Egyptian Journal of Radiology and Nuclear Medicine

RESEARCH Open Access

Can MRI chemical shift imaging replace thymic biopsy in myasthenia gravis patients?

Takeya Ahmed Taymour, Enas Samy Soliman, Enas Hamed Al-Sayyad and Sally Fouad Tadros*

Abstract

Background: Myasthenia gravis is a neuromuscular junction autoimmune condition characterized by muscle weakness. Many people with myasthenia gravis have thymic abnormalities, such as thymic lymphoid hyperplasia and thymic tumors, therefore, the thymus plays a significant role in the disease. The imaging properties of thymic hyperplasia and thymoma on CT and conventional MRI are very similar, yet, MRI has recently revealed promising capability by adding novel sequences. Chemical shift MRI was demonstrated to consistently distinguish thymic hyperplasia from thymus gland tumors. The aim of this study was to determine the value of chemical shift MRI imaging in characterizing thymic lesions in patients diagnosed with myasthenia gravis and its ability to differentiate thymic hyperplasia from thymoma.

Results: MRI showed that thymic lymphoid hyperplasia was more common to be convex in shape while thymoma was more likely to be round or irregular ($P=0.004$). Paired comparison between histopathology and chemical shift MRI showed that MRI had 90% sensitivity and 100% specificity in detecting thymoma with overall diagnostic accuracy 93.3% ($P=0.5$). MRI chemical shift ratio showed 100% sensitivity by using > 0.85 as a cut off value for diagnosis of thymoma, with specificity 83.3% ($P=0.0001$). There was statistically significant difference in chemical shift ratio between thymic lymphoid hyperplasia and thymoma groups, as thymoma group had a higher chemical shift ratio of 1.06 ± 0.06 compared to 0.48 ± 0.13 in thymic hyperplasia group ($P=0.0001$).

Conclusion: MRI chemical shift imaging with chemical shift ratio offers a highly sensitive and specific tool in assessment of thymus lesions in myasthenia gravis patients and it can differentiate between thymic hyperplasia and thymoma using cutoff value of > 0.85, hence, unwarranted invasive procedures as thymic biopsy or thymectomy can be avoided and proper management could be planned.

Keywords: Chemical shift, Thymus, Myasthenia gravis

Background

Myasthenia gravis (MG) is a neuromuscular junction (NMJ) autoimmune condition characterized by muscle weakness; which frequently begins in the ocular extrinsic muscles and progresses to generalized MG in two-thirds of patients. The onset age is bimodal, with a female majority below 40 years (female/male ratio, 3/1), and a male majority above 50 years (female/male ratio, 1/2) [1–3].

With approximately one million MG patients worldwide, MG has a prevalence of 150 per million. The annual incidence is 10–15 per million [4].

Since many people with MG have thymic abnormalities, such as thymic lymphoid hyperplasia (TLH) and thymic epithelial tumors (mainly thymomas and infrequently thymic carcinomas), the thymus plays a significant role in the disease [5].

TLH refers to the presence of thymic tissue with lymphoid germinal centers in the thymic medulla. It is observed in a number of autoimmune diseases, most commonly MG, being seen in up to 65% of MG patients [6].

*Correspondence: sallyfouad86@gmail.com
Faculty of Medicine, Cairo University, Cairo, Egypt

Thymomas are tumors that develop from the thymic epithelium and can be benign or low-grade malignant. About 30–50 percent of thymoma patients develop MG. Furthermore, 15% of patients with MG are discovered to have thymoma [7, 8].

As a result, diagnostic imaging is essential in all patients who have recently developed MG in order to exclude the presence of underlying TLH or thymoma [6].

Moreover, diagnostic imaging aids in the preoperative outlining of MG patients as thymectomy is strongly advocated in all patients with thymoma, and radiological evaluation can help distinguish between non-advanced and advanced disease in order to sort out patients for induction chemotherapy prior surgery [9, 10].

In most previous research, the imaging properties of TLH and thymoma on CT and conventional MRI were very similar [11]. MRI, however, has recently revealed promising capability by adding novel sequences. Chemical shift MRI was demonstrated to consistently distinguish TLH from thymus gland tumors [12].

The aim of this study was to determine the value of chemical shift MRI imaging in characterizing thymic lesions in patients diagnosed with MG and its ability to differentiate TLH from thymoma.

Methods

Local institutional review board approved this study and written informed consent was obtained from all participants or their authorized representatives.

