Stabilization of Tibial Fractures at Risk of Complications With the Bactiguard Intramedullary Nail: Early to Medium Results With a Novel Metal-Coated Device

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Objectives: The purpose of this study was to investigate the safety and early clinical results from the use of a novel, noble metal-coated titanium tibial nail for the definite stabilization of tibial shaft fractures at risk of developing complications.

Design: This is a retrospective case series with prospectively collected data.

Setting: Level I Trauma Centre in the United Kingdom.

Patients and Intervention: Thirty-one patients who were managed with the Bactiguard-coated Natural Nail and achieved a minimum of a 12-month follow-up.

Main Outcome Measurements: The main outcomes of this study were the incidence of adverse events (related to implant safety), complications (particularly infection), and reinterventions.

Results: Thirty-one patients with a mean age of 41.6 years were included in this study. Active heavy smokers or intravenous drug users were 25.8% and 9.7% of them were diabetic. Five fractures were open while 13 had concomitant soft-tissue involvement (Tscherne grade 1 or 2). Twenty-seven patients healed with no further intervention in a mean time of 3.3 months. Three patients developed nonunion and required further intervention. The overall union rate was 96.7%. One patient developed deep infection after union (infection incidence 3.2%). Six patients (6/31; [19.3%]) required reinterventions [2 for the treatment of nonunion, 3 for removal of screws soft-tissue irritation, and 1 for the management of infection).

Conclusions: The management of tibial shaft fractures with a noble metal-coated titanium tibial nail demonstrates encouraging outcomes. Further studies are desirable to gather more evidence in the performance of this innovative implant.

Key Words: tibial fractures, metal-coated nail, Bactiguard, complications

Level of Evidence: Therapeutic Level IV. See Instructions for Authors for a complete description of levels of evidence.

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INTRODUCTION

The gold standard for stabilization of tibial fractures continues to be reamed intramedullary nailing (IMN).[1–4] Numerous studies have reported high rates of union with a low incidence of complications.[3,5–7] However, one of the most dreadful complications remains the development of deep infection.[8] Deep infection has been associated with severe clinical consequences such as sepsis, amputation, and even death; these all have a great impact on the well-being of the patient, his family, and the health care system in resource allocation and costs of treatment. Noteworthy, previous studies have shown that deep infections can increase the overall management cost by 6.5 times compared with noninfected cases.[9,10]

To address this problem, protocols have been developed to identify high-risk patients and to implement preventative strategies focusing on reducing the risk of contamination preoperatively, intraoperatively, and postoperatively.[11,12] Moreover, during the past decade, focus has been given to prevent the development of biofilm formation by designing antibiotic-coated implants (IM nails).[13,14] Preliminary results have been positive but concerns have been raised as to whether such a strategy will lead to antibiotic-resistant bacterial infections, and consequently, the requirement for a new approach for infection prevention has emerged focusing on the development of non–antibiotic-coated implant designs.[15]

Lately, such a new innovation has become available in the trauma reconstruction clinical setting being a noneluting noble IM nail implant having a surface coated with a layer that consists of gold, silver, and palladium metals.[8] Its mechanism of action is based on the generation of a "pico current" (galvanic effect) on contact with moisture, preventing bacterial adhesion and thus the risk of biofilm formation that can

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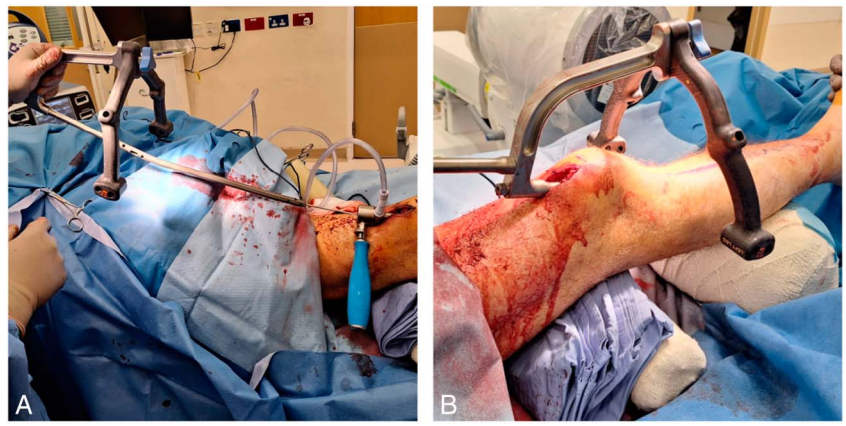

