Carpal Tunnel Syndrome

Evaluation of the Effects of Low-Level Laser Therapy With Ultrasound Strain Imaging

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Objectives—To evaluate the efficacy of low-level laser therapy on median nerve stiffness by using strain elastography in carpal tunnel syndrome (CTS).

Methods—This study included 37 wrists of 34 patients with mild or moderate CTS between January 2016 and August 2016. The control group comprised 17 patients (18 wrists) with CTS who were treated with wrist splinting for 3 weeks. The low-level laser therapy group included 17 patients (19 wrists) with CTS who were treated with a combination of splinting and low-level laser therapy, which was applied 5 times per week for 3 weeks. Clinical assessment scales, including the Symptom Severity Scale (SSS) and Functional Status Score (FSS), were obtained from our database. The cross-sectional area by ultrasound and strain ratio by elastography were studied. The differences in the strain ratio, cross-sectional area, SSS, and FSS between pretreatment and posttreatment periods in the groups were compared by the paired-sample *t* test. The correlations between changes in the strain ratio and the cross-sectional area, SSS, and FSS were analyzed by Pearson correlation coefficients.

Results—The control group included 13 women and 4 men, and the therapy group included 14 women and 3 men. In the therapy group, the mean values of the strain ratio, cross-sectional area, SSS, and FSS decreased significantly after laser therapy ($P < .001$) in contrast to the control group. No significant correlation was observed between the decreasing degree of the strain ratio and the cross-sectional area, SSS, and FSS after laser therapy.

Conclusions—The strain ratio and cross-sectional area of the median nerve decrease after low-level laser therapy. These changes may be related to the therapeutic effects of low-level laser therapy, such as nerve regeneration and improvement of the vascular supply.

Key Words—carpal tunnel syndrome; cross-sectional area; median nerve; musculoskeletal; strain elastography; strain ratio

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Abbreviations

CTS, carpal tunnel syndrome; FSS, Functional Status Score; SSS, Symptom Severity Scale; US, ultrasound

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Carpal tunnel syndrome (CTS) is an entrapment neuropathy caused by compression of the median nerve in the carpal canal, and it is the most common neural entrapment syndrome, with a female predominance.[1] The diagnosis of CTS is generally based on clinical symptoms, the physical examination, and electrophysiologic tests, including electromyography, which is considered the reference standard for the definitive diagnosis.[2] Nevertheless, electrophysiologic tests are invasive and expensive, as well as requiring the patient's cooperation, and several studies also revealed that false-negative rates have ranged from 10% to 20% in electrophysiologic tests for the diagnosis.[3] In addition, electrophysiologic tests cannot provide morphologic information on the median nerve. In recent years, ultrasound (US) has become the best alternative diagnostic tool for CTS because of its advantages of being safe, inexpensive, and easy to perform. Moreover, US yields morphologic information, including the cross-sectional area, flattening ratio, and palmar bowing of the median nerve, and also can show the vascularity of the nerve by using a power Doppler examination.[1,2]

Elastography is a novel, noninvasive US technique that assesses the stiffness of the soft tissues.[4] The principle of elastography is based on an analysis of the displacement of tissue, which is induced by external freehand compression or dynamic stress such as shear wave propagation.[4] Depending on the manner of tissue displacement, 2 main elastographic techniques have been defined. Strain elastography determines the tissue strain generated by external freehand compression of the tissue by means of a US transducer, and the amount of tissue displacement relative to the surrounding normal tissue is measured and defined as the strain ratio. The degree of tissue displacement is greater in harder tissues than that in softer tissues. In contrast to strain elastography, shear wave elastography uses an acoustic radiation force impulse generated by a focused US beam, which enables measurement of the shear wave speeds within the tissue to determine the tissue stiffness quantitatively.[4]

