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대한영상의학회지

Quantification of the Elastic Property of Normal Thigh Muscles Using MR Elastography: Our Initial Experience

자기 공명 탄성 검사를 이용한 대퇴 근육의 탄성도의 정량화: 초기 경험

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Purpose This study aimed to apply MR elastography (MRE) to achieve *in vivo* evaluation of the elastic properties of thigh muscles and validate the feasibility of quantifying the elasticity of normal thigh muscles using MRE.

Materials and Methods This prospective study included 10 volunteer subjects [mean age, 32.5 years, (range, 23–45 years)] who reported normal activities of daily living and underwent both T2-weighted axial images and MRE of thigh muscles on the same day. A sequence with a motion-encoding gradient was used in the MRE to map the propagating shear waves in the muscle. Elastic properties were quantified as the shear modulus of the following four thigh muscles at rest; the vastus medialis, vastus lateralis, adductor magnus, and biceps femoris.

Results The mean shear modulus was 0.98 ± 0.32 kPa and 1.00 ± 0.33 kPa for the vastus medialis, 1.10 ± 0.46 kPa and 1.07 ± 0.43 kPa for the vastus lateralis, 0.91 ± 0.41 kPa and 0.93 ± 0.47 kPa for the adductor magnus, and 0.99 ± 0.37 kPa and 0.94 ± 0.32 kPa for the biceps femoris, with reader 1 and 2, respectively. No significant difference was observed in the shear modulus based on sex ($p < 0.05$). Aging consistently showed a statistically significant negative correlation ($p < 0.05$) with the shear modulus of the thigh muscles, except for the vastus medialis ($p = 0.194$ for reader 1 and $p = 0.355$ for reader 2).

Conclusion MRE is a quantitative technique used to measure the elastic properties of individual muscles with excellent inter-observer agreement. Age was consistently significantly negatively correlated with the shear stiffness of muscles, except for the vastus medialis.

Index terms Magnetic Resonance Imaging; Magnetic Resonance Elastography; Elasticity Imaging; Mechanical Properties; Skeletal Muscle; Thigh

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INTRODUCTION

Manual palpation is a very useful and ubiquitous method of physical examination but also subjective, relative, qualitative, and limited if the lesion is deep-seated in the patient's body (1, 2). The mechanical properties of tissues are frequently affected by disease processes such as cancer, inflammation, and fibrosis (1, 3-5). MR elastography (MRE) is a recently developed technology that quantitatively assesses the mechanical properties of tissue using shear wave techniques regarding tissue stiffness by assessing the propagation of mechanical waves through tissue with motion encoding gradient sequences (2, 3, 6).

The mechanical properties of diseased muscles may differ from those of normal muscles. When a muscle contracts or relaxes, the mechanical properties of muscles can vary (7) MRE has been used in several studies to evaluate skeletal muscles; however, the MRE protocols differed among studies and the elasticity values obtained varied and were inconsistent for numerous reasons (1, 5, 8-11). To establish the standard MRE technique for *in vivo* evaluation and to find the normal reference values of the elastic properties of muscle would be necessary as a first step for comparing abnormal muscle with normal muscle.

In the present study, the feasibility of quantifying the elasticity of the normal thigh muscles using MRE was validated. The relationship between shear stiffness, sex, and age was also evaluated.

MATERIALS AND METHODS

PARTICIPANTS

The present study was approved by the Institutional Review Board. The experimental protocol was explained to all subjects, and written informed consent was obtained from all participants (IRB No. 2020-07-006). Subjects were volunteers who reported normal activities of daily living without knee or hip pain. The subjects were evaluated based on their ability to walk independently and normally without assistance, and all subjects were considered normal and healthy. In addition, the subjects did not have a history of immobilization, orthopedic surgery, or the presence of skeletal muscle disease before enrollment. A total of 10 volunteers were enrolled, and thigh muscles were evaluated using MRE in this prospective study.

