Uniaxial Tensile Properties of Atherosclerotic Carotid Artery After Mobilization of Pushing on Qiao-Gong: A Safety Study Using an Animal Model of Carotid Atherosclerosis

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Abstract

Objectives: This study aimed to preliminarily explore the effects of the soft tissue mobilization of pushing on Qiao-Gong (MPQ) on biomechanical properties of the carotid artery using an animal model of carotid atherosclerosis (CAS).
Methods: Fifty rabbits were randomly divided into 4 groups: animals with CAS treated with MPQ (CAS-MPQ [n = 15]); animals with CAS treated without MPQ (CAS [n = 15]); normal animals treated with MPQ (normal-MPQ [n = 10]); and a blank control group (n = 10). The MPQ procedure consisted of soft tissue mobilization of the Qiao-Gong acupoint on the front edge of the sternocleidomastoid muscle applied from top to bottom, by flat pushing with the thumb repeatedly for 20 times. Disease in the CAS models was induced by carotid artery balloon injury combined with a high-fat diet for 12 weeks. At the end of modeling, carotid color Doppler ultrasonography examination was performed to confirm which animal models were successfully induced with CAS, excluding model rabbits without typical CAS at the same time. Then, MPQ was applied on rabbits in the CAS-MPQ and the normal-MPQ groups for 3 weeks. By contrast, rabbits in the other 2 groups were fed normally without MPQ. Uniaxial failure tests were later performed on carotid arteries in all 4 groups, and at the end of the study, a 2-way factorial analysis of variance of the results was conducted.
Results: (1) At the end of modeling, 10 rabbits in the CAS-MPQ group and 9 in the CAS group were included with typical carotid atherosclerotic characteristics. (2) Young's elastic modulus of the rabbit carotid artery increased more significantly in the CAS-MPQ group than the CAS group. (3) Compared with normal rabbit carotid arteries, atherosclerotic carotid arteries had lower levels of ultimate stress and ultimate strain but higher levels of ultimate load.
Conclusions: The uniaxial tensile mechanical properties of the rabbit atherosclerotic carotid artery were impaired after MPQ. (J Manipulative Physiol Ther 2018;41:164-173)
Key Indexing Terms: *Massage; Medicine, Chinese Traditional; Carotid Arteries; Atherosclerosis*

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Introduction

Manual therapy has been applied worldwide to relieve the symptoms of biomechanical dysfunction.[1-3] Manual therapy to the neck is common in the treatment of cervical musculoskeletal pain or dysfunction, which includes application of accurately determined and specifically directed manual force to the neck.[4-6] Anatomic structures in the neck are both important and vulnerable because the cervical spine is weaker than other spinal areas, as a result of its lower stability and proximity to important neural and vascular structures.[7] As a result, there are concerns about various forms of care that involve inputting force to the neck.

The complications after cervical manipulation have been rarely reported,[8-11] but there is a concern for underreporting because certain complications such as artery dissections could remain silent for days or weeks. Soft tissue mobilization or massage may sometimes cause bruising, soreness, and arterial injury.[11-13] Manipulation has aroused concern about safety with its popularity.[14] However, compared with manipulation, little is known about the side effects of soft tissue mobilization or message.

With regard to the adverse effects on cervical artery, previous studies have mainly focused on the vertebral artery (VA), and almost no studies have focused on the carotid artery (CA).[15-18] The CA is in a more superficial anatomic location compared with the VA, as indicated by the CA pulse being easily felt on both sides of the neck under the jaw. Therefore, a certain manual therapy may be more likely to affect the CA rather than the VA. For instance, in traditional Chinese medicine (TCM), the soft tissue mobilization of pushing on Qiao-Gong (MPQ) is one of the common cervical manual therapies, contributing to the relief of cervical muscle strains, neck pain, tension headaches, hypertension, and dizziness. The MPQ uses a repetitive force of flat pushing and pressing on the linear acupoint of Qiao-Gong from top to bottom. The acupoint of Qiao-Gong is located at the front edge of the sternocleidomastoid muscle, approximately along the superficial projection of the CA.[19,20] It is unclear what adverse effects the repetitive and direct force of MPQ would have on the CA during the procedure.

As one of the major arteries, the CA supplies the blood of the brain and face, and it is vulnerable because of its special anatomic position relative to the neck. It is a common site for atherosclerosis as well. Carotid atherosclerosis (CAS) indicates degradation of the collagen structure, thickening of the intima, and formation of complex plaques that contain regions with a lipid-rich necrotic core, calcifications, and often intraplaque hemorrhage.[21,22] Carotid atherosclerosis also may be one of the potential risk factors contributing to ischemic stroke (IS), possibly because of the occurrence of CA stenosis, unstable plaque, and even rupture.[23-25] This raises the question of whether CAS should be considered a potential contraindication of MPQ. It is uncertain if patients with CAS may be susceptible to IS or other arterial complications if they underwent MPQ therapy.[1,26-28] In addition, related studies mainly explored the effects on vascular hemodynamic properties[29,30] but did not explore the effects on vascular biomechanical properties. It has also been reported that the biomechanical properties of the arterial wall could be closely linked to the risk of the rupture of atherosclerotic plaque.[31,32] Knowing the variations in vascular biomechanical properties would be helpful in determining the risk of cerebrovascular accidents.