Compression of the median nerve causes hyperemia and edematous changes in the nerve in the early period, and after the initial changes, fibrosis, axonal loss, or demyelination becomes prominent over the next month.[5] Fibrosis or demyelination, which may be caused by ischemic injury due to the chronic compression, leads to an increase in the stiffness of the median nerve, which may recover after treatment options, including conservative management, splinting, local steroid injection, US, surgery, and low-level laser therapy.[5–7] In recent years, low-level laser therapy has become a widely used option for mild and moderate CTS, owing to the benefits on clinical and electrophysiologic tests. The possible mechanisms of the therapeutic effects of low-level laser therapy are anti-inflammatory effects, improvement of the vascular supply, and myelin production in the median nerve, which may result in nerve regeneration.[5] Low-level laser therapy was found to be an effective treatment option for pain relief and improvement in motor and sensory nerve conductions in some studies.[8,9] Determination of the median nerve stiffness in pretreatment and posttreatment procedures may provide information about the efficacy of treatment and recovery of the median nerve in CTS. Several studies on median nerve applications of strain elastography have revealed that it has been valuable in detecting nerve stiffness in patients with CTS compared to healthy control groups.[6,7,10,11] To the best of our knowledge, the use of strain elastography for evaluation of the median nerve after low-level laser therapy has not yet been studied. The aims of this study were to determine the stiffness of the median nerve in CTS and to evaluate the efficacy of low-level laser therapy on the median nerve by using strain elastography.

Materials and Methods

Data Acquisition

Our retrospective study was approved by the Institutional Review Board of Baskent University Hospital (approval number KA17/142). Strain elastography was part of the routine clinical protocol for median nerve evaluation at our institution between August 2015 and August 2016. A total of 44 wrists of 41 patients with mild or moderate CTS, which was diagnosed by electrophysiologic tests and treated with wrist splinting or a combination of splinting and low-level laser therapy between January 2016 and August 2016, were examined. Exclusion criteria included radiculopathy, polyneuropathy, brachial plexopathy, pregnancy, systemic diseases such as diabetes mellitus and rheumatoid arthritis, and a history of wrist surgery or severe CTS. Four cases with diabetes mellitus, 2 cases with a ganglion cyst, and 1 case with a bifid median nerve were excluded from the study. This study finally included 37 wrists of 34 patients, which were selected randomly. We divided the patients into 2 groups: control and low-level laser therapy groups. The patients, who were treated with only wrist splinting and also were not suitable for low-level laser therapy or other treatment options were classified as the control group. The patients who were treated with the combination of low-level laser therapy and splinting in this period were defined as the low-level laser therapy group. The control group, including patients with CTS who were treated with only wrist splinting, consisted of 18 wrists in 17 patients. The therapy group consisted of 19 wrists in 17 patients. Electrophysiologic examinations were performed with a Medelec Synergy Multimedia electromyographic/evoked potential machine (Oxford

Instruments, Abingdon, England) in a temperature-controlled room by a physical therapy and rehabilitation specialist with greater than 15 years of experience using a standard clinical protocol based on the American Association of Electrodiagnostic Medicine. The control group comprised 5 wrists with moderate and 12 wrists with mild CTS, whereas the therapy group included 4 wrists with moderate and 15 wrists with mild CTS.

Ultrasound Technique

Ultrasound measurements and elastography were performed between January 2016 and August 2016. All studies were performed with a 9.4-MHz linear array transducer (Acuson 3000; Siemens AG, Erlangen, Germany) by the same radiologist, with 10 years of experience. All examinations were performed while patients were seated facing the examiner with the elbow and fingers flexed and the wrist supinated and relaxed. The transducer was placed on the volar aspect of the wrist, and transverse US images were obtained from the proximal inlet of the carpal tunnel at the scaphoid-pisiform bone level. The cross-sectional area values of the median nerve were measured for each wrist and were measured by performing a continuous boundary trace of the nerve.

Strain Elastography

Strain elastography was performed with eSietouch elasticity imaging technology on an Acuson S3000 system equipped with a 9.4-MHz linear transducer. Strain elastographic images were obtained by repeated compressions of the palm with the transducer. The quality factor option, which provides real-time qualitative feedback for optimizing the acquisition technique, was used to select the optimal images for review and to determine the adequate compression to ensure successful tissue displacement. The compression force applied to the median nerve was adjusted according to a quality factor set on the machine, which was displayed on the screen. A quality factor of 70 or greater was used to ensure adequate median nerve displacement while obtaining the elastogram. The region-of-interest box was placed over the whole cross-sectional area of the median nerve, and the adjacent tissue at the same depth was used as the reference. The images from conventional US imaging and elastography were displayed side by side as a single image. The strain ratio was measured on a static image including coupled B-mode and elastographic images. Calculation of the strain ratio was based on a comparison of the average strain measured in the median nerve and adjacent soft tissue at the same depth. The strain ratio was automatically calculated by the embedded software program in the US unit. Measurements were repeated 3 times, and the mean strain ratio was calculated. All machine settings were preset to fixed values for all patients: the imaging frequency was 8 MHz; dynamic range was 65 dB; frames per second were 16; and imaging depth was 30 mm. All examinations were performed by a radiologist with 5 years of experience in elastography.

