CHAPTER 3

Study I: Structural changes of the cervical muscles in elder women with cervicogenic headache

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3.1 Introduction

Cervicogenic headache is a secondary headache, which has been suggested to be associated with increasing age (26). Functional impairments (reduced strength and endurance) in the cervical muscles have been demonstrated in patients with cervicogenic headache (6, 114, 115). Such changes have also shown to be present in patients with traumatic and non-traumatic neck disorders (123). Interestingly, changes in the structure of the cervical extensors and flexors (fat infiltration) have been quantified in traumatic neck pain (e.g. whiplash) (165, 166), but not to the same magnitude in non-traumatic neck pain. The mechanisms underlying these structural changes in traumatic neck pain are largely unknown but could be the result of traumatic factors (e.g. inflammation, denervation), disuse, or ageing processes (165). To date, little is known about structural changes in the cervical muscle in headache. There exists some evidence that atrophic changes of the upper cervical musculature are present in patients with chronic tension-type headache (128). However, we are unaware if changes in the size and structure (cross-sectional area (CSA), fat infiltration and lipid content) of the entire cervical musculature are present in a cohort of elderly patients with -r cervicogenic headache.

A recent study conducted by Abaspour et al (121) demonstrated no difference in CSA of the longus colli between patients with cervicogenic headache and healthy controls and between affected and non-affected side in patients with cervicogenic headache utilizing diagnostic ultrasonography. Conversely, Jull et al (6) using ultrasonography demonstrated reduced CSA on the symptomatic side for the semispinalis capitis in comparison with the non-symptomatic side in patients with

cervicogenic headache. Whilst ultrasound has been shown to be a valid and reliable measurement of muscle size, its poor resolution and anisotropic nature poses a challenge to interpretation of findings (167). Magnetic resonance imaging (MRI) is the gold-standard for soft-tissue demonstrating value for quantifying muscle atrophy and fat infiltration on a macroscopic scale (123, 166). MR spectroscopy (MRS) is also a measure of metabolic imaging with MRI that quantifies the lipid content of muscle (132). To our knowledge, macroscopic changes in cervical muscle have not been established in patients with cervicogenic headache.

It is our contention that changes in the size and structure of the cervical muscles may help explain some of the functional impairments common to patients with cervicogenic headache, and in particular elderly females. Accordingly, the purpose of this study was to investigate the size and macroscopic content of fat structure (fat infiltration and lipid content) in the cervical muscles using conventional MRI in elder women with cervicogenic headache compared to those without headache.

3.2 Methods

3.2.1 Sample size calculation

The sample size was calculated based on relative cross-sectional areas of the suboccipital muscles in the previous study of headache (128). The minimum number of at least 10 participants per group was required for the study (power = 0.80, alpha = 0.05 and effect size = 1.36).

3.2.2 Participants 1^O by Chiang Mai University

Fourteen elder women with cervicogenic headache, aged between 60-75 years, were sought for the study from the headache clinic at Maharaj university hospital and the local community by advertising on local radio and flyers. All participants with cervicogenic headache were screened and diagnosed by a neurologist according to the Cervicogenic Headache International Study Group (CHISG) (105). Inclusion criteria were headache frequency for at least one per month over the past year and neck pain \geq 3/10 on a visual analog scale. They were not considered if they reported two or more types of headache. Age and gender matched controls were recruited from the local

community by advertising through local radio and flyers. The control group had no previous history of headache and neck pain in the past 12 months. Participants of both groups were excluded if they had a previous history of injury and surgery of head and neck; musculoskeletal problems/disorders (e.g. cervical radiculopathy, myopathy, advanced osteoporosis); neurological problems/diseases (e.g. Parkinson's disease, stroke); metabolic syndromes (e.g. diabetes, hypo-/hyperthyroidism) and any contraindication to magnetic resonance imaging (MRI). They were also excluded if they had abnormal fasting blood sugar (fasting blood sugar (FBS) > 110 mg/dL) and lipid profile levels (total cholesterol > 200 mg/dL, and a low-density lipoprotein (LDL) > 130 mg/dL) (168).

