

## Metacarpal Bone Density in Carpal Tunnel Syndrome Patients Without Thenar Atrophy

### Tenar Atrofisi Olmayan Karpal Tünel Sendromlu Hastalarda Metakarpal Kemik Yoğunluğunun Değerlendirilmesi

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#### Abstract

**Objective:** Bone loss due to thenar atrophy was reported in the metacarpal bones in premenopausal patients with carpal tunnel syndrome (CTS). The present study was designed to assess bone density in the metacarpal bones in patients with CTS without thenar atrophy and to correlate the metacarpal bone density with the electrophysiological findings, hand strength and Boston Questionnaire (BQ).

**Patients and Methods:** Thirty premenopausal patients with CTS without thenar atrophy were enrolled in this study. Thirty-two consecutive premenopausal women were included in the study as controls. The severity of symptoms and the functional status of CTS patients were assessed with Boston Questionnaire (BQ). Muscle strength of both hands was tested first with a Jamar dynamometer followed lateral pinch using a manual pinch meter in both groups. Bone mineral density (BMD) was measured by dual energy X-ray absorptiometry (DXA) at the second to fourth metacarpal bones of right hand. Electrodiagnostic testing was performed in CTS group.

**Results:** BMD values at the metacarpal bones did not differ between the CTS group and controls ( $0.49 \pm 0.07$  gr/cm<sup>2</sup> vs  $0.50 \pm 0.07$  gr/cm<sup>2</sup> respectively,  $p > 0.05$ ). Hand grip strength ( $23.98 \pm 5.50$  kg vs  $23.88 \pm 3.76$  kg respectively,  $p > 0.05$ ) and lateral pinch strength ( $6.70 \pm 1.44$  vs  $6.99 \pm 1.17$  kg respectively,  $p > 0.05$ ) of CTS group and controls was similar. Electrophysiological findings, hand strength and BQ were not correlated with the bone density at the metacarpal bones in patients with CTS without thenar atrophy ( $p > 0.05$ ).

**Conclusion:** Thenar atrophy seems be the most important predicting factor for the low bone density at the metacarpal region in patients with CTS. (*Rheumatism 2007; 22: 15-9*)

**Key words:** Carpal tunnel syndrome, bone density, DXA, metacarpal bones, nerves

#### Özet

**Amaç:** Premenopozal karpal tünel sendromlu (KTS) kadınlarda tenar atrofiye bağlı olarak metakarpal kemik yoğunluğu kaybı olduğu bilinmektedir. Bu çalışmanın amacı, tenar atrofi olmayan KTS'li hastalarda metakarpal kemik mineral yoğunluğunu değerlendirmek, metakarpal kemik yoğunluğu ile elektrofizyolojik bulguları, el gücü ve Boston Anketi arasındaki ilişkiyi belirlemektir.

**Hastalar ve Yöntem:** Çalışmaya tenar atrofi olmayan 30 KTS'li premenopozal hasta ile 32 premenopozal kontrol olgu alındı. KTS'li hastaların semptom şiddeti ve fonksiyonel durumları Boston Anketi ile değerlendirildi. Grupların el güçleri Jamar dinamometresi ve pinçmetre ile ölçüldü. Kemik mineral yoğunluğu sağ elin 2-4. metakarpallarından dual enerji X-ray absorpsiyometri cihazı (DXA) ile ölçüldü. KTS'li grupta elektrodiagnostik incelemeler yapıldı.

**Bulgular:** Metakarpal kemik yoğunluğu değerleri KTS ve kontroller arasında farklı değildi ( $0.49 \pm 0.07$  gr/cm<sup>2</sup> ve  $0.50 \pm 0.07$  gr/cm<sup>2</sup>,  $p > 0,05$ ). KTS ve kontrollerin el kavrama gücü değerleri ( $23.98 \pm 5.50$  kg ve  $23.88 \pm 3.76$  kg,  $p > 0.05$ ) ile lateral tutma güçleri ( $6.70 \pm 1.44$  ve  $6.99 \pm 1.17$  kg,  $p > 0.05$ ) benzerdi. Elektrofizyolojik bulgular, el gücü ve Boston Anketi değerleri metakarpal kemik yoğunluğu ile korele değildi ( $P > 0.05$ ).

