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Percutaneous Autologous Bone-Marrow Grafting for Nonunions

Surgical Technique

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ABSTRACT

BACKGROUND:
Bone marrow aspirated from the iliac crest contains progenitor cells that can be used to obtain bone-healing of nonunions. However, there is little available information regarding the number and concentration of these cells that are necessary to obtain bone repair. The purpose of this study was to evaluate the number and concentration of progenitor cells that were transplanted for the treatment of nonunion, the callus volume obtained after the transplantation, and the clinical healing rate.

METHODS:
Marrow was aspirated from both anterior iliac crests, concentrated on a cell separator, and then injected into sixty noninfected atrophic nonunions of the tibia. Each nonunion received a relatively constant volume of 20 cm³ of concentrated bone marrow. The number of progenitor cells that was transplanted was estimated by counting the fibroblast colony-forming units. The volume of mineralized bone formation was determined by comparing preoperative computerized tomography scans with scans performed four months following the injection.

INTRODUCTION

The percutaneous technique of autologous bone-marrow grafting is a minimally invasive treatment. The effectiveness of this technique for the treatment of atrophic nonunions has been confirmed by several authors. However, the efficacy appears to be related to the number of progenitor cells in the graft. Here, we describe a technique for obtaining progenitor cells by marrow aspiration, a method of concentration for increasing the number of progenitors in the graft after aspiration, and a technique of intraosseous reinjection into the site of a tibial fracture nonunion.

SURGICAL TECHNIQUE

Patient Positioning and Preparation
With the patient under general anesthesia, the procedure is performed with an internal fixation device used to stabilize the atrophic tibial nonunion. The patient is placed on the operating table in a supine position with the arms stretched out to the sides. The affected leg and both iliac crests are prepared and draped in a sterile fashion. A c-arm fluoroscope is draped with a sterile cover in a manner that will allow access for anteroposterior and lateral views of the nonunion site.
Marrow Aspiration
Bone marrow harvesting is most conveniently done by two surgeons working simultaneously on one anterior iliac crest each (Fig. 1). Under sterile conditions, a 2-mm skin incision is made at the level of the anterior iliac crest so that the tip lies between the inner and outer tables. The bone marrow is aspirated into a 10-cm³ plastic syringe. If no mar-

RESULTS:
The aspirates contained an average (and standard deviation) of 612 ± 134 progenitors/cm³ (range, 12 to 1224 progenitors/cm³) before concentration and an average of 2579 ± 1121 progenitors/cm³ (range, 60 to 6120 progenitors/cm³) after concentration. An average total of 51 × 10³ fibroblast colony-forming units was injected into each nonunion. Bone union was obtained in fifty-three patients, and the bone marrow that had been injected into the nonunions of those patients contained >1500 progenitors/cm³ and an average total of 54,962 ± 17,431 progenitors. The concentration (634 ± 187 progenitors/cm³) and the total number (19,324 ± 6843) of progenitors injected into the nonunion sites of the seven patients in whom bone union was not obtained were both significantly lower (p = 0.001 and p < 0.01, respectively) than those in the patients who obtained bone union. The volume of the mineralized callus measured at four months on the computerized tomography scans of the patients who had union ranged from 0.8 to 5.3 cm³ (mean, 3.1 cm³). There was a positive correlation between the volume of mineralized callus at four months and the number (p = 0.04) and concentration (p = 0.01) of fibroblast colony-forming units in the graft. There was a negative correlation between the time needed to obtain union and the concentration of fibroblast colony-forming units in the graft (p = 0.04).

CONCLUSIONS:
Percutaneous autologous bone-marrow grafting is an effective and safe method for the treatment of an atrophic tibial diaphyseal nonunion. However, its efficacy appears to be related to the number of progenitors in the graft, and the number of progenitors available in bone marrow aspirated from the iliac crest appears to be less than optimal in the absence of concentration.
row is obtained, the needle should be reoriented within the ilium and the aspiration should be repeated. It may be necessary to change the trocar insertion site if no marrow is obtained.

At a given depth where marrow is successfully aspirated, the trocar is turned 45° during successive aspirations to reorient the bevel, thereby affording aspiration from the largest possible space. After one full turn, the trocar is withdrawn 1 cm toward the surface through the same insertion site, and successive aspirations are begun, with the trocar always turned 45° after each aspiration. The marrow is aspirated in small (4-cm³) amounts to reduce the degree of dilution by peripheral blood. Three, four, or five perforations are made in the iliac crest through the same skin opening, with the perforations spaced at approximately 2 cm from the others to avoid dilution by aspiration from the previous area. All aspirates are pooled in plastic bags containing an anticoagulant solution (citric acid,

**CRITICAL CONCEPTS**

**INDICATIONS:**

- An uninfected nonunion following a closed fracture of the tibia treated with a cast or following an open fracture treated with external fixation.
- The best indication is an atrophic nonunion. The technique may also be used as an adjuvant for a hypertrophic nonunion; however, the surgeon should remember that the cause of the hypertrophic nonunion is usually the failure of the fixation. If a true synovial pseudarthrosis is encountered, the fluid should be removed by aspiration.
sodium citrate, and dextrose).