The study was approved by a research ethics committee of Faculty of Associated Medical Sciences, Chiang Mai University. Written informed consent was obtained from each participant prior to commencement of the study.

3.2.3 Questionnaires

3.2.3.1 General questionnaire

A general questionnaire was developed to include demographic data, anthropometric data, health status and physical activity. Details of this questionnaire are provided in Appendix A.

3.2.3.2 Headache questionnaire

A headache questionnaire was used to include characteristics of headaches according to the IHS (104) and CHISG (105) classification criteria. Details of this questionnaire are provided in Appendix B.

3.2.3.3 Neck Disability Index-Thai version (NDI-TH)

The NDI-TH was used to measure levels of neck pain and disability. It has been translated from its original version in English and shown to have good reliability (169). The NDI-TH consists of 10 items designed to assess participant-determined disability resulting from neck pain, including pain intensity, personal care, lifting, reading, headache, concentration, work, driving, sleeping and recreation. The

score for each item ranges from 0 (highest level of function) to 5 (lowest level of function). The item scores was summed to a total score and a total score was calculated as a percentage of disability. A total score of 10-29 indicates mild disability, 30-49 moderate disability, 50-69 severe disability and \geq 70 complete disability (170). Details of this questionnaire are provided in Appendix C.

3.2.3.4 Visual Analog Scale questionnaire

A VAS was used to measure intensity of neck pain and headache. It consists of a 10 cm line, where 0 = no pain and 10 = the worst pain imaginable. The participants were asked to make a mark along the line corresponding to their pain. The VAS was shown to have good validity and reliability for assessing pain in young and older populations (171). Details of this questionnaire are provided in Appendix D.

3.2.4 Magnetic resonance system

3.2.4.1 Magnetic resonance imaging (MRI)

MRI was performed using a 1.5 Tesla superconducting magnet (Achieva, Philips Medical Systems, Best, The Netherlands) and a dedicated neck coil was used as receiver coil. All images were conducted on conventional T1-weighted spin echo (172). The measurement parameters consist of 384×384 pixel matrix, 180 mm field of view, 5 mm of slice thickness, 600 ms of repetition time (TR), and 20 ms of echo time (TE). The axial MRI slices were taken from the base of the occipital lobe through the upper portion of the C4 vertebral body and aligned parallel to the C2/3 intervertebral disc which was marked as reference point (173). Relative cross-sectional areas (rCSAs) of the cervical muscles were reported in order to reduce measurement errors (173).

The rCSAs for the cervical muscles were bilaterally measured by manually tracing the area of interest within the fascia border around using Image J software version 1.48 (Java-based version of the public domain NIH Image Software) (128, 173). The rCSAs of cervical muscles were measured on axial images at cervical certain levels as described previously by Elliott et al (166, 173). The rCSAs measures for the suboccipital muscles (rectus capitis posterior minor, RCPMIN; and major, RCPMAJ) were taken at the C1 and C2 vertebral levels, the cervical extensors (multifidus, MUL; semispinalis capitis, SECP; and splenius capitis, SPC) at the C3 vertebral level, and the cervical flexors (longus capitis/colli, LCa/LCo; sternocleidomastoid, SCM) at the C2 vertebral level.

Each image was measured three times and the mean value was used for analysis. The ICCs for intra-rater reliability in this study were 0.75-0.96, indicating good reliability. Detail of reliability is provided in Appendix G.

The quantification of fat infiltration of the cervical muscles on T1weighted MRI was determined as previously described (166, 174). An index of fat within the cervical muscle was obtained from a ratio between pixel intensity over the cervical muscle relative to pixel intensity over the standardized area of intermuscular fat at inferior of C2 on the right side (174). The image was measured manually tracing area of interest (ROI) on the axial T1-weighted images with MRIcro software (www.mricro.com). Each image was measured three times and the mean value was used for analysis. The ICCs for intra-rater reliability in this study were 0.84-0.99, indicating good reliability. Detail of reliability is provided in Appendix H.

