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Evaluation of Bone Mineral Density after Replantation or Revascularization Surgery in the Upper Extremity

Üst Ekstremite Replantasyon ve Revaskülarizasyonu Sonrası Kemik Mineral Yoğunluğunun Değerlendirilmesi

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Summary

Objective: This study was undertaken to examine bone mineral density (BMD) of the hand after replantation or revascularization surgery in the upper extremity and to investigate the relationship between BMD and muscle strength, range of motion and motor activity.
Materials and Methods: Fourteen patients who underwent a replantation or revascularization surgery in the upper extremity were included in this study. Total active motion (TAM), handgrip and lateral pinch strength were evaluated. Motor activity was assessed using the Purdue Pegboard Test (PPT) and BMD was estimated by radiographic absorptiometry (ALARA). The results of the injured and non-injured sides were compared.
Results: The average length of time that had elapsed after surgery was 5.36±3.08 years. Handgrip and pinch strength, TAM of the fingers and thumb as well as the PPT of the replanted extremity were significantly decreased ($p<0.05$). No significant difference in BMD was observed between the injured and non-injured hands ($p>0.05$). There was a positive correlation between lateral pinch strength and BMD and a negative correlation between age and BMD ($p<0.05$).
Conclusion: Although replantation affected the muscle strength, functional level and TAM, there were no differences in BMD estimates between the operated and non-operated hands. Motor activity and lateral pinch strength are related to BMD. *Turk J Phys Med Rehab 2011;57:73-9.*
Key Words: Bone mineral density, replantation, upper extremity

Özet

Amaç: Bu çalışmada, üst ekstremitede replantasyon veya revaskularizasyon cerrahisi sonrası elde kemik mineral yoğunluğunu (KMY) değerlendirmek ve KMY ile kas gücü, eklem hareket açıklığı ve motor aktivite arasındaki ilişkiyi belirlemek amaçlandı.
Gereç ve Yöntem: Çalışmaya üst ekstremitede replantasyon veya revaskularizasyon cerrahisi geçiren 14 hasta alındı. Total aktif hareket(TAH), el kavrama ve lateral kavrama güçleri değerlendirildi. Motor aktivite Purdue Pegboard Test (PPT) ile, KMY radyografik absorbsiyometri (ALARA) kullanılarak değerlendirildi. Etkilenen ve etkilenmeyen tarafın sonuçları karşılaştırıldı.
Bulgular: Cerrahi sonrası ortalama geçen süre 5,36±3,08 yıldı. El kavrama ve lateral kavrama güçleri, başparmak ve diğer parmakların TAH'ları ve PPT skoru replante edilmiş ekstremitede anlamlı olarak daha az bulundu ($p<0,05$). Etkilenen ve etkilenmeyen el arasında KMY açısından anlamlı fark yoktu ($p>0,05$). Lateral kavrama gücü ile KMY arasında pozitif korelasyon, yaş ile KMY arasında negative korelasyon saptandı ($p<0,05$).
Sonuç: Replantasyon kas gücü, fonksiyonel düzey ve TAH'i etkilemesine rağmen opere edilen ve opere edilmeyen eller arasında KMY açısından fark bulunmadı. Motor aktivite ve lateral kavrama gücü KMY ile ilişkili bulunmuştur. *Türk Fiz Tıp Rehab Derg 2011;57:73-9.*
Anahtar Kelimeler: Kemik mineral yoğunluğu, replantasyon, üst ekstremite

Introduction

The primary aim of replantation is the salvage of the amputated digit or extremity. Many factors, including the level of amputation, type of injury, duration of ischemia, age, surgical technique and rehabilitation, affect the outcome of the surgery (1). Recent technological advances as well as a better understanding of the tissue response to trauma and of the tissue

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regeneration have led to a higher survival rate of the replanted upper limbs, now placing more emphasis on the functional outcome compared to past. Although many studies have reported satisfactory functional results, the replanted hand may not perform as well as the non-operated hand functionally (2-3).

