Periosteum: Resorption or Formation Area?

Periost Rezorpsiyon Alanı mı Formasyon Alanı mı?

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Abstract

Periosteum is a membrane that lines the outer surface of all bones, except at the joints of long bones. Endosteum lines the inner surface of all bones. Periosteal formation is observed in every stage of life, especially in childhood and early adulthood. Formation continues mechanically as a response to load. Periosteal resorption is observed especially in the flat bones in the growing period. In adulthood, resorption is a part of remodeling. The periosteal surface contains fewer osteoclasts than does the endosteal surface, and remodeling on the periosteal surface is much slower. For this reason, adult periosteum is defined as a formation area. *Turk Jem 2008; 12: 28-31*

Key words: Periosteum, resorption, formation, osteoporosis

Özet

Periost uzun kemiklerin birleşme yerleri dışındaki tüm kemiklerde dış yüzü kaplayan bir membrandır. Endosteum ise tüm kemiklerin iç yüzünü kaplar. Periost formasyonu hayatın tüm evrelerinde, özellikle çocukluk ve erken erişkin döneminde gözlenir. Mekanik olarak yüke bir cevap olarak devam eder. Periost rezorpsiyonu büyüme periyodunda özellikle düz kemiklerde gözlenir. Erişkinde yeniden yapılanmanın bir parçasıdır. Periostal yüzey endosteal yüzeye göre daha az miktarda osteoklast içerir ve yeniden yapılanma daha yavaştır. Bu nedenle erişkin periostu bir formasyon alanı olarak tanımlanır. *Turk Jem 2008; 12: 28-31*

Anahtar kelimeler: Periost, rezorpsiyon, formasyon, osteoporosis

As a bone structure, periosteum was discovered very late. In 1757, the anatomist and surgeon Duhamel du Monceau explained that periosteum is an osteogenic layer in 1757. In 1800, Baron Guillaume Dupuytren suggested that fracture develops from the periosteum and bone marrow. In 1912, Sir William Macewan reported that periosteum is not osteogenic but a kind of visceral capsule. Nevertheless, in 1945, John Victor Lacroix showed that periosteum has osteogenic capacity.

Using data from periostial biology and anatomy, this review defines another point of view of periosteum as a dynamic bone tissue. Limited data are available from clinical trials. Specifically, periosteal cells appear to differ from endosteal cells; each cell population responds differently both qualitatively and quantitatively to a wide variety of hormones and growth factors.

Periosteum covers the external surface of most bones to serve as a transitional region between the cortical bone and the overlying soft tissue or musculature. Long bones exhibit a continuous periosteal surface, yet this surface may not be covered by an intact periosteum. Periosteum is absent from articular surfaces, tendon insertions, and sesamoid bone surfaces (1) and is present in locations at high risk for fracture, such as the femoral neck, the distal radius, and vertebrae. The existence of periosteum at the femoral neck has been questioned; early observational (2,3) and histological (4) studies suggested that the femoral neck lacked a periosteal cambium layer.

Periosteum contains osteogenic cells that regulate the outer shape of bone and work in coordination with inner cortical endosteum to regulate cortical thickness, size, and position of a bone in space. Periosteum is a thin layer of osteogenic and fibroblastic cells in a well-developed nerve and microvascular network, located along the periosteal cortex of cortical bone. Because there are ligament and tendon muscle attachments, and fibrocartilage, on some areas of the periosteal surface, the different physical environments to which periosteal cells are exposed are quite unlike those of the more frequently studied endosteal cells, which are bathed in hematopoietic marrow. Compared with endosteal osteoblasts, periosteal osteoblasts exhibit greater mechanosensitivity to strain (5), a lower threshold of responsiveness to osteogenic compounds such as parathyroid hormone (PTH) (6), and higher levels of expression of proteins such as periostin (7-9). For example, compared with endosteal osteoblasts, periosteal osteoblasts produce seven times more

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bone matrix protein and and estrogen-alpha receptors are more strongly expressed in periosteal osteoblasts (10).

Anatomically, the outermost fibrous layer of periosteum is composed of fibroblasts, collagen, and elastin fibers (11), along with a distinctive nerve and microvascular network (12,13). The inner layer, called cambium, contains adult mesenchymal progenitor cells, differentiated osteogenic progenitor cells, osteoblasts, fibroblasts, (14) microvessels, (12) and sympathetic nerves (13). The cambium is positioned in direct contact with the bone surface, is highly cellular, and is composed of three to four cell lines (Figure 1). Sympathetic nerve density in the cambium is significantly higher than that in the endosteum. Periosteum is thickest in the long bone diaphysis, 2 mm to 3 mm, and is thinnest within the metaphysis and epiphysis.

Periosteal Formation

Periosteal formation is observed in every stage of life, and is greatest in childhood and early adulthood. Periosteal formation continues mechanically secondary to endosteal bone loss as a response to load and also nonmechanically in the metatarsi and skull in adulthood.

Periosteal Resorption

Periosteal resorption is observed during the growing period, especially in the flat bones such as the pelvis, mandibule, and skull. In adulthood, resorption is a part of remodeling. The periosteal surface contains fewer osteoclasts than does the endosteal surface, and the remodeling is much slower. For this reason, adult periosteum is defined as a formation area (16).