**Sonuç:** Tenar atrofi, KTS'li hastaların metakarpal bölgelerinde saptanan düşük kemik yoğunluğunun en önemli belirleyicisi olarak görülmektedir. (*Romatizma 2007; 22: 15-9*)

**Anahtar kelimeler:** Karpal tünel sendromu, kemik yoğunluğu, DXA, metakarpal kemikler, sinirler

#### Introduction

Carpal tunnel syndrome (CTS) is the most common peripheral compressive neuropathy (1). The nerve degeneration and muscle weakness leads to thenar atrophy as the disease advances. Bone loss in the forearm and metacarpal bones of

the affected extremities of CTS patients with thenar atrophy was recently reported and the bone loss was explained with the presence of thenar atrophy and disuse (2). The relationship between the the metacarpal bone density and electrophysiological findings has never been evaluated before in patients with CTS. Depending on the strong evidence sug-

gesting that nervous system influences bone metabolism directly (3), we aimed to determine whether a disorder of a nerve, such as in CTS, without causing muscle atrophy, influence the metacarpal BMD. We also evaluated the effects of the hand strength and the severity of CTS symptoms and the functional status of the hand on bone density at the metacarpal region.

## Patients and Methods

### Study Design

The local research ethics committee of our faculty approved the study and informed consent was obtained from all patients. Thirty-eight premenopausal patients with clinically and electrophysiologically diagnosed CTS without thenar atrophy who admitted to Suleyman Demirel University Physical Medicine and Rehabilitation outpatient clinic between September 2003 and April 2005 were enrolled in this study. We choose the thenar atrophy free patients in order to exclude the possible effect of muscle atrophy on bone density. Thirty-two premenopausal women were selected as controls. All cases were selected among housewives in order to eliminate the occupational influences on hand strength measurements. No subjects had any past history of neurological disorder, diabetes mellitus or renal dysfunction. Six patients who have an illness or drug treatment known to influence bone mass were excluded. The left hands of the CTS group and the left hands of the control group were not included in the study as controls in order to eliminate the hand dominance on metacarpal bone density. All the women underwent laboratory analysis, including a complete blood count, serum protein electrophoresis and serum levels of calcium, phosphorus. Two women whose laboratory tests were out of the normal range were excluded from the study. For each participant, body weight and height were measured, and body mass index (BMI) was calculated as weight (kg)/height (m<sup>2</sup>). The severity of symptoms and the functional status of CTS patients were assessed with Boston Questionnaire (BQ) (4). The following factors influencing bone mass were considered: age, body weight, body height, body mass index, and daily calcium intake and the duration of regular exercise in a week. The mean daily calcium intake was assessed by interviewing study subjects on frequency of dairy product intake. The calcium content of dairy products was based of the content given by the USDA National database as, milk, 1 cup: 285 mg; plain yoghurt, 1 bowl: 275 mg; feta cheese, 1 wedge: 140 mg. All subjects underwent BMD measurements at both forearms and hands. Strength of both hands was tested first with a Jamar dynamometer followed by lateral pinch using by a manual pinch meter.

### Bone mineral density assessment

Bone mineral density (BMD) (g/cm<sup>2</sup>) was measured by dual energy X-ray absorptiometry (DXA) (Norland XR-46 bone densitometer, with dynamic filtration, Norland Corp, Fort Atkinson, USA) at the AP lumbar spine (L2-L4), femoral neck, distal third of the radius and ulna, and second to fourth metacarpal bones of right hand, by the standard array mode of acquisition. The Norland XR-46 was calibrated daily, 30 min

after turning the apparatus on. Quality control was performed using calibration standard and QC phantom. Analyses of the different subareas were carried out on the image of the hands on the screen using a region of interest (ROI) for the metacarpal region. To minimize the interobserver variations were carried out by the same technician. The in vitro precision of BMD measurements, according to the coefficient of variation (CV), was %3.7 during the study period.