Because of this knowledge gap, we tested the hypothesis that MPQ may impair the biomechanical properties of the atherosclerotic CA, which may be one of the risks leading to the occurrence of adverse events. Therefore, the purpose of this study was to preliminarily explore the potential adverse effects of MPQ on the CA by applying it on the rabbit models of CAS, along with some unidirectional failure tests.

Methods

Animals

All procedures were approved by the Institutional Animal Care and Use Committee of China Academy of Chinese Medicine Science (No. 201506034). Fifty healthy male purebred New Zealand white rabbits aged 3 months (weight range: 2.0-2.4 kg) were housed in a pathogen-free facility in microisolator cages (China Academy of Chinese Medicine Science Experimental Animal Center, Beijing, China). All animal care was done in accordance with the "Guide for the Care and Use of Laboratory Animals" (Office of Science and Health Reports CPRR/NIH 1996).

All rabbits were randomly divided into 4 groups: animals with CAS treated with MPQ (CAS-MPQ [n = 15]); animals with CAS treated without MPQ (CAS [n = 15]); normal animals treated with MPQ (normal-MPQ [n = 10]); and a blank control group (n = 10).

Atherosclerosis Modeling

In the CAS-MPQ group and the CAS group, the atherosclerosis model was induced by CA balloon injury combined with a high-fat diet (1% cholesterol, 5% lard, 7.5% egg yolk, 86.5% common feed; Beijing Jin Muyang Experimental Animal Feed Science and Technology, Beijing, Beijing City, China). The model rabbits were fed with the high-fat diet (120 g/d) after adapting to the environment for 1 week; then, the model rabbits were anesthetized with 3% pentobarbital sodium (22.5 mg/kg intravenously [IV]), followed by balloon injury procedures on the left common CA in accordance with the previously described method.[33,34] The 3.0-mm balloon catheter was gently inflated and retracted, and it was pushed and pulled 3 times inside the left common CA of each model rabbit. A postoperative muscular injection of ampicillin (50 mg/kg/d for 5 days) was given to the subjects to prevent infection. The high-fat diet continued for 12 weeks after the surgery. During the entire experiment, the normal rabbits in the normal-MPQ group and the blank control group were fed a regular diet (120 g/d) for the same time. All rabbits were given free access to water.

Ultrasonography Examination

As a noninvasive technique, ultrasonography examination was carried out on all rabbits to detect the presence of atherosclerosis at the 12th week after modeling, in accordance with the previously described method.[35] For preparation, the rabbits were lightly anesthetized with 3% pentobarbital sodium (20 mg/kg IV) and fixed in the dorsal position with shaved neck skin. Warm ultrasound

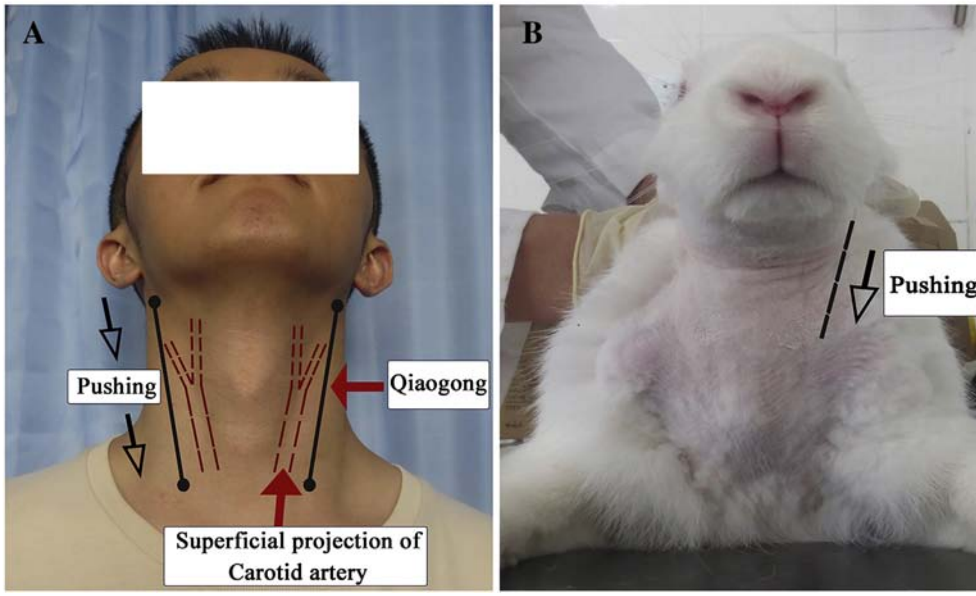

Fig 1. *Qiao-Gong acupoint and flat pushing procedure. (A) Qiao-Gong acupoint is located on the front edge of sternocleidomastoid muscle, which is also approximately along the superficial projection of carotid artery. (B) Qiao-Gong acupoint was located in the rabbit referring to the location in human body.*