3.2.4.2 Magnetic resonance spectroscopy (MRS)

The ¹H-MR spectroscopy (proton MRS) was performed with the same 1.5 Tesla MR scanner (Achieva, Philips Medical Systems, Best, The Netherlands) by using a dedicated neck coil. The ¹H-MRS was performed using single voxel point-resolved spectroscopy (PRESS) sequence (TR=2000 ms, short echo time=37.6 ms; 128 average). For localization of the ¹H-MRS volume of interest (VOI), T1-weight images in three planes (axial, sagittal and coronal plane) were acquired for the placement of the ¹H-MRS voxel. The ¹H-MRS voxel of $5 \times 5 \times 5$ mm was positioned close to the center of each muscle as possible in order to prevent partial volume averaging artifacts. Due to relatively long scan times and small volume of the cervical muscle tissue, the ¹H-MRS was obtained from the bilateral RCPMAJ, SECP and SPC muscles.

Analysis of the ¹H-MRS data was processed as previously described (175). For curve fitting, the Totally Automatic Robust Quantitation in NMR

(TARQUIN) software was used. Resonance frequencies and linewidth parameters were fitted with the standard metabolite library provided by TARQUIN (175). The peak height and area of the lipid peak was determined: intramyocellular lipid (IMCL) methyl protons peak at a resonance of 0.9 ppm, extramyocellular lipid (EMCL) methyl protons peak at a resonance of 1.1 ppm, intramyocellular lipid (IMCL) methylene protons peak at a resonance of 1.3 ppm and extramyocellular lipid (EMCL) methylene protons peak at a resonance of 1.5 ppm (176). The area under each prominent peak was calculated using Origin 8.0 (OriginLab Corporation, Northampton, MA) and the integrated areas (0.9-1.5 ppm) were used for analysis. 210262

3.2.5 Procedure

All participants with headache were screened by a neurologist. All eligible participants completed the general questionnaire and those with headache also completed the headache, VAS and NDI questionnaires. Then, participants were positioned on the examination table in a supine position with a pillow under knees and a standard foam was used to support participant's head and neck. Participants were instructed to breathe normally and relax as well as stay still to maintain their position during imaging. The MRI and MRS of the cervical muscles were performed by a radiologist blind to participant's condition. The total scan time was 30-45 minutes for each participant.

3.2.6 Statistical analysis

Paired t-tests were preliminarily conducted to determine differences between the left and right sides in the rCSAs, fat indexes and lipid content. There were no differences between the left and right sides in all outcomes for both headache and control groups (all p > 0.05). The mean values of the left and right sides were considered for between-group comparisons.

An independent t-test was performed to test differences between groups in age, BMI and FBS and lipid profile levels. Preliminary analyses were performed to determine if the assumptions of analysis of variance (ANOVA) and of covariance (ANCOVA) were met. The Shapiro-Wilk test was used to test the assumption of normality. All outcome data were normally distributed, except for the fat indexes of the RCPMAJ and the lipid content of the RCPMAJ, SECP and SPC muscles. A transformation based on the logarithm was performed for the fat indexes of the RCPMAJ muscle. Non-parametric analysis was considered for the lipid content data. Levene's test was used to test the assumption of homogeneity of variance. A Pearson's correlation analysis investigating the relationship between the body mass index (BMI) and the rCSAs of the cervical muscles revealed no significant correlations between BMI and the cervical rCSAs, except for the rCSAs of the RCPMAJ (r = -0.47, p = 0.01), SECP (r = 0.50, p = 0.01) and SPC (r = 0.43, p = 0.02). The correlation analysis investigating the relationship between the BMI, FBS, lipid profile levels and the fat indexes and lipid content of the cervical muscle also revealed that there were no significant correlations among these variables (all p > 0.05).