### Boston Questionnaire

BQ is a self-administered questionnaire which assesses the severity of symptoms and the functional status of CTS patients. BQ had been translated into Turkish, and has been validated in a preliminary study (5). The symptom severity scale consists of 11, and the functional status scale of eight, questions. Each question has a 1-to-5 scale, in which 1 indicates no symptom and 5 indicates the severe symptoms. The symptom severity scale assesses the symptoms with respect to severity, frequency, time and type. The functional status scale assesses the effect of the carpal tunnel syndrome on daily living.

### Electrodiagnostic testing

All studies were performed with the patient supine, at a room temperature of 25°C, using a Nihon Kohden-Neuropack MEB 5504K (Tokyo, Japan), according to the American Association of Electrodiagnostic Medicine (AAEM) guidelines (6). The filter band-pass was 2 Hz to 3 kHz for the motor studies and 20 Hz to 3 kHz for the sensory studies. The compound muscle action potential was recorded with surface electrodes over the abductor pollicis and adductor digiti minimi muscles. The median and ulnar nerves were stimulated 8 cm proximal to the anodal electrode by a hand-held stimulator with a 2 cm inter-electrode distance. Stimulus duration was 0.2 ms, sweep speed was 2 ms/division and amplitude gain was 5 mV. Measurements were made with a tape measure. Sensory nerve action potentials were obtained antidromically and were recorded with ring electrodes placed at the proximal and distal interphalangeal joints. The distance between the stimulator and the recording electrode was 14 cm. Sweep speed was 2 ms/division and the gain was 10µV. An average of ten responses for sensory and five responses for motor evaluation were obtained from each stimulation site. The amplitudes of the sensory nerve action potentials and compound muscle action potentials were measured from peak-to-peak and distal latency from the onset point. Concentric needle electromyographic investigations were performed to exclude other causes of the hand symptoms. The electrophysiological criterion used to diagnose carpal tunnel syndrome was a median-ulnar sensory distal latency difference of greater than 0.5 ms (7). The normal limits routinely used in our laboratory were as follows: distal motor latency from the wrist to abductor pollicis brevis >4.2 msec, median nerve sensory conduction velocity <42 m/s, and median sensory conduction velocity less than 40 m/s at wrist-to-palm segment.

### Handgrip and Pinch Strength Measurements

Grip strength was tested first with a single calibrated Jamar dynamometer (Sammons Preston, Inc., Bollingbrook, IL) followed by lateral pinch using by a manual pinch meter

(Sammons Preston, Inc., Bollingbrook, IL). For each tests of hand strength, the standard test position approved by the American Society of Hand Therapists (ASHT) was used (8). This testing position is described as sitting in a straight-backed chair with feet flat on the floor, the shoulder adducted and neutrally rotated, elbow flexed at 90 degrees, forearm in a neutral position, and the wrist between 0 and 30 degrees extension and between 0 and 15 degrees ulnar deviation. In all cases the arm should not be supported by the examiner or by an armrest. For grip strength measurement, the dynamometer is presented vertically and in line with the forearm to maintain the standard forearm and wrist positions. For standardization, the handle of Jamar dynamometer is set at the second handle position (3.8 cm) for all subjects. For pinch strength the pinch gauge was positioned between the pad of the thumb and the radial side of the middle phalanx of the index finger. For each strength test the scores of three successive trials were recorded and the mean of three trials was used. For the final analysis, only grip strength of the right hand was used.

**Statistical analysis**

Results were given as mean ± standard deviation (SD) and range. The difference between the groups was evaluated with a two-tailed Student's t-test. Pearson's correlation analysis was used to express the strength of the association between two variables. The relationship between metacarpal bone density (as a dependent variable) and the median nerve sensory distal latency and SNCV (as independent variables) was examined using multiple stepwise regression analysis. The significance level was set at P<0,05 for all tests. Analyses were performed using the soft ware programme SPSS Statistics 11,0 (SPSS International BV, Chicago, IL, USA).

