Injectable Recombinant Human Platelet-derived Growth Factor in Collagen Carrier for Hindfoot Fusion

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KEYWORDS

• rh-PDGF • Hindfoot arthrodesis • Medial approach • Surgical technique

KEY POINTS

- Autogenous bone graft harvest is associated with significant risks and morbidity.
- Recombinant human platelet-derived growth factor is a safe, effective alternative to autogenous bone grafting in the setting of hindfoot arthrodesis.
- A single medial approach can provide adequate access to both the subtalar and talonavicular joints for double arthrodesis of the hindfoot.

INTRODUCTION

The hindfoot (minus the ankle) is composed of the talus and calcaneus, and their articulations including the subtalar joint (STJ), talonavicular joint (TNJ), and calcaneocuboid joint (CCJ). The hindfoot allows for inversion and eversion of the foot primarily through motion at the STJ and TNJ.[1,2] Its importance in normal gait lies in its ability to transform the foot from a flexible shock absorber at heel strike into a rigid lever at toe-off.[1,2] Dysfunction of the hindfoot complex may occur as a result of disease or deformity. Degenerative joint disease (inflammatory, posttraumatic, idiopathic) and/or substantial deformity can all contribute to pain and dysfunction of the hindfoot.[3–6] When nonoperative management of these problems fails, arthrodesis of 1 or more of the articulations of the hindfoot may be necessary.

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In any arthrodesis procedure, nonunion (pseudoarthrosis) is a potential risk. The rate of nonunion in hindfoot fusions varies dramatically depending on the study.[3,6–12] Studies include isolated STJ fusions, double and triple fusions, and variable methods of determining union. The rate of nonunion of isolated STJ fusions may be as high as 20% and may be even higher in triple fusions.[3,6–12] Smoking has been found as a consistent risk factor for development of nonunion after hindfoot fusion procedures.[6,7] Other risk factors include poorly controlled diabetes mellitus, vasculopathy, obesity, inadequate stability at the fusion site, fusion site gaps, avascular necrosis, and noncompliance with weightbearing restrictions.[13] Rates of nonunion reported in the literature are largely based on radiographs, and this may overestimate union rates.[10] Coughlin and colleagues[10] found that radiographs consistently overestimated union rates in hindfoot fusions when compared with computed tomography scan. They also found that orthopedic surgeons tend to overestimate union rates when compared with radiologists.[10] Regardless of the true nonunion rate, symptomatic nonunion after hindfoot arthrodesis is the most common reason for revision surgery. Avoiding this complication would certainly reduce rates of reoperation.

Bone grafting to enhance healing has been used extensively for decades. Although no consensus exists on the necessity of bone grafting, surgeons must take into account many factors when making the decision to use any type of bone graft material. Both clinical and radiographic factors play a role. Common reasons for the use of bone graft include nonunion surgery, history of nonunion at other sites, smoking, diabetes, renal disease, osteonecrosis, bone loss, and significant deformity.[14] Autogenous iliac crest bone graft has historically been the most common source for bone graft material.[15–17] Other sources for autogenous bone graft material have also been extensively reported included the proximal and distal tibia, greater trochanter, and calcaneus.[15] Each of these sites has their own risks associated with bone harvest, with common complications including pain, infection, and nerve injury.[12,15–19] Synthetic alternatives to autogenous bone graft offer an alternative method of enhancing bone growth while preventing the potential morbidity of bone graft harvest.[17]

Platelet-derived growth factor (PDGF) is a cytokine secreted by platelets and cells of mesenchymal origin at the site of fracture and soft tissue injury.[20–22] This growth factor acts as a chemotactic and mitogenic agent, attracting mesenchymal cells to the area of injury, and inducing replication and differentiation into osteogenic cells.[20–23] In addition, PDGF is proangiogenic, resulting in increased blood flow to the area of injury.[20–22] Recombinant human PDGF (rhPDGF-BB) is a subtype of PDGF synthesized for use in research and clinical settings. Numerous animal and basic science studies have demonstrated the efficacy and safety of PDGF and rhPDGF-BB for use in bone and soft tissue healing.[20–22]

Recent clinical studies examining the efficacy of rhPDGF in patients undergoing ankle and hindfoot fusions have demonstrated at least equivalent fusion rates when compared with cancellous autograft.[24,25] Data from a large Canadian randomized controlled trial suggest that fusion rates may even be greater for rhPDGF delivered in a collagen-based matrix than for autograft.[24] These clinical studies have also further validated the safety of using PDGF in foot and ankle surgery.

INDICATIONS AND CONTRAINDICATIONS

Indications for rh-PDGF can be grouped as disease- and patient-specific factors that increase the risk of nonunion (**Box 1**). Contraindications are few and most are related to clinical situations in which the safety of rhPDGF is unknown (**Box 2**).