Maintenance of skeletal mass depends largely on mechanical loading applied to the bone by tendon pull and force of gravity. Bone mass will increase with repeated loading stresses and will decrease in the absence of muscle activity or with the elimination of gravity (4). In addition, bone fractures, immobilization and paralysis, painful clinical conditions (reflex sympathetic dystrophy, infection and inflammation), total joint replacement, internal fixation devices (plates and screws) are mechanical causes of localized osteoporosis (5). Thus, bone loss appears to be an inevitable consequence of replantations.

In replant patients, the incidence of bone non-union is disproportionately high, probably due to poor vascularization of the bone in the distal amputation fragment. Impaired vascularity may also affect bone quality and mineral density. Presence of vasomotor and neural stasis plays an important role in bone remodeling and recovery (6). During the rehabilitation program care must be exercised not to exert excessive stress on the healing tissues. Despite clinical awareness regarding early changes in a replanted extremity that affect the bone recovery, little is known as to what happens to the bone mineral density (BMD) after the recovery of vasomotor and neural stasis in the long term. Although factors such as bed rest, microgravity, immobility and a lack of muscle activity have been proven to significantly reduce the BMD, the effect of replantation on this parameter has not been very well studied.

This study was based on the hypothesis that BMD of the injured hand after upper extremity replantation would be statistically significantly lower than the uninjured side, and that this local occurrence of osteoporosis and decreased BMD may help to predict the fracture risk in replanted extremities. Our aim was to assess the BMD of replanted hand and to investigate the relationship between BMD and muscle strength, motor activity and range of motion.

Materials and Methods

Forty-one patients were screened for this study. Twenty-two subjects met the inclusion criteria, but 8 of them were excluded according to the exclusion criteria. Fourteen patients with successful replantation and/or revascularization of the upper extremity, who were followed up between 2006–2007 in the Department of Physical Medicine and Rehabilitation, Dokuz Eylül University Medical School, were included in this study. The study protocol was approved by the Institutional Ethics Committee. All cases were operated by a surgical team at the Department of Hand Surgery. All patients provided informed consent after through explanation of the protocol. Age, sex, injured side, level of amputation, duration of follow-up, and the type and extent of injury were recorded. Inclusion criteria were at least six months of follow-up after operation and suitability of the patient's hand to the BMD scanning device. Exclusion criteria included conditions that could affect either the recovery process (e.g. diabetes mellitus, infection, malignancy, immune deficiency, previous radiotherapy or chemotherapy) or BMD (e.g. osteoporosis, hyperthyroidism and medications such as steroids and anticonvulsants). Except for some individual minor modifications, all patients underwent the same postoperative rehabilitation protocol as follows:

1 to 3 weeks: gentle, protected passive range of motion of joints in a dorsal thermoplastic splint, wound care and edema control. Active, active assisted and passive range of motion exercises to all non-involved joints proximal to the replanted part to avoid joint tightness that may occur proximal to the replantation;

3 to 6 weeks: protected range of motion for injured joints, passive and active, protected tenodesis exercises in the splint until splint was discontinued at sixth week; at 4 to 6 weeks: minimal gentle functional activities to pick up light objects or assist in minimal activities of daily life;

6 to 12 weeks: scar mobilization as well as active, active assisted and passive range of motion exercises; after 8 weeks: resistive exercises for full excursion and blocked positions as well as protective splinting in public or when sleeping. Dynamic splinting after fractures is stable; and sensory re-education, if necessary.

After 12 weeks: the patients were allowed to return to work if there was no problem with bone healing. All home exercises for range of motion, sensory re-education and strengthening were continued during follow-up visits.

Evaluation of BMD in replanted hand was the primary endpoint; the secondary endpoint of the study was to assess the relationship between BMD and muscle strength, motor activity and range of motion.

