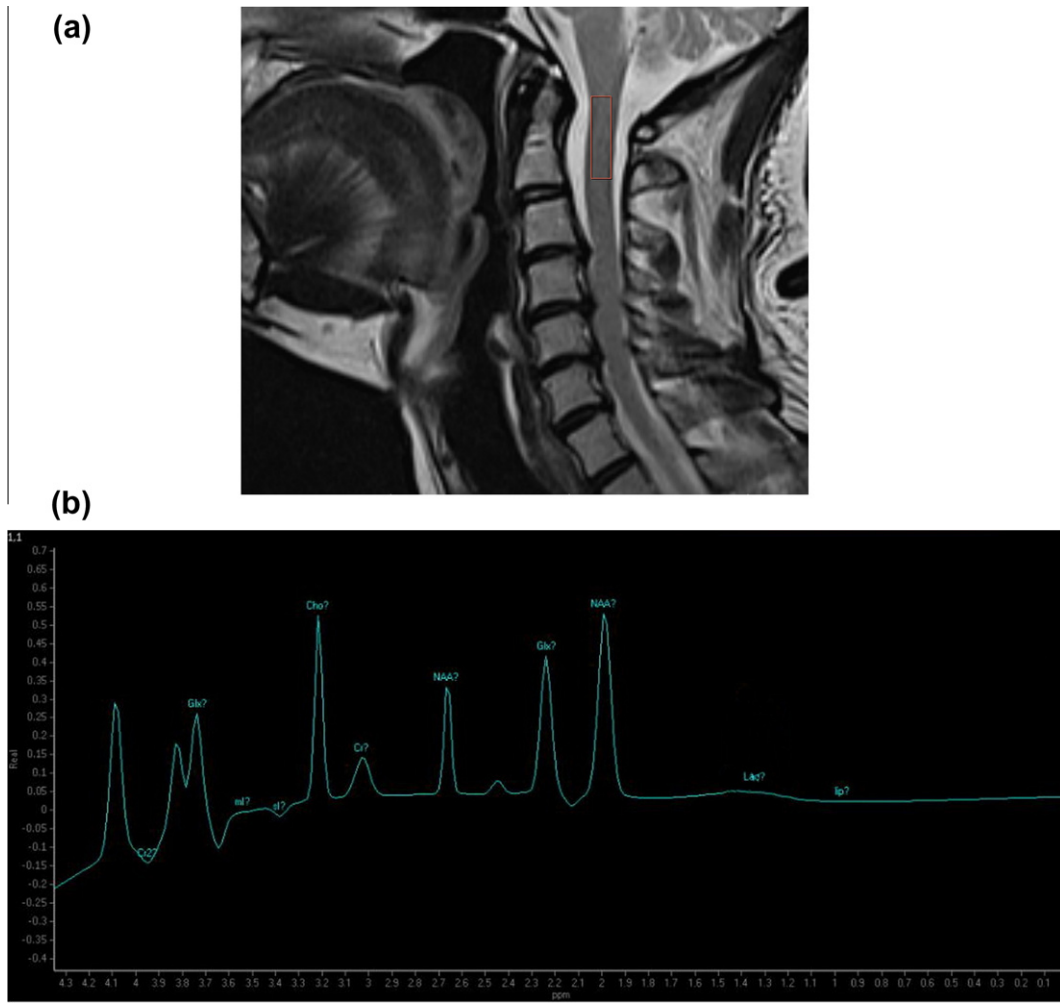


Fig. 4 Patient with cervical spondylotic myelopathy (a) sagittal cervical spine MR with cord compression, voxel box is placed opposite C-2 spinal cord level (b) MR spectra showing reduced NAA/Cr ratio but no Lac peak.