FIGURE 1. A and B, Intraoperative images demonstrating the insertion of the Bactiguard-coated Tibial Natural Nail through the supra-patellar portal.

lead to the development of infection. This combination of metals has previously been used in a variety of tubes and catheters, with optimal outcomes in infection risk reduction.[16–19]

Because this technology has now been introduced in the design of IM nails implanted for stabilization of tibial shaft fractures, the purpose of this study was to investigate the safety and the early clinical results from the use of a novel, noble metal-coated titanium tibial nail (Bactiguard, Zimmer Biomet) for the management of tibial shaft fractures in patients being at risk of developing complications in a single Major Trauma Centre Hospital.

MATERIALS AND METHODS

Between January 2021 and May 2022, after receiving approval from the local institutional review board, a retrospective study with prospectively collected data was conducted in our institution. All adult patients managed with the Bactiguard (Bactiguard AB, Tulligen, Sweden)-coated Natural Nail (Zimmer Biomet, IN) for tibial shaft fractures being at high risk of developing complications were eligible to participate in this study. Exclusion criteria were patients who were lost to follow-up, pathological tibial fractures requiring IMN, and patients who had not completed their course of treatment with a follow-up time of at least 12 months.

Characteristics of tibial fractures being at increased risk of development of complications (infection) included all types of open fractures, closed fractures with features of internal degloving, compartment syndrome, and patients with comorbidities such as diabetes, peripheral vascular disease, and being immunocompromised.

Patient demographics, medical history, injury mechanism, associated injuries, fracture type, operation details (if a staged management was performed), time from presentation to operation, time to bone union, and local or systemic complications were collected and analyzed. Finally, the functional outcomes for each patient were assessed by evaluating the range of motion of the knee and ankle joints in comparison with the opposite uninjured side. Safety of the device was assessed regarding development of any adverse events related to local or systemic allergic reactions.

Fractures were classified according to the OTA/AO classification.[20] For grading of severity of open fractures, the Gustilo–

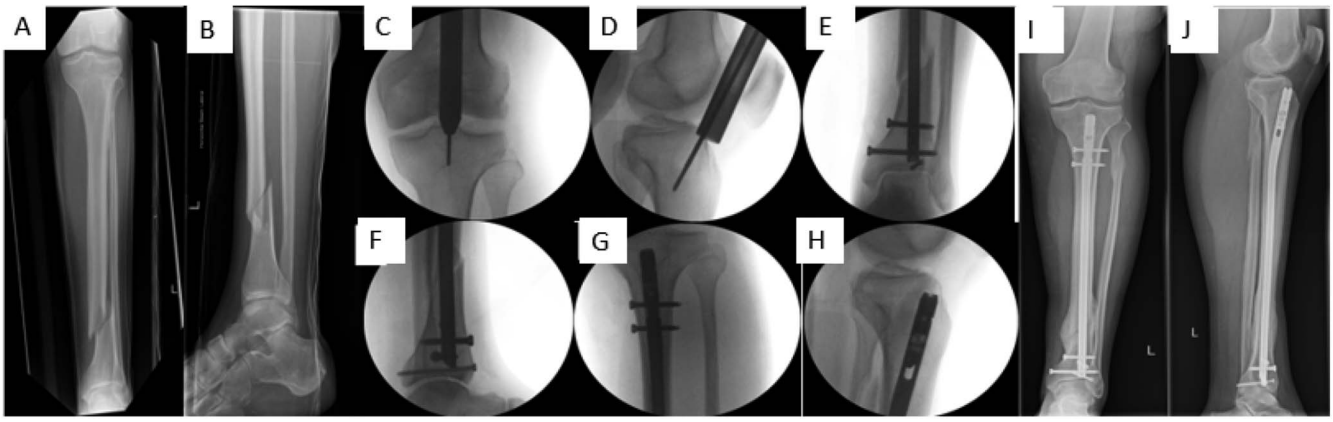

FIGURE 2. A 32-year-old man sustained a closed distal tibial shaft fracture while playing football. A and B, Preoperative tibia radiographs showing the fracture pattern. C, D, E, F, G, and H, Intraoperative fluoroscopic images showing the stabilization of the fracture with the Bactiguard-coated natural nail. I,J, Postoperative radiographs showing fracture union 4 months postoperatively.