A one-way analysis of variance was performed to determine significant differences in the rCSAs and the fat indexes of the cervical muscles between groups. The exception was the rCSAs of the RCPMAJ, SECP and SPC were analyzed using analysis of covariance (ANCOVA), which BMI was entered as a covariate. Kruskal-Wallis test was used to analyze between-group differences in the lipid content of the RCPMAJ, SECP and SPC muscles.

All statistical analyses were performed using SPSS statistical package (version 17.0). Significance was set at p < 0.05.

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3.3.1 Participant characteristics

Demographic characteristics of the participants are presented in Table 3.1. The BMI was higher in the cervicogenic headache group compared to the control group (p = 0.001). The preliminary results revealed no significant correlations between the BMI and the rCSAs of the cervical muscles (p > 0.05), except for the rCSAs of the RCPMAJ, SECP and SPC muscles (p < 0.05). There were no correlations between the BMI, FBS, lipid profile levels and the fat indexes and lipid content of the cervical muscles (all p > 0.05).

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3.3.2 Cross sectional area

The mean and standard deviation of the rCSA, fat indexes and lipid content of the cervical muscle are present in Table 3.2. The cervicogenic headache group had significantly decreased rCSAs of the RCPMAJ and MUL muscle compared with controls (p < 0.05). There were no significant differences between groups in the rCSAs of the RCPMIN, SECP, SPC, LCa/LCo and SCM muscles (all p > 0.05). Figure 3.1 shows the rCSA of bilateral RCPMAJ muscle.

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3.3.3 Fat infiltration

The fat indexes of the RCPMIN, RCPMAJ and SPC muscles were significant higher in the cervicogenic headache group when compared with that in the control group (p < 0.05). There was also a trend for the cervicogenic headache group to have higher fat index of the SECP muscle compared with controls (p = 0.056). No significant difference between groups in the fat index of the MUL, LCa/LCo and SCM muscles was found (p > 0.05). Figure 3.2 shows histogram of pixel intensity profile of right RCPMAJ.



Variables	CEH (n = 14)	Control $(n = 14)$	<i>p</i> -value
Age (yrs)	63.36 ± 3.30	64.21 ± 4.02	0.54
BMI (kg/m ²)	25.84 ± 2.66	22.70 ± 1.57	0.001
Headache frequency (days/week)	3.27 ± 2.27	-	
Headache intensity (VAS, 1-10)	4.05 ± 1.89	-	
Headache durations (hrs/day)	3.28 ± 2.95		
Headache history (yrs)	3.76 ± 3.14	2/2	
NDI (0-100)	27.68 ± 9.56	- 321	
Side of pain (n)	78<	13	
Left	7	-1-1	
Right	2 mg	- 383	
FBS (mg/dL)	93.71 ± 12.31	93.36 ± 8.17	0.93
Cholesterol (mg/dL)	178.86 ± 21.54	181.07 ± 23.88	0.80
LDL-C (mg/dL)	95.83 ± 21.63	104.41 ± 26.00	0.35
HDL-C (mg/dL)	56.50 ± 16.03	59.57 ± 15.43	0.61

Table 3.1 Demographic characteristics of participants

Data are mean \pm SD unless otherwise indicated.