Study population

This cross sectional study involved 30 MG patients with thymic lesions. All patients were referred from the Neurology department to our Radiology department for MRI of the chest during the period from December 2020 to September 2021.

Inclusion criteria

Patients diagnosed as MG based on their history, neurological examinations and electrophysiological studies, above the age of 15 years, regardless of gender with radiological finings in CT suggestive of thymic lesion.

Exclusion criteria

Any contraindication to MRI such as: cardiac pace-makers, claustrophobia, and cochlear implants.

Methods

MRI technique

All patients underwent MRI of the chest using a 1.5 T unit (Achieva; Philips Medical Systems, Best, The Netherlands). A dedicated torso phased-array surface coil was used to acquire the following sequences:

1. Axial T1WI, T2WI
2. Coronal T1WI, T2WI
3. Sagittal T1WI, T2WI
4. Axial in phase and out of phase.

Imaging parameters were as follows:

- 275–400-mm field of view
- 256 × 256 image matrix
- 5 mm section thickness
- 0.5 mm intersection gap
- flip angle of 90°
- time of examination 15–20 min

MRI interpretation and image analysis

- *Qualitative assessment* We determined whether there was apparent signal drop in the signal intensity of the thymus gland on the opposed-phase image compared to the in-phase.
- *Quantitative assessment* Chemical-shift ratio (CSR) was obtained by measuring the signal intensity of the thymus and chest muscles in both in-phase and opposed-phase images after placing the region of interest (ROI) at the same site in both sequences. The CSR was obtained using the following equation: CSR = (tSIop/mSIop)/(tSIin/mSIin)

Histopathological assessment

For all cases with thymic neoplasm after thymectomy.

Statistical analysis

Statistical analysis was conducted using SPSS 22nd edition, numeric variables were presented in mean ± standard deviations and compared using Mann whiney u test after normality testing. Categorical variables were presented in frequency and percentage and compared using Chi2 test. Paired comparison was conducted using McNemar's test. Any P value < 0.05 was considered significant.

Results

Demographics & clinical manifestations

A total of 30 patients were included in our final analysis; 60% were females and 40% were males. They had a mean age of 34.8 ± 7.6 years old.

Ocular muscles were the commonest affected group in 21 (70%) patients, followed by bulbar muscles in 14 (46.7%), facial muscles in 11 (36.7%), upper limbs muscles in 9 (30%) and lower limbs muscles in only 2 (6.7%) patients (Fig. 1).