The patients were evaluated at the baseline and at the end of the treatment. The baseline cross-sectional area and strain ratio values were obtained for each patient in both the therapy and control groups on the same day as electromyography. After 3 weeks, cross-sectional area and strain ratio measurements were repeated in both the therapy and control groups at the end of the therapy. All parameters were obtained from the database of the Nucleus program (Mentor Graphics, Erlangen, Germany). Representative elastographic images in a patient with CTS are shown in Figures 1 and 2.

Low-Level Laser Treatment

For the source of the low-power laser, a gallium-aluminum-arsenide diode laser device (Encre Intelect laser; Hixon Manufacturing and Supply Co, Fort Collins, CO) was used with a power output of 100 mW and a wavelength of 670 nm. A total of 5 points across the median nerve trace were irradiated with the laser transducer. The patients received 15 sessions of laser irradiation at each point of the skin overlying the median nerve on the volar side at the wrist. The total dose per treatment was 4 J, and the accumulated dose for 15 treatments was 60 J. All treatments were applied once per day, 5 days per week, with a total duration of 3 weeks. All patients were treated by the same physiotherapist.

Clinical Assessment

The Symptom Severity Scale (SSS) and Functional Status Score (FSS), which were developed by Levine et al,[12] are used for clinical follow-up in CTS. The SSS and FSS evaluations were performed in all patients at the baseline and at the end of the 3 weeks. The data SSS and FSS data for the patients were obtained from our database. The SSS has 11 items, consisting of pain, nocturnal symptoms, numbness, tingling, and weakness. The FSS has 8 items, including difficulty in writing, buttoning clothes, holding a book, gripping a telephone receiver, opening jars, household chores, carrying grocery bags, bathing, and dressing. The severity of each symptom was graded from 1 (no symptoms or no difficulty) to 5 (very severe symptoms completely preventing the activity).

Statistical Analyses

Statistical analyses were performed with SPSS version 22.0 software (IBM Corporation, Armonk, NY). The Kolmogorov-Smirnov test was used to analyze the normal distribution of data. All measurements are expressed as means ± 2 SDs. We used the paired-sample *t* test to compare pretreatment and posttreatment measurements (cross-sectional area, strain ratio, SSS, and FSS) in both the therapy and control groups. The differences of changes in the values of the strain ratio, cross-sectional area, SSS, and FSS at the end of the treatment between the therapy and control groups were studied by the independent-sample *t* test. The correlations between

