REMOBILIZATION RESTORES CANCELLOUS BONE MASS BUT NOT MICROARCHITECTURE AFTER LONG-TERM DISUSE IN OLDER ADULT DOGS

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Introduction: Disuse results in not only a dramatic loss of bone mass, but also changes in bone architecture (1-3). In cancellous bone, these changes result from a combination of thinning, perforation and ultimately complete loss of trabecular elements. Bone mass that is lost during disuse can substantially recover with restoration of the normal loading (remobilization). However, whether bone architectural changes caused by long-term disuse can recover following remobilization is unknown. In the current study, we examined both the bone mass and microarchitectural bases of cancellous bone recovery from long-term disuse osteoporosis.

Methods: Right forelimbs of 5-7 years old retired breeder Beagle dogs (N=32) were immobilized (IM) with a jacket-type plastic splint, placing the elbow flexed at 90 degrees and the carpal joint volar-flexed slightly. Immobilization lasted for either 3 or 6 months. At the end of these times, animals were either sacrificed (3IM and 6IM), or remobilized (RM: allowed to resume normal weight-bearing in kennel runs) for an additional 12 months (3IM-12RM and 6IM-12RM) prior to sacrifice. Nonimmobilized age-matched animals served as controls. Before sacrifice, all animals received double fluorescent-labels injections. All procedures were approved by the Institutional Animal Care Committees of the Henry Ford Hospital and Mount Sinai School of Medicine. Changes in cancellous bone were examined using histomorphometry on undecalcified MMA embedded longitudinal sections from the distal metacarpal metaphyses. Bone architectural changes were assessed from trabecular bone area (%Tb.Ar/T.Ar), trabecular number (Tb.N) and trabecular width (Tb.Wi). Osteoclastic activity was assessed from eroded surface (%Er.Pm) and osteoblastic activity assessed from labelled surface (%L.Pm), mineral appositional rate (MAR) and surface-based bone formation rate (BFR/B.Pm). Differences among groups were tested using ANOVA with Fisher's PLSD for post-hoc testing; significance is reported at $p<0.05$.

Results: *Immobilization*: After 3 months IM, there was a marked reduction of trabecular bone area (%Tb.Ar/T.Ar, -38%; Fig.1a), accompanied by a significant decrease in trabecular width (Tb.Wi, 45%; Fig. 1b) and number (Tb.N, -17%; Fig.1c). Bone formation (L.Pm/B.Pm, MAR and BFR/B.Pm) and resorption indices (Er.Pm/B.Pm) were significantly higher in 3IM group compared to control group (Table 1), suggesting that disuse osteoporosis results from high bone turnover. Continued loss of bone mass up to 6 months IM occurred through loss of trabecular number (Tb.N, - 23% compared to control group), but without further decrease in Tb.Wi.
Remobilization: In both 3IM-12RM and 6IM-12RM groups, bone mass recovered to control levels. This recovery occurred through thickening of existing trabeculae (Tb.Wi, +7% in 3IM-12RM and +15% in 6IM-12RM groups compared to the control group, respectively; Fig.1b). However, microarchitecture did not recover from long-term disuse osteoporosis. Trabecular number remained significantly lower in both 3IM-12RM (-12%, $p<0.09$) and 6IM-12RM (-25%) groups when compared to the control group (Fig.1c).

Discussion: The present study shows that cancellous bone mass in older animals can recover from long-term disuse osteoporosis. However, architecture of the restored cancellous bone remains significantly different from that in normal bone. Previous studies of recovery from disuse osteoporosis showed contradictory results. Jaworski and Uhthoff (1) found only partial recovery of bone mass in young and old dogs; however, the duration of remobilization in their experiment was about half that examined in the present study. Lane et al (2) showed that bone mass in very young adult dogs recovers fully within 32 weeks when exercise was incorporated. Our results suggest that given enough time, cancellous bone mass in older animals will recover from long-term disuse osteoporosis.