CEH, cervicogenic headache; VAS, visual analog scale; FBS, fasting blood sugar; LDL, low-density lipoprotein cholesterol, HDL, high-density lipoprotein cholesterol

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Variables	Muscle	CEH (n = 14)	Control $(n = 14)$	<i>p</i> -value
rCSA	RCPMIN	80.18 ± 17.40	83.30 ± 13.11	0.60
	RCPMAJ	61.62 ± 9.45	72.20 ± 5.60	0.03 ^a
	MUL	55.88 ± 11.69	66.29 ± 14.30	0.045
	SECP	213.06 ± 34.56	191.48 ± 29.04	0.80 ^a
	SPC	166.94 ± 19.72	147.84 ± 21.34	0.22 ^a
	LCa/LCo	67.36 ± 14.82	69.11 ± 6.36	0.69
	SCM	101.23 ± 26.73	100.60 ± 7.15	0.93
MFI	RCPMIN	0.46 ± 0.02	0.42 ± 0.04	0.002
	RCPMAJ	0.42 ± 0.04	0.37 ± 0.04	0.004 ^b
	MUL	0.42 ± 0.03	0.40 ± 0.05	0.18
	SECP	0.32 ± 0.02	0.30 ± 0.02	0.056
	SPC	0.32 ± 0.02	0.29 ± 0.02	0.02
	LCa/LCo	0.25 ± 0.02	0.25 ± 0.02	0.71
	SCM	0.32 ± 0.02	0.33 ± 0.02	0.12
Lipid content	RCPMAJ	0.011 ± 0.009	0.011 ± 0.006	0.82 ^c
ຨຑ	SECP	0.008 ± 0.005	0.008 ± 0.004	0.96°
Co	SPC	0.010 ± 0.005	0.008 ± 0.004	0.53°

 Table 3.2 Mean and standard deviation of rCSAs, fat infiltrates and lipid content of the cervical muscles between the headache and control groups

Data were analyzed using ANOVA, unless otherwise indicated. ^a after controlling for BMI, ^b using log algorithm data, ^c Data were analyzed using Kruskal-Wallis test CEH, cervicogenic headache; rCSA, relative cross sectional area; MFI, muscle fat infiltration; RCPMIN, rectus capitis posterior minor; RCPMAJ, rectus capitis posterior major; MUL, multifidus; SECP, semispinalis capitis; SPC, splenius capitis; LCa/LCo, longus capitis/colli; SCM, sternocleidomastoid



Figure 3.1 Bilateral axial MR image for rCSA of rectus capitis posterior major between control (a) and cervicogenic headache (b)



Figure 3.2 Axial T1-weighted spin echo image with histogram of pixel intensity profile for right rectus capitis posterior major between control (a) and cervicogenic headache (b)

3.3.4 Lipid content

Figure 3.3 shows MRI and corresponding MRS spectra of the lipid content of right RCPMAJ in a participant with cervicogenic headache. There were no significant differences between groups in the lipid content of the RCPMAJ, SECP and SPC muscles (p > 0.05).



Figure 3.3 MRI and corresponding MRS spectra for right rectus capitis posterior major in cervicogenic headache. IMCL (CH₃), intramyocellular lipid methyl protons; EMCL (CH₃), extramyocellular lipid methyl protons; IMCL (CH₂), intramyocellular lipid methylene protons; EMCL (CH₂), extramyocellular lipid methylene protons.

3.4 Discussion

The purpose of this study was to examine the changes in the structures of the cervical flexors and extensors in older women with cervicogenic headache. The results demonstrated decreased rCSAs in the deep cervical extensor muscles (rectus capitis posterior major and multifidus) and increased fatty infiltration in the suboccipital (rectus capitis posterior minor and major) and splenius capitis muscles in elders with cervicogenic headache compared to those without headache. There were no differences between groups in the rCSAs of the rectus capitis posterior minor, semispinalis capitis, splenius capitis, longus capitis/colli and sternocleidomastoid muscles and fatty infiltration in the multifidus, semispinalis capitis, longus capitis/colli and sternocleidomastoid muscles in lipid content in the rectus capitis posterior major, semispinalis capitis and splenius capitis muscles in lipid content in the rectus capitis posterior major, semispinalis capitis and splenius capitis muscles in lipid content in the rectus capitis posterior major, semispinalis capitis and splenius capitis muscles in lipid content in the rectus capitis posterior major, semispinalis capitis and splenius capitis muscles in lipid content in the rectus capitis posterior major, semispinalis capitis and splenius capitis muscles in lipid content in the rectus capitis posterior major, semispinalis capitis and splenius capitis muscles in lipid content in the rectus capitis posterior major, semispinalis capitis and splenius capitis muscles in lipid content in the rectus capitis posterior major, semispinalis capitis and splenius capitis muscles in lipid content in the rectus capitis posterior major, semispinalis capitis and splenius capitis muscles in lipid content in the rectus capitis posterior major, semispinalis capitis and splenius capitis muscles in lipid content in the rectus capitis posterior major.

