A Retrospective Clinical Evaluation of Using Recombinant Human Platelet-Derived Growth Factor in Revisional Rearfoot Arthrodesis

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Statement of Purpose

The primary aim of this study is to review and assess the safety and effectiveness of recombinant human platelet-derived growth factor as a bone graft substitute for revisional arthrodesis in rearfoot reconstruction surgery

Hypothesis: The hypothesis for this study was that fusion rates for recombinant human platelet-derived growth factor will compare favorably to historical autograft controls when used in revision rearfoot arthrodesis, and without major or minor complications associated with the use of the grafting material.

Literature Review

Failure to achieve successful arthrodesis with the initial procedure causes a great deal of burden on the patient and surgeon. The results are poor patient satisfaction, the possibility of chronic disability, and increasing burden on the cost of healthcare for that individual. Nonunion rates of 40% have been reported for ankle arthrodesis, 16% for subtalar joint arthrodesis, and 17-30% for tarsometatarsal joint arthrodesis (1-4). Arner and Stantrock recently reported an approximately 10% nonunion rate in their ankle and hindfoot fusions with a statistically significant increased risk of nonunion rate associated with smoking, avascular necrosis and surgical error (5).

Once confronted with this dreaded complication, the outlook is poor. O'Connor and colleges reported on retrospective review of case logs from January 2007 to September 2014, identifying nonunion arthrodesis revision cases. They found that the overall nonunion rate was 23%. Furthermore, they found a statistically significant linear relationship between subsequent revision attempts & risk for nonunion reporting an odds ratio of 2.83 (1.24–6.47) for nonunion after prior operative treatment for nonunion (6).

Autograft has long been considered the "gold standard." However, harvesting iliac crest bone graft can cause significant comorbidity and subsequent increased healthcare expenditure. Investigations have reported an average overall cost of harvesting iliac crest bone graft to be $2,365 (7). Common complaints and postoperative complications of iliac crest bone graft harvesting are well known to include persistent pain of the donor site which may eclipse the patient's pain from the primary surgical site and procedure (8). Other complications also include bleeding, infection and chronic pain to the donor site. Allografts may provide a method of circumventing drawbacks found with autograft harvest; but they also include risks such as disease transmission, variable preservation practices, potential structural weaknesses, cost, variable availability, as well as possible increased risk of nonunion or failure (9,10).

An ideal grafting material is one that significantly reduces the risk of these type of complications, has a low or nonexistent potential for transmission of disease, and possesses osteo-inductive and osteo-conductive properties to facilitate faster healing of high risk arthrodeses (11).

Platelet derived growth factor (PDGF) helps to stimulate fibroblastic activity in the healing cascade (12). When utilized with beta tri-calcium phosphate granules, this also biologic provides an osteo-conductive and osteo-inductive graft substitute (13-25). DiGiovanni and colleagues published on the utility of rhPDGF–BB in foot and ankle reconstructive surgery with 397 patients from 37 centers in the United States and Canada. When they compared clinical healing between the autograft group and the rhPDGF–BB with beta-tricalcium phosphate, the only finding with clinical significance at 52 weeks was chronic graft site pain from the autograft group. They concluded that Rh PDGF–BB/beta-tricalcium phosphate is safe and effective alternative to autologous bone graft when utilizing the hindfoot and ankle arthrodesis (26-30).

Methodology

Study Design: Level IV Retrospective Multi-Center Case Series

Conflict of Interest: Wright Medical Technology (JL), Wright Medical Technology (PB)

Population: N = 12 patients, 12 feet. Mean 14 month follow up (range 10 to 22 months).

Inclusion Criteria: All patients who underwent revision rearfoot arthrodesis which utilized recombinant human platelet derived growth factor bone grafting at one of two institutions with a minimum of 10 months of follow up.

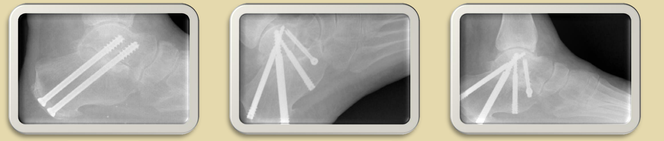
Exclusion Criteria: Patients with less than 10 months of follow up at time of submission of this poster.

Procedures: Patients underwent revisional arthrodesis surgery for one of the following joints using recombinant human platelet-derived growth factor: talo-navicular, calcaneal-cuboid, subtalar and ankle joints.