MRI AND MRE

All MR studies were acquired on a 3T MRI unit (Ingenia 3T, Philips Healthcare, Best, the Netherlands) at our institution using a body coil (Philips Medical System) with the subject in the supine position. The MRE of the dominant thigh was acquired in addition to the conventional T2 fast spin echo axial image for anatomical evaluation of the thigh. A readily available pneumatic wave transducer, designed for liver elastography, was used. An active acoustic driver (Resoundant, Mayo Clinic, Rochester, MN, USA) was used to generate 60-Hz mechanical waves. The vibration pad was placed on the skin of the posterior aspect of the thigh and secured with Velcro straps. To avoid dispersing the vibration of acoustic waves, the transducer was kept from touching the table below the subject (Fig. 1). MRE acquisitions were performed with a two-dimensional multi-echo balanced fast field echo (gradient echo) using a

Fig. 1. Setup for MR elastography acquisition in the 3T MRI system.
A. Subjects are placed in the supine position on the table to characterize thigh muscles (vastus medialis, vastus lateralis, adductor magnus, and biceps femoris). The pneumatic driver (arrow) is attached to the posterior thigh and secured with straps.
B. The pneumatic transducer is used to produce 60 Hz mechanical wave.

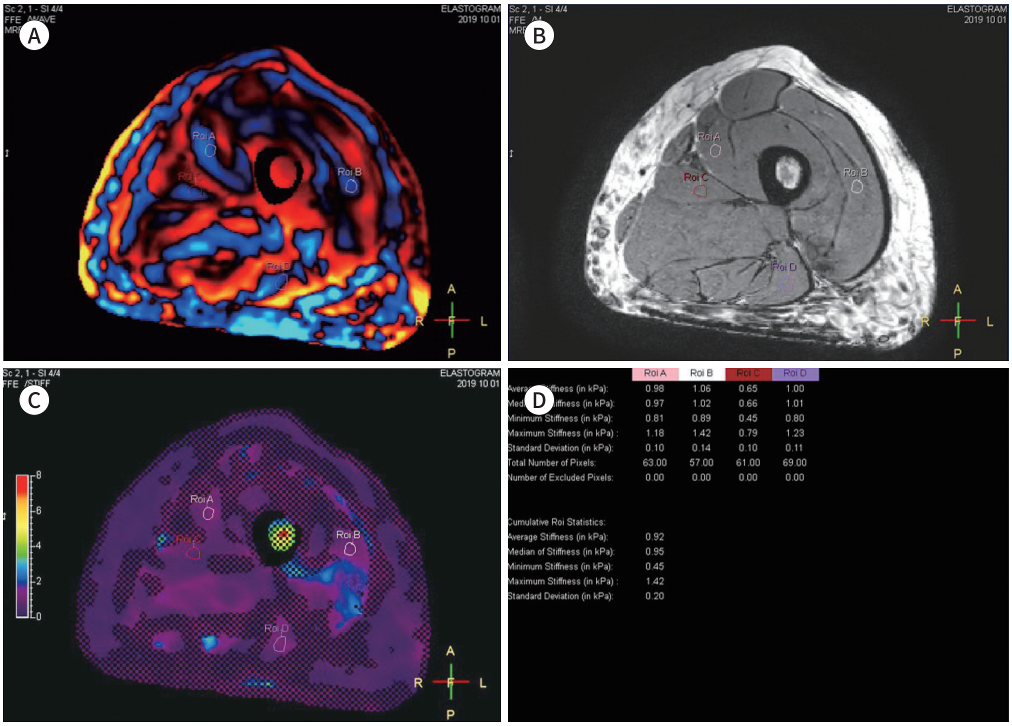
motion-encoding gradient with the following parameters: repetition time/echo rime 100/10 ms, 20° flip angle, 200 × 200 mm field of view, 128 × 128 acquisition matrix, 2 number averages, 2 mm slice thickness, and 40 seconds total acquisition time (four phase offsets with interpolation). The readout gradient direction was set perpendicular to the rectus femoris muscle fibers.