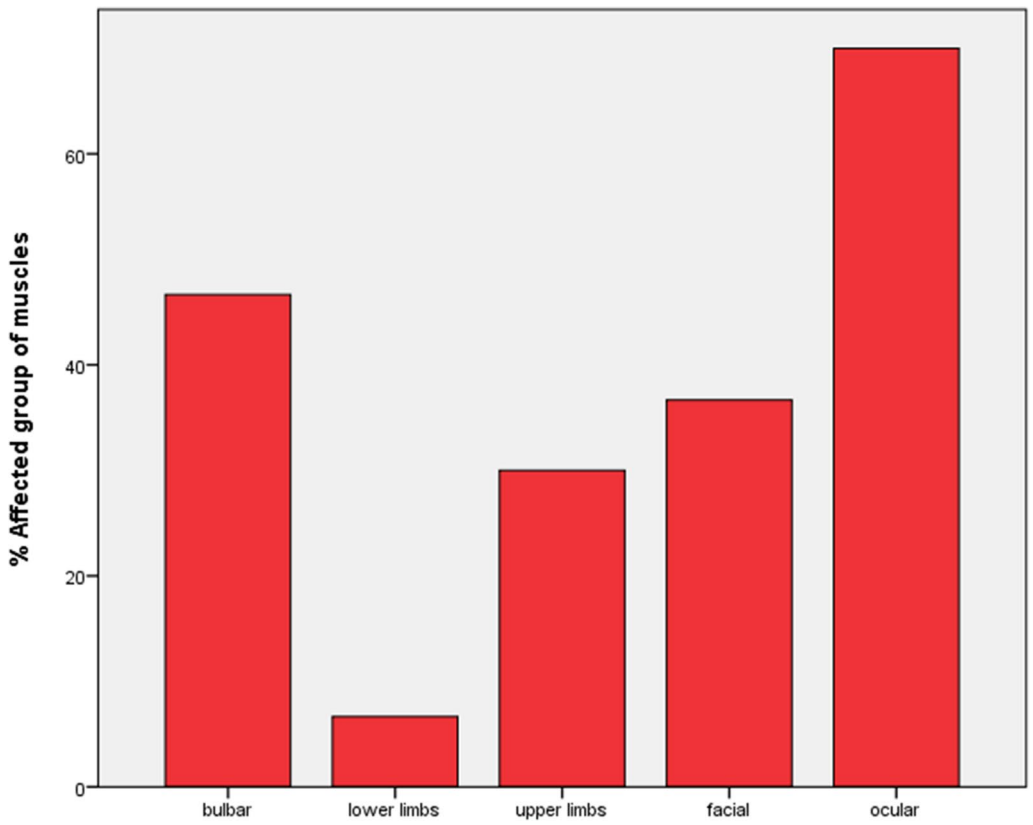

Fig. 1 Bar chart showing percentage of affected muscle groups

There was no significant difference in age, gender, or affected muscles based on histopathology with *P* values > 0.05.

MRI findings

Regarding the shape of the thymus gland, 8 (26.7%) of the patients had a convex gland, 6 (20%) were round, 6 (20%) were oval, 5 (16.7%) were irregular, 3 (10%) were lobulated, and 2 (6.7%) were pyramidal in shape.

MRI showed that TLH was more common to be convex in shape while thymoma was more likely to be round or irregular (*P* value 0.004) (Fig. 2).

Opposed-phase imaging showed no changes in 20 (60%) cases and signal drop in 10 (40%) cases, while CSR had a mean of 0.83 ± 0.3 among the included patients.

Paired comparison between histopathology and chemical shift MRI showed that MRI had 90% (95% CI 68.30–98.77%) sensitivity, 100% specificity in detecting thymoma, and overall diagnostic accuracy 93.3% (95% CI 77.9–99.2) with *P* value 0.5 (Table 1).

MRI CSR showed 100% sensitivity by using > 0.85 as a cut off value for diagnosis of thymoma, with specificity 83.3% (AUC = 0.92 and *P* value 0.0001).

There was statistically significant difference between CSR in TLH and thymoma groups; as thymoma group had a higher CSR of 1.06 ± 0.06 with a range of 0.95–1.15 compared to 0.48 ± 0.13 in thymic hyperplasia group ranging from 0.29–0.76 with *P* value 0.0001.

Histopathology

Histopathology revealed that 60% of the included patients had thymoma and 40% were diagnosed with TLH.

Discussion

MG is a relatively uncommon autoimmune disease characterized by muscle weakness. The thymus gland plays an important role in the pathogenesis of MG. Approximately 90% of patients with MG display thymic abnormalities; namely TLH (70 %) and thymoma (20%) [13].

The differentiation of thymoma from TLH is critical in the evaluation of surgical treatment. Thymectomy is strongly recommended in all thymoma cases, whereas the surgical indication in hyperplasia cases should be only considered when conservative treatments are ineffective [14].

Thymoma is seen as a focal soft tissue mass, while, thymic hyperplasia shows a diffuse symmetric