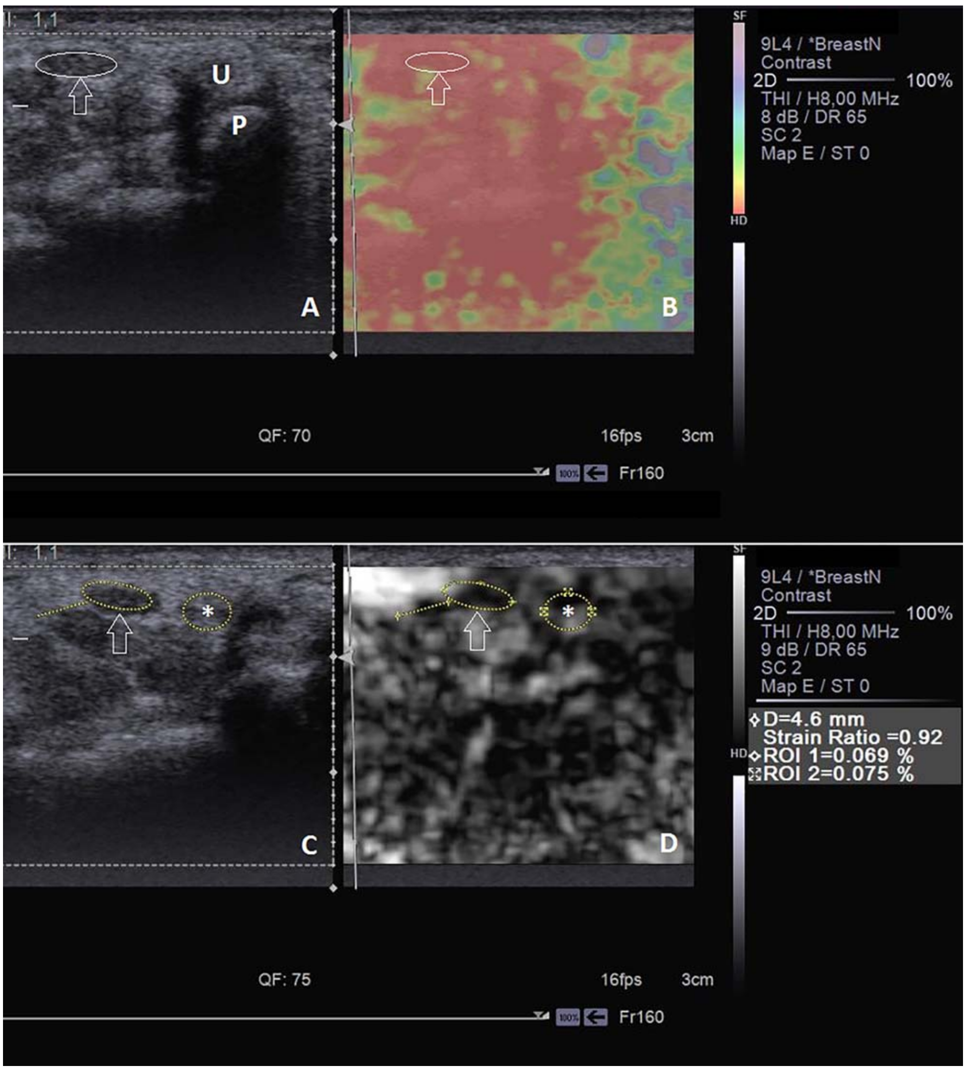


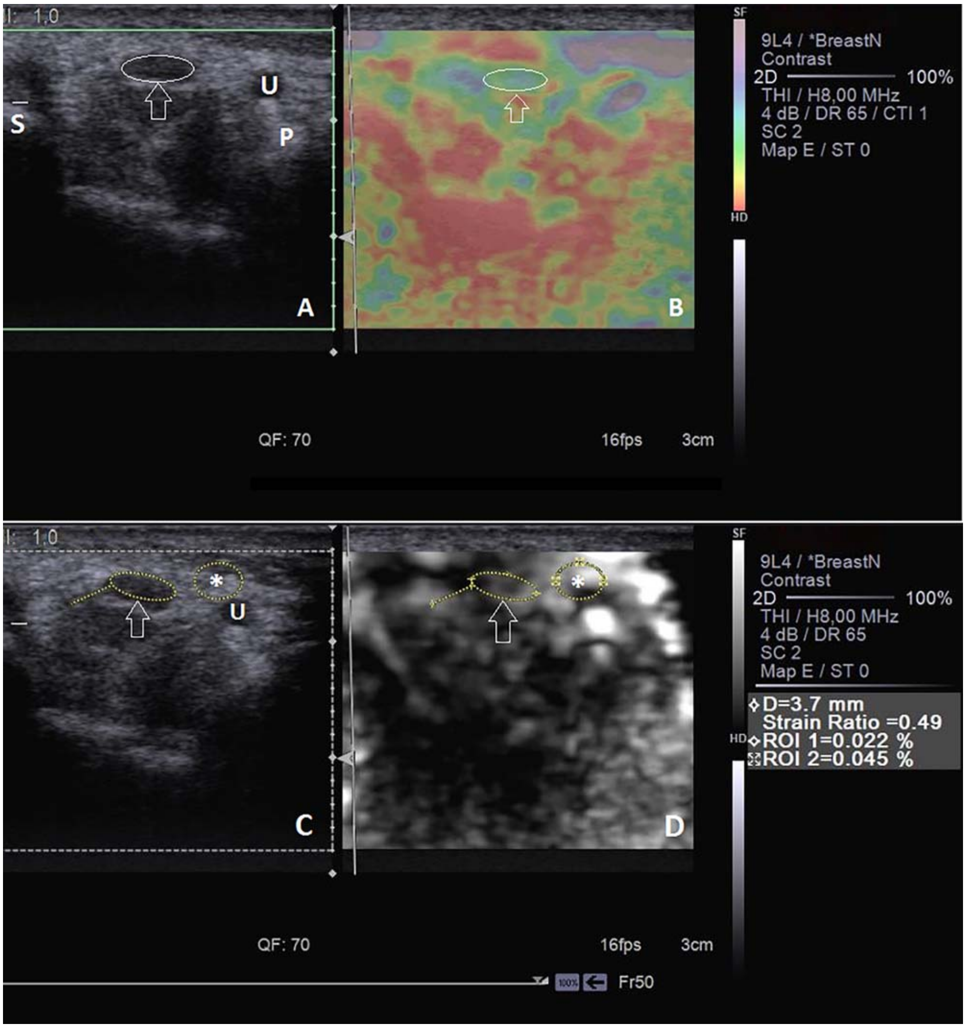
Figure 1. Images from a 55-year old woman with untreated mild CTS. **A**, Conventional B-mode image shows the median nerve (white oval with arrow), ulnar artery (U) and pisiform (P). **B**, Color-coded elastogram represents the stiffness of the median nerve (white oval with arrow) in the region of interest. The color scale ranges from blue for softest tissues to red for stiffest tissues. **C** and **D**, Conventional B-mode image (**C**) and strain elastogram (**D**) show the median nerve (yellow ovals with arrows) and adjacent fat (asterisks). The strain ratio was calculated by determining the ratio of the strain from the median nerve compared to that of fat. In this case, the strain ratio was 0.92.