Total active motion (TAM), handgrip and pinch strength, motor activity and BMD were evaluated. TAM was calculated in each finger with finger goniometry using the following formula: [TAM= active flexion (distal interphalangeal + proximal interphalangeal + metacarpophalangeal) - active extension deficit (distal interphalangeal + proximal interphalangeal + metacarpophalangeal)]. For the thumb, the formula 'active flexion (interphalangeal + metacarpophalangeal) – extension deficit (interphalangeal + metacarpophalangeal)' (7) was used. Grip strength of both hands was measured by a Jamar hydraulic hand dynamometer (Sammons Preston, Bolingbrook, IL, USA). During testing, the subjects sat with their shoulder adducted, elbow flexed at 90° and their forearm and wrist in neutral position. The patients were then instructed to grip the

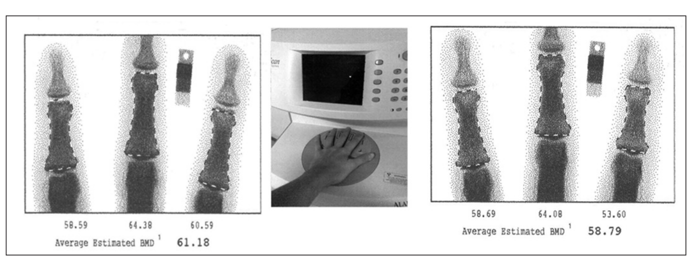

Figure 1. Alara. Metriscan Bone Densitometer

Table 1. Clinical data of cases.

PN	Age	Gender	DH	IH	Level of amputation	Type of amputation	S2PD IH	S2PD NIH	F TAM NIH	F TAM IH	T TAM IH	T TAM NIH	BMD NIH	BMD IH	T score IH	T score NIH	Extent of injury
1	31	M	R	R	wrist	guillotine	protective	4	238	270	155	170	52.36	60.22	-1.09	0.8	total
2	26	M	R	L	thumb-distal phalanx	crush	5	5	258	260	145	160	60.43	61.68	0.85	1.15	subtotal
3	25	M	R	R	2-middle phalanx	guillotine	protective	5	225	282	150	145	61.76	58.38	1.17	0.35	total
4	49	M	R	L	thumb-distal phalanx	guillotine	protective	5	262	271	140	155	57.86	56.75	0.23	-0.30	total
5	20	F	R	L	1-transmetacarpal	guillotine	protective	5	260	262	35	130	58.79	61.18	1.03	0.45	total
6	39	F	R	R	2-proximal phalanx	guillotine	5	5	202	270	130	145	60.75	57.34	0.53	0.18	subtotal
7	26	F	R	L	4-distal phalanx	degloving	7	3	227	257	140	150	49.38	55.04	-1.85	-0.44	total
8	50	M	R	L	distal forearm	crush	anesthetic	5	223	241	120	115	53.85	61.79	-0.73	1.18	subtotal
9	19	F	R	L	3-distal phalanx	guillotine	5	5	282	286	150	150	55.95	58.72	-0.22	0.44	subtotal
10	20	M	L	L	1-transmetacarpal	degloving	5	5	246	260	60	150	58.35	59.48	0.35	0.62	subtotal
11	55	M	R	L	2-middle phalanx	avulsion	12	4	206	227	120	135	52.23	52.32	-0.20	0.20	total
12	54	M	R	L	distal forearm	avulsion	protective	5	149	276	5	165	50.02	53.23	-0.30	0.23	total
13	21	M	R	L	Wrist	guillotine	protective	5	96	232	95	145	50.93	54.73	-1.48	-0.57	subtotal
14	59	M	R	L	3-distal phalanx	degloving	9	5	251	250	145	170	47.44	61.01	-2.27	0.99	subtotal

PN: Patient number, F: Female, M: Male, IH: Injured hand, DH: Dominant hand, IH: Injured hand, NIH: Non-injured hand, S2PD: Static two-point discrimination (in millimeters), F TAM: Finger total active motion (in degrees), T TAM: Thumb total active motion (in degrees), BMD: Bone mineral density (in arbitrary units).

dynamometer as hard as possible for 3 seconds without pressing the instrument against the body. Lateral pinch strength was measured with pinch-meter (Irvington, NY10533, US) at the same position. Three measurements were recorded and the mean values were calculated.