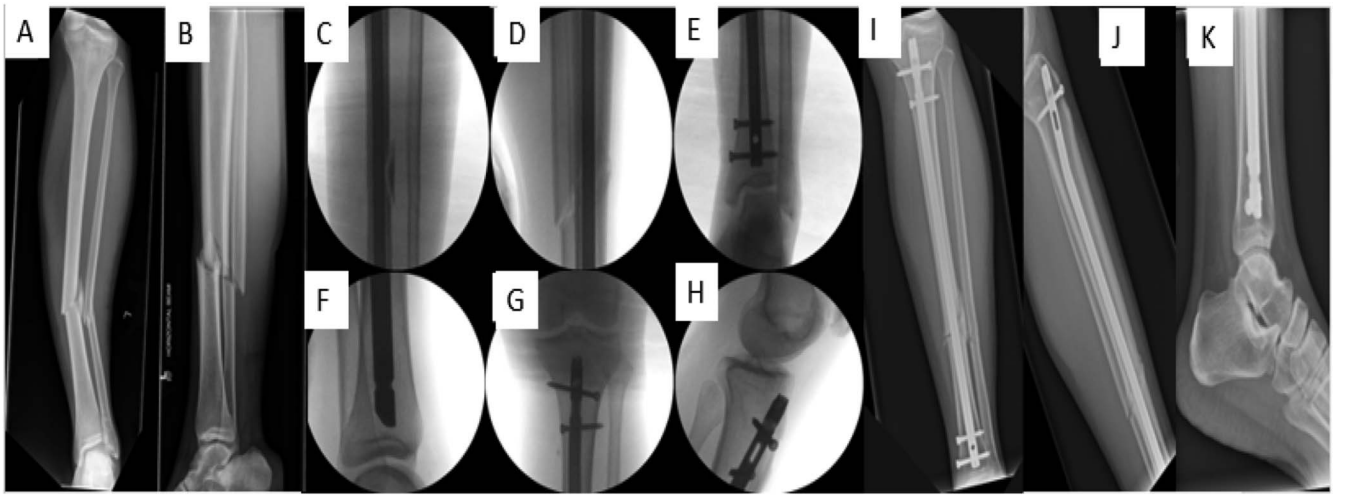

FIGURE 3. A 24-year-old woman sustained a road traffic collision and suffered an open tibial shaft fracture. A and B, Preoperative tibia radiographs demonstrating the fracture. C, D, E, F, G, and H, Intraoperative fluoroscopic images showing the stabilization of the fracture with the Bactiguard-coated natural nail. I, J, and K, Postoperative radiographs showing the fracture union 3 months postoperatively.

Anderson classification[21] was used, and for soft-tissue degloving in closed fractures, the Tscherne grade system was applied.[22]

All patients presenting with open or suspected open fracture were administered 1.2 g of intravenous amoxicillin–clavulanate. Subsequently, the same antibiotic regime was prescribed 8-hourly in open fractures until the wound was closed. All operations occurred under general anesthesia on a radiolucent fracture table with the patient in a supine position after sterile draping. Preoperative for closed fractures one dose only of antibiotic prophylaxis (flucloxacillin and gentamycin) was prescribed. The nail entry point was defined by the surgeon's preference and experience, and therefore, the knee was positioned accordingly (semiextended position for suprapatellar entry and flexed for transpatellar entry) (Fig. 1).

Postoperatively, patients were able to mobilize as comfort allowed, and thromboprophylaxis medication (tinzaparin 3500 IU, subcutaneous injections) was administered for 6 weeks after hospital discharge. Throughout the hospitalization, local and systemic complications were monitored and documented. On discharge, patients were given regular outpatient follow-up appointments at 6, 12, 24, 36, and 52 weeks for clinical and radiological assessment.