alterations of the strain ratio and cross-sectional area values at the end of the 3 weeks were calculated by Pearson correlation coefficients in both the therapy and control groups. We also used Pearson correlation coefficients to analyze the correlation between alterations of the strain ratio values and changes in the SSS and FSS at the end of the treatment in the therapy group. The paired-sample *t* test was used to compare strain ratio and cross-sectional area values according to CTS grade, including mild and moderate, in both the therapy and control groups. The differences in the initial strain ratio values between patients with mild and moderate CTS were studied by the independent-sample *t* test. Statistical significance was accepted at $P < .05$.

Results

The control group included 13 women and 4 men (age range, 36–65 years; mean age, 53.4 years). The low-level laser therapy group included 14 women and 3 men (age range, 32–64 years; mean age, 47 years).

Figure 2. Images from a 55-year old woman with mild CTS after low-level laser therapy (3 weeks after Figure 1 was obtained). **A**, Conventional B-mode image shows the median nerve (white oval with arrow), ulnar artery (U), pisiform (P), and scaphoid (S). **B**, Color-coded elastogram represents the median nerve, which is encoded with green and blue (white oval with arrow). **C** and **D**, Conventional B-mode image (**C**) and strain elastogram (**D**) show the median nerve (yellow ovals with arrows) and adjacent fat (asterisks), which were used to calculate strain ratio. The strain ratio changed to 0.49 after laser therapy.



The mean cross-sectional area, strain ratio, SSS, and FSS values for the therapy and control groups are summarized in Table 1. In the control group, we found no significant differences in the strain ratio, cross-sectional area, FSS, and SSS values between pretreatment and posttreatment examinations (Table 1 and Figure 3). As shown in Table 1, the mean values for the strain ratio, cross-sectional area, SSS, and FSS decreased significantly after laser therapy in the therapy group ($P < .001$; Figure 3). In comparing the decreasing degree of the strain ratio ($P = .081$) and cross-sectional area ($P = .12$) values at the end of the treatment in the therapy and control groups; no significant difference was observed between the groups (Table 1). However, the changes in both the SSS (P < .001) and FSS (P < .001) values after treatment showed significant differences between the groups (Table 1). We found no significant correlation between the decreasing degree of cross-sectional area and strain ratio values at the end of the laser therapy in the therapy group ($P = .603$). We also analyzed the correlation between the decreasing degree of cross-sectional area and strain ratio values in the control group, and no significant correlation was observed among those values ($P = .67$).