In contrast to bone mass, architecture of the restored cancellous bone remains significantly different from that in normal bone. Specifically, bone mass recovery occurred by thickening of the existing trabeculae, such that trabecular width in recovered bone was significantly greater than that in control bone, but trabecular number was equivalent to that in severe, long-term disuse osteoporosis. In conclusion, the current study indicates that cancellous bone mass can recover from long-term disuse osteoporosis, but the changes in bone microarchitecture are not reversible. Cancellous bone mechanical properties are strongly dependent on microarchitecture (4). Accordingly, the failure to restore bone microarchitecture may have important implications for determining whether bone recovery from osteoporosis is adequate to mechanical integrity.

Bone Mass and Architectural Changes with Long-term Disuse and Recovery

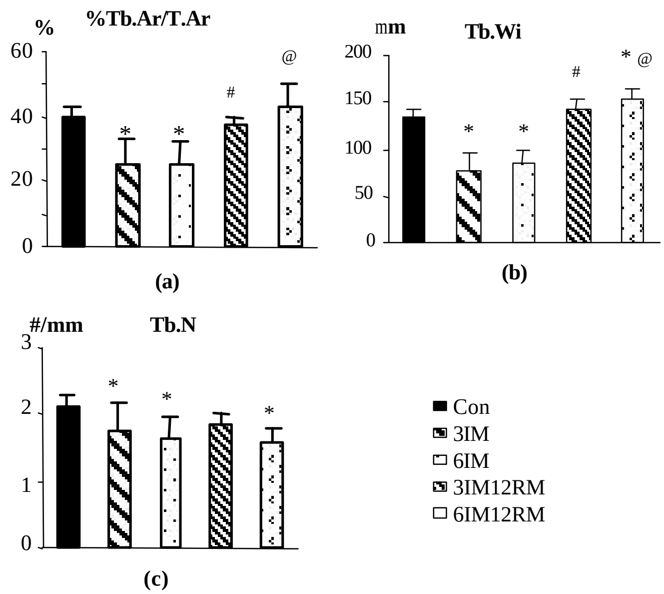

Figure.1. (**a**) Trabecular bone area, (**b**) trabecular width, and (**c**) trabecular number in experimental groups; *$p<0.05$ *vs*. control; #$p<0.05$ *vs*. 3IM; @$p<0.05$ *vs*. 6IM.

Table. 1. Dynamic measurements in distal metacarpal metaphyses.

Groups	%L.Pm	MAR	BFR/B.Pm	%Er.Pm
	%	µm	$\mu m^2/\mu m$ /d	%
Control	1.1±1.1	0.4 ± 0.4	0.2 ± 0.4	1.6 ± 0.6
3IM	7.1 ± 5.9*	0.9 ± 0.1*	2.5 ± 2.2*	8.5 ± 3.1*
3IM12RM	1.3 ± 0.8#	0.1 ± 0.3#	0.1 ± 0.2#	1.9 ± 0.8#
6IM	3.4 ± 2.5	0.7 ± 0.4	0.9 ± 0.6	3.6 ± 2.5
6IM12RM	1.8 ± 1.3	0.0 ± 0.0@	0.0 ± 0.0	1.2 ± 0.5@

Data are presented as means ± SD; L.Pm, labeled perimeter; MAR, mineral apposition rate; BFR/B.Pm, bone formation rate; Er.Pm, eroded perimeter; *$p<0.05$ *vs*. control; #$p<0.05$ *vs*. 3IM; @$p<0.05$ *vs*. 6IM.

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References

1. Jaworski and Uhthoff. Bone 7:431-439, 1986.
2. Lane et al., Calcif Tissue Int 59:401-406, 1996.
3. Grynpas et al., Bone 17:225S-232S, 1995.
4. Goulet et al, Trans Orthop. Res. Soc., 14: 73, 1989.