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Original Article

Clinical outcomes of natural bone matrix grafting in foot and ankle surgery

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Abstract

Objective: This study evaluated outcomes following bone grafting in the foot or ankle using a natural bone matrix with porcine collagen (NBM-PC) composite.

Methods: Sixty-six patients were enrolled in this prospective, single-arm, multicenter study. After signing the informed consent, all patients underwent standard-of-care treatment involving bone grafting on their foot or ankle. Patients were seen at 6 weeks, 3 months, 6 months, and 12 months after surgery. Patients also underwent a radiological examination, either radiograph, computed tomography, or magnetic resonance imaging.

Results: The most common surgery was arthrodesis (n = 35), followed by skeletal deformity corrections (n = 12). At the 12-month follow-up, 53 patients were evaluated, and radiological examinations indicated a fusion rate of 85%. There was osteolysis of < 1 cm^2 in 5% of patients, while six patients presented with non-union or pseudoarthrosis. The most common serious adverse events were pseudoarthrosis (n = 2) and wound infection (n = 2), unrelated to the NBM.

Conclusions: The radiographic fusion rate of 85% at the 12-month follow-up for this NBM is consistent with that reported for bone grafts other than void fillers. The lack of adverse events related to the use of NBM indicates it is safe and can provide an alternative to autografts in foot and ankle surgery.

Level of evidence: IV; Prospective cohort study

Keywords: Arthrodesis; Bone graft; Bone defect; Collagen.

Introduction

Bone grafts are an essential tool in orthopedic surgery, and their use in surgical procedures is a firmly established practice[1]. Demand for such procedures is steadily rising. Every year, half a million bone grafting procedures are performed in the United States of America and the European Union[2]. In Germany, bone defect reconstruction increased by 15% over a decade[3]. The demand for bone grafting is projected to double by 2040, primarily due to osteoporotic fractures in an aging population[4]. Thus, there is an apparent clinical need for bone grafts, whether autograft, allograft, or synthetic, each carrying its own set of benefits, risks, and limitations.

Autografts are often defined as the gold standard among bone grafts due to their non-immunogenic, osteoconductive, osteoinductive, and osteogenic properties[5]. Unfortunately, autograft has limitations, including limited availability and donor site morbidity[6]. Additionally, the harvesting of autografts is associated with a long surgical time and excessive blood loss[7].

Study performed at Schön Klinik München Harlaching, Munich, Germany and Fachklinik 360 Grad GmbH, Ratingen, Germany.

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In trauma cases, using a bone graft substitute (BGS) has significantly reduced operating times and yielded positive clinical outcomes in 95% of cases[8]. These factors have prompted the development of alternatives to autograft. Published data on options such as allograft, bone morphogenetic protein, or BGS have produced mixed outcomes[2]. Recombinant human bone morphogenetic protein has been associated with significant perioperative and postoperative morbidity[9].

Most papers on bone grafting outcomes have focused on the spine. A large meta-analysis found no difference in fusion rates among autograft, allograft, and BGS, with similar complication rates[10]. Another systematic review reported that synthetic BGS showed fusion rates comparable to the use of iliac crest bone graft[11]. In the foot and ankle, evidence is not as abundant, yet there are data to support the role of BGS in foot and ankle surgery. Thordarson and Kuehn (2003) [12] reported a 90% fusion rate when BGS is used in complex ankle or hindfoot fusion cases. While promising, it was a small case series employing two BGS instances. In a more extensive case series, positive outcomes regarding fusion rate and complications were observed when demineralized bone matrix was used in primary ankle arthrodesis[13]. However, poor outcomes have been reported in a small case series involving bovine structural allografts in subtalar fusion[14].

Given the growing demand for alternatives to bone autograft, it is imperative to present clinical outcome data for using BGS in lower extremity surgery. One such material is a natural bone matrix (NBM) in granule form that has been used in spinal trauma[8] and in lower extremity trauma[15]. Additionally, there is a composite of NBM that adds 10% porcine collagen (NBM-PC) (Orthoss® Collagen, Geistlich Pharma AG, Wolhusen, Switzerland) to enhance handling and adaptability to the shape of the defect site. However, clinical data on NBM-PC outcomes following ankle and foot surgeries are limited. Therefore, we conducted a prospective, single-arm, observational, uncontrolled, multicenter clinical investigation to evaluate outcomes following the use of NBM-PC in foot and ankle surgeries.

Methods

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki, the Good Clinical Practice guidelines, and the European Union's Commission Directives. Ethical approval was received before the start of any study activities at both sites (Approval No. 272/18_mp-me and 2019286).