transmission gel was liberally applied to ensure optimal image quality. Then, B-mode ultrasound and color Doppler images from the left common CA were obtained with a mini probe (L15-7io; Philips, Amsterdam, The Netherlands) attached to the ultrasound machine (IU22; Philips, Amsterdam, The Netherlands). In terms of thickness and roughness of the arterial wall, loss of alignment or protrusion into the lumen, abnormal echo, and lumen stenosis, CAS formation was identified compared with normal common CAs. The rest of the rabbits without typical CAS after modeling were excluded from the rest of the experiment process.

MPQ Intervention

With successful CAS model, the rabbits in the CAS-MPQ and the normal-MPQ groups underwent MPQ intervention, whereas the others were fed normally without the soft tissue mobilization.

The detailed procedure of intervention was as follows. For preparation, rabbits were placed in a prone position, with the maxilla lifted up to expose the neck area. After locating the Qiao-Gong acupoint on the front edge of the sternocleidomastoid muscle, soft tissue mobilization was applied along the linear acupoint Qiao-Gong from top to bottom, by flat pushing with thumb repeatedly for 20 times on the left side (Fig 1).

This intervention was performed by the same experienced TCM manual therapist, at a frequency of 1 time per day for 3 weeks. During the MPQ procedure, these animals were not sedated, and we observed the rabbits at the same time to identify whether a certain manifestation of discomfort appeared or not.

Histology

At the end of the entire MPQ intervention, 1 rabbit was randomly selected from each group to be euthanized by air embolism. Then the left common CAs were harvested completely and washed with phosphate-buffered saline buffer to remove the excessive fat and connective tissues. Subsequently, 5-μm sections were collected from the samples embedded in paraffin, guided by rotary microtome imaging (Nikon Eclipse CI; Nikon, Tokyo, Japan), using hematoxylin and eosin to stain the tissue sections to identify the histologic characteristics.

Uniaxial Tensile Test

Materials and Specimen Preparation. At the end of the experiment, all the rabbits in the 4 groups were euthanized by air embolism. Complete segments of their left common CAs (from the common CA branch points to arcus aortae) were harvested. The excessive fat and connective tissues were removed after washing with phosphate-buffered saline buffer (in mmol/L): NaCl 150, KCl 2.7, $Na2HPO_4$ 10, NaH_2PO_4 2, pH 7.4.[36] Each artery was dissected in a similar manner. Then the artery was opened up longitudinally (Fig 2A), and a longitudinal strip, 2 mm wide and 15 mm long, was obtained (Fig 2B) and immediately preserved in a solution of 0.90% w/v of NaCl at 4°C to 5°C before the uniaxial tensile test.

Experimental Setup and Unidirectional Failure Test. The tensile test was performed using a unidirectional tensile testing machine (Instron 5848, Micro Tester, Norwood, Massachusetts) adapted for testing biological specimens. The strips were removed