Motor activity was evaluated with Purdue Pegboard Test (PPT) (8-9). This test is used for the assessment of motor activity of the hand. Two types of activity are measured: one involving the gross movement of hands, fingers and arms and the other involving primarily what may be called an assembly or fingertip dexterity. In this test, motor activity was evaluated in three stages within thirty seconds. First was left hand coupling, second was right hand coupling and third was bilateral coupling. All tests were done three times and an average value was calculated. Sensory recovery was measured by the static two-point discrimination (S2PD) test for each finger. BMD was measured using ALARA (As Low As Reasonably Achievable) Metriscan (10) (Figure 1), which is a compact digital radiographic absorptiometry device capable of determining phalangeal BMD in arbitrary units from the second phalanges of the middle three digits. For an exposure, the patient removes any jewelry from the hand, and places the hand on the molded support plate. Hand placement is checked to ensure the fingers are flat but not too much pressed down and that the second phalanges of the middle three digits are within the region of interest marked on the plate. With exposure, a cone beam X-ray image (tube voltage, 60 kV; current, 0.333 mA) of the region of interest is projected onto a curved storage phosphor plate mounted on a rotating drum. The drum is rotated and scanned by a laser in order to excite photons to an electronic signal pulse proportional to the number of incident photons. A second light source then erases the plate ready for the next acquisition. An aluminum step wedge of known thickness built into the device within the region of interest provides the calibration for each image. The geometric distortion inherent to projecting the image onto a drum is corrected by software before the final digital image is displayed on an LCD screen. Bone mass estimates are determined through comparison with the step wedge and T and Z scores (i.e. the number of standard deviations from normal young or age matched individuals, respectively) are derived from reference data. BMD score is given in an arbitrary unit rather than the usual g/cm^2 (10). All evaluations were done for both hands and the results for the injured versus non-injured hand were compared.

Statistical evaluation was performed by using SPSS 11.0 statistical soft ware. Mean and median values, standard deviations and inter-quartile ranges (IQR) were calculated and compared using Wilcoxon test. Spearman correlation test was done to assess the relationship between BMD and muscle strength, range of motion and functional level. Significance level was accepted as $p<0.05$.

Results

Fourteen patients (9 males and 5 females) were included in this study. The age ranged from 19 to 59 years with an average of 35.29±15.07 years. Average time after the surgery was 5.36±3.08 years (1-10 years). Seven (50%) patients had total amputation and seven (50%) patients had subtotal amputation with revascularization. Total amputation is defined as a completely amputated distal part, without any physical connection between the severed part and the patient, and subtotal amputation is defined as an incomplete amputation in which some of the soft tissue (skin, nerves or tendons) is intact. However, in all cases of subtotal amputation in our study, the distal part was attached to the proximity only with a small skin bridge. The non-dominant hand was replanted in 10 subjects. There was no patient who experienced any fracture in their replanted extremities. Level of amputation, type of injuries, and functional and BMD data are shown in Table 1. Average duration of rehabilitation was 3.50±1.91 (1–6) months. TAM for the fingers and thumb, lateral pinch strength, and hand grip strength were significantly lower for the replanted hand compared to the contralateral non-injured hand ($p<0.05$) (Table 2). PPT results were better for the non-injured side ($p<0.05$) (Table 2). The thumb and finger TAM in the injured side were 76% and 85% of the non-injured side, respectively. The hand grip strength for the injured side was 51% and lateral pinch strength was 68% of the non-injured side. BMD estimates of the

Table 3. Comparison of bone mineral density of injured hand and non-injured hand.

	Injured hand median (IQR 25-75%) N=14	Non-injured hand median (IQR 25-75%) N=14	p value
BMD (au)	56.90 (51.28-60.02)	59.10 (56.89-61.13)	0.175
T score	0.005 (-1.38-0.77)	0.445 (-0.18-0.94)	0.182

(BMD: Bone Mineral Density, au: arbitrary unit; IQR: Inter-range quartiles

Table 2. Active motion, strength, and motor activity results of the study group.