IMAGE PROCESSING AND DATA ANALYSIS

Two readers (one dedicated musculoskeletal radiologist with 24 years of experience and one third-year radiology resident) independently measured the muscle shear modulus on MRE images. The MRE technique provides phase images showing the propagation of introduced waves and stiffness maps and displays color-coded maps based on the degree of estimated shear stiffness of muscles. In the MRE analysis, anatomical magnitude images were shown together and used to identify the exact anatomy, which was separately acquired as a conventional T2-weighted image. Each reader first identified the exact location of the four thigh muscles, vastus medialis, vastus lateralis, adductor magnus, and biceps femoris, and drew the region of interest (ROI) on the anatomical magnitude image. Then, another ROI was automatically set for the same areas along the muscles on the stiffness map. The mean shear modulus was calculated automatically from the stiffness map (Fig. 2). The readers drew the ROIs in areas with homogeneous low stiffness in a relatively large area within the muscle, while avoiding vessels and edges of the muscle and tendon. Based on the confidence area overlapped on the stiffness map, the number of pixels for ROIs drawn on the stiffness maps that were included were assessed. The two readers ensured that every resulting ROI included 50 to 70 pixels, and all included pixels were reliable on the confidence map. If a pixel was considered unreliable, it was marked with a checkered pattern on a confidence-area-overlapped stiffness map and automatically excluded from the analysis. In addition, the excluded pixels in each ROI were confirmed to be 0.

Mean shear modulus data were obtained and are presented as mean ± standard deviation. SPSS version 27 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Intraclass

Fig. 2. Estimation of shear stiffness of thigh muscles on MR elastography scans.
After identifying the exact locations of muscles to be measured at anatomical magnitude images, freehand ROIs are drawn, and the same ROI is simultaneously defined in the same areas along the muscles on the stiffness map. Finally, the shear stiffness is estimated automatically from the stiffness map. Unreliable pixels on the confidence-area-overlapped stiffness maps are easily identified as excluded pixels (checkered pattern), and the results show the number of included pixels and excluded pixels in the ROIs.
A. Wave images.
B. Anatomical magnitude image.
C. Stiffness map with overlapped confidence area.
D. Estimated shear stiffness.
ROI = region of interest



	Roi A	Roi B	Roi C	Roi D
Avera ffness (in kPa):	0.98	1.06	0.65	1.00
Med tiffness (in kPa):	0.97	1.02	0.66	1.01
Minimum Stiffness (in kPa):	0.81	0.89	0.45	0.80
Maximum Stiffness (in kPa) :	1.18	1.42	0.79	1.23
Standard Deviation (in kPa):	0.10	0.14	0.10	0.11
Total Number of Pixels:	63.00	57.00	61.00	69.00
Number of Excluded Pixels:	0.00	0.00	0.00	0.00

Cumulative Roi Statistics:

Average Stiffness (in kPa):	0.92
Median of Stiffness (in kPa):	0.95
Minimum Stiffness (in kPa):	0.45
Maximum Stiffness (in kPa) :	1.42
Standard Deviation (in kPa):	0.20

coefficients were estimated to measure inter-reader agreement. The mean shear modulus values were compared between sexes and among the four thigh muscles using the Mann-Whitney U test and one-way analysis of variance, respectively. Pearson's correlation coefficients were calculated for the relationship between age and mean shear modulus to determine the influence of aging on the mean shear modulus values of the muscles. Statistical significance was set at $p < 0.05$.

RESULTS

BASELINE CHARACTERISTICS OF PARTICIPANTS

Of total 10 participants, the mean age was 32.5 years (range, 23–45 years) and the mean body mass index (BMI) was approximately 23.8 kg/m^2 (range: 18.7-32.7 kg/m^2); 3 subjects were male and 7 were female.

