Correlations between alveolar bone microstructure and bone turnover markers in pre- and post-menopausal women

Emi Yamashita-Mikami, DDS, PhD,[a] Mikako Tanaka, DDS, PhD,[a] Naoki Sakurai, DDS, PhD,[a] Yoshiaki Arai, DDS, PhD,[b] Akira Matsuo, DDS, PhD,[c] Hayato Ohshima, DDS, PhD,[d] Shuichi Nomura, DDS, PhD,[a] and Sadakazu Ejiri, DDS, PhD[e]

Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; Niigata University Medical and Dental Hospital, Niigata, Japan; Tokyo Medical University, Tokyo, Japan; and Asahi University School of Dentistry, Gifu, Japan

Objective. Alveolar cancellous bone biopsy samples were extracted during dental implant preparation for investigating microstructural changes due to menopause and relationships between these changes and bone turnover markers.

Study Design. Subjects were 18 women receiving mandibular implants: premenopausal (n = 5), early postmenopausal (≤5 years; n = 3), and late postmenopausal (>5 years; n = 10). Bone turnover markers were measured and the samples analyzed using microscopic computerized tomography and 3-dimensional bone morphometry.

Results. The alveolar bone volume was significantly less in late postmenopausal women than in premenopausal ones. The trabeculae in early postmenopausal women were more separated and rod-like than in premenopausal ones ($P < .05$). Each alveolar bone parameter was significantly ($P < .05$) related to at least 1 bone turnover marker.

Conclusions. Alveolar cancellous bone structure begins changing even in early postmenopausal women, and this structure varies in close relationship to bone turnover markers. (Oral Surg Oral Med Oral Pathol Oral Radiol 2013;115:e12-e19)

Osteoporosis has been described as "a skeletal disorder characterized by compromised bone strength predisposing a person to increased risk of fracture," with bone strength being evaluated based on bone mineral density (BMD) and bone quality.[1] Diagnosing osteoporosis usually involves dual-energy X-ray absorptiometry (DXA) to evaluate BMD loss in the lumbar vertebrae.[2] For osteoporosis screening, quantitative ultrasound has recently become popular, because it is noninvasive.[3,4]

Bone quality is usually evaluated based on the architecture, turnover, damage accumulation, and mineralization of bone tissue,[5,6] with turnover being used to reveal the level of cell activity within such tissue.[7–9] Clinically, bone turnover markers have been used in assessing risks of osteoporosis and fracture before such problems appear.[10–12] Unlike BMD, which only reveals existing bone loss, bone turnover markers can reveal presently ongoing bone metabolic activity, thereby making it possible to predict future changes in bone dynamics before actual bone loss occurs.

To obtain more direct information about bone tissue, it is also useful to investigate its microstructure. An examination of the microstructure of rat tibiae revealed that their trabecular architecture had already begun to deteriorate 2 weeks after ovariectomy.[13]

Although medical X-ray equipment in common use today (computerized tomography [CT], DXA, etc.) can evaluate the overall BMD of a bone (including both its cortical and cancellous areas) as well as the condition of its cortical bone, their resolution is insufficient for revealing the bone microstructure. If microscopic computerized tomography (microCT) is used for better resolution, there then remains the problem of the invasive extraction of a biopsy sample. For patients with bone metabolic disorders, bone biopsies have been taken from the iliac crest or rib.[14,15] However, such invasive biopsies can not be performed on large numbers of healthy subjects for osteoporosis screening purposes.

Statement of Clinical Relevance

Our method permits a direct inspection of a patient's alveolar bone tissues and could offer a useful well founded technique for clinically evaluating a patient's general bone health, thereby allowing practitioners to identify early signs of osteoporosis.

Supported by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (no. 23890061).

[a]Division of Comprehensive Prosthodontics, Department of Tissue Regeneration and Reconstruction, Niigata University Graduate School of Medical and Dental Sciences.

[b]Temporomandibular Joint Clinic, Niigata University Medical and Dental Hospital.

[c]Department of Oral and Maxillofacial Surgery, Tokyo Medical University.

[d]Division of Anatomy and Cell Biology of the Hard Tissue, Department of Tissue Regeneration and Reconstruction, Niigata University Graduate School of Medical and Dental Sciences.

[e]Department of Oral Anatomy, Division of Oral Structure, Function and Development, Asahi University School of Dentistry.