In the therapy group, we found no significant correlation between alterations of strain ratio and SSS values at the end of the laser therapy compared to baseline measurements ($P = .72$; $R = 0.08$). Similarly, at the end of the treatment, no significant correlation was observed between the changes in strain ratio and FSS values in the therapy group ($P = .2$; $R = –0.3$).

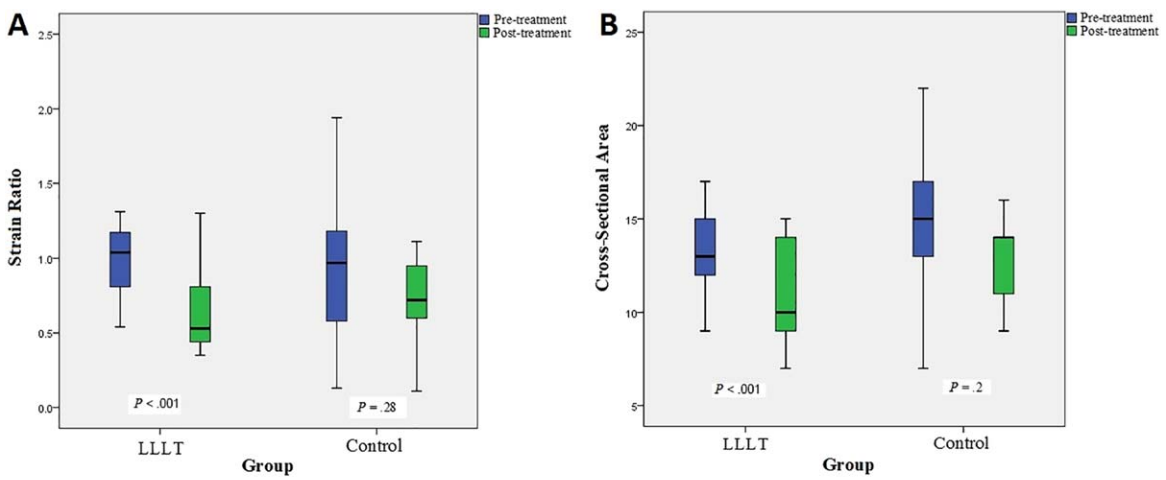
The initial mean cross-sectional area values were found to be significantly higher in the patients with moderate CTS (n = 9; mean value, 16.2 mm) compared to those with mild CTS (n = 27; mean value; 12.8 mm; $P = .01$). The initial mean strain ratio of the median

Table 1. Ultrasound and Strain Elastographic Findings for the Therapy and Control Groups

	Therapy			Control			
Parameter	**Pretreatment**	**Posttreatment**	***P***	**Pretreatment**	**Posttreatment**	***P***	***P*[a]**
Strain ratio	0.98 ± 0.21	0.63 ± 0.24	<.001	0.94 ± 0.44	0.81 ± 0.43	.28	.081
Cross-sectional area, mm^2	13.0 ± 2.9	10.8 ± 2.4	<.001	14.4 ± 4.06	13.5 ± 3.7	.20	.12
SSS	2.5 ± 0.37	2.0 ± 0.32	<.001	2.25 ± 0.56	2.26 ± 0.65	.94	<.001
FSS	2.4 ± 0.59	1.9 ± 0.49	<.001	2.20 ± 0.71	2.25 ± 0.75	.32	<.001

Data are presented as means ± 2 SDs.
[a]Therapy versus control.

Figure 3. Box plots showing the distributions of the strain ratio (**A**) and cross-sectional area (**B**) values of the median nerve in the pretreatment and posttreatment periods in the low-level laser therapy (LLLT) and control groups. As shown, the strain ratio and cross-sectional area values decreased significantly after treatment in the therapy group in contrast to the control group.



nerve in the patients with moderate CTS (n = 9) was 1.23 ± 0.12, which was significantly higher than the mean strain ratio in the patients with mild CTS (n = 27; 0.87 ± 0.05; *P* = .005). In the therapy group, the mean strain ratio values were significantly decreased after laser therapy in both the mild (*P* < .001) and moderate (*P* = .002) CTS groups (Table 2). We found no significant difference in the mean strain ratio values between pre– and post–3-week examinations in both the patients with mild (*P* = .61) and moderate (*P* = .393) CTS in the control group (Table 2).