Table 1. Estimated Shear Stiffness Values of the Four Thigh Muscles at Rest in the Study Subjects

Sex	Age (Years)	BMI	Estimated Shear Stiffness (kPa)							
			Reader 1				Reader 2			
			VM	VL	AM	BF	VM	VL	AM	BF
Female	23	21.3	0.63	1.13	1.81	1.84	0.54	1.13	2.09	1.59
Female	23	26.7	1.05	1.31	0.76	1.12	1.07	1.26	0.71	1.05
Female	24	32.7	1.55	2.07	1.15	1.34	1.50	2.02	1.28	1.36
Male	25	20.6	1.37	1.65	1.41	0.95	1.40	1.56	1.16	0.96
Female	29	18.7	1.09	0.85	0.74	0.72	1.15	0.72	0.71	0.63
Male	33	29.9	0.81	0.95	0.79	0.94	0.81	0.88	0.94	0.89
Female	40	20.5	0.89	0.64	0.67	0.78	1.11	0.75	0.62	0.74
Female	40	20.0	0.52	0.70	0.52	0.51	0.52	0.68	0.56	0.54
Female	43	20.6	1.08	0.88	0.63	0.79	1.12	0.86	0.66	0.77
Male	45	26.6	0.76	0.79	0.65	0.91	0.76	0.82	0.61	0.91
Mean ± SD			0.98 ± 0.32	1.10 ± 0.46	0.91 ± 0.41	0.99 ± 0.37	0.98 ± 0.32	1.10 ± 0.46	0.91 ± 0.41	0.99 ± 0.37

AM = adductor magnus, BF = biceps femoris, BMI = body mass index, SD = standard deviation, VL = vastus lateralis, VM = vastus medialis

ESTIMATED SHEAR STIFFNESS VALUES OF THIGH MUSCLES AT REST

The estimated shear stiffness values of the four thigh muscles at rest for all subjects for each reader are listed in Table 1. The mean shear modulus was 0.98 ± 0.32 kPa and 1.00 ± 0.33 kPa for vastus medialis, 1.10 ± 0.46 kPa and 1.07 ± 0.43 kPa for vastus lateralis, 0.91 ± 0.41 kPa and 0.93 ± 0.47 kPa for adductor magnus, and 0.99 ± 0.37 kPa and 0.94 ± 0.32 kPa for biceps femoris, with reader 1 and 2, respectively.

INTER-READER AGREEMENT FOR MEASURING SHEAR STIFFNESS OF THIGH MUSCLES

Inter-reader agreement was excellent for all the four thigh muscles. The estimated intraclass coefficients were 0.984 [95% confidence interval (CI); 0.941–0.996] for vastus medialis, 0.994 (95% CI; 0.976–0.998) for vastus lateralis, 0.975 (95% CI; 0.902–0.994) for adductor magnus, and 0.983 (95% CI; 0.926–0.996) for biceps femoris muscles.

COMPARISONS OF SHEAR STIFFNESS BETWEEN MUSCLES AND SEX

The differences in shear stiffness among the four thigh muscles were not statistically significant between the two readers ($p = 0.771$ for reader 1, $p = 0.868$ for reader 2). The differences in shear stiffness for all four thigh muscles between males and females were also not significant between the two readers ($p > 0.05$) (Table 2).

RELATIONSHIPS BETWEEN ESTIMATED SHEAR STIFFNESS OF MUSCLES AND AGE

The estimated correlation coefficient between the shear stiffness of the four thigh muscles and the age of each reader is shown in Table 3. Despite notable variation of shear stiffness in each subject, muscles, except vastus medialis, consistently showed negative correlation with age in both readers and the coefficient ranged from -0.65 to -0.73 with statistical significance.

Table 2. Comparison of Shear Stiffness Values of Muscles Based on Sex

Thigh Muscles	Reader 1			Reader 2		
	Mean Stiffness (kPa)		*p*-Value*	Mean Stiffness (kPa)		*p*-Value†
	Male	Female		Male	Female	
VM	0.98 ± 0.34	0.97 ± 0.34	1.000	0.91 ± 0.45	1.00 ± 0.48	1.000
VL	1.13 ± 0.46	1.08 ± 0.49	0.833	1.04 ± 0.46	1.06 ± 0.48	0.667
AM	0.95 ± 0.40	0.90 ± 0.45	0.667	0.89 ± 0.30	0.95 ± 0.56	1.000
BF	0.93 ± 0.02	1.01 ± 0.46	0.833	0.80 ± 0.23	0.95 ± 0.39	0.833

Statistical significance was set at $p < 0.05$.

*Comparison of stiffness values between sexes by reader 1 using the Mann-Whitney U test.