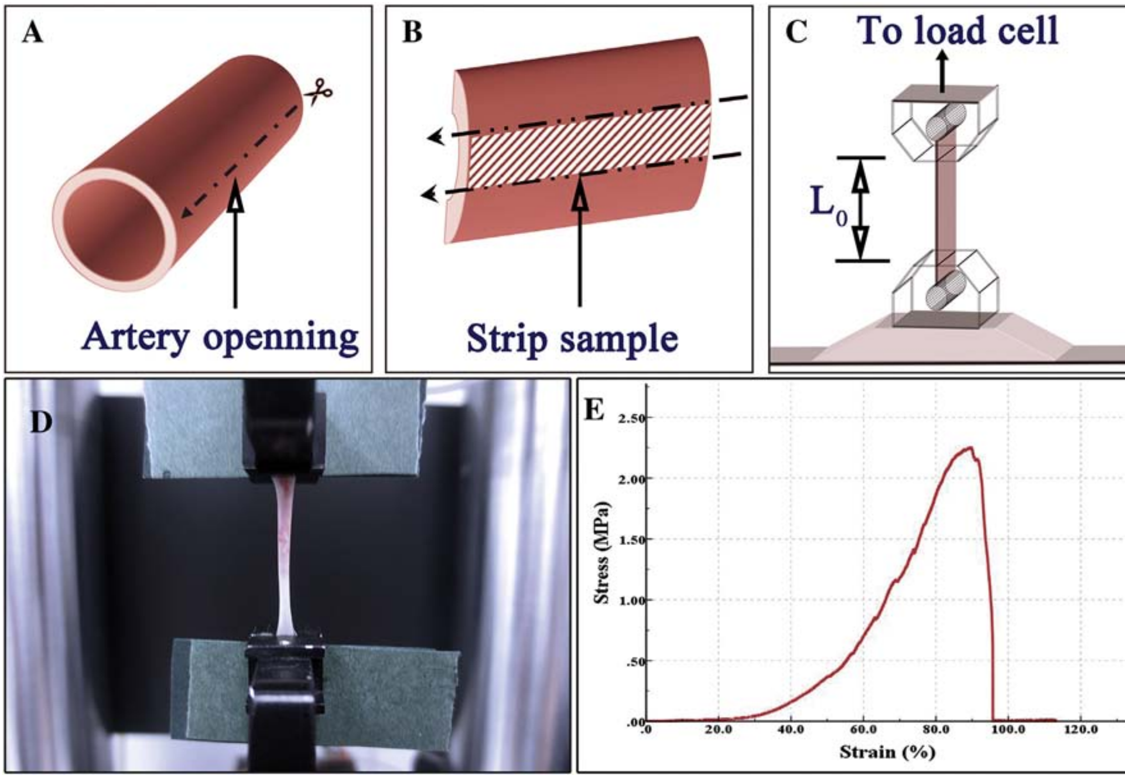

Fig 2. *Uniaxial tensile test. (A) The harvested artery was opened up longitudinally with tissue scissors. (B) Strip sample, 2 mm wide and 15 mm long, was obtained from former opened artery. (C) Sketch diagram of unidirectional failure test. (D) A picture of unidirectional failure test during tensile process. (E) A representative stress-strain curve during the tensile process.*

from the physiological saline and mounted on the tensile test machine (Fig 2C and D). The initial thickness of the strip was measured via a laser beam micrometer (LS-3100, Keyence Corp., Osaka, Japan). Because the thickness of the tissue varied along the strips, 5 measurements were taken for each strip, and the average value was used. To ensure a firm fixation of samples between the jaws of the machine, a small tensile preload of 0.05 N was applied to each machine, and rough sandpaper was used between the jaw and the sample to ensure a no-slip surface. Because the length of our strip specimen is relatively long relative to its width, 15:2; and because this work is focused on discussing the biomechanical behavior of a particular, decomposed, longitudinal sample, we neglected edge effects, in accordance with previous study.[37,38] Moreover, to minimize the effect of viscoelastic phenomena and obtain constant and reproducible stress-strain curves, each strip was subjected to 10 successive cycles before the measurement.[39] The longitudinal force (F) was applied onto the strip, and the initial length of the strip between the 2 jaws was measured by the tension device with a frequency of 50 Hz. Each strip was stretched at a constant tensile speed of 5 mm/min until failure occurred, and the stretch ratio was calculated based on a gauge length that is a grip-to-grip displacement instead of optical strain measurement to minimize the effects of boundary conditions and local deformation at the tip of the grip. At the same time, the stress-strain curves were recorded (Fig 2E). In addition, a tensile test was performed within 6 hours of tissue harvesting to preserve biomechanical properties.[40] During the process of tensile test, the strips were kept moist by dripping phosphate buffered saline onto the surface of the tissue.[41]

Mechanical Data Analysis. The previous research indicated that the engineering definitions of strain and stress were no longer applicable when deformations of the materials (eg, elastomers, polymers, and soft biological tissues) were sufficiently high. Therefore, other definitions, such as true strain and true stress, were selected instead.[42,43] The CA walls were assumed to be incompressible material. The hypothetical incompressibility of the CA indicates a zero change of volume during the process of the tensile test. Therefore, $A \times L = A_0 \times L_0$, where *A* is the current cross-sectional area of the strip, *L* is the current length, A_0 is the initial cross-sectional area, and L_0 is the initial length. The true stress was defined as $\sigma_T = F / A = (F \times L) / (A_0 \times L_0) = (F \times L) / (H_0 \times W_0 \times L_0)$, where H_0 is the initial thickness of the strip and W_0 is the initial width (2 mm). The true strain was defined as $\varepsilon_T = \ln (L / L_0) = \ln\lambda$, where λ is the stretch ratio and defined as L / L_0. Furthermore, the ultimate true strain (in %), ultimate true stress (in MPa), ultimate load (in N), and elastic modulus derived from 0.3 to 0.5 (in MPa) with approximately linear trend in stress-strain curves were measured before the failure occurred.