**Results**

Thirty CTS patients were included in the study. Twenty-one patients had bilateral CTS and 4 patients had unilateral CTS. The mean duration of the disease in CTS patients was 38.08 months (6-120 months). The mean age of patients with CTS and controls was 38.00±5.48 years (range 26-43 years) and 38.27±4.84 years (range 27-42 years) respectively (p=0.84). The mean weight of the patients with CTS was

72.68±11.86 kg and 70.17±11.13 kg in controls (P=0.43). The mean height of the patients with CTS was 1.57±0.05 cm and 1.58±0.04 cm in controls (p=0.42). The mean BMI of patients with CTS and controls was 29.19±5.39 and 27.42±4.21 respectively (P=0.19). None of the subjects engaged in regular exercise. The mean daily calcium intake was not different between the patients and the controls (571.36±261.47 mg vs 593.10±191.18 mg, P=0.73). Comparison of age, BMD and daily calcium intake of the groups is presented in Table 1. The mean grip strength and lateral pinch strength was not different between the groups (23.98±5.50 kg to 23.88±3.76 kg, p=0.94 and 6.70±1.44 kg to 6.99±1.17 kg, P=0.43 respectively) (Table 2).

The mean functional scale score was 2.01±0.81 (1-3.63) and the mean severity scale score was 1.46±0.59 (0.73-2.64) in the patients with CTS.

The electrophysiologic findings of the right hand of CTS patients were summarized in Table 3. Electrophysiological findings were not correlated with BQ scores (P>0.05 ).

BMD values in AP lumbar spine (L2-L4), femoral neck, Ward's triangle, distal third of the radius and ulna, and second to fourth metacarpal bones did not differ between the groups (P>0.05). BMD values are presented in Table 4.

Age, height, weight and duration of the disease was not correlated with the BMD of second to fourth metacarpal bones (r=0.32, P=0.17, r=0.16, P=0.90, r=0.16, P=0.50 and r=0.16, P=0.53 respectively). Daily calcium intake was not correlated with the BMD of second to fourth metacarpal bones (r=-0.1, P=0.55). Grip strength and key pinch strength was not correlated with the BMD of second to fourth metacarpal bones (r=-0.93, P=0.70 and r=-0.93, P=0.51 respectively). The mean BMD of second to fourth metacarpal bones was not correlated with the symptom severity scale scores and the functional status scale scores (r=0.24, P=0.7 and r=0.32, P=0.7).

Significant correlation was observed between the mean BMD of second to fourth metacarpal bones and the median nerve sensory distal latency and SNCV in patients with CTS in Pearson correlation analysis (r=0.65, P=0.005 and r=-0.63, P=0.006 respectively). However no significant correlation was found in the multiple stepwise regression analysis (Adjusted R square= 0.398, P=0.011) between the metacarpal

**Table 1.** Comparison of demographic features and daily calcium intake of the groups

	CTS patients (n=30)	Controls (n=32)	P
Age (years)(range)	38.00±5.48 (26-43)	38.27±4.84 (27-42)	0.84
BMI (kg/m <sup>2</sup> )(mean±SD)	29.19±5.39	27.42±4.21	0.19
Daily calcium intake (mg) (mean±SD)	571.36±261.47	593.10±191.18	0.73

**Table 2.** Comparison of hand strength values of the groups

	CTS patients (n=30)	Controls (n=32)	P
Grip strength (kg) (mean±SD)	23.98± 5.50	23.88± 3.76	0.94
Lateral pinch strength (kg) (mean±SD)	6.70± 1.44	6.99± 1.17	0.43

bone density and median nerve sensory distal latency (Standardized coefficient ( $\beta$ ): -0.39,  $P=0.198$ ) and SNCV (Standardized coefficient ( $\beta$ ): 0.34,  $P=0.262$ ). Median nerve motor distal latency was not correlated with the mean BMD of second to fourth metacarpal bone in Pearson correlation analysis ( $r=-0.36$ ,  $P=0.17$ ).