† Comparison of stiffness values between sexes by reader 2 using the Mann-Whitney U test.

AM = adductor magnus, BF = biceps femoris, VL = vastus lateralis, VM = vastus medialis

Table 3. Estimated Correlation Coefficients between Shear Stiffness and Age

	Reader 1		Reader 2	
	Correlation Coefficient (r^*)	*p*-Value*	Correlation Coefficient ($r^\dagger$)	*p*-Value†
VM	-0.448	0.194	-0.328	0.355
VL	-0.728	0.017	-0.685	0.029
AM	-0.709	0.022	-0.658	0.039
BF	-0.651	0.041	-0.645	0.044

Statistical significance was set at $p < 0.05$.

*Pearson's correlation coefficient between stiffness values of muscle and age by reader 1.

† Pearson's correlation coefficient between stiffness values of muscle and age by reader 2.

AM = adductor magnus, BF = biceps femoris, VL = vastus lateralis, VM = vastus medialis

However, the vastus medialis did not show statistical significance ($p = 0.194$ for reader 1 and $p = 0.355$ for reader 2).

DISCUSSION

MRE was used to measure the stiffness of the skeletal thigh muscles in previous studies. Bensamoun et al. (8) reported the shear stiffness of the vastus muscles with values of 3.91 ± 1.15 kPa for vastus medialis and 3.73 ± 0.85 kPa for vastus lateralis. In the present study, the values obtained for the vastus muscle were much lower. This discrepancy could be due to basic differences in the experimental setups. In previous studies, the measured stiffness values were more likely to be higher when a higher mechanical wave frequency was used (9, 10).

The aging process can affect muscles as early as the 3rd decade of life; however, the gross morphology remains somewhat similar until a specific time point. The significant reduction in muscle mass, a condition known as sarcopenia, usually starts around the 6th decade of life, and these alterations are known to reduce the extensibility of muscles, thus affecting muscle stiffness (11-13). The present study results showed a tendency for shear stiffness to gradually decrease as age increased and muscle stiffness was statistically significantly reduced in the elderly group. There was no statistically significant correlation between the results obtained by both readers for the vastus medialis muscle; however, this might be due to the small sample size. The correlation between muscle stiffness and aging has been investigated in previous *in vivo* studies using various methods, including transient elastography, ultrasound-shear wave ultrasonography (US-SWE), and MRE; however, the results of previous studies were inconsistent. Akagi et al. (14) studied age-related differences in shear modulus in the lower extremity using US-SWE and reported significant shear modulus reduction in the rectus femoris and lateral head of the gastrocnemius muscle in the elderly group, which was similar to our results. In contrast, Eby et al. (12) also investigated the effects of aging on the shear stiffness of the biceps brachii muscle and reported a positive correlation between shear stiffness and age. Furthermore, Wang et al. (15) studied the effects of age on shear stiffness in the vastus intermedius muscle and reported no significant difference based on age, because the age effects on shear stiffness were inconsistent among studies and the present study results might have been affected by the small sample size and exclusion of older subjects, further investigation is needed.

Chleboun et al. (16) reported that passive joint torque in many joints was greater in men than in women, which was supported by subsequent studies. Passive joint torque is one parameter that might affect muscle shear modulus; thus, the differences in shear stiffness of muscle based on sex were also investigated in the present study. However, significant differences in stiffness based on sex were not observed in thigh muscles studied. Wang et al. (15) also investigated differences in shear stiffness of skeletal muscles based on sex and showed similar results. However, Eby et al. (12) reported higher stiffness values for females than males, passive joint torque, and many other parameters, such as muscle cross-sectional area, are also associated with muscle shear stiffness, and differences in joint torque might be less significant compared with other parameters. Therefore, further studies should be conducted to determine the influence of sex on the shear modulus values of skeletal muscles.