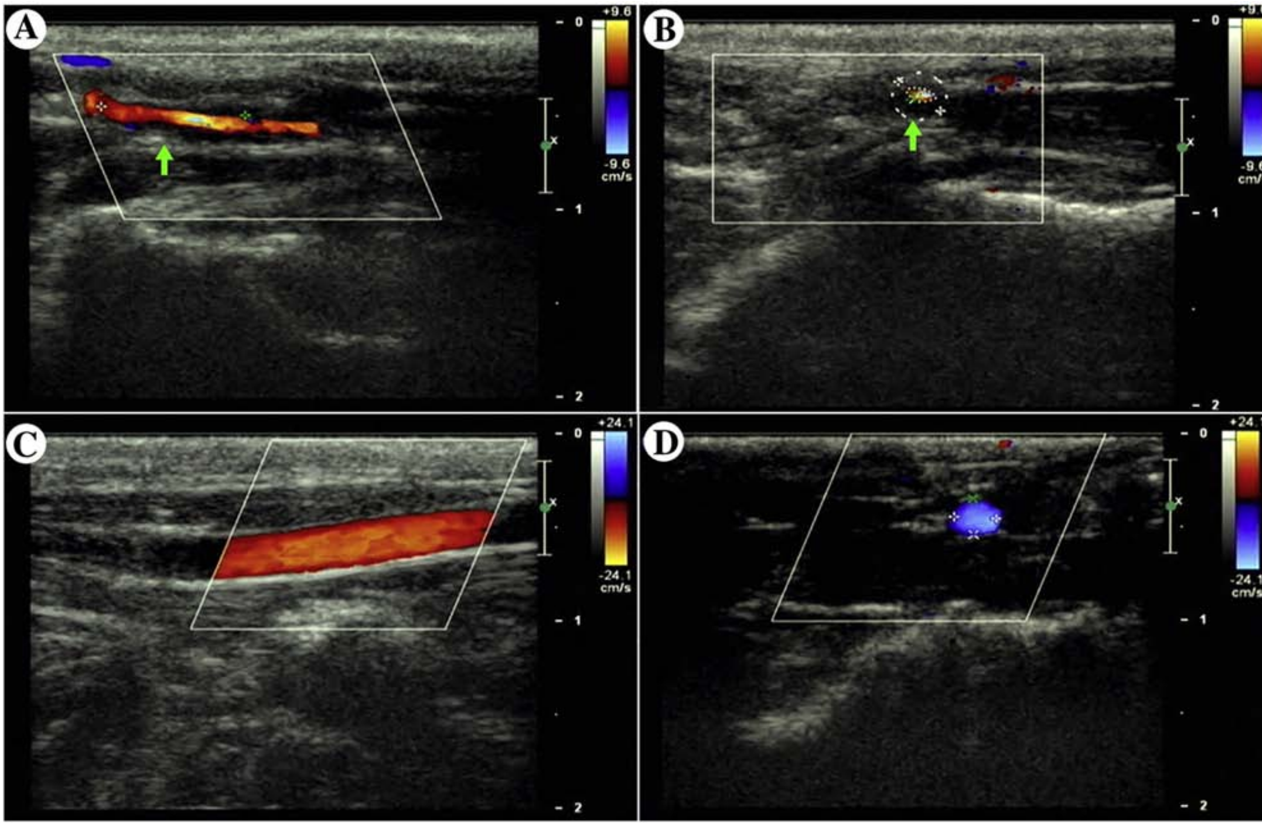

Fig 3. *Carotid ultrasonography. (A) Longitudinal image of atherosclerotic carotid artery showed arterial wall thickening and plaque formation (arrow). (B) Cross-section image of atherosclerotic carotid artery showed arterial wall thickening and lumen stenosis (arrow). (C) Longitudinal image of normal carotid artery showed arterial wall smoothness. (D) Cross-section image of normal carotid artery showed regular vessel lumen.*

Statistical Analysis

All data were presented using mean with standard error. A 2-way factorial analysis of variance was used to examine the effects of MPQ and atherosclerosis, and a multiple comparison test was performed using the Bonferroni method for assessing differences in terms of biomechanical properties (Young's elastic modulus, ultimate strain, ultimate stress, and ultimate load) among the 4 groups. A result of $P < .05$ was considered significant. All analyses were performed by SPSS 20.0 software (IBM, Armonk, New York).

Results

Ultrasonography Examination

A total of 19 rabbits with typical CAS were included: 10 in the CAS-MPQ group and 9 in the CAS group. In detail, CA stenosis was obvious, with observations of arterial wall thickening and high-level or mixed echo plaque protruding into the artery vessel (Fig 3A and B). By contrast, no lumen stenosis, arterial wall thickening, and plaque were detected in the other 2 groups (Fig 3C and D). In addition, the histologic findings confirmed the development of CAS (Fig 4).

Tensile Test

For the changes in ultimate load, ultimate stress, and ultimate strain, the main effects of CAS were considered significant ($P < .05$; Table 1), whereas the main effects of MPQ were significant for Young's elastic modulus ($P < .05$; Table 1). No interaction between MPQ and CAS was found to be significant ($P > .05$; Table 1), in terms of changes in ultimate load, ultimate stress, ultimate strain, and elastic modulus.

In addition, Young's elastic modulus increased significantly in the CAS-MPQ group compared with the CAS group ($P < .05$; Table 1, Fig 5). In contrast, no significant difference was detected when comparing the normal-MPQ group with the blank control group ($P > .05$; Table 1, Fig 5).