## Discussion

There is not so much data about the BMD at the metacarpal region in CTS patients in the literature. In the very first study of Schorn (9), it was reported that, metacarpal bone density was increased following a ligament-releasing operation according to radiometric findings in CTS patients. After this study, Erselcan et al. (2) assessed the bone mineral density at the metacarpal bones in CTS patients with thenar atrophy and they found that bone mass was decreased approximately 7% in the forearm region and 18% in metacarpal bones. The authors explained the low bone density at the metacarpal bones with the presence of thenar atrophy and disuse of the affected extremity. The duration of CTS was significantly correlated with the decrease in metacarpal bone density. They found no significant BMD modification in the bone density of forearm or metacarpal bones in the thenar atrophy free patients. Our results are similar with the results of Erselcan et al (2). However in their study the relationship between the metacarpal bone density and electrophysiological parameters and the effect of hand muscle strength on metacarpal bone density was not examined in their patients with and without thenar atrophy.

Evidence now suggests roles for neural control in bone mass and osteoporosis (10). The nerve lesions, central or peripheral, are suspected to contribute directly to abnormal bone metabolism through direct peripheral nerve signaling (3). Potential transmitters of this influence include glutamate (11), calcitonin gene-related protein (CGRP) (12), substan-

ce P (13), vasoactive intestinal peptide (VIP) (14), pituitary adenylate cyclase activating polypeptide (PACAP) (15), leptin (16), and catecholamines (17). It is known that nerves, even sensory efferents, clearly deliver signaling molecules in a unique way to the immediate milieu around bone cell surface receptors (3). The bone loss detected in CTS patients was explained with the presence of muscle atrophy and disuse (2). It is well known that disuse, reduction of mechanical stress on bone, can lead to loss of bone mass in an individual bone (18). The effects of sciatic neurectomy have been used extensively as a standard model of disuse osteopenia, as loss of musculature from denervation effectively stops active motion in the limb. However neurectomy itself may have direct effects on bone cells from lost bone innervation, above and beyond denervation of muscle and disuse of the limb (19). A hemiplegic stroke patient may be osteoporotic in both involved extremities, and this osteoporosis is totally independent of pre-existing body muscle composition or weight (20). This implies that effects from more than muscle inactivity alone are at play. A bone maintenance role for peripheral nerves rather than disuse osteoporosis has been implicated in spinal cord injury (21).

We found no correlations with the electrophysiological parameters and bone density at the metacarpal region in thenar atrophy free patients. According to our results, metacarpal bone density seems not to be effected in the absence of thenar atrophy in patients with CTS. However nerve signals to bone are not necessarily the master controllers, but they are recognized as part of vasty complex system for metabolic regulation of the bone (3). Therefore our findings do not totally exclude the influence of nervous system on bone density. The severity of the nerve damage may be important and our patients had a milder form of CTS. The neuro-osseous transmission disruption might not be severe enough to cause low bone density in our patients.

Hand strength was similar between the study groups and hand strength in our patients was not correlated to the metacarpal bone density. There is much discrepancy in the literature concerning relationships between muscle strength and local bone mass. A positive correlation has been found between handgrip strength and distal radius bone density (22,23) and metacarpal bone mass (24). However some authors stated that the effect of muscle strength on bone mass is more systemic than site specific (25) and still others found no link between handgrip strength and local bone density (26,27). Our results support the data that muscle strength is not the only factor in the bone density. Multiple factors are involved in the pathogenesis of osteoporosis, and these may be partially responsible for much of the vari-

**Table 3.** Electrophysiological findings of CTS patients (n=30)

	Mean±SD
Distal motor latency (msec)	4.33±0.89
Motor amplitude (mvolts)	13.75±4.20
Distal sensory latency (msec)	3.39±0.61
Sensory amplitude (microvolts)	23.53±29.39
SNCV* (msec)	39.12±7.20
Median-ulnar sensory distal latency difference (msec)	0.89±0.67

\*Sensory nerve conduction velocity

**Table 4.** BMD values of the patients and the controls

BMD (g/cm <sup>2</sup> ) (mean±SD)	CTS patients (n=30)	Controls (n=32)	P
AP lumbar spine (L2-L4)	1.04±0.20	1.00±0.18	0.53
Femoral neck	0.94±0.11	0.92±0.12	0.54
Distal third of the radius and ulna	0.33±0.06	0.34±0.04	0.43
Second to fourth metacarpal bones	0.49±0.07	0.50±0.07	0.73

ation. And also the different study designs and different techniques for measuring bone mineral density and muscle strength may be responsible for the conflicting results.