During the follow-up visits, main parameters evaluated were wound healing, range of motion of the affected and the uninjured extremities, signs of development of local or systemic complications, and progress of fracture healing by radiological control. Union was defined clinically as the ability to pain-free full weightbearing and, radiographically, as cortical apposition in ¾ fracture cortices.[23] The need for reoperation and further interventions was also recorded and analyzed. Fracture-related infection was defined as per the recently suggested definition.[24]

Descriptive statistics were used with parametric and nonparametric tests for the variable analyzed where appropriate. P value was set <0.05.

RESULTS

During the prespecified period, 47 patients met the inclusion criteria and were eligible to participate in this study. However, 5 patients were lost to follow-up and 11 had not completed a minimum follow-up of 12 months, and therefore, 31 patients (23 male) with a mean age of 41.6 years (range 18–82) formed the basis of this study.

Most of the patients (19/31, 61.3%) did not have any comorbidities. Eight patients (25.8%) were heavy smokers or intravenous (IV) drug users at the time of the operation. Moreover, 3 patients were diabetic (9.7%), a further 2 had hypertension (6.5%), and 1 suffered from hypothyroidism (3.2%), Table 1.

Regarding injury mechanism, the main cause of tibial shaft fractures was a fall (14 patients, 45.2%; from a height >1 m [n = 6], or <1 m [n = 8]). Six patients (19.4%) sustained their injuries after a road traffic collision. In addition, sporting activities, including football, rugby, and horse riding, resulted in 8 tibial fractures (25.8%). Assault occurred in 3 cases (6.5%).

Regarding fracture pattern, 5 fractures were open (16.1%), and 3 of them necessitated additional plastic surgery intervention for soft-tissue coverage (raise of a gastrocnemius flap and skin graft in 1 case, a gracilis flap in 1 case, and a simple skin graft in another case). The remaining 2 open fractures were primarily closed after thorough debridement and washout.

In 24 patients, tibial fracture was an isolated injury, while in 7 individuals, other injuries were observed. More specifically, 2 patients sustained polytrauma,[25] whereas 5 patients, although suffered concomitant injuries, they did not fulfill the criteria of the polytrauma definition. Details about fracture classification, additional injuries, and management are summarized in Tables 2 and 3.

TABLE 1. Most Common Comorbidities

Comorbidity	N (%, Incidence)
Smoking/IVDU	8 (25.8)
Diabetes	3 (9.7)
HTN	2 (6.5)
Depression	2 (6.5)
Psoriasis	2 (6.5)
Epilepsy	2 (6.5)
Hypothyroidism	1 (3.2)
Asthma	2 (6.5)

HTN, hypertension; IVDU, intravenous drug user.

TABLE 2. Additional Injuries

Additional Injuries	N	Details
Head	1	SDH operatively treated
Thorax	2	Ribs fractures
Pelvis	2	LC1, APC2
Spine	1	Thoracic vertebra fracture
Abdomen	1	Bowel bleeding
Upper limb	2	Clavicle fracture, metacarpal fracture
Lower limb	5	Femoral neck fracture, calcaneal fracture, metatarsal fracture, toe fracture, toe fracture

AP, anteroposterior compression; LC, lateral compression; SDH, subdural hemorrhage.

At a mean follow-up period of 14.3 months (range 12–24), 27 fractures (87.1%) united without any further procedure in a mean time of 3.3 months (range 2–7) (Figs. 2 and 3), Comparing the time to union between male and female patients, no statistical difference was noted, $P > 0.05$. Three fractures required additional intervention to achieve union (2 cases underwent exchange nailing and implantation of stem cells and BMP-2; 1 case was prescribed exogen (bone stimulator) due to delayed union), Table 4. The overall union rate was 96.7% (30/31 fractures).

In addition, 1 patient died 1-month postoperatively before fracture healing completion. This was due to hospital-acquired pneumonia. All but 1 patient who primarily achieved union (26/27, 96.3%) could demonstrate full range of motion of their adjacent knee and ankle joints and had full functional capacity to return to their previous preinjury activity level.