Discussion

The high prevalence of CAS, one of the potential risk factors of IS, has been noticeable among middle-aged and senior people. In the early stage of the disease, it always is asymptotic and is easily ignored by patients themselves. Neck pain and other cervical dysfunctions are commonly comorbid with CAS in these patients. Unaware of potential

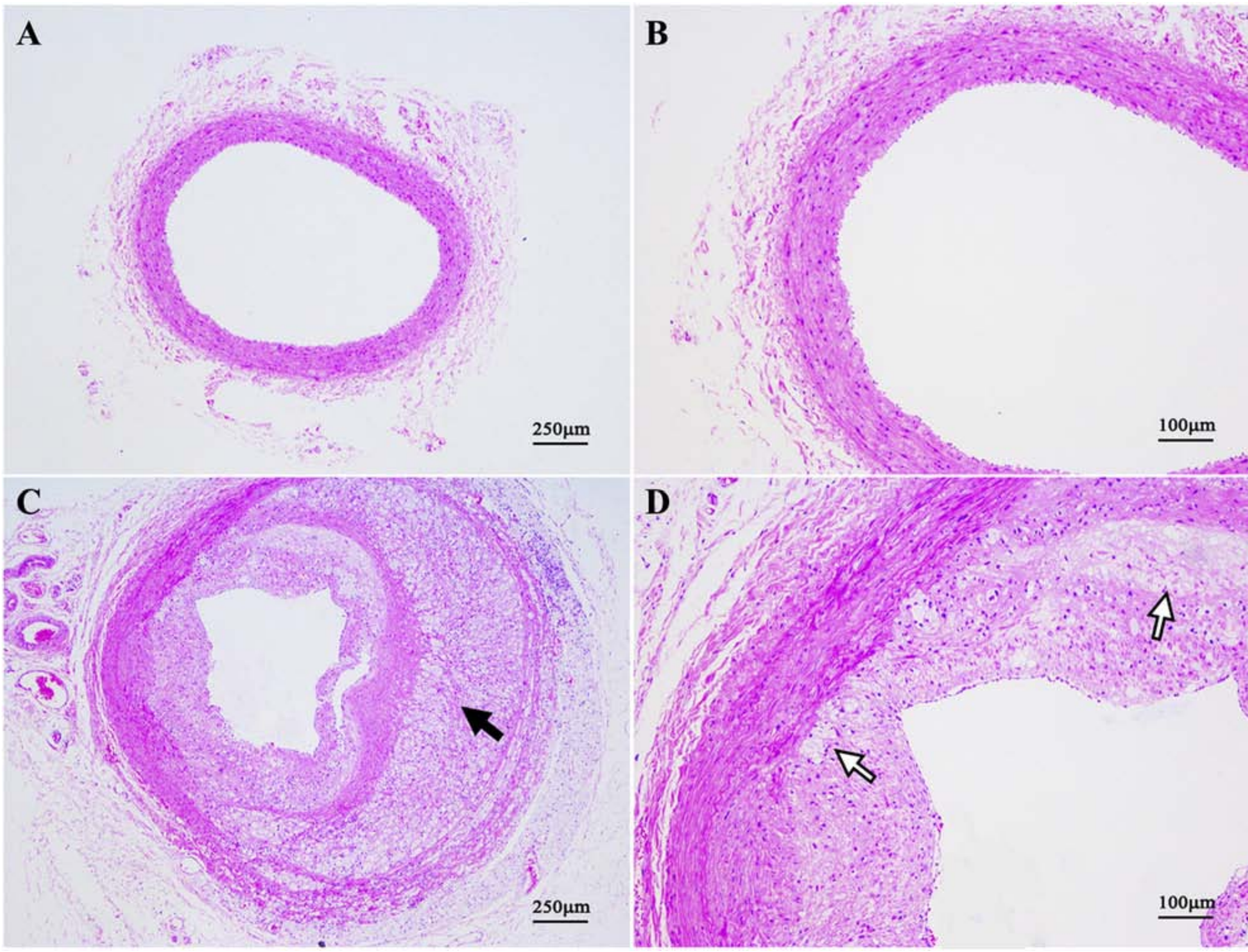

Fig 4. *Histologic observation of left common carotid artery by hematoxylin and eosin stain. (A) At low magnification, the arterial wall was normal with uniform thickness and regular fiber arrangement in the blank control group and the normal animals treated with soft tissue mobilization of pushing on Qiao-Gong (MPQ) (normal-MPQ) group. (B) At high magnification, no foam cells and atherosclerotic plaques were found in the blank control group and normal-MPQ group. (C) At low magnification, the lumen stenosis was obvious and the intima of carotid arteries had typical atherosclerotic characteristics with disordered cell arrangements and fuzzy structures (black arrow) in the animals with carotid atherosclerosis treated with MPQ (CAS-MPQ) and the CAS group. (D) At high magnification, accumulation of foam cells (white arrows) and enlarged area of cell discoloration were observed in the CAS-MPQ and the CAS group.*

underlying vascular diseases such as CAS, patients sometimes undergo cervical manual therapy (CMT), even though they are unsure of its therapeutic benefit, let alone the potential risk involved.[44-46] In brief, the safety of these therapies is still controversial and inconclusive.[47]