Discussion

In recent years, the application of median nerve elastography has become widespread for diagnosis of CTS in combination with grayscale US, with regard to evaluation of the elasticity of the tissues. Most of the studies performed up to date analyzed the efficacy of elastography in the diagnosis of CTS by comparing the elasticity of the median nerve in healthy volunteers and patients with CTS.[5,7,10,13,14] However, few studies compared the stiffness of the median nerve in pretreatment and posttreatment periods for CTS.[6,15] Our study evaluated the median nerve stiffness by using strain elastography to determine whether the strain ratio can be used for clarifying the efficacy of low-level laser therapy for CTS.

Histopathologic features of CTS include thickening of the tendon sheath, edema, fibrosis of the tenosynovium with thickening of vessel walls, intimal hyperplasia, and thrombosis.[16] In the early period, the median nerve is more hyperemic and edematous; however, after initial changes, fibrosis, demyelination, and axonal degeneration may gradually develop in the nerve.[17] The increased intracarpal tunnel pressure and continuously shearing stress result in fibroblast invasion, which gradually increases fibrosis in the median nerve.[18] Additionally, ischemic injury caused by chronic compression results in focal demyelination and axonal degeneration in the median nerve, and these degenerative changes lead to an increase in the stiffness of the median nerve.[6,7]

Previous studies showed that low-level laser therapy had some potential benefits, including anti-inflammatory and anti-edematous effects, increased adenosine triphosphate production and cellular respiration, and improvement of the vascular supply to the median nerve, in the treatment of CTS.[5,19] Furthermore, low-level laser therapy leads to an increase in myelin production, which results in nerve regeneration.[19] In addition to low-level laser therapy, wrist splinting is a widely used option for conservative treatment of CTS, especially in patients with mild or moderate CTS.[20,21] Although some studies demonstrated that splinting provided significant improvement, especially in clinical symptoms of CTS, most of the studies revealed that the combination of low-level laser therapy and splinting had better therapeutic outcomes for both clinical symptoms and electrophysiologic tests compared to splinting alone in the treatment of CTS.[21–23] Our study showed that the stiffness of the median nerve was decreased significantly after the combination of low-level laser therapy and splinting in both the mild and moderate CTS groups. This finding may be related to the fact that laser therapy has the potential for nerve regeneration and improvement in the blood supply, which reduces the ischemic injury and fibrosis of the median nerve. We found no significant change in the elasticity of the median nerve in the control group, which received only wrist splinting without any other treatment options. However, interestingly, the decreasing degree of strain ratio values at the end of the 3 weeks was not significantly different between the therapy and control groups. In a study performed by Miyamoto et al,[7] which evaluated the effect of corticosteroid injection on the intracarpal tunnel by comparing strain ratio and cross-sectional area values, significant decreases in strain ratio and cross-sectional area values were detected at the end of the therapy compared to the baseline measurements. In a similar study

Table 2. Strain Elastographic Characteristics of CTS Subgroups

	Therapy			Control		
Subgroup	Pretreatment Strain Ratio	Posttreatment Strain Ratio	*P*	Pretreatment Strain Ratio	Posttreatment Strain Ratio	*P*
Mild CTS	0.97 ± 0.22	0.60 ± 0.24	<.001	0.75 ± 0.08	0.70 ± 0.08	.61
Moderate CTS	0.99 ± 0.21	0.73 ± 0.24	.002	1.41 ± 0.39	1.07 ± 0.64	.393

Data are presented as means ± 2 SDs.

performed by Yoshi et al,[15] in which the strain of the median nerve before and after surgery was compared, a significant increase in the strain of the median nerve was observed after carpal tunnel release surgery. We think that strain elastography may provide additional information for evaluating the efficacy of low-level laser therapy, as for other treatment options, which were analyzed in the previous studies.[7,15]