cervicogenic headache compared with controls. These results suggest selective increased fatty infiltration in the cervical extensor muscles and atrophy of the deep cervical extensor muscles in older adults with cervicogenic headache.

The results of decreased rCSAs in the rectus capitis posterior major and multifidus muscles in elders with cervicogenic headache in this study are in agreement with previous studies in chronic neck pain suggesting that greater atrophy could occur in the deep suboccipital and multifidus muscles (123, 177). A possible explanation for these results may be explained by pain adaptive theory (178). The atrophy in the cervical extensors may reflect avoidance to use muscle due to pain, indicating disused atrophy. Alternatively, changes in muscle size may occur due to inflammatory mechanism in the cervicogenic headache (179) caused by cervical degenerative joint disease in older persons (27), resulting in nerve root irritation (180). However, the results of the present study are not supported by a previous study conducted in younger adults with cervicogenic headache. Jull et al (6) found atrophy of the semispinalis capitis on the symptomatic side compared with the non-symptomatic side. This discrepancy may be due to differences in methodology. Our study investigated muscle size by using MRI to measure at C3 level, but the study of Jull et al. (6), investigated at C2 level using ultrasound. The present study showed no significant differences between groups in rCSAs of the cervical flexors. Similar to the findings from Abaspour et al.'s study (121), they found that there was no difference in CSA of the longus colli between younger populations with cervicogenic headache compared with controls, and between the affected and non-affected side in cervicogenic headache group using ultrasound imaging. The result was unexpected, since patients with cervicogenic headache have demonstrated impaired cervical flexor synergy as revealed by craniocervical flexion test (6). The reason why there were no changes in morphology of cervical flexors in elders with cervicogenic headache is unknown, thus further investigation is still required.

Previous studies have demonstrated increased fatty infiltration in the cervical muscles in younger populations with chronic neck pain (7, 165). As yet, there is no evidence of changes in fatty infiltration in patients with cervicogenic headache. This study demonstrated increased fatty infiltration in the cervical extensor muscles in elders with cervicogenic headache compared with controls and the largest amounts of fatty

infiltration were found in the deep layer. Our results are supported by the previous study, which has demonstrated similar pattern of fatty infiltration in the extensor muscles in patients with chronic neck pain (165). The possible explanations for the increase in fatty infiltration are muscle disuse and inflammatory mechanism, similar to the cause of atrophy. Conversely, we found no differences in fatty infiltration of the cervical flexor muscles between elders with and without cervicogenic headache. The reason for this is still not known, thus requires further investigation. It is known that cervical muscles provide 80% of mechanical support of the cervical segment (181). The deep cervical muscles is an important stabilizer of cervical spine for functional activities in daily living (181). A reduction in muscle size and increased muscle fatty infiltration in the cervical extensor muscles, notably in the deep cervical muscles in older adults with cervicogenic headache may compromise the stability of the cervical movement. A recent study reported that the morphology of cervical muscle can be modified with exercise in women with chronic whiplash (182). Further research is needed to determine whether structural changes in the cervical muscles could be restored by specific exercise, and influence clinical symptoms in this population.