Studies on this issue in the human body are limited because of ethics and safety considerations. Because rabbit models of CAS were previously confirmed available for replicating CAS in the human body,[33] this study preliminarily explored the adverse effects of traditional Chinese CMT on CAS, specifically the MPQ, on the biomechanical properties. The result supported our hypothesis to some extent.

Typical pathologic characteristics associated with the development of atherosclerotic plaques within arterial vessels have been reported to result in significant alterations to the biomechanical properties of the diseased arterial wall.[38,48] Multiple studies have reported impaired biomechanical characteristics in the atherosclerotic artery.[34-43,48-50] However, few studies performed tensile tests to investigate the biomechanical properties of atherosclerotic arteries after CMT. As a fundamental materials science test in which a sample is subjected to a controlled tension until failure, tensile test has been widely used in measuring the biomechanical properties of biological tissues, such as muscle tendons, bone, cartilage, and vessels.[38,43,50,51] Using such a test would be helpful to further study whether certain CMTs would impair the biomechanical properties of the atherosclerotic CA. In addition, recent studies of tensile tests on vessels mainly used excised strips of vessels instead of entire vessels.[52,53] During the process of tensile test on vessel strips, their biomechanical properties may be easier to calculate without the effect of changing lumen; therefore, we selected the CA strips as samples to perform a uniaxial tensile test in reference to related experiments.

Table 1. *Differences in Tensile Mechanical Properties Among 4 Groups*

Trait	CAS-MPQ Group	CAS Group	Normal-MPQ Group	Blank Control Group
Ultimate load (N) [a]	4.92 ± 1.76	3.99 ± 1.49	1.96 ± 0.48	1.99 ± 0.87
Ultimate stress (MPa) [a]	4.78 ± 1.96	3.17 ± 1.11	6.62 ± 3.43	5.38 ± 0.91
Ultimate strain (%) [a]	77.50 ± 26.92	82.20 ± 29.36	117.25 ± 13.35	134.76 ± 63.22
Young's elastic modulus (MPa) [b,c]	5.19 ± 1.63	3.78 ± 1.16	4.57 ± 1.07	3.61 ± 0.84

CAS, carotid atherosclerosis; *MPQ,* mobilization of pushing on Qiao-Gong.
Two-way analysis of variance results:
[a] Significant $P < .05$ CAS main effect, $P > .05$ MPQ main effect.
[b] Significant $P < .05$ MPQ main effect, $P > .05$ CAS main effect.
[c] $P < .05$ significance of comparisons for CAS-MPQ group vs CAS group.

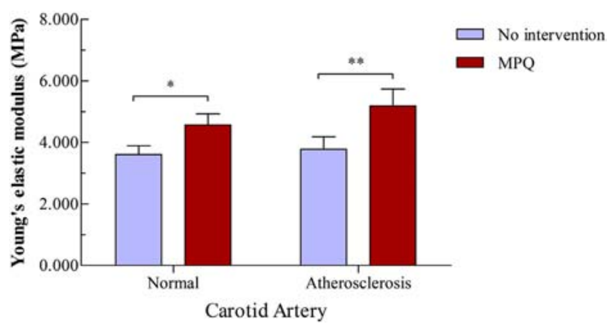

Fig 5. *Young's elastic modulus (MPa) of carotid arteries in 4 groups (mean, standard error). *P > .05, **P < .05.* MPQ, *mobilization of pushing on Qiao-Gong.*

Consequently, the rabbit models of CAS were prepared, and we intervened with MPQ. Comparing the biomechanical characteristics among different groups through conducting a tensile test, we found that the atherosclerotic CAs had decreased levels of ultimate stress and ultimate strain but an increased level of ultimate load at the same time. It may indicate that the decrease of flexibility in the CA was a result of increasing thickness of intima, disordered arrangement of elastic fibers, or even broken and disappearing fibers, which is in accordance with histologic changes in the CAS-MPQ and CAS groups. These findings could also explain why the biomechanical properties of the atherosclerotic artery would be more impaired than those of the normal artery.