	Injured hand (n=14) Median (IQR 25-75%)	Non-injured hand (n=14) Median (IQR 25-75%)	p value
Hand grip strength (kg)	14.24 (2.53-25.41)	24.66 (20.04-36.08)	0.008*
Lateral pinch strength (kg)	14.66 (7.62-17.16)	18.16 (14.87-21.91)	0.021*
Thumb TAM	135.00 (86.25-146.25)	150.00 (142.50-161.25)	0.011*
Finger TAM	232.50 (205.56-258.50)	261.00 (247.81-272.31)	0.008*
PPT	10.16 (8.25-13.24)	14.00 (13.66-15.58)	0.001*

(TAM=Total Active Motion, PPT=Purdue Pegboard Test, *p<0.05) replanted and non-injured hands were not significantly different (p>0.05) (Table 3). There was a positive correlation between BMD and lateral pinch strength (r=0.62, p=0.001) and a negative correlation between BMD and age (r=-0.53, p=0.04). In addition, there was a positive correlation between BMD and bilateral motor activity as assessed by PPT (p=0.039, r=0.556). However, no significant correlation could be found between BMD and grip strength or TAM (p>0.05).

Discussion

The aim of the present study was to investigate the BMD of the hand after upper extremity replantation. The BMD values in the injured and non-injured hands did not differ significantly. Our literature search revealed only a single study assessing the BMD after replantation (11). In that report, five patients were evaluated following traumatic amputation only with radiographies. Levels of amputation were the wrist (2), mid forearm (2) and knee (1). Following upper limb replantation, rapid development of osteopenia has been reported in the bones of the hand in all cases. However, a gradual resolution of bone changes were noted in three of the four cases where follow-up exceeded 5 years. Following lower limb replantation, there was no evidence of bone loss (11). However, in that report, bone loss was only evaluated by X-rays and, no other BMD measurements were performed. Moreover, the authors pointed out the possibility that their results could be related with reflex sympathetic dystrophy syndrome. In contrast, our patients had no significant evidence of bone loss following upper extremity replantation. We assume that this may be related with the duration of time that has elapsed after replantation. The average length of time after replantation was 5.36 years, which might have been an adequate length of time for BMD to recover. Also, despite significant decrease in muscle strength and functional level in the injured side, our patients had sufficient motor activity and most of them were satisfied with the performance of their extremities during daily activities.

Patients who were on medications that can lead to osteoporosis or who had conditions that may impair the recovery process were excluded from the study. Smoking is also a factor that could affect the BMD. However, such an effect is expected to involve both hands. Also, dominant hand has been shown to have a higher BMD compared to the other hand (7). Unfortunately, our small sample size precluded a meaningful comparison between the dominant and non-dominant injured extremities. Surprisingly, we could not detect any differences in BMD between the injured and uninjured sides, although the non-dominant extremity was injured in most of our patients.

BMD assessment plays an important role in the evaluation of patients with potential osteoporosis (12). Osteoporosis increases the risk of fracture and disability, and BMD has a predictive value for the fracture risk such that one standard deviation decrease in BMD of an age-matched norm is associated with a 50-100% increase in the risk of fracture (13). Studies examining localized osteoporosis following tendon or ligament injury are scarce in number (14-15).

There are a number of devices available for assessing BMD in the peripheral skeleton such as ALARA for the hand, dual-energy X-ray absorptiometry (DXA) for the forearm and ultrasound for the heel (16). The ALARA Metriscan, which was chosen for our study, is a compact digital radiographic absorptiometry device capable of measuring bone mineral content of the second phalanges of the middle digits. It is possible that we could have found different results with DXA. However, ALARA was chosen on the basis of practicality, cost-effectiveness, and lower radiation exposure compared to DXA.

The limitations of our study include the small sample size, which is partly related to our patient selection criteria, and the differences between the patients with regard to the level of amputations and type of injuries. Most of our cases had finger replantation that has better functional results, consistent with the satisfactory outcomes observed in all of our patients with proximal injury.