CTS is a frequent cause of disability and impaired upper extremity functional status (28). However BQ which assesses the symptom severity and the functional status of CTS patients was not correlated to metacarpal BMD in our study. The reason for this result may be that our patients had a milder disease and they had only sensory symptoms. BQ and electrophysiological findings was not correlated in our study. This result is in line with result of the study of Mondelli et al. who stated that BQ was not correlated with EMG findings because BQ considers different aspects of CTS with respect to nerve conduction studies (29).

In conclusion, our data suggests that CTS without thenar atrophy does not cause a decrease in bone density at the metacarpal region. Thenar atrophy seems to be the major predictive factor for the low metacarpal bone density detected in premenopausal CTS patients. However, the relationship between the electrophysiological findings and the metacarpal bone density in patients with CTS with thenar atrophy still remains to be clarified.

## References

1. Kerwin G, Williams CS, Seiler JG 3rd. The pathophysiology of carpal tunnel syndrome. *Hand Clin* 1996;12: 243-51.
2. Erselcan T, Topalkara K, Nacitarhan V, Akyuz A, Dogan D. Carpal tunnel syndrome leads to significant bone loss in metacarpal bones. *J Bone Miner Metab* 2001;19: 317-20.
3. Jones KB, Mollano AV, Morcuende JA, Morcuende JA, Cooper RR, Salzman CL. Bone and brain: A review of neural, hormonal, and musculoskeletal connections. *Iowa Orthop J* 2004; 24: 123-32.
4. Levine DW, Simmons BP, Koris MJ, Daltroy LH, Hohl GG, Fossel AH, et al. A self-administered questionnaire for the assessment of severity of symptoms and functional status in carpal tunnel syndrome. *J Bone Joint Surg* 1993;75A: 1585-92.
5. Heybeli N, Özerdemoglu RA, Aksoy OG, Mumcu EF. Functional and symptomatic scoring used for the assessment of outcome in carpal tunnel release. *Acta Orthopaedica et Traumatologica Turcica* 2001; 35: 147-51.
6. Jablecki CK, Andary MT, So YT, Wilkins DE, Williams FH. Literature review of the usefulness of nerve conduction studies and electromyography for the evaluation of patients with carpal tunnel syndrome. *Muscle Nerve* 1993; 16: 1392-414.
7. Uncini A, DiMuzio A, Awad J, Manente G, Tafuro M, Gambi D. Sensitivity of three median-to-ulnar comparative tests in diagnosis of mild carpal tunnel syndrome. *Muscle Nerve* 1993; 16: 1366-73.
8. Mathiowetz V, Weber K, Volland G, Kashman N. Reliability and validity of grip and pinch strength evaluations *J Hand Surg* 1984; 9A: 222-6.
9. Schorn D, Hoskinson J, Dickson RA. Bone density and the carpal tunnel syndrome. *Hand* 1978; 10: 184-6.
10. Castellano-Garcia JM, Diaz-Herrera P, Morcuende JA. Is bone a target-tissue for the nervous system? New advances understanding of their interactions. *Iowa Orthop J* 2000; 20: 49-58.
11. Gu Y, Genever PG, Skerry TM, Publicover SJ. The NMDA type glutamate receptors expressed by primary rat osteoblasts have the same electrophysiological characteristics as neuronal receptors. *Calcif Tissue Int* 2002; 70: 194-203.
12. Hukkanen M, Kontinen YT, Santavirna S, Paavolainen P, Gu XH, Terenghi G, et al. Rapid proliferation of calcitonin gene-related peptide-immunoreactive nerves during healing of rat tibial fracture suggests neural involvement in bone growth and remodeling. *Neuroscience* 1993; 54: 969-79.