The edema in the early period and fibrosis in the late period may lead to morphologic changes in the median nerve.[16] In clinical practice, the cross-sectional area is the most popular and commonly used parameter among the US indicators for evaluation of morphologic changes or nerve thickening in the median nerve. Previous studies demonstrated that the cross-sectional area had significant diagnostic value in CTS and also could be used in the follow-up after treatment.[6,15,24,25] In contrast to some studies that indicated no significant difference in the cross-sectional area among the severity grades of CTS, we observed that cross-sectional area values in moderate CTS were significantly higher than those in mild CTS ($P = .01$).[6,26] Similar to our results, some studies stated that the cross-sectional area was found to be significantly associated with the severity of CTS.[3,13,14] Additionally, we also found a significant decrease in cross-sectional area values in the therapy group in contrast to the control group at the end of the treatment. Similarly, Miyamoto et al[7] reported that cross-sectional area values of the median nerve decreased after corticosteroid injection. Although in our study, a significant decrease in both the cross-sectional area and strain ratio of the median nerve was observed after low-level laser therapy, no correlation was found between the decreasing degree of cross-sectional area and strain ratio values. The cross-sectional area is a quantitative assessment of nerve thickening and may change for any reason, which leads to nerve swelling. However, tissue elasticity is a parameter that indicates the amount of tissue displacement and is frequently associated with fibrosis in the tissue. For this reason, the strain ratio may not routinely correlate with the cross-sectional area because of the variable pathologic features of the median nerve, including edema, hyperemia, and fibrosis.[16]

In addition to electrophysiologic tests and imaging modalities, an evaluation of symptoms and the functional status provides a more accurate assessment for determining the treatment success in CTS.[5,8,9] We found a significant improvement of the SSS and FSS in the therapy group, which may have been related to the therapeutic effects of low-level laser therapy, such as anti-inflammatory effects and selective inhibition of nociceptive activation, which may lead to relief of pain and an improvement in the functional status.[5] In the literature, after low-level laser therapy, recovery of the median nerve, including nerve regeneration or myelin production and symptomatic or functional improvement, was reported in many studies.[8,9,17,27] Although the strain ratio, SSS, and FSS showed significant decreases after low-level laser therapy, we also analyzed the correlation between the decreasing degree of the strain ratio and clinical assessment parameters to determine whether tissue elasticity may be correlated with symptomatic improvement after therapy. However, no significant correlation was observed between the decreasing degree of the strain ratio and clinical assessment parameters. This finding may have been related to the fact that the duration of the recovery period for the median nerve, including nerve regeneration or regression of fibrosis and improvements in clinical symptoms or the functional status, may not occur at the same time or synchronically after low-level laser therapy. Also, the amount of fibrosis and the duration of CTS (early or late period) may influence the duration of pathologic and clinical responses to therapy. Although we found a significant decrease in the tissue elasticity of the median nerve as well as the SSS and FSS after low-level laser therapy in this study, the results of this study cannot be generalized because of the small sample size; thus, the diagnostic value of strain elastography must be clarified with a larger sample size in a more-generalized group.

The literature on strain ratio measurements for the evaluation of the severity of CTS is limited. Two previous studies revealed that mean tissue strain values were lower in patients with CTS compared to healthy volunteers; however, they found no significant difference in the tissue strain of median nerve between mild and moderate or severe CTS.[6,28] In contrast, a previous study by Kantarci et al,[13] which analyzed median nerve stiffness by shear wave elastography, demonstrated that the median nerve stiffness was higher in severe CTS compared to mild or moderate CTS. Similarly, in this study, we showed that the strain ratio values in moderate CTS were significantly higher than those in mild CTS. We also found that the strain ratio values decreased significantly in both mild and moderate CTS after low-level laser therapy. However, in the control group, no significant decrease in the strain ratio values was observed for both mild and moderate CTS.

This study had some limitations, which have to be pointed out. First, it was designed as a retrospective study. As a result, intraobserver and interobserver variabilities were not analyzed. Second, measurements were obtained from only the proximal carpal tunnel inlet; therefore, the changes in the cross-sectional area and strain ratio at the tunnel outlet were not analyzed. The durations of mild and moderate CTS and severe CTS were not evaluated in this study, and we believe that studies comparing the overall severity grades and disease durations to elastographic findings are necessary to determine more accurate results. Furthermore, we evaluated the short-term efficacy of low-level laser therapy for CTS by using strain elastography; however, evaluating the long-term effectiveness in a larger sample size is needed to determine whether the strain ratio can also be used in long-term follow-up after treatment.

In conclusion, our study demonstrated that the stiffness and cross-sectional area of the median nerve decrease after low-level laser therapy for CTS. The decreased stiffness may be attributed to the possible mechanisms of the laser therapy, such as having the potential for nerve regeneration and an improvement in the blood supply.

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