Received for publication Aug 16, 2011; returned for revision Oct 4, 2011; accepted for publication Oct 6, 2011.

2212-4403/$ - see front matter

http://dx.doi.org/10.1016/j.oooo.2011.10.028

Table I. Subject characteristics

	Case no.	Age, y	Years since menopause	Biopsy region	Period since tooth loss or extraction	Cause of tooth loss or extraction
Premenopausal group	1	23	—	Premolar	15 y	Congenitally missing
	2	33	—	Premolar	25 y	Congenitally missing
	3	37	—	Premolar	30 y	Congenitally missing
	4	47	—	Premolar	20 y	Dental caries
	5	48	—	Molar	14 y	Periapical periodontitis
Early postmenopuasal group	6	52	5	Premolar	5 y	Marginal periodontitis
	7	53	1	Molar	23 y	Dental caries
	8	58	5	Molar	23 y	Dental caries
Late postmenopausal group	9	60	25	Molar	2 y 3 mo	Periapical periodontitis
	10	60	19	Molar	20 y	Periapical periodontitis
	11	61	8	Molar	20 y	Dental caries
	12	61	26	Molar	30 y	Unknown
	13	65	20	Premolar	10 y	Unknown
	14	66	22	Molar	10 y	Dental caries
	15	67	17	Molar	25 y	Dental caries
	16	67	12	Molar	30 y	Dental caries
	17	68	21	Molar	5 y	Dental caries
	18	75	25	Premolar	30 y	Unknown

Unknown: the patient's previous tooth had not been extracted at the authors' hospital, and the reason for the loss or extraction was unknown.

During preparations for a dental implant, alveolar bone tissue is surgically removed where the implant will be installed, and recently there have been reports of using the tissue removed during this preparation process as alveolar bone biopsy samples.[16,17] Such samples can be more easily and less invasively obtained than from the iliac crest or rib, and by inspecting the bone microstructure of these alveolar bone samples, it is possible to investigate how this microstructure is reacting to the systemic bone metabolic dynamics.

In recent years, there has been a growing desire in dentistry to be able to diagnose osteoporosis. Studies have reported that erosion of the mandibular inferior cortex as seen on dental radiographs is correlated with lumbar BMD,[18–20] as is mandibular cortical thickness.[21] Furthermore, osteoporosis has been reported to adversely affect bone formation in the dental implant area[22,23] and impede osseointegration.[24,25] Animal studies have also shown that the alveolar bone microstructure in estrogen-deprived monkeys is more fragile.[26] The above studies clearly demonstrate the responsiveness of the mandible and alveolar bone to systemic osteoporosis.

The present study examined microstructural changes in the cancellous bone arising due to the bone-metabolism changes accompanying menopause, using microCT analysis of biopsy samples of alveolar bone extracted during the surgical preparation of implant sites. These changes in alveolar bone microstructure were also compared with systemic bone turnover markers, and the correlations between these two were evaluated for the purpose of investigating the viability of using such alveolar bone samples to reveal early-stage osteoporosis.

MATERIALS AND METHODS

Subjects

Subjects consisted of 18 Japanese women, divided into 3 groups (Table I): a premenopausal group (PRE [n = 5], 23-48 years old, mean age 37.6 ± 10.4 years), an early postmenopausal group (EPOST, ≤5 years since menopause [n = 3], 52-58 years old, mean age 54.3 ± 3.2 years), and a late postmenopausal group (LPOST, >5 years since menopause [n = 10], 60-75 years old, mean age 65.0 ± 4.7 years). All subjects were patients receiving dental implant treatment at the Niigata University Medical and Dental Hospital. Each of them gave her informed consent. Patients who had been treated for osteoporosis in the past were excluded from the study, and inclusion required that the implant site (i.e., alveolar bone biopsy site) was in the lower molar or premolar region, also that >2 years had passed since the original tooth had been extracted or lost (Table I).

Systemic measurements

Before surgery, bone turnover markers, including serum bone-specific alkaline phosphatase (BAP), serum osteocalcin (OC), serum type I collagen cross-linked N-telopeptide (NTX), and urinary deoxypyridinoline (DPD), were examined as part of a biochemical testing of systemic bone metabolism. In general, the values of these markers tend to increase after menopause, reflecting the postmenopausal rise in bone metabolic activity. The calcaneal bone density was measured using speed of sound (SOS) with an ultrasound device (CM-200; Furuno Electric Co.,