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Autologous bone graft: Is it still the gold standard?☆

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ABSTRACT

Bone grafting has over 100 years of successful clinical use. Despite the successes of autograft bone transplantation, complications of bone grafting are significant, mostly at the donor site. This article reviews the biology of fracture healing, the properties of bone grafts, and reviews the specific advantages and problems associated with autograft bone. Recent techniques such as the Reamer Irrigator Aspirator are described, which has dramatically reduced complications of bone autograft harvesting.

Introduction

Autologous bone grafting has been used with increasing success for centuries and remains in common use today. This paper reviews the pre-requisites for bone healing, the biology of bone graft incorporation, and discusses the ideal characteristics of a bone graft and the physiologic function of bone grafts or bone substitutes. The overall goal is to provide the reader with a broad overview of autologous bone grafts to serve as the comparison "gold standard" for the papers which follow.

History of Bone Grafting

Examples of successful bone grafting have been found worldwide in the skeletal remains of prehistoric peoples, including the Egyptians, Khurits, and Aztecs [1]. The first medical description of a bone grafting procedure was in 1668, when Jacob van Meekeren described a successful xenograft from a dog calvarium to a soldier's skull [2]. In 1863, A Scottish surgeon, William MacEwen, performed the first documented human allograft bone transplant in a young boy in 1879 [3]. By the 1920's, bone-grafting was a well-known procedure, with Albee reported on 1600 successful bone graft operations in 1919 [4]. Well-known surgical techniques, such as the Phemister cortico-cancellous graft, were reported in this period [4], and continue to be used today. Despite the tremendous interest in developing artificial bone graft substitutes, bone remains the second most common tissue transplanted in the U.S., with over 2 million bone graft procedures now performed per year world-wide.

Prerequisites for Successful Bone Healing

The biology and biomechanics of bone healing are complex and continue to be the focus of research. It is currently considered that successful bone healing requires the presence of viable osteogenic cells (or their progenitors), an appropriate connective tissue matrix, adequate vascularity, the presence of multiple growth factors that have both temporal and special specificity within the fracture site, and appropriate degree of mechanical stability (which changes as bone formation progresses). These concepts have been popularized by Giannoudis et al. in what they term the "Diamond Concept" [5].

Typical bone formation proceeds through several well-defined steps: hematoma formation, formation of "soft callus" (unmineralized cartilage), which is then replaced by a fibrous matrix that represents nascent bone and which undergoes progressive mineralization to form "hard callus" and eventually remodeled bone [6]. Alternatively, these events can be considered in both metabolic phases (anabolic and catabolic), as well as biological stages (inflammation, endochondral bone formation, and remodeling) [6].

Biology of Bone Graft Incorporation

Although successful bone grafting must essentially re-capitulate these same steps of fracture healing, the biological steps in bone graft incorporation are usually described using different terms that are also used to describe potential functions or physiological properties of a specific bone graft material: osteogenesis, osteoinduction, and osteoconduction [7,8]. Bone grafts also provide varying degrees of mechanical support, often considered separately from (although obviously related to) their biologic function.

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Physiologic Properties of Bone Grafts

Structural Support: Bone grafts have varying ability to withstand mechanical load. Cortical grafts can withstand reasonable mechanical loads, while cancellous graft can only resist compression, and even that only to a degree. It has been shown that the mechanical properties of human bone graft vary according to the donor site. In craniofacial surgery, these properties of autologous bone graft are thought to affect the long-term structural integrity of the graft and the propensity of the graft to undergo resorption [9].

Osteogenesis: describes the ability for the graft to promote *de novo* bone formation driven by cells that are derived from the graft itself, such as surviving osteoblast precursors. Such grafts contain the cellular elements, growth factors and matrix that are required to form new bone, and are capable of inducing the angiogenesis and ingrowth of mesenchymal stem cells that are also necessary (osteoinduction) [7,8].

Osteoinduction: refers to the protein- (growth factor-) mediated recruitment, proliferation, and differentiation of host mesenchymal stem cells into chondroblasts and osteoblasts. Bone grafts with osteoinductive properties contain one or more of the bone morphogenetic proteins [7,8].

Osteoconduction: refers to the microscopic connective tissue matrix that provides the scaffold for hosting the cellular population to drive bone formation, and upon which bone formation can occur. All bone grafts and bone substitutes (other than bone marrow or plasma – based preparations) provide this function; some types of bone grafts provide only this function [7,8]. Without an appropriate scaffold, bone formation may be inhibited, even if osteogenic and/or inductive material present.

Ideal characteristics of a bone substitute

An ideal bone graft material must have all of the physiologic properties of autogenous bone: it must be biocompatible, bioresorbable, osteoconductive, and osteoinductive. The material would be easy to use and handle, must be safe, and should be cost-effective. For bone substitutes, the material should be structurally similar to bone with respect to porosity and mechanical properties.