Primary outcome: Primary outcomes for the study were three fold: (1) fusion rates for the population; (2) average time to fusion; (3) adverse affects related to the grafting material.

Methods: Retrospective chart and radiographic/CT review of all patients meeting the aforementioned inclusion criteria.

Procedures: Revision Rearfoot Arthrodesis with rhPDGF-BB/β-TCP



Figures 1-3: Patient developed a subtalar joint nonunion. She required a revisional subtalar joint fusion with new hardware and rhPDGF-BB. She had a CT scan that showed fusion at 10 weeks

Figures 4-7: Patient had previous charcot reconstruction 2 years prior and nonunion of the T-N and midfoot joints. He required revisional arthrodesis with new hardware and rhPDGF-BB. CT scan confirmed fusion at 12 weeks.

Figures 7-12: Patient had previous charcot reconstruction devloped broken hardware and nonunion. He required removal of hardware application of external fixator with use of rhPDGF-BB. CT scan at 16 weeks confirmed fusion.

Results

Table 1: Demographics

Variable	N
Patients	12
Average Age	57 years
Average follow-up	14 Months
Male:Female	5:7
Neuropathic	8/12 66.7%
Diabetic	4/12 33.3%
Charcot Arthropathy	5/12 41.7%
HTN	4/12 33.3%
GERD	1/12 8.3%
Smoking History	2/12 16.7%

Table 2: Primary Outcomes

Primary Outcome	N
Fusion Rate	11/12 patients (91.7%)
Average Time to Fusion	12.9 weeks
Adverse Reactions Pertaining to Grafting Material	None

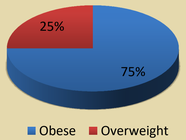


Table 3: Individual Case Results

Patient	Previous surgery	Revision Site	Augment (mL)	Time to union (weeks)	Return to activity (weeks)	Follow Up (Months)
1	Subtalar fusion	STJ	1.5	12	17	22
2	Triple arthrodesis	STJ, TNJ, CCJ	3	14	20	22
3	Ankle fusion	Ankle	3	14	17	10
4	TNJ fusion	TNJ	1.5	nonunion	nonunion	11
5	Medial column fusion	TNJ	3	12	16	17
6	Medial column fusion	TNJ	3	14	19	11
7	medial column fusion	TNJ	3	15	18	14
8	Subtalar and Medial column	STJ, TNJ	3	14	15	11
9	Subtalar fusion	STJ	3	8	10	18
10	Triple arthrodesis x2	STJ, TNJ, CCJ	3	14	20	10
11	Malunion ankle	Ankle	3	13	15	10
12	Malunion ankle	Ankle	3	12	16	13

Analysis & Discussion

A total of 12 patients underwent revisional rearfoot arthrodesis using recombinant human platelet-derived growth factor. There was an 91.7% fusion rate (11/12) in the series with an average time to fusion of 12.9 weeks, with fusion being defined by radiographic consolidation and clinical findings. Two cases of 12 (16.7%) were complicated by infected hematoma, one resolving with oral antibiotics and the second requiring multiple incision and drainage with intravenous antibiotics before resolution on infection but both patients went on to fusion. One patient went on to develop a nonunion which required further surgical management. CT scans were obtained in all patients to confirmed fusion or nonunion on average of 14 weeks. There were no adverse reactions or complications specifically related to the grafting material.

Fusion rates for the recombinant human platelet-derived growth factor compared favorably to historical autograft controls, especially in this high risk non-union revision arthrodesis patient population (1). We did not find any complications associated specifically with the use of rhPDGF in this study, in stark contrast to the potential complications seen with autograft or allograft (7-10). In the neuropathic and diabetic patients we had 100% union rate 8/12 patients. This supports the use of recombinant human platelet-derived growth factor as a safe and effective way to achieve high rates of fusion in a population with multiple high risk factors for non unions.

In their study comparing the use of either autograft or rhPDGF-BB/beta-TCP, DiGiovanni and colleges reported fusion rates of 61.2% and 62% respectively at 6 months, with clinical healing of 87.6% and 86.2% at 52 weeks respectively (26). It was also notable that fewer side effects were also reported in the PDGF group (26). The results of the present case series compares similarly and favorably to these results, and does so despite a very high risk patient population.

Limitations to the present study include a small sample size and multiple surgeons.

In conclusion, rhPDGF-BB/B-TCP is a suitable graft material with minimal complications and should be considered an acceptable alternative to autograft, even in high risk patients requiring revision hindfoot arthrodesis.

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