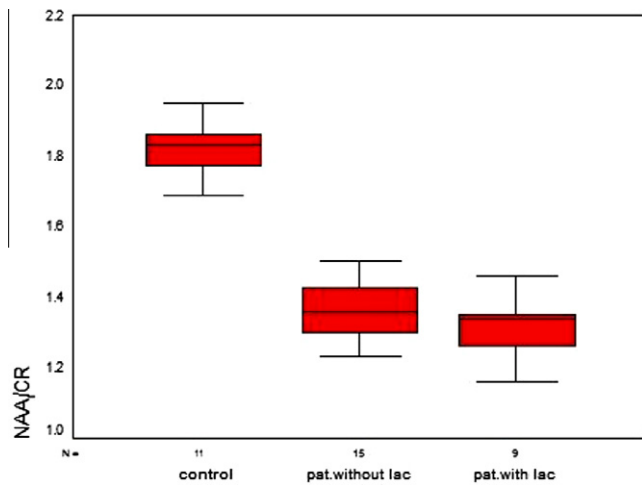


Fig. 5 Box plots showing NAA/Cr ratio in controls, CSM patients without Lac peak and CSM patients with Lac peak.

can be attributed to the fact that conventional MRI gives excellent information about macroscopic anatomy but limited

Table 2 Mean NAA/Cr and Cho/Cr ratio in patient and control groups.

	No	Mean NAA/Cr	Mean Cho/Cr
All patients	24	1.34 ± 0.09	0.82 ± 0.12
Patients without Lactate peak	15	1.36 ± 0.09	0.84 ± 0.11
Patients with Lac peak	9	1.31 ± 0.10	0.80 ± 0.13
Controls	11	1.82 ± 0.08	0.75 ± 0.14

Table 3 *t*-Test and *p* value compared to control group.

	No	Mean NAA/Cr		Mean Cho/Cr	
		<i>t</i> -test	<i>p</i> value	<i>t</i> -test	<i>p</i> value
All patients	24	15.17	<0.0001	1.74	0.09
Patients without Lactate peak	15	14.10	<0.0001	1.89	0.07
Patients with Lac peak	9	13.33	<0.0001	0.93	0.37

evaluation at microscopic and cellular function levels [16]. Metabolic information can be provided by MRS, a non invasive technique that can detect some biochemical markers

including NAA, Creatine (Cr), Choline (Cho) and Lactate (Lac). NAA is contained almost exclusively within neurons and axons, [12,13,21,22] so it can be used as a measure of neural density and marker of normal functioning neurons as well as neural integrity [10,11]. Choline is associated with cellular membrane turnover and so its peak changes with altered neural membrane synthesis and degradation [12]. Creatine is relatively constant as it measures global cellularity metabolic activity, so Cr can be used as internal control [10]. Presence of Lactate is a sign of anaerobic metabolism that may be related to inflammation or ischemia [23].

Cooke et al. [16] described an optimized proton spectroscopy protocol for examination of the human cervical spinal cord by combining field maps and experimental data, and they determined the metabolite concentrations in the cervical cord in six healthy controls by short-echo point-resolved spectroscopy (PRESS) volume localization.

The application of MRS in cord pathology seems a logical extension of its use in the brain, but in comparison has received relatively little attention. In preliminary study carried out by Gomez-Anson et al. [13] and included 6 healthy volunteers, the mean value of NAA/Cr ratio was 1.28 ± 0.48 and Cho/Cr was 0.45 ± 0.17 and they concluded that MRS appears potentially useful in spinal cord investigation.

In a more recent study, Marliani et al. [18] demonstrated the feasibility of MRS – using 3T system – in obtaining main metabolite concentration ratios in 10 healthy subjects and showed a significant difference between spinal cord NAA, Cr and Cho concentration ratios in comparison to brain stem. They concluded that: total NAA/Cr was 1.4 ± 0.3 , Cho/Cr was 0.5 ± 0.1 .

MRS was used to evaluate some spinal cord pathology especially MS, where several studies have showed that the NAA concentration within cervical cord is reduced and Cho/Cr is increased in MS patient in comparison with healthy control [14,15,17,18].