Autogenous Bone Grafts

The physiologic properties of autogenous bone graft has defined the “gold standard” for bone grafting, and the efficacy of bone graft alternatives are therefore compared to the known results of grafting bone defects with autogenous bone. Given the demonstrated efficacy of autogenous bone, the issue of donor site morbidity is of primary concern to both patients and surgeons [10]. New methods of autogenous bone graft harvesting have been introduced and will be described.

Bone grafts, whether autograft or allograft, are described as cortical or cancellous, depending on the type of bone harvested. Autograft bone can be further classified as non – vascular or vascularized.

Cancellous autograft consists of a porous three-dimensional scaffold that is highly osteoconductive, contains osteocytes and stem cells that are osteogenic, as well as growth factors that are osteoinductive. Although cancellous bone graft offers poor initial structural support, it can begin to provide structural support as bone is formed. Cancellous autograft is typically harvested from the iliac crest, the posterior superior iliac spine, the distal femur, the proximal or distal tibia, distal radius, or olecranon. More recently, reamings from the femoral medullary canal obtained using the Reamer Irrigator Aspirator system (RIA, Depuy Synthes, West Chester, PA) has become a popular source of cancellous graft due it’s large volume of potential graft, decreased donor site morbidity and equivalent efficacy to more traditional sources of cancellous graft (Figs. 1-7).

Fig. 1. Anteroposterior and lateral radiographs of the right tibia of a 30-year-old male injured in a motorcycle accident. He had a comminuted fracture of the tibia and fibula with a wound over his anterior tibial crest.

Fig. 2. Clinical photograph of the leg after debridement and external fixation, showing the distal tibial shaft and bone void distally.

Cortical bone grafts, even when autogenous, are primarily osteoconductive and have less biologic activity compared to cancellous bone. Cortical bone is less porous, has less surface area and less cellular matrix than cancellous bone. Therefore, cortical bone

Fig. 3. Anteroposterior and lateral radiographs of the right tibia after IM nailing, soleus flap, and placement of a polymethylmethacrylate spacer in the tibial bone defect.

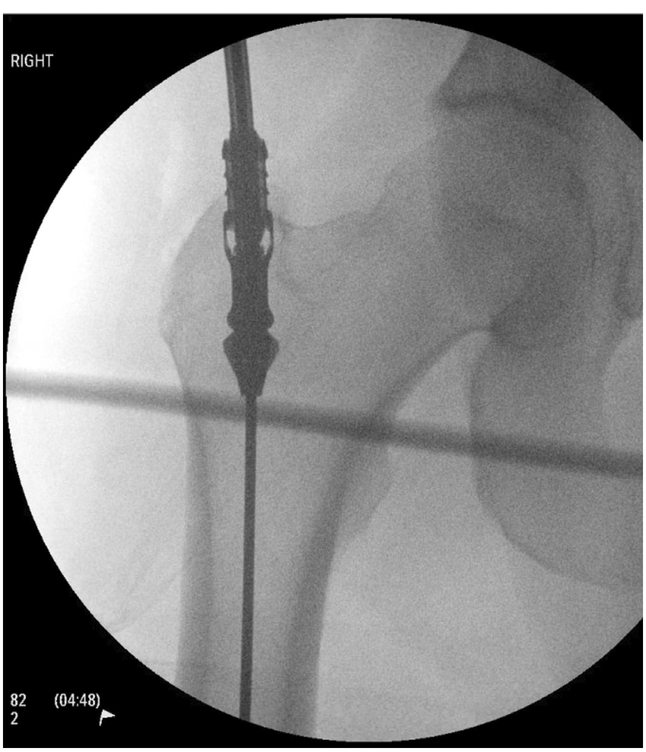

Fig. 4. Harvesting of femoral autograft using the Reamer Irrigator Aspirator device (RIA, Depuy Synthes, West Chester, PA).

Fig. 5. Intra-operative images after removal of the spacer (left panel) and filling of the bone defect with autograft cancellous bone obtained using the RIA (right panel).

takes longer to revascularization, but this may be offset by the increased structural support that cortical bone provides. Cortical bone grafts can be used to span bone defects, and vascularized cortical bone can be obtained, either as rotational or free tissue transfers. Vascularized cortical grafts provide better structural support than non-vascularized grafts due to their earlier incorporation, and also can have osteogenic and osteoinductive properties, especially if periosteum is also transferred.

Benefits and Risks of Autogenous Bone Graft

Autogenous bone graft is osteogenic, clearly histocompatible, can provide structural support, and has no risk of disease transmission [7]. Drawbacks to the use of autogenous bone graft are its limited supply, the fact that the magnitude of surgery is increased by the need to harvest bone graft with increase time and blood loss, and the possible need for general (as opposed to regional) anesthesia. Of greatest concern is the potential for donor site morbidity. Younger and Chapman reviewed 243 autogenous bone graft procedures and documented an overall major complication rate of 8.6% [10]. These complications included infection, prolonged wound drainage, reoperation, pain persisting more than 6 months, and sensory loss. Minor complications, described as superficial infection, minor wound problems, temporary sensory loss, and mild or resolving pain occurred in 20.6 % of patients [10].