Periosteum and Childhood

In childhood, periosteum is closely attached only to the metaphysis; in adulthood, periosteum is closely attached to both the diaphysis and metaphysis. In childhood, periosteum is thicker and more elastic than in adulthood and wraps the bone more firmly. These differences explain the occurrence of subperiosteal and greenstick fractures in childhood in which the integrity of the periosteum is protected. In adulthood, periosteum is thinner, less elastic, and less firm. In fractures in adults, periosteum integrity is usually impaired. Periosteum does not play a major role in longitudinal growth of bone but does in intramembraneous growth, ensuring cortical thickness, development of the Haversian canals, and above all, formation of the endosteum (17).

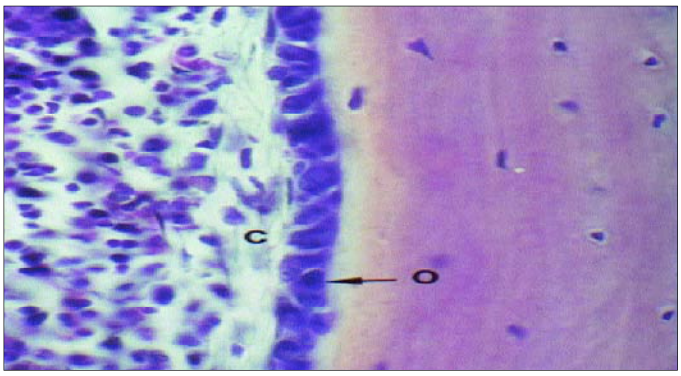

Figure 1. Histological imaging of periosteum. C: collagen outer layer, O: osteoblastic inner layer. (From Hohmann EL, Elde RP, Rysavy JA, Einzig S, Gebhard RL. Innervation of periosteum and bone by sympathetic vasoactive intestinal peptide-containing nerve fibers. Science 232: 868-871, 1986; with permission.)

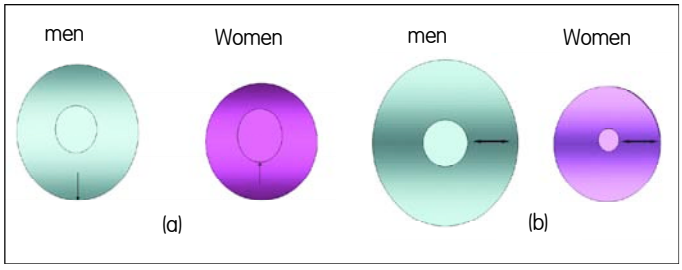

Figure 2. . Periosteum and aging. Prepubertal cortex (a) and postpubertal cortex (b) in men and women.

Periosteum in Puberty

Androgens have a positive effict on periosteal formation, whereas estrogens have a negative effect. In puberty, periosteal growth comes to a halt by the advance of estrogens. The growth is toward the endosteum in girls. Androgens stimulate periosteal growth and thus the bone expands toward the periosteum (Figure 2a). Endocortical expansion is limited to 25% in women. Medullary diameter does not change in men. The narrowing of the medullary diameter provides an almost equal cortical thickness in men (Figure 2b). Mechanical stimulation is much greater in men than women (17-19).

Periosteum and Aging

Periosteal growth occurs at various rates according to the stage in life, and is highest in childhood and early adulthood. Disorders that compromise movement, mobility, and weight-bearing at any stage in life can greatly reduce bone density.

Periosteal activity decreases with age. This reduction in osteoblast numbers may contribute to the apparent atrophy and thinning of the cambium layer that occurs with age (20). Periosteal fibroblast numbers and fibrous layer thickness decrease with age (21), although atrophy of the fibrous layer is less than that of the cambium layer (12,20). Vessel density throughout the periosteum also declines with age (12); however, vessels retain the capacity to increase when activated by mechanical load or fracture repair (12). These age-induced changes may help explain why periosteal cells from older subjects fail to form mineralized nodules in culture (21) and why the rates of periosteal bone formation (22) and responsiveness to hormones and cytokines (23) decline with age. Whether such changes in periosteal cells are also due to age-related changes in circulating hormones known to influence the periosteum, such as growth hormone and sex steroids (24), deserves further study.

Due to its high vascularity, the periosteum contains an abundance of endothelial pericytes (25). Pericytes are cells in physical contact with capillary endothelial cells. Pericytes have the ability to differentiate into numerous cell types, including osteoblasts, under appropriate culture conditions (26,27). Pericytes may serve as a supplementary source of osteoprogenitor cells (25) and may be more important in periosteal bone formation because of their greater abundance in periosteum (28) than in endosteal bone surface apposition (26). Cultured pericytes mineralize in vitro and synthesize the osteoblast marker alkaline phosphatase (28), as well as bone matrix proteins, including osteocalcin (12,28), osteonectin, osteopontin, and bone sialoprotein (12). These cells form an osteogenic tissue that mimics bone-derived tissue, both spatially and temporally (12), and responds to osteogenic stimuli, such as bone morphogenetic protein and PTH (27). A potential role for pericytes as a source of osteoblasts in periosteum has not been investigated.