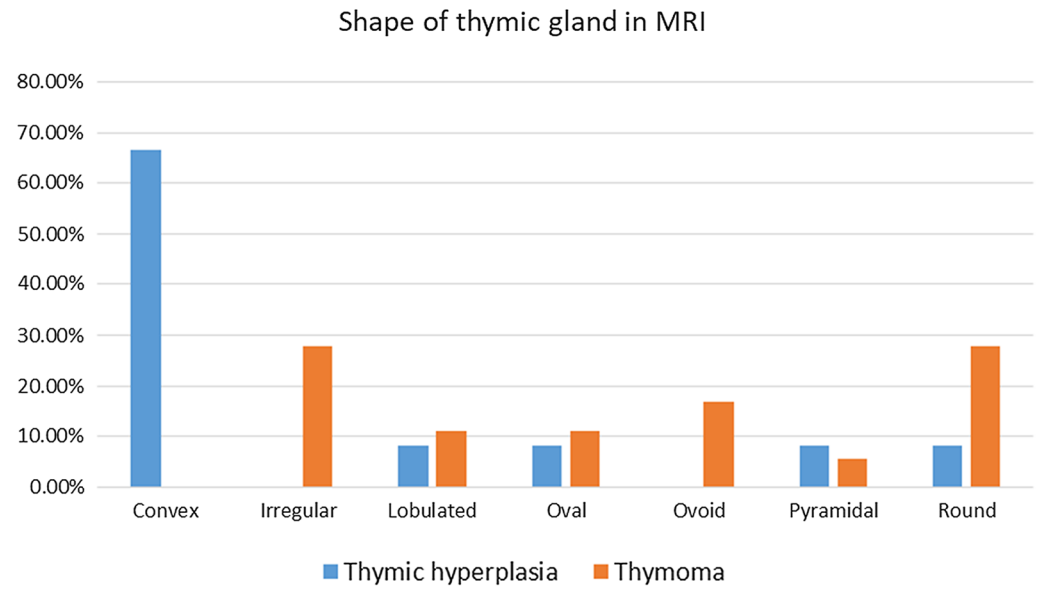

Fig. 2 Bar chart showing shape of thymic gland by MRI based on histopathology findings

Table 1 Paired comparison between chemical shift MRI and histopathology findings

	Histopathology				*P* value
	Thymic hyperplasia (n = 12)		Thymoma (n = 18)		
	Count	Row N %	Count	Row N %	
Opposed-phase imaging					
No change	0	0.0%	18	100.0%	1.0
Signal drop	12	100.0%	0	0.0%	

enlargement of the gland. However, it is difficult to differentiate the two conditions on CT because of high inter-rater variation [15].

TLH may display a focal soft tissue mass; in contrast, thymoma may demonstrate diffuse enlargement in both lobes. In these cases, CT results in indeterminate findings, whereas chemical shift MRI can differentiate the two pathologies by detecting fat in tissue showing signal intensity loss on opposed-phase imaging compared to in-phase imaging [16]. Moreover, it can specifically outline the boundaries of thymoma and its relationship with surrounding tissues [17].

Demographics of our study were similar to those reported in several previous studies as the mean age was mostly in the third and fourth decade of life [18].

The results of our study showed that ocular muscles was the commonest affected group followed by bulbar muscles. The current evidence in literature points out that ocular muscles are the first group of muscle to be affected in patients with MG presenting with squint or ptosis, followed by bulbar muscles and limb muscles [19, 20].

Our findings showed that there was no significant difference in age, gender, or affected muscles based on histopathology. These results were inconsistent with the results of many studies which stated that patients with thymoma are significantly older than patients with TLH [21].

In our study, histopathology revealed that 60% of the included patients had thymoma and 40% were diagnosed with TLH. This finding was similar to literature as it is estimated that prevalence of thymoma in patients with MG is 62 % versus 38% for TLH [21].

Our MRI findings showed that the most common shape of thymus gland in MG patients was convex gland, followed by round, oval, irregular, and lobulated while pyramidal shape was the least common. We also found that TLH was more common to be convex in shape and thymoma was more likely to be round or irregular.

Our findings were supported by results of similar studies. Inaoka et al demonstrated in a study of 41 patients with MG (23 with TLH and 18 with thymoma) that in the hyperplasia group, there was convex enlargement of the gland without lobulation in 73% and with lobulation in 26%. In the thymoma group, the thymus gland was round in 83.3 % of the cases, had diffuse enlargement without lobulation in 11.1% and had an irregular shape in one patient [12].

All patients in the thymoma group in our study showed no decrease in the signal intensity on the out-phase image

compared to the in phase (Figs. 3, 4, 5). Accordingly, we found that chemical shift MRI had 90% sensitivity and 100% specificity in detecting thymoma with overall diagnostic accuracy of 93.3%. These findings are similar to the ones reported by Tuan et al., who stated that opposed phase imaging showed sensitivity 97.0% and 90% specificity in detection of thymoma in MG patients [21].

Such high reliability of chemical shift MRI in detecting fat in tissue and discriminating thymoma from TLH in our study is comparable to that of several other studies. Popa et al. also demonstrated that none of the patients in the thymoma group showed a decrease in the signal intensity of the thymus gland [22].

In our study, all the patients in the hyperplasia group demonstrated a homogeneous decrease in the signal intensity of the thymus gland on the opposed-phase image relative to the in-phase image (Figs. 6, 7) except for two cases; an 18-year-old male and a 21-year-old female. Their chemical shift MRI showed no signal drop on the opposed phase images and their CSR values were 1.01 and 1.10, respectively. These cases were proven to be TLH with minimal fat infiltration on histopathology. These findings were consistent with Ackman et al. study illustrating a pathologically proven case of normal thymus in a 21-year-old woman that displayed no fat replacement on the opposed-phase chemical shift MRI with CSR = 1.1 [23].