Regarding complications, in addition to the patient who died of pneumonia, 2 patients developed systemic complications postoperatively, including Staphylococcus bacteremia and an acute kidney injury type III; these complications were both managed with advice from the microbiology and renal physician teams. Another patient who had sustained an open fracture, after fracture union, developed a local complication 8 months postoperatively (deep infection associated with a discharging sinus). He necessitated excision of sinus, removal of nail, reaming and irrigation of the intramedullary canal, and prescription of antibiotics for a period of 6 weeks. The overall fracture-related infection rate in this patient cohort was 3.2%.

Five patients complained of ongoing aching discomfort after fracture union due to soft-tissue irritation around the locking screws. Three individuals underwent removal of the symptomatic screws, with the remaining 2 individuals opting to not having a further procedure for their removal. Finally, 1 patient was diagnosed with partial extensor hallucis longus tendon rupture postoperatively, but he did not require any further treatment, Table 4.

Nail removal for the treatment of above complications was necessary in 3 cases (9.7%) (2 nonunions; 1 late infection) while screw removal was performed in 3 patients (9.7%). Therefore, the overall reoperation rate was 19.3%.

Regarding the safety evaluation of the Bactiguard implant, no adverse events were observed related to any local or systemic allergic reactions to the metal alloy.

DISCUSSION

The subcutaneous location of the tibia and the lack of a good muscular bed all around, particularly at the distal half of the bone, make tibial fractures vulnerable to an increased risk of infection and nonunion. The management of fracture-related infection is one of the biggest challenges in Trauma and Orthopaedics, and many efforts have been made to minimize this infection risk through the development of various strategies and innovations.[26] One of such innovations is the antibiotic-coated nails, such as the Expert Tibial Nail, which has demonstrated very good results in infection prevention in open fractures with fewer infection numbers, reduced inpatient days, and reoperations reported in the literature.[27] However, concerns have been raised with its use for the risk of development of antibiotic-resistant bacteria. Another technique is the application of injectable synthetic calcium bone substitute mixed with gentamycin or vancomycin over the inserted implant, with a similar action and adverse effects.[28,29]

Recently, Zimmer Biomet launched a novel Titanium Natural Nail implant combined with the Bactiguard technology for the treatment of femoral and tibial fractures. Regarding this novel Bactiguard IMN device, there is only one reported study in the literature, from a single center in Malaysia with the authors reporting an infection rate of 8.6%.[8] However, in this Malaysian study, all the patients had sustained open fractures. The different injury characteristics may explain the lower infection rate noted in our patient population. In our study, 1 patient developed deep infection and osteomyelitis. This was a 40-year-old IV drug user with a Tscherne Type 1, closed 42 A fracture, that subsequently underwent nail removal after union, 1-year postoperatively. Interestingly, it should be noted that this was a closed fracture, which is unusual, as it is widely accepted that open fractures (often grade IIIB according to the Gustilo–Anderson classification), are 4 times more likely to be complicated with infection, compared with closed pathology.[30,31] However, we speculate that what must have contributed to the development of this late infection complication could be his immunocompromised profile (due to the chronic intravenous drug abuse) and the previous episodes of groin infections and cellulitis that were treated with antibiotics due to his drug injection habits. In our study, we identified 5 open fractures,

TABLE 3. Classifications and Management of the Injuries

Patients	AO/OTA Classification	Gustilo–Anderson Classification	Tscherne Classification	Initial Stabilization	Definite Stabilization	Approach
	42A (n = 21)	Grade I (n = 0)	Grade 0 (n = 13)	2 ex-fix	Ex-fix to nail time: 4 d	19 TP
		Grade II (n = 1)	Grade 1 (n = 8)			
31	42B (n = 10)	Grade IIIA (n = 1)	Grade 2 (n = 5)	29 nails	Diagnosis to nail insertion time:	12 SP
(23M/ 8F)		Grade IIIB (n = 3)	Grade 3 (n = 0)		41.4 h (range 4–3000)	
	42C (n = 0)	Grade IIIC (n = 0)				

ex-fix, external fixator; F, female; M, male; SP, suprapatellar; TP, transpatellar.

with 3 being open grade IIIB; none of these patients developed infection.