Periosteal ossification may increase to compensate for decreased endosteal ossification due to age (Figure 3).

Periosteum Imaging

It is difficult to demostrate the early stage or minimal changes of the periosteum with noninvasive methods. Cortical bones, tendons, ligaments, and periosteum may be demonstrated radiologically with ultrashort time echo pulsed sequence within magnetic resonance imaging systems (29). Less expensive, safer, and more widely available techniques are needed.

Periosteum in Osteoporosis

It is now known that bone size is an important factor in determining the risk of fracture because periosteum is directly related to bone size. Periosteal expansion in the cortical area helps to improve bone strength independently of local bone mineral density (29).

Current pharmacological interventions to stimulate bone growth include anabolic and antiresorptive agents. Both these modes of treatment reduce the risk of osteoporotic bone fracture, in part by increasing bone density. Anabolic agents, such as PTH, increase bone modeling (30) and remodeling (31). Antiresorptive agents, such as the bisphosphonates, and estrogenic compounds (estrogen, raloxifene) decrease bone remodeling through suppression of osteoclast resorption and increased osteoclast apoptosis. Knowledge of the effects of approved osteoporosis drugs on cortical bone biology is limited. Antiresorptive and anabolic osteoporotic drugs may regulate periosteal cells differently than endosteal cells. For mechanical reasons, periosteal stimulation may provide better antifracture efficacy than agents that primarily target endosteal and trabecular cell populations (32).

It is know that, after considering the limited published data on therapeutic interventions for osteoporosis, substantial work should be undertaken to assess the ways in which current drugs influence periosteal cells. It is speculated that selective and specific drug targets within the periosteum can be activated independently of endocortical or trabecular surfaces. Expanding the periosteal perimeter would represent a novel mechanism to dramatically improve bone strength and reduce fracture risk, independent of the well-accepted effects of increasing bone density.

In vivo studies in animals (33) and studies in postmenopausal women (34,35) have revealed differences in the osteogenic response on periosteal and endosteal surfaces, indicating a potential to preferentially target the periosteal surface cells and increase bone circumference, thereby reducing the risk of osteoporotic fracture. Selective targeting of the periosteum requires identification of genes and proteins that are unique to periosteum or present in greater concentrations in periosteum.

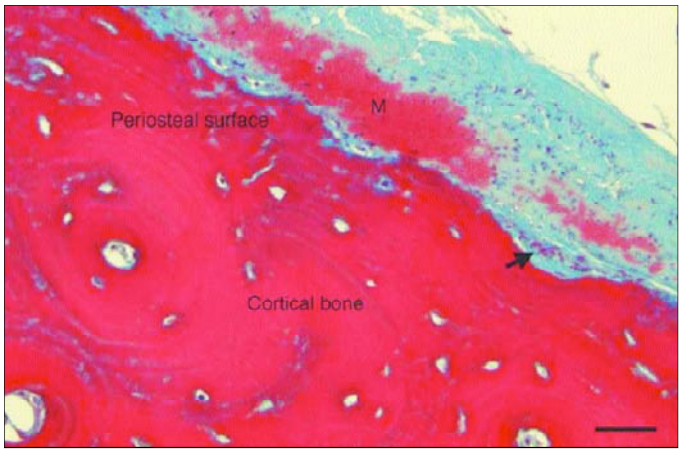

Figure 3. Histological imaging of periosteum. C: collagen outer layer, O: osteoblastic inner layer. (From Hohmann EL, Elde RP, Rysavy JA, Einzig S, Gebhard RL. Innervation of periosteum and bone by sympathetic vasoactive intestinal peptide-containing nerve fibers. Science 232: 868-871, 1986; with permission.)

Periosteum and Bisphosphonates

Few data document whether bisphosphonate-induced reductions in bone remodeling have an impact on periosteal expansion. The increased rate of periosteal apposition observed in these studies was transient and occurred early during treatment (34,35).

Periosteum and Selective Estrogen Receptor Modulators

Limited data suggest that selective estrogen receptor modulators have little or no effect on periosteal apposition in humans. Data from iliac crest biopsies document a nonsignificant increase in cortical bone width after 2 years of raloxifene treatment compared with a decrease in placebo-treated subjects (35).

Periosteum and Parathyroid Hormone

Once-daily PTH treatment increases cortical bone width through referential modeling on both periosteal and endosteal surfaces (36-39). Clinical studies using dual-energy X-ray absorptometry (DXA scan) document significant increases in vertebrae (40) and radius (41) cross-sectional area following 12 to 18 months of PTH treatment in postmenopausal women. Histological (30,42) data document PTH-induced increases in cortical wall thickness. Paradoxically, continuous exposure to PTH and hyperparathyroidism in humans.... (38).

In conclusion, bone strength is associated with bone mass, material features, micro-architecture, size, and geometry. It is known that periosteum affects all of these parameters. For this reason, periosteum is the layer that directly affects bone strength and thus deserves special attention. We speculate that an alternate strategy to protect human bones from fracture may be through targeting of the periosteum, either using electrical current or novel agents.

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