A Retrospective Clinical Evaluation of Using Recombinant Human Platelet-Derived Growth Factor in Revisional Forefoot and Midfoot 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 forefoot and midfoot 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 forefoot and midfoot arthrodesis, and that there would be no 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 = 8 patients, 8 feet. Mean 12.5 month follow up (range 10 to 17 months).

Inclusion Criteria: All patients who underwent revisional forefoot and midfoot arthrodesis utilizing recombinant human platelet derived growth factor bone grafting at one of two institutions with a minimum of 10 months of follow up.

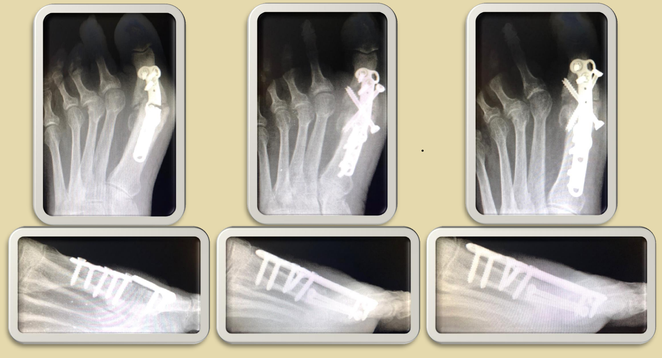
Exclusion Criteria: Patients with less than 10 months of follow up at time of submission of this poster.

Procedures: Patients underwent revisional arthrodesis surgery for one of the following joints using recombinant human platelet-derived growth factor: 1st metatarsal-phlanageal, tarsometatarsal and navicular-cunieform joints.

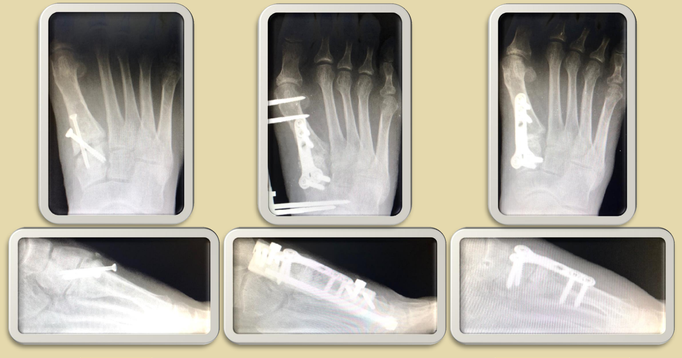
Primary outcome: Primary outcomes for the study: (1) fusion rates for the population; (2) average time to fusion; (3) adverse affects related to the grafting material.

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

Procedures: Revision Midfoot/Forefoot Arthrodesis with rhPDGF-BB/β-TCP



Figures 1-6: Patient had previous 1st MPJ fusion and sustained a broken plate that required a revisonal 1st MPJ fusion with new hardware and use of rhPDGF-BB. She went on to fuse with no complications.



Figures 7-12: Patient had two previous 1st TMT fusion attempts with no fusion. She had a revisional 1st TMT arthrodesis with plate and screws along with external fixator and use of rhPDGF-BB She went on to fuse with CT scan confirmation at 16 weeks.

Results

Table 1: Demographics

Variable	N
Patients	8
Average Age	61 years
Average follow-up	12.5 Months
Male:Female	2:6
Neuropathic	4/8 50%
Diabetic	3/8 37.5%
Charcot Arthropathy	3/8 37.5%
HTN	1/8 12.5%
COPD	1/8 12.5%
Smoking History	1/8 12.5%

Table 2: Primary Outcomes

Primary Outcome	N
Fusion Rate	7/8 patients (87.5%)
Average Time to Fusion	12.6 weeks
Adverse Reactions Pertaining to Grafting Material	None

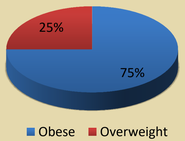


Table 3: Individual Case Results

Patient	Previous surgery	Revision Site	Augment (cc)	Time to union (weeks)	Return to activity (weeks)	Follow Up (Months)
1	1st TMT fusion x 2	1st TMTJ	1.5	13	16	14
2	1st MPJ fusion	1st MPJ	1.5	-	-	-
3	1st MPJ fusion	1st MPJ	1.5	9	14	10
4	1st TMT fusion	1st TMTJ	1.5	11	13	11
5	Medial column fusion	NCJ	1.5	12	16	17
6	Medial column fusion	NCJ	1.5	14	19	11
7	Medial column fusion	NCJ and TMTJ	3	15	18	14
8	Medial column fusion	NCJ and TMTJ	3	14	15	11

Analysis & Discussion

A total of 8 patients underwent revisional forefoot and/or midfoot arthrodesis using recombinant human platelet-derived growth factor. There was a 87.5% fusion rate (7/8) in the series with an average time to fusion of 12.6 weeks. Fusion was defined by radiographic consolidation and clinical findings. One patient developed a infected nonunion of the 1st MPJ requiring a partial ray amputation because of her noncompliance and diabetes. We did not encounter any adverse reactions or complications specifically related to the grafting material.

Fusion rates for the recombinant human platelet-derived growth factor compared very favorably to historical autograft controls, especially in this high risk revision arthrodesis patient population (1). There were also no complications associated specifically with the use of rhPDGF in this study. We find this in stark contrast to the potential complications seen with autograft or allograft (7-10). 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 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 high risk patient population.

Limitations to the present study include a small sample size, multiple surgeons, and a lack of CT confirmed arthrodesis in all cases.

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 forefoot and midfoot arthrodesis.

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