Moreover, it was also noted that Young's modulus of the atherosclerotic CA increased significantly with application of MPQ. In contrast, no significant difference was identified between the normal-MPQ group and the blank control group with the normal common CA. Young's modulus, which is also known as the elastic modulus, is a mechanical property of linear elastic solid materials. It defines the relationship between stress and strain of a material. For instance, it predicts how much a material sample could extend under tension in this experiment. Young's modulus directly applies to cases of uniaxial stress, which is tensile or compressive stress in one single direction without any stress in the other directions. In addition, elastic modulus is usually used in measuring the elasticity and stiffness of soft tissues, such as arteries, veins, ligaments, and muscles. Generally, a material with a high Young's modulus is considered rigid, indicating that it is a stiff material that requires more force to deform compared with a less rigid material.[39,47,49] Based on this, the atherosclerotic CA may become rigid and stiff with low elasticity in tensile mechanical properties after treatment of MPQ. Multiple studies have reported that increased arterial stiffness and diminished arterial elasticity are associated with incident stroke and symptomatic CA disease.[48,54] This suggests that impairment of biomechanical properties of the atherosclerotic CA after MPQ may be one of the potential risks leading to adverse vascular events.

In TCM, MPQ and cervical rotatory manipulation (CRM) are both common CMTs. The safety of MPQ has rarely been considered because MPQ was usually considered gentler than CRM.[19,20] Cervical rotatory manipulation, similar to high-velocity and low-amplitude thrust in Western medicine, both require high-velocity and low-amplitude power on the cervical spine area, which would apply a tensile force rapidly along the length of the pressurized vessel. Further, Zhang et al[55] have found that CRM may decrease the uniaxial tensile properties of the rabbit arteriosclerotic CA, indicating a trend of increasing elastic modulus similar to our result. By contrast, the MPQ procedure applies a linear slow load superficially to the soft tissue of the neck along the length of the vessel. The loading profiles for the artery are different during the 2 procedures. In detail, the slow loading of the vessel in MPQ may allow for tissue creep, whereas the rapid loading of the vessel in CRM will allow the tissue to behave elastically. Because of repetitive tissue creep and press-push force on the nearby region of the superficial projection of the CA, it is reasonable to discuss the potential adverse effects of MPQ procedure on the arterial wall, especially in biomechanics. In this experiment, we attempted to add a uniaxial load on the vessel strips, which was easy to perform, to preliminarily represent the potential physiological loading on the local arterial wall in vivo during the MPQ procedure. Finally, the result supported that MPQ may impair the uniaxial tensile biomechanical properties of the rabbit atherosclerotic CA and might have similar effects on human atherosclerotic CA, which was helpful in guiding the use of MPQ in clinics.

Limitations

In ultimate load, ultimate stress, and ultimate strain, no significant difference was found in the effects of MPQ on atherosclerotic CAs. This result could be attributed to the sample size, objective conditions, measurement errors, and features of the animal model in the study. Second, the CAS models still had different degrees of atherosclerosis because of individual differences and objective condition restrictions, despite the same modeling procedure. Third, the MPQ were carried out by the same TCM manual therapist to standardize the intervention as far as possible; however, using a human thumb on a rabbit to simulate the MPQ on human body seems to be a large point. Mobilization of pushing on Qiao-Gong used on animals is only similar to MPQ used on human body, but it is not the same. Forth, uniaxial tensile test on isolated strips only could not entirely indicate the mechanical properties of vessels without other mechanical tests. Test on strips was different from pressurized whole vessels because of noncontinuity of the vessel's collagen matrix during loading and the different mechanical properties as a result of artery opening, including increased Poisson ratio and strain-stress. This may influence the result to a certain extent. Although the largest sample size possible was used for these tensile tests, the 15- × 2-mm gauge length might be insufficient to fully prevent edge effects from the clamps. Because these limitations existed, the experiment was a preliminary research about the biomechanical effect of MPQ on CA by using animal models. It is not yet certain if the findings in the rabbit model can be translated to humans.

Conclusion

In conclusion, the uniaxial tensile mechanical properties of the rabbit atherosclerotic CA was impaired after MPQ.

Practical Applications

- An animal model of rabbit CAS could replicate CAS in human body, which was helpful to evaluate the effects of MPQ on CAS, avoiding serious adverse events during a clinical trial.
- We evaluated MPQ in TCM, which may have effects on CA with reduplicated power of pressing and pushing on the approximate position of the surface projection of CA.
- Our experiment showed the effects of pushing on Qiao-Gong on the atherosclerotic CA—decreasing artery mechanical properties of the CA—through animal experiments.

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Authors Ji Qi, Shaoqun Zhang, Lei Zhang, and Ruiyue Ping contributed equally to this work.

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Contributorship Information

Concept development (provided idea for the research): Y.L.
Design (planned the methods to generate the results): J.Q., S.Z., L.Z., R.P., Y.L.
Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): J.Q., S.Z., L.Z., R.P.
Data collection/processing (responsible for experiments, patient management, organization, or reporting data): J.Q., S.Z., L.Z., R.P., D.Y., H.S.
Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): K.P., Y.C.
Literature search (performed the literature search): J.Q., S.Z., L.Z., R.P.
Writing (responsible for writing a substantive part of the manuscript): J.Q., S.Z., L.Z., R.P., D.Y.
Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): D.Y.

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