Proton magnetic resonance spectroscopy has been used for quantifying intramuscular lipid concentration in patients with chronic musculoskeletal pain (132, 183). However, no previous study has investigated the lipid content of cervical muscles in patients with cervicogenic headache. There were no significant differences in lipid content in any cervical extensor muscles studied between elders with and without cervicogenic headache. There is evidence that signal to noise ratio (level of the signal relative to background noise) is proportional to voxel volume (184). It is possible that the absence of high lipid content in the cervical extensors in elders with cervicogenic headache compared with controls may be due to insufficient signal to noise ratio (SNR) as a consequence of small voxel volume of each cervical muscle. Previous study suggested that increasing magnetic field strength will improve SNR (185). Saupe et al. (185) demonstrated that T1-weighted spin echo with identical image parameters, the SNR of muscle and bone at 3 tesla were 1.1 and 1.28 times, respectively higher than 1.5 tesla. Thus, further research is required to determine lipid content in the cervical muscles by using higher magnetic field strength (3 tesla) to better understand the mechanism of changes in lipid concentration associated with cervicogenic headache.

The current study demonstrated inconsistent results of fat deposition, as determined by fatty infiltration and lipid content in the cervical muscles in elders with cervicogenic headache. This study showed an increase in fatty infiltration in cervical extensor muscles, but not for lipid content in cervicogenic headache. Lipid content within the muscle was found in two discrete locations: fat deposits in the muscle cells (intramyocellular lipid, IMCL) and along the fascia (extramyocellular lipid, EMCL) (131). It has been found that EMCL is a lipid which turns over very slowly and serves as a long-term fat deposit (186) and might be related to changes in fatty infiltration. However, the result of a small signal of lipids and an overlapping of signal intensity for EMCL and IMCL of the cervical muscles did not find any significant difference in lipid content between the groups, and was unable to determine whether lipid within or outside the muscle cell was associated with fatty infiltration of the cervical muscles in elders with cervicogenic headache. Thus, these results of the changes in lipid content in cervical muscles need to be interpreted with caution. Although morphological changes (size and fatty infiltration) would be expected in patients with cervicogenic headache, especially in the deep muscles; this study demonstrated changes in both muscle atrophy and increased fatty infiltration only for rectus capitis posterior major (the power is 0.93 and 0.89, respectively), but not in other deep extensor muscles (rectus capitis posterior minor and multifidus). It failed to reach significant differences between groups in rCSA for rectus capitis posterior minor and fatty infiltration for multifidus muscle probably due to low power to detect differences between groups (0.08 for rectus capitis posterior minor and 0.24 for multifidus). Additionally, measurement of rCSA and fatty infiltration for the rectus capitis posterior major exceeds the measurement error (standard error of measurement, SEM). This study has demonstrated changes in rCSA that exceed 2.10 mm², and in muscle fatty infiltrations that exceed 0.0031. Thus, the values of rCSA and fatty infiltration are reliable, and a significant difference between groups in rCSA and fatty infiltration imply real changes.

There are some limitations to this study. Previous studies have provided evidence that quantification of metabolite concentration using magnetic resonance spectroscopy required large voxel volume in order to obtain sufficient amounts of signal in relative to background noise (184, 187). However, it is difficult to obtain a large voxel volume in the small area of each cervical muscle. The morphological has commonly been measured perpendicular to the muscle fibers (188). Since the cervical spine is surrounded with a complex of cervical musculature arrangement, it would be difficult to identify the anatomical structure of cervical muscle accurately. Accordingly, further research is required to determine the cervical muscle morphology and fatty infiltration in perpendicular to the cervical muscle fibers.

3.5 Conclusion

The study provides preliminary evidence towards quantifying muscle atrophy with increased fatty infiltration in the cervical extensor muscles in older women with cervicogenic headache. This suggests that clinicians need to keep in mind that exercise of the extensor muscles shall be only modest at best. In addition, further research is required to identify the presence and its significance of cervical muscle atrophy and fat composition in the cervical muscles associated with cervicogenic headache.



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