Autologous Bone Graft: When Shall We Add Growth Factors?

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Despite the ongoing advances in the treatment of fractures and understanding of the fracture repair processes, impaired healing continues to be one of the most debilitating complications of fractures. Up to 10% of the 6.2 million fractures occurring annually in the United States are associated with impaired healing.[1] Many of these cases of impaired fracture healing demonstrate unique characteristics posed not only by the initial trauma sustained with bone defects and impaired vascularity of the area but also as a result of previous treatment modalities. Many of these patients require lengthy treatments associated with both functional and psychosocial impairment. Not less worthy is the economical burden to the patient and the health system.[2]

The standard treatment of most aseptic nonunions is mechanical stabilization with or without biologic stimulation depending on the assessment and classification of the nonunion.[3]

The current gold standard for any given situation requiring bone grafting and especially in situations of fracture nonunion is autologous bone grafting (ABG). Autologous cancellous bone grafting remains a unique biologic method promoting union by stimulating the local biology at the nonunion site.[4–7] Autologous bone has all three components necessary to promote or enhance bone regeneration: an osteoconductive scaffold, endogenous bioactive molecules, and cells that are able to respond to these signals. Unfortunately, although autogenous bone is considered as the best graft option, significant complications have been reported related to the harvesting site,

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most often being the anterior iliac crest of the pelvis.[8] Furthermore, the desirable quantity of the required graft at times may be insufficient.[8]

For these reasons, over the years other biologically based strategies have been developed. These include electrical, ultrasound, and shockwave stimulation, a wide range of bone graft substitutes with either osteoconductive or both osteoconductive and osteoinductive properties, and biologic response modifiers that are administered either locally or systemically, including bone morphogenetic proteins (BMPs), platelet-derived growth factors, and parathyroid hormone.[9–11] These biologic response modifiers, appear to have been used successfully in managing nonunions.[12–14] In addition to nonunion, the administration of these molecules has been used in many other orthopedic situations, including stabilization of implants,[15,16] restoration of large segmental bone defects,[15,17] treatment of osteonecrosis of the femoral head,[18] fusion of joints, cartilage regeneration,[19,20] augmentation of periprosthetic fractures, and acceleration of fracture healing, especially in patients at high risk of fracture nonunion.[21]

Nonetheless, there are still adverse clinical settings where despite providing the best mechanical environment modification complemented with ABG, failure has occurred.[22–27] In addition, there are circumstances where the application of growth factors in isolation would not seem enough to promote successful bone healing.[28]

In this study, therefore, we consider in what clinical situations implantation of autologous bone grafting may need enhancement with commercially available growth factors (BMP-2 and BMP-7) to promote successful bone healing.

THE USE OF AUTOLOGOUS BONE GRAFTING OR REAMING BY-PRODUCTS

Tibia is the most common long bone to sustain a fracture. It has a high risk of developing nonunion because of the compromised soft tissue envelope especially over its anterior medial area.[25,29] Consequently, it represents the bone with the highest overall incidence of nonunion, and the "nonunion model."[25]

In the atrophic nonunions, the biologic factor is considered to be mostly the problem, despite the perception that the vascularity at the nonunion site is not compromised. The oligotrophic and even more the atrophic nonunions present insufficient blood supply, or insufficient quantities of bone-forming cells. As a result, augmentation of this poor biologic environment through graft expansion is considered mandatory in achieving union in these difficult nonunion cases.[27,30–34] Several reports exist in the literature illustrating the efficacy of autologous iliac crest bone graft (AICBG) in isolation but also in combination with other materials. Overall the success rate with AIGBG is approximately 80% to 90%.[35–42]

The biologic properties of the "by-products" of reaming (RBP) have gained special interest very early in the history of reamed intramedullary nailing (IMN), representing an internal autografting procedure during closed reamed nailing.[17,43–45] IMN and reaming offers the unique biomechanical advantages of an intramedullary splinting fixation, in association with the osteoinductive stimulus of the "by-products" of reaming.[23,44–46] The vascular flow between endosteum and periosteum of the long bones retains nutrition and healing of the nonunion sites even after the temporary destruction of the endosteal blood flow until it is restored.[47] Although it is debatable in the literature whether to perform the IMN procedure openly or closed, it seems that surgeons open the nonunion site in those cases where the existing hardware needs to be removed, in cases with severe malalignment, and in those cases where additional bone graft needs to be added owing to massive bony defects.[43,48–53] Reckling and Waters[54] reported favorable results in the series of 33 noninfected tibial nonunions

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