In current study, NAA/Cr ratio was significantly lower in CSM patients (mean = 1.34 ± 0.09) in comparison to controls (mean = 1.82 ± 0.08), ($p < 0.0001$). This can be attributed to axonal and neuronal damage even with no apparent abnormalities at conventional MRI. This result agrees with Holly et al. [14] who showed a trend of significant reduction of NAA/Cr in patients with cervical spondylotic myelopathy in comparison to controls (1.27 vs 1.83, respectively, $p < 0.0001$).

In this study, Cho/Cr ratio was not significantly different in patients (mean = 0.82 ± 0.12) in comparison to controls (mean = 0.75 ± 0.14), this is in agreement with Holly et al. [14], who also concluded that Cho/Cr ratio was not significantly different between the patient and the control groups.

In the current study nine patients with CSM had Lac peaks (37.5%) while none of the controls showed these peaks. In the study carried out by Holly et al. [14], they detected Lac peak in one third of their patients with CSM while Lac peaks were not noted in any of their controls, they explained that by the role of cellular ischemia in the pathogenesis of CSM.

Furthermore comparison was done between patients with Lac peaks and patients without Lac peak, this revealed that patients with Lac peak had a lower NAA/Cr ratio (mean = 1.31 ± 0.10) than patients without Lac peak (mean = 1.36 ± 0.09), however the difference was not statistically significant ($p = 0.20$). Regarding Cho/Cr ratio, there was

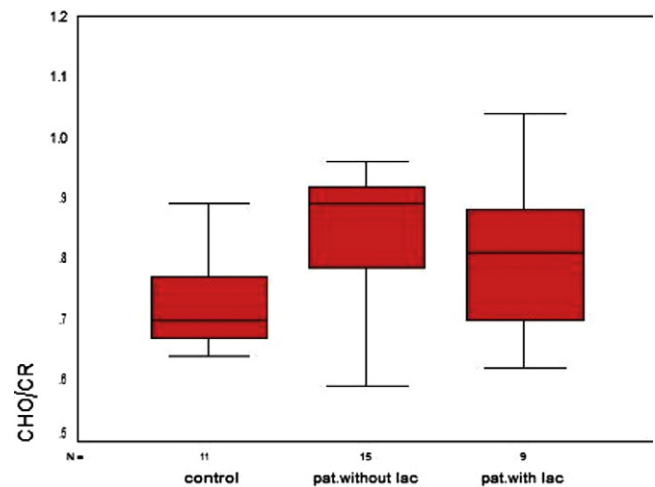


Fig. 6 Box plots showing Cho/Cr ratio in controls, CSM patients without Lac peak and CSM patients with Lac peak.

no significant difference in its value in the case of presence or absence of Lac peaks ($p = 0.48$).

Currently, MRS of the spinal cord has some potential limitations which make it technically challenging. Firstly the pulsatile flow of CSF which causes the spinal cord to move slightly with each heartbeat. The cerebrospinal fluid (CSF) that flows around the cord within the spinal canal presents another challenge because of the motion artifacts produced. The relatively small cross-section of cervical cord especially in patients with CSM presents another problem as an optimal balance of image resolution and the volume of tissue that can be imaged without contamination must be determined. It is known that microstructure abnormalities were reported in the spinal cord proximal to compression level using tensor diffusion imaging [24], so, in this study, voxels were placed at the C2 level as we thought this may reduce the artifact and improve the signal-to-noise ratio which is hampered by the small cross section of the cord.

Further improvements and advances are still to be expected so it may be available to use smaller voxels to increase resolution and thus MRS may be used to detect changes and follow up earlier than conventional MRI.

5. Conclusion

MRS can be used to obtain valuable information to understand the microstructure and metabolic abnormalities in patients with cervical spondylotic myelopathy even in normally looking-areas. A significant reduction in NAA/Cr ratio in patients with CSM compared to controls, and Lac signal indicates that ischemia plays a role in the pathogenesis of CSM. A larger cohort and follow-up will be necessary to determine whether MRS findings have prognostic significance.

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