Priola et al. also reported a true hyperplasia case in a 60-year-old female being treated with corticosteroids without fat infiltration on chemical shift MRI [24]. Furthermore, Phung et al. reported a case of a 22-year-old woman with MG that showed no drop in signal intensity on the opposed phase images and was diagnosed as thymic tumor. Post-operative histopathological findings proved TLH with only a few fat cells, which was not

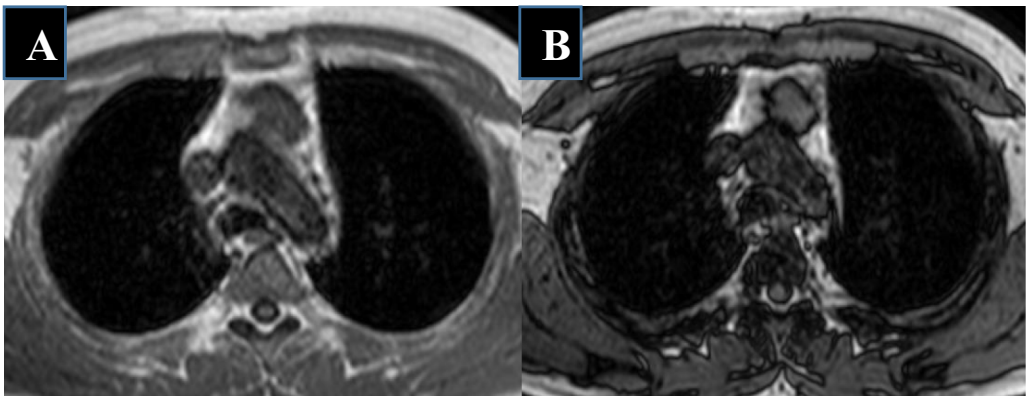

Fig. 3 MRI chemical shift imaging in a 38-year-old male patient complaining of weakness in both upper limbs diagnosed as MG. **a** In phase and **b** out of phase MR images show the mass eliciting intermediate signal to the surrounding muscles with no apparent signal drop in the out of phase series. CSR value is 1.05. Histopathological diagnosis was thymoma

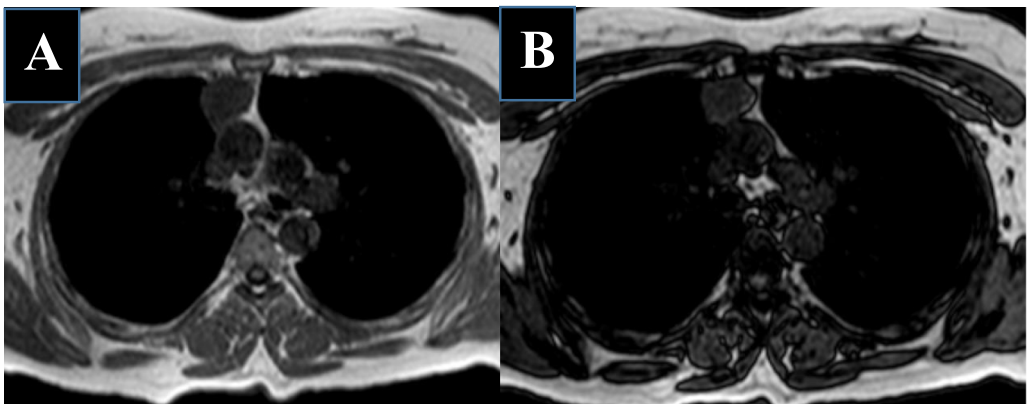

Fig. 4 MRI chemical shift imaging in a 40-year-old female patient complaining of drooping of both eyelids and dysphagia diagnosed as MG. **a** In phase and **b** out of phase MR images show the mass eliciting intermediate signal to the surrounding muscles with no apparent signal drop in the out of phase series. CSR value is 1.01. Histopathological diagnosis was thymoma