Regarding bone union, 87.1% of our fractures uneventfully united without any further intervention. Three patients developed nonunion/delayed union, and in 1 patient, union could not be primarily assessed. In this instance, the patient was a 70-year-old man with a medical history of liver disease who unfortunately died after a hospital-acquired pneumonia 1-month postoperatively. The 3 patients who developed nonunion/delayed union were a 20-year-old woman with a 42B open grade II tibial fracture and concomitant pelvic fracture, and a 30-year-old man with a 42B open grade IIIB fracture; both underwent exchange nailing and implantation of BMP-2 and stem cells 1-year postinitial operation for the treatment of their nonunion. They both united 4 months later. The third patient, a 73-year-old diabetic man with a 42A closed Tscherne type 0 fracture presented with slow-healing progress 6 months postoperatively; this individual was treated with the exogen ultrasound bone-stimulating system and eventually healed 3 months after this nonsurgical intervention.

Metal ions applied on orthopaedic implants is a current trend, demonstrating significant benefits.[32,33] Nevertheless, silver-coated implants have been associated with increased osteoclast formation, grey skin discoloration, and peripheral neurological deficit from argyria.[34] None of these complications were identified in our cohort. It is proven that most of the silver ions that are not excreted remain bound to proteins without any functional activity.[35]

This study has several limitations that have to be acknowledged. First, the number of patients recruited was small. Second, it was a retrospective study lacking the elements of randomization. Third, the follow-up was 12 months, and one may argue that despite union, late episodes of infection may still occur. Fourth, there was no control group for comparison.

TABLE 4. Complications

Patient	Sex	Comorbidities	Type of Injury	Complication	Timing of Complication	Intervention	Outcome
P1	F	Nil	Open grade II	Nonunion	12 mo	Exchange nail + stem cells + BMP2	Union in 6 mo
P4	M	Nil	Closed	Pain around the proximal locking screw	6 mo	Conservative	Tolerated
P5	M	IVDU	Closed	Acute kidney injury stage III	5 d	Conservative	Resolved
P9	M	ADHD, PTSD, schizophrenia, epilepsy	Open	Staph. bacteremia	3 d	ABX	Resolved
P11	M	Nil	Closed	Pain around the distal screws	9 mo	Removal of distal locking screws	Resolved
P13	M	Diabetes	Closed	Delayed union	5 mo	Exogen	Union in 3 mo
P17	F	HTN	Closed	EHL partial rupture	2 wk	Conservative	Resolved
P19	F	Alcohol abuse, asthma	Closed	Pain around distal screws	8 mo	Conservative	Tolerated
P21	M	HIV	Closed	Pain around distal screws	14 mo	Removal of distal locking screws	Pain relief
P24	M	Nil	Open	Pain around the proximal screws	18 mo	Removal of proximal locking screws	Pain relief
P26	M	IVDU	Closed	Osteomyelitis	12 mo	Nail removal + ABX	Infection eradication
P28	M	Alcoholic liver disease	Closed	Hospital-acquired pneumonia	1 mo	ABX	Death
P31	M	Nil	Open Grade IIIB	Nonunion	12 mo	Exchange nail + stem cells + BMP2	Union in 5 mo

ABX, antibiotics; ADHD, attention deficit hyperactivity disorder; BMP2, bone morphogenetic protein 2; EHL, extensor hallucis longus; F, female; HTN, hypertension; IVDU, intravenous drug user; M, male; PTSD, posttraumatic stress disorder.

Finally, no generic functional outcome score was used to evaluate the health-related quality of life and function of the patients. Strengths of this study include the recruitment of patients at risk of developing complications, and the fact that this study was conducted in a single Level I Major Trauma Centre, highlighting the consistency in surgical procedures and a reduction in confounding factors.

In conclusion, the Bactiguard-coated intramedullary nailing device demonstrated favorable outcomes, and it can constitute another weapon in the armamentarium of the orthopaedic surgeons, especially for the treatment of patients and fractures with a high risk of developing postoperative complications. This is the first study in the literature, which evaluates the clinical outcomes of noneluting noble metal-coated titanium tibial IMNs, having included patients' demographics and comorbidities, fracture classification, time from injury to operation, union time, complications (including further interventions), and functional outcomes with range of motion. Overall, it can constitute the foundation of future studies to evaluate further the clinical performance of this new coated intramedullary nailing device for the treatment of tibial shaft fractures.

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