The morbidity of autologous bone harvest clearly depends on the choice of donor site. Younger and Chapman noted that there was a much higher complication rate (17.9% major complication rate) when the incision used for the surgery was also used to harvest the bone graft [10]. The morbidity of using the iliac crest has been well-documented, and includes bleeding, fracture, neurologic injury, and significant pain. There may be fewer complications associated with use of the posterior iliac crest compared to the anterior crest [11]. However, the morbidity of iliac crest grafts appears to be less with smaller grafts. Suda et al. had only minor complications when iliac crest bone was used for the repair of distal radial fractures [12].

Fig. 6. Anteroposterior and lateral radiographs of the right tibia 4 weeks after bone-grafting.

Fig. 7. Anteroposterior and lateral radiographs of the right tibia taken 1 year postoperatively, showing mature bone callus.

A significant advance that may be primarily responsible for the continued popularity of autologous cancellous bone graft is the Reamer Irrigator Aspirator (RIA) technique. Originally developed to reduce the risk of pulmonary bone marrow embolism during intramedullary nailing of the femur, the device removes bone and bone marrow from the femoral medullary canal that is trapped in a filter and readily available for use. Femoral reamings contain cortical bone, blood and bone marrow elements. In 2004, Frölke et al. used a sheep model to study whether femoral reamings contained viable cells [13]. Femoral reamings were comparable to iliac crest biopsies in ability to culture cells, and in the physiologic response of the cells in response to vitamin D stimulation [13]. The osteogenic potential of RIA-derived graft has been demonstrated in many animal and human studies [14-16]. The overall complications of bone graft harvest using RIA appear to be low [17]. In one series reporting 204 RIA cases, there were 4 complications (2%); all related to fracture or cortical perforation [18]. The potential for biomechanical compromise of the femur as a consequence of using the RIA has been investigated. In a cadaver study using matched femora, the torsional strength of the reamed femur was unchanged from the opposite unreamed femur [19]. One specimen had eccentric reaming of the anterior cortex and fractured during loading, illustrating this as a potential complication [19]. In another cadaver study, Finnan et al. showed that with either a trochanteric, “piriformis fossa”, or retrograde portal, mechanical strength of the femur after reaming with the RIA remained sufficient to allow unsupported single-leg weight-bearing [20].

Results of Autologous Bone Grafting

Reporting or comparing the outcome of any bone-grafting technique is complicated by the heterogenous nature of reported studies, many of which are simple case series, the varied etiologies of the bone defect, the site of the defect, differences in patient selection, differences in the technique of graft harvest, preparation, or insertion, and the method of bone stabilization used. Flierl et al. reviewed 192 patients with long-bone nonunions treated at two trauma centers, comparing autograft (n =105), allograft (n = 38), combined allograft / autograft (n = 16), and recombinant human bone morphogenetic protein-2 (rhBMP-2) with or without bone graft (n=23) [21]. The nonunions treated with autograft had a statistically significantly shorter time to union than the other groups. Furthermore, the autograft cohort had fewer surgical revisions and need for revision bone grafting compared the other types of bone grafts. Finally, the new-onset postoperative infection rate was significantly lower in the autograft group (12.4%), compared to the allograft cohort (26.3%) [21]. Autograft appears to be equally efficacious in the elderly patient as in the young [22].

The results of the RIA technique have been compared to the more traditional iliac crest bone graft in several studies. Belthur et al. reported a 90 % union rate after using RIA compared with 80% union rate after iliac crest grafting [23]. Furthermore, in this study the RIA group reported lower pain scores, while complications were more frequent after iliac crest bone graft harvest [23]. More recently, Dawson et al. reported 82 % union following RIA comparted to 86% union after iliac cresting grafting [24]. No statistically significant differences were noted in rates of union or complication rate, of which both were about approximately 8% [24]. Lastly, Dimitriou and colleagues performed a systematic review of 92 published studies evaluating the results of RIA or iliac crest bone grafting [25]. In their study, the complication rate following RIA bone graft harvest was 6% (14 complications in 233 patients), compared to 19 % after iliac crest bone graft harvesting (1249 complications in 6449 patients) [25].

Conclusions

Despite intensive research and development of potential bone graft alternatives, autologous bone graft remains the gold standard of care for treatment of bone defects. The union rate associated with autograft bone appears greater than with alternative bone grafts. The major impetus for the development of bone graft substitutes was to mitigate the complications associated with the harvest of autologous bone. However, the development of the RIA device and application of RIA to harvest of intramedullary bone graft has significantly reduced donor site complications. For the foreseeable future, for most nonunions, autograft bone remains the gold standard.

Declarations of interest

None.

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