Mechanical stress is a major determinant of BMD, morphology and strength. Therefore, immobilization accelerates bone resorption, especially of the cancellous bone, so the bone becomes atrophic and fragile. Osteocytes respond to the mechanical load and changes in the bone metabolism (17-19) and they play an important role in transmitting the mechanical load through intracellular (cAMP and cGMP) and extracellular (PGE2, IGF-I, IGF-II and TGF-β) signal transmitters to induce bone formation by osteoblasts, inhibition of bone resorption by osteoclasts or a combination of the two (20,21). Bone loss has been related to immobilization and muscle strength in some studies (22,23). In a study by Erdem and Kekilli, patients surgically treated for acute clean-cut tendon injuries at the volar wrist level were examined, and a significant bone loss was observed as early as 6 weeks which continued up to 4 months after the operation. These authors emphasized the importance of early active mobilization (24). However, the long-term effect on BMD is not known.

Probably vasomotor stasis is an important determinant in these patients. For instance, following spinal cord injury, sympathetic nervous system affects the circulation in bone and causes transformation of mesenchymal cells into osteoclastic cells (25,26). Nerve injury also affects the BMD via the neuro-osteogenic system (27,28). Osseal neurons contain neurotransmitters, which have been identified in bone cells. These neurotransmitters can modulate bone remodeling. Therefore, bone loss is an inevitable consequence in a denervated bone. However, reversibility of such changes after reinnervation is not known. A solid microsurgical technique for vascular microanastomosis and nerve coaptation enables a good nerve and vessel healing, perhaps partly explaining our BMD findings in our patients. Also, in our study, BMD measurements were performed long after the reinnervation was done. In our cases, a significant relationship between lateral pinch strength and BMD was observed. This suggests that in addition to extrinsic muscle strength, the intrinsic muscle strength, which is a marker of motor innervation and was measured by finger lateral pinch test, may be more directly related to the BMD in fingers. It can be hypothesized that since recovery in the intrinsic muscle function and sensory function of the fingers are associated with sympathetic reinnervation of the bone, a correlation between BMD and sensory recovery in the skin of replanted digits may exist. However, the small sample size again precluded reaching any conclusions on the relationship between the BMD and 2PD test results.

In some experimental studies, unilateral nerve section have been found to disrupt neuronal signaling in the ipsilateral side, but some studies have also identified alterations in contralateral nerve anatomy, function and transmitter expression following nerve section (29). Some studies found that patients with stroke were at increased risk of developing osteoporosis both in paretic and non-paretic upper extremities in acute and chronic phase (30,31). Impairment of local neurotransmitters can reduce neuronal signaling, therefore inducing bone loss in contralateral side (32). Absence of a significant BMD difference between injured and non-injured sides in our study can be related to bilateral BMD loss caused by the impairment of neuronal signals. However, we did not compare our patients with healthy controls in terms of BMD of the upper extremities, pointing out another possible limitation of our study.

Muscle strength has been reported to be associated with the bone composition (33,36). Impairment of muscle function reduces the function of the replanted hands and could be related to BMD. Therefore, we assessed the relationship between BMD and muscle strength in our patients and found a positive correlation between lateral pinch strength and BMD. This finding suggests that muscle strength affects bone density. However, no such correlation was observed for hand grip strength, which can be explained on the basis of the fact that this test measures the total hand grip strength. The most frequently used assessment tool for hand grip strength is the JAMAR dynamometer, which was also used in our study. But our patients found it difficult to hold the hand-held dynamometer and to squeeze it well enough. We did not use a sphygmomanometer which is a light device. This could have caused a technical problem in measurement that affects our results. This problem is a limitation of our study. Motor activity in the injured upper extremity was significantly lower compared to the non-injured side, and there was a positive correlation between BMD and bilateral motor activity as assessed by PPT, suggesting a link between BMD and motor function.

In conclusion, we were unable to show a long-term effect of upper extremity replantation on BMD of the injured hand, and the injured and non-injured sides had similar BMD estimates after replantation and revascularization surgery. Another observation in the present study was the correlation between BMD and motor activity and lateral pinch strength. While interpreting these results, some limitations of our study such as small and heterogeneous sample and absence of healthy controls should be borne in mind. Further studies are warranted to confirm the associations observed here.

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