journal of prosthodontic research xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Journal of Prosthodontic Research

journal homepage: www.elsevier.com/locate/jpor

Review

A paradigm shift for bone quality in dentistry: A literature review

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ARTICLE INFO

Article history:
Received 21 February 2017
Received in revised form 18 May 2017
Accepted 24 May 2017
Available online xxx

Keywords:
Bone quality
Collagen
Biological apatite (BAp)
Osteocytes
Prosthodontic dentistry

ABSTRACT

Purpose: The aim of this study was to present the current concept of bone quality based on the proposal by the National Institutes of Health (NIH) and some of the cellular and molecular factors that affect bone quality.
Study selection: This is a literature review which focuses on collagen, biological apatite (BAp), and bone cells such as osteoblasts and osteocytes.
Results: In dentistry, the term "bone quality" has long been considered to be synonymous with bone mineral density (BMD) based on radiographic and sensible evaluations. In 2000, the NIH proposed the concept of bone quality as "the sum of all characteristics of bone that influence the bone's resistance to fracture," which is completely independent of BMD. The NIH defines bone quality as comprising bone architecture, bone turnover, bone mineralization, and micro-damage accumulation. Moreover, our investigations have demonstrated that BAp, collagen, and bone cells such as osteoblasts and osteocytes play essential roles in controlling the current concept of bone quality in bone around hip and dental implants.
Conclusion: The current concept of bone quality is crucial for understanding bone mechanical functions. BAp, collagen and osteocytes are the main factors affecting bone quality. Moreover, mechanical loading dynamically adapts bone quality. Understanding the current concept of bone quality is required in dentistry.

Contents

1. Introduction 00
2. Bone quality based on collagen 00
   2.1. Collagen in bone 00
   2.2. Post-translational modifications of type I collagen 00
   2.3. Collagen cross-linking 00
3. Bone quality based on biological apatite (BAp) 00
   3.1. Crystallographic texture and preferential orientation of BAp crystals and collagen molecules in bone 00
   3.2. Contribution of the BAp *c*-axis orientation to bone mechanical property-validity as a bone quality parameter 00
   3.3. Usefulness of the BAp *c*-axis orientation in bone assessment, bone medication, and implantology 00
   3.4. Artificial induction and control of the BAp orientation 00
4. Bone quality based on osteocytes 00
   4.1. Osteocytes in bone tissue 00
   4.2. Mechanosensation in osteocytes 00
   4.3. Osteocytes improve bone quality through drug therapies 00
5. Conclusion and future direction 00

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http://dx.doi.org/10.1016/j.jpor.2017.05.006
1883-1958/

Acknowledgments 00
References 00

1. Introduction

Bone tissue, which plays an essential role in skeletal homeostasis, responds to mechanical load. A well-known anatomist Georg Hermann von Meyer and a structural engineer and mathematician Karl Culmann discovered marked similarity between the trabecular structure of the proximal femur and stress trajectory patterns in 1867 [1]. Julius Wolff also found an association between trabecular morphology and stress trajectories in 1869 [2,3]. This famous theory is referred to as "Wolff's law," which indicates bone adaptation to mechanical load [4]. For instance, bones of the stroke forearm and hand increase bone density, diameter, and length compared with those of the contralateral arm of professional tennis players [5]. Moreover, athletes, who perform much strength training, have greater bone mineral densities (BMDs) than non-athletes [6]. Conversely, although astronauts who had been in space 4–6 months demonstrated decreased bone mass ranging 2–9%, their BMDs recovered up to 50% within 9 months after returning to Earth due to gravity [7]. Therefore, mechanical load positively and negatively changes skeletal bone mass (bone quantity) and BMD.

Another famous theory, "mechanostat," was proposed by Harold Frost in 1987 [8]. This theory states that bone strains induced by mechanical load determine bone reactions. Bone strains $\geq$1500–3000 microstrain induce bone modeling to increase cortical bone mass, while strains $<$100–300 microstrain rapidly proceed basic multicellular unit (BMU)-based remodeling, which removes existing cortical and trabecular bone. BMU couples initial bone resorption to a final bone formation process. Normal lamellar bone is fractured when bone strain reaches 25000 microstrain [9]; 1000 microstrain indicates bone length change of 0.1% compared with the original length. Bone strains are converted to various mechanical stimuli such as fluid shear stress [10,11], hydrostatic pressure [12], and direct deformation of osteocytes that reside in the bone matrix [13–15], which suggest that osteocytes, but not bone itself, regulate bone homeostasis in response to mechanical load.