**Preparation of Bone Marrow Graft**

In our cellular and molecular therapy unit, the bone marrow is first filtered to separate cellular aggregates and fat (Hemoset NSR LP; B-Braun, Bethlehem, Pennsylvania). The concentrated buffy coat is obtained after a five-minute centrifugation at 1200 g on a cell separator (Cobe 2991; Gambro BCT, Lakewood, Colorado). This centrifugation forces the polynuclear cell layer, which is heavier as a result of the volume of its nuclei, to the periphery, where it can be collected and separated from the remainder. The lighter layer with anuclear red cells is found in the center and is also removed. This centrifugation method reduces a typical 300-cm³ bone-marrow aspirate to a concentrated buffy coat of about 50 cm³, which is placed into a syringe for injection.

The buffy coat contains progenitor cells. To measure the

**Critical Concepts**

**Contraindications:**

- Absence of a completely healed wound
- A gap between fragments exceeding 5 mm
- Preexisting angular deformity or shortening, both of which must be addressed with direct access to the non-union site
number of connective-tissue progenitor cells that were transplanted, we use the fibroblast colony-forming unit (CFU-F) as an indicator of stromal cell activity. Results are expressed as the mean number of fibroblast colony-forming units per one million bone-marrow cells. The number of nucleated cells present in the crude marrow aspirates from the individual patients in our study ranged from 1 to 24 million/cm$^3$, with a mean of $18 \pm 7$ million/cm$^3$. The mean number of fibroblast colony-forming units per one million nucleated cells present in the crude marrow aspirates for the individual patients ranged from 7 to 51, with a mean of $33 \pm 8$. Therefore, the number of fibroblast colony-forming units obtained in the samples incubated in vitro averaged one progenitor cell per $30 \times 10^3$ bone-marrow nucleated cells, and the bone marrow obtained by aspiration from the iliac crest contained an average of $612 \pm 134$ progenitor cells/cm$^3$ (range, 12 to 1224 progenitor cells/cm$^3$).

The bone marrow graft obtained after concentration contained an average of $2579 \pm 1121$ progenitor cells/cm$^3$ (range, 60 to 6120 progenitor cells/cm$^3$). Each nonunion site received a mean of $20 \text{ cm}^3$ (range, 17 to 22 cm$^3$) of bone marrow graft. The total number of progenitor cells received by each patient was represented by the product of the concentration of progenitor cells in the bone marrow graft obtained after concentration and the volume of the graft. Thus, the average total number of fibroblast colony-forming units injected into each nonunion was $51 \times 10^3$ (range, 1200 to $122 \times 10^3$).

**Intraosseous Reinjection**

The same trocar that had been used to aspirate the bone marrow is placed into the nonunion gap.
and around the bone ends. The position of the tip of the trocar is monitored with biplane fluoroscopy (Figs. 3 and 4). The trocar should not be placed adjacent to tendons or major neurovascular structures, and its tip should be applied directly to the surfaces of the bone. For a tibial fracture, the skin is perforated on the lateral part of the anterior tibial crest. Through this single skin perforation it is possible to position the trocar both in the nonunion site and on the medial, lateral, and posterior tibial surfaces. No attempt is made to remove the intervening callus or fibrous tissue from the nonunion site with the trocar. The marrow is injected slowly, at a rate of about 20 cm³/min, with a 10-cm³ syringe to a total volume of 20 cm³ (Fig. 5). In some cases, high pressure is required to inject the marrow and the marrow may leak through the trephine site. If that happens, it is necessary to change the position of the tip of the trocar. After injection, the trocar, with the stylet in place, is gradually withdrawn with small oscillating motions (backward and forward) to fill the path of the trocar. The skin perforation is closed with a circumferential suture to avoid leakage of marrow.

**Postoperative Care**

For patients with an atrophic nonunion and mobility at the fracture site, external fixation is maintained and weight-bearing is not allowed during the first month following injection to avoid mechanical disruption of the process of tissue regeneration and bone-healing. After one month, if (and only if) callus is observed radiographically, partial weight-bearing is allowed with the external fixation in place or with a plaster cast. There is a one-month transition period between the beginning of partial weight-bearing and that of full weight-bearing. At the end of that month, if the patient has no pain and there is cortical bridging or disappearance of the fracture lines on at least three of the four cortices viewed on the anteroposterior and lateral radiographs, the plaster cast or the external fixation is removed.

### CRITICAL CONCEPTS | continued

**AUTHOR UPDATE:**

The procedure has not changed since the time of writing of the original article.

**REFERENCES**