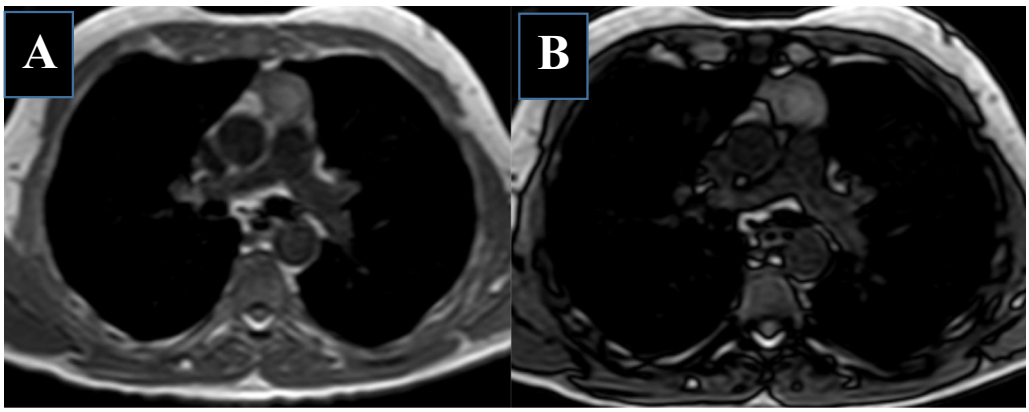

Fig. 5 MRI chemical shift imaging in a 34-year-old male patient complaining of drooping of both eyelids and weakness in both lower limbs diagnosed as MG. **a** In phase and **b** out of phase MR images show the mass eliciting intermediate signal to the surrounding muscles with no apparent signal drop in the out of phase series. CSR value is 1.01. Histopathological diagnosis was thymoma

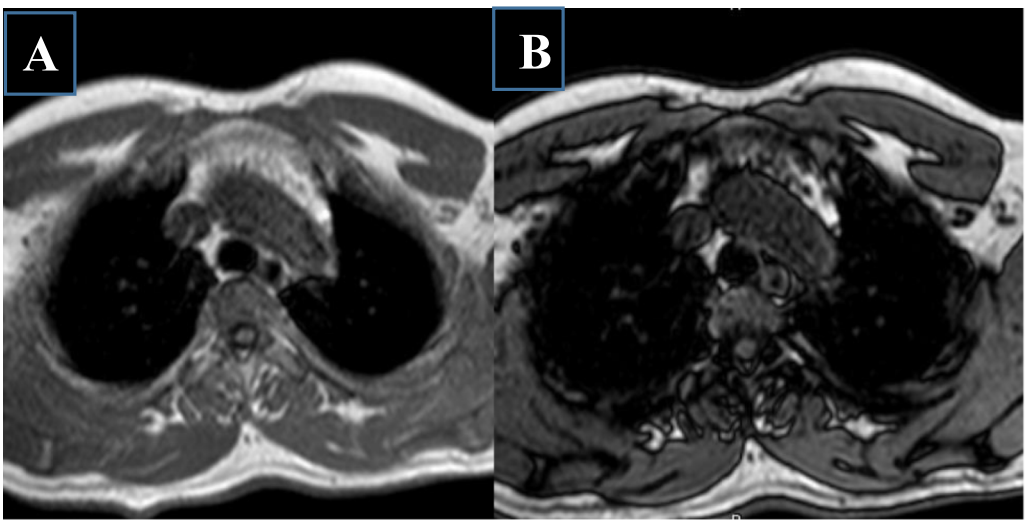

Fig. 6 MRI chemical shift imaging in a 34-year-old male patient complaining of dysphagia and weakness in both upper limbs diagnosed as MG. **a** In phase and **b** out of phase MR images show the lesion eliciting a hyperintense signal relative to the surrounding muscles in the in-phase series with apparent signal drop in the out of phase series. CSR value is 0.61. Histopathological diagnosis was thymic hyperplasia

sufficient to detect the decrease of signal intensity on chemical shift MRI [13].

In our study, CSR showed 100% sensitivity by using >0.85 as a cut off value for diagnosis of thymoma with specificity 83.3%. Our results were consistent to Priola et al. study which included 83 patients diagnosed as MG who underwent surgical intervention and were assessed using MRI preoperatively; their results showed that MRI had a sensitivity 100% and specificity 96.7% at cutoff point >0.85 CSR [25].

Our findings also more or less agreed with a cross-sectional study of 53 participants conducted in Vietnam where 53 MG patients were included; comparison between CT and MRI findings showed that MRI had sensitivity 100% and specificity 95% when using >0.75 as a cutoff value of MRI chemical shift [21].

Limitations of our study included the small sample size. A larger number of patients is necessary to clarify the utility of the chemical shift MRI imaging for differentiating thymic hyperplasia from tumors of the thymus gland in MG patients [25].