Until 2000, bone strength was considered to be synonymous with BMD. However, a new clinical parameter, "bone quality," was proposed by the National Institutes of Health (NIH) in 2000 [16]. Bone quality, which is defined as "the sum of all characteristics of bone that influence the bone's resistance to fracture" is completely independent of BMD. Therefore, to determine bone strength, not only BMD but also bone quality must be evaluated. A lower BMD induces greater fracture risk in bone [17]. However, the relationship between increased BMD by antiresorptive therapy and reduced fracture risk is not proportional [18], indicating that increased BMD does not always lead to decreased fracture risk. The NIH defines bone quality as comprising bone architecture, bone turnover, bone mineralization, and microdamage accumulation [19] (Fig. 1). In addition, recent investigations have proposed novel and promising bone quality parameters focusing on the bone microstructure such as osteocytes, biological apatite (BAp), and collagen fibers. Indeed, Nakano et al. proposed that BAp orientation is one of the major determinants of bone quality because BAp orientation strongly depends on the anatomical bone portion, especially in mandible, closely related to the *in vivo* stress distribution [20]. In addition, Ishimoto et al. clearly demonstrated that degree of BAp orientation is more strongly correlated with bone strength than BMD using a regenerative bone defect model in rabbit ulna [21]. Kuroshima et al. demonstrated that osteocytes, BAp, and collagen fibers could become new clinical parameters to evaluate bone quality in implant dentistry [22], suggesting that understanding bone quality is clinically relevant.

In dentistry, the effect of mechanical load on jaw bone has been well documented. Jaw bones constitutively receive functional loads such as mastication and swallowing and parafunctional loads such as grinding, clenching and tapping. Mandibular and palatal tori, which are bone outgrowths, are associated with mechanical stresses such as functional and parafunctional loads [23,24]. Orthodontic force via natural teeth dynamically proceeds bone modeling and remodeling around the teeth [25]. Occlusal force often acts as traumatic occlusion in patients with periodontitis, resulting in the destruction of periodontal tissue and alveolar bone [26]. Moreover, it is believed that occlusal overload may lead to bone loss around stable dental implants [27]. Some of the confusion surrounding the term "bone quality" is that this term has already been used in dentistry. In contrast to the current concept of "bone quality," which is independent of BMD, "bone quality" in dentistry has largely been synonymous with BMD based on radiographic and sensible evaluations [28–30]. Although, the paradigm of bone quality has already shifted from BMD-based assessments to microstructural evaluations of bone, BMD-based diagnosis remains the gold standard in dentistry. Hence, accepting and understanding the current concept of bone quality is actually required in dentistry. However, further research based on this concept of bone quality is necessary prior to its clinical application in prosthodontic dentistry.

The aim of this literature review is to present the current concept of bone quality according to collagen, BAp orientation, and bone cells, such as osteoblasts, and osteocytes, to consider bone strength in dentistry and discuss innovative dental research based on the current concept of bone quality.

2. Bone quality based on collagen

2.1. Collagen in bone

Collagen is the main component of bone organic constituents. The composition and structure of collagen components have long been recognized as important contributors to bone quality [31–33]. The importance of collagen components in bone mechanical properties has been demonstrated through irreversible collagen manipulations, such as formalin fixation [34], heat denaturation [35,36], and X-ray irradiation [37,38]. Studies demonstrate that collagen manipulations affect bone mechanical properties; collagen contributes predominantly to bone toughness, whereas mineral contents contribute to stiffness and strength [39–41].

Osteogenesis imperfecta (OI) is a genetic bone disorder characterized by fragile bones. Approximately 90% of OI cases are caused by dominant mutations in the genes encoding type I collagen (i.e., *COL1A1* and *COL1A2*), which affects the amount and structure of bone collagen. It has been reported that polymorphisms in type I collagen genes increase the risk of fractures, independent of changes in BMD [42]. For many years, no causative genes were identified for the remaining 10% of OI cases; however, other mutations causing recessive forms of OI have been recently discovered. Part of them are genes related to post-translational modifications of type I collagen [43].

Please cite this article in press as: S. Kuroshima, et al., A paradigm shift for bone quality in dentistry: A literature review, J Prosthodont Res (2017), http://dx.doi.org/10.1016/j.jpor.2017.05.006