Patients

All study participants were patients under the care of one of the two principal investigators. Before enrolment, all patients were informed about the study's purpose and gave their informed consent. We calculated that 64 patients were necessary to achieve 80% power to detect non-inferiority over a reference success rate of 90%, assuming a significance level of 5%. At the conclusion of this study, there were 66 patients in total, with a planned follow-up of 12 months.

Procedure

All patients were seen by one of the two participating surgeons during standard-of-care visits. The conditions for which patients were treated required bone grafting, whether arthrodesis, to treat pseudoarthrosis and fractures, or to fill surgically created osseous defects. Surgeries followed the standard-of-care without deviations from the normal treatment algorithms. All patients who consented to be in this study received NBM-PC as part of the grafting procedure.

Outcomes

The focus of this study was assessing whether NBM-PC could provide successful bone fusion in various indications for foot and ankle surgery. Primary outcome was bone fusion and graft consolidation 12 months after surgery. Secondary outcome was the safety of NBM-PC; therefore, all serious adverse events (SAE) were recorded. Outcomes were presented as a percentage of the total. Data were retrieved from each patient's medical records and radiographs.

Results

Demographic data of patients

The sample consisted of 35 women, representing 53% of the patients included, with a mean age of 51 years (range 18–81). Mean body mass index was 26.87 kg/m^2 (range 18.65–41.0). All demographic data of patients are presented in Table 1.

Table 1. Patient demographic data

Variables	
Age (years)	
Mean (SD)	51.09 ± 17.54
Median	55
Range	18–81
Sex	
Male	31 (47%)
Female	35 (53%)
BMI	
n	66
Mean (SD)	26.87 ± 4.73
Median	26.2
Range	18.65–41.0
Substance use	
Tobacco use	9 (14%)
Alcohol use	2 (3%)

SD: Standard deviation; BMI: Body mass index.

Half of the surgical procedures were performed on the ankle, while midfoot surgeries accounted for almost a third of the interventions. Detailed data regarding the number of surgeries relative to the general anatomical sites are presented in Table 2. Lastly, arthrodesis was the primary indication for using the NBM-PC graft during these surgeries. Table 3 presents the specific surgeries performed requiring bone grafting.

Bone fusion and integration

Of the 66 patients treated in our study, one was lost to follow-up. Radiographic data were available for 53 patients at the 12-month follow-up. Of these, radiographic imaging showed that 45 patients had a consolidated fusion site, while 44 patients presented with complete integration of the bone graft. This represents a fusion rate of 85% of patients (95% confidence interval [CI] 73%–92%). In three patients, there was osteolysis of < 1 cm^2 (6% of patients), while six patients (11%) presented with non-union or pseudoarthrosis at the 12-month follow-up.

Safety

Regarding SAE, there were six events among five patients, categorized as serious due to hospitalizations following the SAE occurrence (overall incidence 9%, 95% confidence interval [CI] 5%–19%). Most common SAE were pseudoarthrosis (n = 2) and wound infection (n = 2), while there was one reported case of wound healing deficiency and one case of contralateral arthrodesis to the first metatarsophalangeal joint. None of these were determined to be related to the NBM-PC implanted during the index surgery.

Table 2. Site where fusion was performed

Surgical site	N (%)
Ankle	33 (50%)
Hindfoot	5 (8%)
Midfoot	21 (32%)
Forefoot	7 (11%)

Table 3. Type of bone fusion/reason for the bone graft

Bone fusion	N (%)
Arthrodesis	35 (53%)
Skeletal deformities	12 (18%)
Fractures	9 (14%)
Pseudarthrosis	4 (6%)
Osteochondral defect	3 (5%)
Benign bone tumor/cyst	3 (5%)

Discussion

The cohort of 66 patients experienced a successful outcome, as demonstrated by radiographic evidence of consolidation at the fusion site in 85% of patients and complete integration of the bone graft in 84% of patients by the end of follow-up. Concerning safety, none of the SAE were considered related to the NBM-PC, while two SAE were possibly related to the procedure.

Documented outcomes are consistent with those reported in the literature concerning bone fusion following the implantation of BGS. Fusion rate observed in our data (85%) is in line with a case-control study that reported fusion rates of 85% for autografts and of 90% for allografts[16]. Similarly, another comparative study found that allograft implantation resulted in 82% fusion, while autografts demonstrated an 85% fusion rate[17]. This is also supported by a systematic review that reported union rates of 70% to 100%, depending on the graft type, treatment site, and follow-up duration[18]. Some authors presented more varied data, including BGS, in their review of bone grafting in trauma surgery[5]. They presented union rates of 70%–100%, reflecting a substantial heterogeneity in reviewed papers. These included various conditions, such as acute injuries, osteoporotic fractures, and atrophic non-union, as well as differing follow-up lengths.