13. Imai S, Matsusue Y. Neuronal regulation of bone metabolism and anabolism: calcitonin-gene-related peptide-, substance P-, and tyrosine hydroxylase-containing nerves and bone. *Microsc Res Tech* 2002; 58: 61-9.
14. Mukohyama H, Ransjo M, Taniguchi H, Ohyama T, Lerner UH. The inhibitory effects of vasoactive intestinal peptide and pituitary adenylate cyclase-activating polypeptide on osteoclast formation are associated with upregulation of osteoprotegerin and downregulation of RANKL and RANK. *Biochem Biophys Res Commun* 2000; 271: 158-63.
15. Winding B, Wiltink A, Foged NT. Pituitary adenylate cyclase-activating polypeptides and vasoactive intestinal peptide inhibit bone resorption by isolated rabbit osteoclasts. *Exp Physiol* 1997; 82: 871-86.
16. Ducy P, Amling M, Takeda S, Priemel M, Schilling AF, Beil FT, et al. Leptin inhibits bone formation through a hypothalamic relay: a central control of bone mass. *Cell* 2000; 100: 197-207.
17. Imai S, Tokunaga Y, Madea T, Kikkawa M, Hukuda S. Calcitonin-gene-related peptide, substance P, and tyrosine hydroxylase-immunoreactive innervation of rat bone marrows: an immunohistochemical and ultrastructural investigation on possible efferent and afferent mechanisms. *J Orthop Res* 1997; 15: 133-40.
18. Takata S, Yasui N. Disuse osteoporosis. *J Med Invest* 2001; 48: 147-56.
19. Zeng QQ, Jee WS, Bigornia AE, King JG Jr, D'Souza SM, Li XJ, et al. Time responses of cancellous bones to sciatic neurectomy in growing female rats. *Bone* 1996; 19: 13-21.
20. Ramnemark A, Nyberg L, Lorentzon R, Olsson T, Gustafson Y. Hemiosteoporosis after severe stroke, independent of changes in body composition and weight. *Stroke* 1999; 30: 755-60.
21. Garland DE, Stewart CA, Adkins RH, Hu SS, Rosen C, Liotta FJ, et al. Osteoporosis after spinal cord injury. *J Orthop Res* 1992; 10: 371-8.
22. Tsuji S, Tsunoda N, Yata H, Katsukawa F, Onishi S, Yamazaki H. Relationship between grip strength and radial bone mineral density in young athletes. *Arch Phys Med Rehabil* 1995; 76: 234-38.
23. Di Monaco M, Di Monaco R, Manca M, Cavanna A. Handgrip Strength is an independent predictor of distal radius bone mineral density in postmenopausal women. *Clin Rheumatol* 2000; 19: 473-6.
24. Osei-Hyaiman D, Ueji M, Toyokawa S, Kano K. Influence of grip strength on metacarpal bone density in postmenopausal Japanese women: A cross-sectional study. *Calcif Tissue Int* 1999; 64: 263-6.
25. Sinaki M, Fitzpatrick LA, Candace RK, Montesano A, Wahner H. Site-specify of bone mineral density and muscle strength in women: Job-related physical activity. *Am J Phys Med Rehabil* 1998; 77: 470-6.
26. Bayramoglu M, Sözüy S, Katatas M, Kilinc S. Relationships between muscle strength and bone mineral density of three body regions in sedentary postmenopausal women. *Rheum Int* 2005; 25: 513-7.
27. Madsen OR, Lauridsen UB, Sorensen OH. Quadriceps strength in women with a previous hip fracture: relationships to physical ability and bone mass. *Scand J Rehab Med* 2000; 32: 37-40.
28. Heybeli N, Kutluhan S, Demirci S, Kerman M, Mumcu EF. Assessment of outcome of carpal tunnel syndrome: A comparison of electrophysiological findings and a self-administered Boston questionnaire. *J Hand Surg* 2002; 27: 259-64.
29. Mondelli M, Reale F, Sicurelli F, Padua L. Relationship between the self-administered Boston Questionnaire and electrophysiological findings in follow-up of surgically-treated carpal tunnel syndrome. *J Hand Surg* 2000; 25: 128-34.