In the present study, all four thigh muscles were evaluated in a single axial plane simultaneously, and to the best of our knowledge, the shear stiffness of several different muscles together in one scan has been estimated in only a few studies. The stiffness of muscles may be calculated by manually measuring the shear wavelength along a one-dimensional profile drawn in the direction of the primary wave propagation along the muscle fibers due to the anisotropy of muscles, which has been used in many previous studies to evaluate muscles (1, 2, 17). However, in clinical settings, applying planes individually for each muscle is difficult because of the high number of acquisitions necessary and time limitations. Instead, the axial plane, which is nearly perpendicular to the fibers of thigh muscles, was applied because the thigh muscles measured in the present study were grossly aligned semi-vertically, and the actual stiffness measurements of the thigh muscles were consistent. This approach may require further validation to ensure repeatability and reliability, but could be a good option for MRE acquisition in clinical settings.

The present study had several limitations. First, the sample size was small, and all subjects were recruited volunteers who were healthy, active, and well educated and might not represent the general population. Data including BMI and performance status were collected using a simple questionnaire; thus, some degree of inherent inaccuracy may have existed. In addition, individual habits such as exercise and posture could not be strictly controlled during the scan, which could have influenced MRE acquisition. Furthermore, as mentioned earlier, the direction of the readout gradient was set perpendicular to the rectus femoris muscle, and all four muscles were evaluated simultaneously; thus, the wavelengths of the propagated waves in each muscle could not be manually measured. However, this method could be practical in clinical settings in terms of scan time and complexity, although the putative advantages require further validation with larger samples and prospective designs.

In conclusion, MRE techniques were shown to be useful for the quantitative estimation of the shear stiffness of thigh muscles, with excellent inter-observer agreement. There were no significant differences based on sex or muscle strength. However, aging was consistently negatively correlated with the shear stiffness of muscles, with statistical significance, except for the vastus medialis.

Author Contributions

Conceptualization, K.J., R.J.A.; data curation, K.J.; formal analysis, K.J.; investigation, all authors; methodology, all authors; project administration, K.J.; resources, all authors; supervision, R.J.A.; validation, K.J., R.J.A.; visualization, K.J.; writing—original draft, K.J.; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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자기 공명 탄성 검사를 이용한 대퇴 근육의 탄성도의 정량화: 초기 경험

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목적 정상 대퇴 근육의 탄성도를 정량적으로 측정함에 있어 자기 공명 탄성 검사의 실현 가능성을 확인하고 정상 대퇴 근육의 탄성도를 측정한다.

대상과 방법 이 전향적 연구는 일상적인 보행에 지장이 없는 자원자를 대상으로 대퇴부의 T2 강조 축상 영상과 대퇴 근육의 자기 공명 탄성 검사를 시행하였고 최종적으로 10명의 피실험자가 포함되었다[평균 연령, 32.5세, (범위, 23~45세)]. 탄성 특성은 휴식 상태에서 각 대퇴 근육에서의 전단 탄성 계수를 정량적으로 다음 4개의 대퇴 근육에 대해 측정하였다; 내측넓은근, 외측넓은근, 대내전근, 대퇴이두근.

결과 대퇴 근육의 평균 전단 탄성 계수는 각각 두 명의 판독자에서 내측넓은근은 0.98 ± 0.32 kPa, 1.00 ± 0.33 kPa, 외측넓은근은 1.10 ± 0.46 kPa, 1.07 ± 0.43 kPa, 대내전근은 0.91 ± 0.41 kPa, 0.93 ± 0.47 kPa, 대퇴이두근은 0.99 ± 0.37 kPa, 0.94 ± 0.32 kPa으로 측정되었다. 성별에 따른 전단 탄성 계수의 차이는 유의미하지 않게 나타났다($p < 0.05$). 내측넓은근(판독자 1; $p = 0.194$; 판독자 2; $p = 0.355$)을 제외한 나머지 대퇴 근육에서 연령은 각 근육의 전단 탄성 계수와 유의미하게 일관된 음의 상관관계를 보였다.

결론 자기 공명 탄성 검사는 개별적인 근육의 탄성 특성을 정량적으로 측정할 수 있는 유용한 검사이다. 내측넓은근을 제외한 대퇴 근육에서 나이는 근육의 전단 탄성계수와 통계학적으로 유의미한 일관된 음의 상관관계를 보였다.

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