While generally demonstrating outcomes comparable to autograft, data on BGS demonstrate certain limitations. In cervical disc fusion, it was observed that fusion rates and time to fusion with BGS were inferior to those achieved with autologous bone grafts. However, authors did note the advantage of avoiding donor site morbidity[19]. Specifically in the lower extremities, a small case series indicated that patients who received a structural BGS experienced persistent pain and signs of non-union. This led the authors to recommend the use of autograft in subtalar fusion[14]. These outcomes, however, could also be influenced by factors such as the site of surgery, fixation technique, or patients' comorbidities. For instance, diabetic patients have shown worse outcomes following subtalar arthrodesis[20]. Additionally, the type of fixation and smoking status both affect the rate of non-union in patients undergoing tarsometatarsal arthrodesis[21].

In addition to the fusion rate, we have documented an adverse event rate that is consistent with that of peer-reviewed literature. A review by Baldwin et al.[5] reported complication and failure rates ranging from 5.5% to 26%[5]. Therefore, the adverse event rates observed in our study are comparable to those reported in the peer-reviewed literature.

Outcomes observed following bone grafting with NBM-PC are aligned with those of studies published on the granular form of the NBM. In the spine, the granular form of NBM demonstrated successful outcomes for spinal posterolateral fusion[22]. In spinal trauma, a radiographically observed fusion rate of 85% and a successful treatment rate of 92% were reported, with significantly shorter surgery times when NBM was used without additional autologous bone graft[8]. Additionally, positive outcomes have been reported in treating pathologic fractures of bone cysts in children[23]. A case-

control study comparing NBM to allograft cancellous bone found comparable outcomes with a very low rate of adverse events for both cohorts[24]. Although there is limited clinical data on the granular form of the NBM we have implanted, published data indicate its utility in providing positive outcomes and a favorable safety profile.

When bone grafting is a surgical necessity, multiple factors affect graft choice. While autograft is considered the gold standard, surgeons must consider factors such as the additional surgical time for harvesting and donor site morbidity. Alternatives to autografts have been shown to reduce surgical time and blood loss[7]. The handling of the material also plays a role in the choice of graft, and the addition of collagen, which is osteoconductive, provides a bone graft that conforms to the shape and size of the defect to be treated. Such a scaffold offers a structural support that is absent in particulate bone graft materials[25]. Donor site morbidity is another crucial factor in surgical planning, as it is a common consequence of autograft harvesting[2]. Moreover, donor site morbidity may have cosmetic impacts, such as local deformity of the bone or scarring, which can also affect the patient's well-being.

The properties of various BGSs have been extensively discussed elsewhere, in numerous publications. All BGSs share the common function of providing an osteoconductive material, making an autologous bone graft and its associated comorbidity unnecessary. Differences in their material properties arise from their composition and processing. Consequently, the risks and benefits of each BGS vary slightly, as shown in Table 4. These grafts also exhibit different handling characteristics, which is another important consideration. The addition of collagen to the mineral component of the graft we implanted, NBM-PC, allows for better filling of irregularly shaped defects with difficult access. The formability of these materials ensures high contact with the surrounding vascularized bone, which is essential for bone ingrowth and graft success[26]. Data from a preclinical test showed that NBM-PC has a good level of ingrowth to the host bone after implantation, as shown in Figure 1. A more detailed photomicrograph, shown in Figure 2, shows the NBM-PC (labeled as T1) and the new bone formation (labeled as NFB).

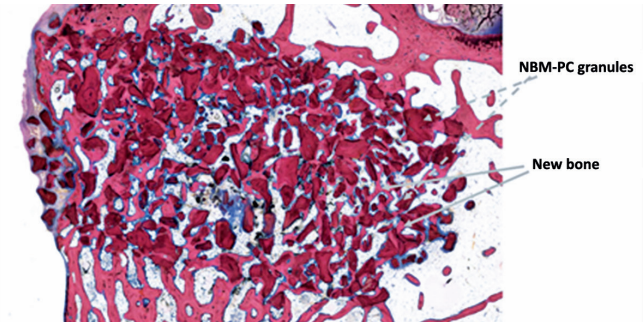

Figure 1. Integration of NMB-PC with the host bone in a small animal model 12 weeks after implantation.