Also, in few cases especially in young patients and early adulthood, chemical shift MRI may be not solely enough for differentiation between TLH and thymoma. In such

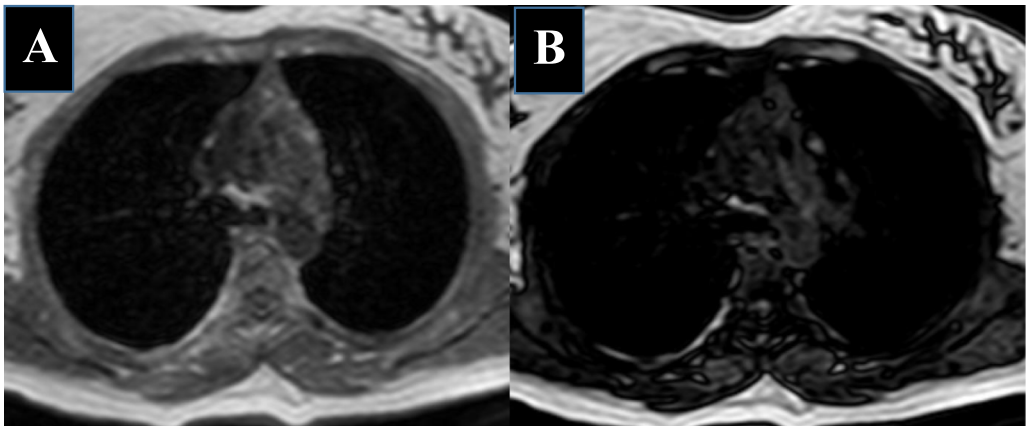

Fig. 7 MRI chemical shift imaging in a 44-year-old female patient complaining of drooping of both eyelids diagnosed as MG. **a** In phase and **b** out of phase MR images show the lesion eliciting a hyperintense signal relative to the surrounding muscles in the in-phase series with apparent signal drop in the out of phase series. CSR value is 0.41. Histopathological diagnosis was thymic hyperplasia

cases, complementary Diffusion weighted MRI would be helpful to allow proper diagnosis. Furthermore, overlapping CSR values between normal or hyperplastic thymus and tumors can be expected in early adulthood as cases of lipid-poor normal or hyperplastic thymus may occur.

Conclusion

In conclusion, MRI chemical shift imaging with CSR offers a highly sensitive and specific tool in assessment of thymus in MG patients and can differentiate between thymic hyperplasia and thymoma using cutoff value of >0.85, hence, unwarranted invasive procedures as thymic biopsy or thymectomy can be avoided and proper management could be planned.

Abbreviations

CRS: Chemical shift ratio; MG: Myasthenia gravis; NMJ: Neuromuscular junction; ROI: Region of interest; TLH: Thymic lymphoid hyperplasia.

Acknowledgements

Not applicable.

Authors' contributions

SFT and ESS reviewed the images. SFT, ESS, EHA and TAT analyzed and interpreted the patient data. SFT wrote the manuscript and TAT reviewed it. All authors have read and approved the manuscript.

Funding

The authors state that this work has not received any funding.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Approval of the ethical committee of the 'Radiology department, Faculty of Medicine, Cairo University' was granted before conducting this prospective study; Reference number: not applicable Local institutional review board approval was granted before conducting this cross sectional study, and written informed consent was obtained from all patients.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study. If the patients were less than 16-year-old, deceased, or unconscious when consent for publication was requested, written informed consent for the publication of this data was given by their parents or legal guardians.

Competing interests

The authors declare that they have no competing interests.

Received: 22 November 2021 Accepted: 5 February 2022
Published online: 15 February 2022

References

1. McGrogan A, Sneddon S, De Vries CS (2010) The incidence of myasthenia gravis: a systematic literature review. Neuroepidemiology 34(3):171–183
2. Grob D, Brunner N, Namba T, Pagala M (2008) Lifetime course of myasthenia gravis. Muscle Nerve 37(2):141–149
3. Huang X, Liu WB, Men LN, Feng HY, Li Y, Luo CM, Qiu L (2013) Clinical features of myasthenia gravis in southern China: a retrospective review of 2,154 cases over 22 years. Neurol Sci 34(6):911–917
4. Andersen JB, Engeland A, Owe JF, Gilhus NE (2010) Myasthenia gravis requiring pyridostigmine treatment in a national population cohort. Eur J Neurol 17(12):1445–1450
5. Nasseri F, Eftekhari F (2010) Clinical and radiologic review of the normal and abnormal thymus: pearls and pitfalls. Radiographics 30(2):413–428
6. Spillane J, Higham E, Kullmann DM (2013) Was versteht man unter einer Myasthenia gravis?
7. Wright CD, Mathisen DJ (2001) Mediastinal tumors: diagnosis and treatment. World J Surg 25(2):204–209
8. Strollo DC, de Christenson MLR, Jett JR (1997) Primary mediastinal tumors. Part 1*: tumors of the anterior mediastinum. Chest 112(2): 511–522.
9. Skeie GO, Apostolski S, Evoli A, Gilhus NE, Illa I, Harms L, Hilton-Jones D, Melms A, Verschuuren J, Horge HW (2010) Guidelines for treatment of autoimmune neuromuscular transmission disorders. Eur J Neurol 17(7):893–902
10. Silvestri NJ, Wolfe GI (2012) Myasthenia gravis. Semin Neurol 32(03):215–226

11. Pirronti T, Rinaldi P, Batocchi AP, Evoli A, Di Schino C, Marano P (2002) Thymic lesions and myasthenia gravis: diagnosis based on mediastinal imaging and pathological findings. Acta Radiol 43(4):380–384
12. Inaoka T, Takahashi K, Mineta M, Yamada T, Shuke N, Okizaki A, Nagasawa K, Sugimori H, Aburano T (2007) Thymic hyperplasia and thymus gland tumors: differentiation with chemical shift MR imaging. Radiology 243(3):869–876
13. Phung T, Nguyen T, Tran D, Phan N, Nguyen H (2018) (2018) A thymic hyperplasia case without suppressing on chemical shift magnetic resonance imaging. Case Rep Radiol 2018:73056194
14. Onodera H (2005) The role of the thymus in the pathogenesis of myasthenia gravis. Tohoku J Exp Med 207(2):87–98
15. Takahashi K, Inaoka T, Murakami N, Hirota H, Iwata K, Nagasawa K, Yamada T, Mineta M, Aburano T (2003) Characterization of the normal and hyperplastic thymus on chemical-shift MR imaging. AJR Am J Roentgenol 180(5):1265–1269
16. Priola AM, Priola SM (2014) Imaging of thymus in myasthenia gravis: from thymic hyperplasia to thymic tumor. Clin Radiol 69(5):e230–e245
17. Li K, Yang DW, Hou SF, Xu XH, Gong T, Chen HB (2014) Chemical shift and fat suppression magnetic resonance imaging of thymus in myasthenia gravis
18. Abdel Razek AAK, Khairy M, Nada N (2014) Diffusionweighted MR imaging in thymic epithelial tumors: correlation with World Health Organization classification and clinical staging. Radiology 273(1):268–275
19. Nair AG, Patil-Chhablani P, Venkatramani DV, Gandhi RA (2014) Ocular myasthenia gravis: a review. Indian J Ophthalmol 62(10):985
20. Kim SJ, Park GY, Choi YM, Sohn DG, Kang SR, Im S (2017) Bulbar myasthenia gravis superimposed in a medullary infarction diagnosed by a fiberoptic endoscopic evaluation of swallowing with simultaneous tensilon application. Ann Rehabil Med 41(6), 1082.
21. Tuan PA, Vien MV, Dong HV, Sibell D, Giang BV (2019) The value of CT and MRI for determining thymoma in patients with myasthenia gravis. Cancer Control 26(1):1073274819865281
22. Popa GA, Preda EM, Scheau C, Vilciu C, Lupescu IG (2012) Updates in MRI characterization of the thymus in myasthenic patients. J Med Life 5(2):206
23. Ackman JB, Mino-Kenudson M, Morse CR (2012) Nonsuppressing normal thymus on chemical shift magnetic resonance imaging in a young woman. J Thorac Imaging 27(6):W196–W198
24. Priola AM, Priola SM, Ciccone G, Evangelista A, Cataldi A, Gned D, Pazè F, Ducco L, Moretti F, Brundu M, Veltri A (2015) Differentiation of rebound and lymphoid thymic hyperplasia from anterior mediastinal tumors with dual-echo chemical-shift MR imaging in adulthood: reliability of the chemical-shift ratio and signal intensity index. Radiology 274(1):238–249
25. Priola AM, Gned D, Veltri A, Priola SM (2016) Chemical shift and diffusion-weighted magnetic resonance imaging of the anterior mediastinum in oncology: current clinical applications in qualitative and quantitative assessment. Crit Rev Oncol Hematol 98:335–357

Publisher's Note