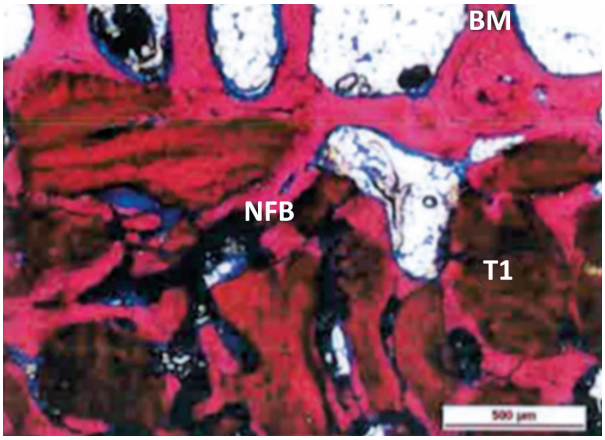

Figure 2. Photomicrograph showing new bone formation 12 weeks after NBM-PC implantation in a small animal model.

Table 4. Risks and benefits of different bone graft substitutes

Bone graft substitute	Benefits	Risks
Allograft	Large availability, low cost, variable amount of growth factors.	Disease transmission, inflammation, no living cell depending on the preservation/sterilization, variable or no growth factor.
Demineralized bone matrix (DBM)	Large availability, low cost.	Amorphous, no mineral fraction, variable or no growth factor, no cell, no structural analogy with porous bone, disease transmission, inflammation.
Ceramics (ß-TCP, synthetic HA, biphasic mineral implants)	Large availability, long shelf life, potential carrier for growth factors, potential extender when mixed with auto-/allograft, structurally sound, no immunogenicity.	No live cells, no growth factors, no organic matrix, brittle, porosity, limited compressive strength.
Naturally derived HA Bone Graft Substitutes	Large availability, high interconnected porosity and high internal surface exposure, inorganic components of the bone matrix, rapid bone ingrowth and development. Potential extender when mixed with auto-/allograft, bone marrow aspirate, structurally sound. Long term stability of the bone graft.	No live cells, no organic matrix, limited compressive strength.

Table 5. Outcomes with various bone graft substitutes

Bone graft substitutes	Reported fusion rate
Allograft	90%–100% (28)
Orthoss® Collagen (NBM-PC)	85%–95% (15,8)
Tricalcium phosphates	73% (29)
Calcium sulfate	85% (30)

In addition to the risks and benefits, the potential for clinical success is a critical consideration in choosing a BGS. While synthetic grafts offer advantages such as low cost, availability, and various forms (e.g., powder or putty), they are not as reliable as other grafts. For example, although tricalcium phosphate has shown positive results, its degradation can be unpredictable, making it suboptimal for load-bearing areas[27]. Hydroxyapatite, another option, can be derived from various sources but tends to have poor mechanical strength[2]. Table 5 presents the success rates documented in peer-reviewed literature. Available data show that the BGS used in our case series yielded results comparable to those reported in the literature, confirming its efficacy and reliability.

However, this study has limitations. Although 66 patients is a respectable number for assessing the safety and performance of a medical device, it should be noted that all treated defects were in the foot and ankle. Therefore, a follow-up study could determine whether comparable successful outcomes would be seen in other surgical sites. Furthermore, our outcome assessment was based solely on radiographic assessment of bony fusion. At the same time, it has been noted that patient-reported outcomes are essential for assessing meaningful changes from the patient's perspective. Accordingly, any follow-up study should include a patient-reported outcome instrument.

Conclusion

The use of bone grafts in orthopedic surgery has increased steadily in recent years, and as the average age of the population increases, the demand for bone grafts is likely to continue to grow. Unfortunately, with such an aging population, it is realistic to expect that the availability of autografts may not be sufficient to meet the demand. Thus, there is a clear need for an alternative. The composite graft used in this study, NBM-PC, which contains a collagen component, has shown consolidation and fusion rates comparable to autograft, while demonstrating a good safety profile. Therefore, NBM-PC can provide a reliable addition to the orthopedic surgeon's options, capable of delivering positive patient outcomes.

Authors' contributions: Each author contributed individually and significantly to the development of this article: MW *(https://orcid.org/0000-0003-1122-1303) Conceived and planned the activities that led to the study, Clinical examination, Performed the surgeries, Data collection, Survey of the medical records, Interpreted the results of the study, Participated in the review process, Statistical analysis, Bibliographic review, Formatting of the article; JG *(https://orcid.org/0009-0004-2651-1463) Conceived and planned the activities that led to the study, Clinical examination, Performed the surgeries, Data collection, Survey of the medical records, Interpreted the results of the study, Participated in the review process, Bibliographic review, Formatting of the article; RZ *(https://orcid.org/0000-0001-9692-5283) Participated in the review process, Statistical analysis, Interpreted the results of the study, Bibliographic review, Formatting of the article. All authors read and approved the final manuscript. *ORCID (Open Researcher and Contributor ID).

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