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ORIGINAL PAPER

A cost analysis of treatment of tibial fracture nonunion by bone grafting or bone morphogenetic protein-7

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Abstract The parameter of health economics in the use of any contemporary medical module plays a dominant role in decision making. A prospective nonrandomised comparative study of the direct medical costs on the first attempt of treating aseptic nonunions of tibial fractures, with either autologous-iliac-crest-bone-graft (ICBG) or bone morphogenetic protein-7 (BMP-7), is presented. Twenty-seven consecutive patients, who were successfully treated for fracture nonunions, were divided into two groups. Group 1 (n = 12) received ICBG and group 2 (n = 15) received BMP-7. All patients healed their nonunions, and the financial analysis presented represents a best-case scenario. Three out of 12 of the ICBG group required revision surgery while just one out of 15 required it in the BMP-7 group. Average hospital stay was 10.66 vs. 8.66 days, time-to-union 6.9 vs. 5.5 months, hospitals costs £2,133.6 vs. £1,733.33, and theatre costs were £2,413.3 vs. £906.67 for the ICBG and BMP-7 groups, respectively. The BMP-7 cost was £3002.2. Fixation-implant was £696.4 vs. £592.3, radiology £570 vs. £270, outpatient £495.8 vs. £223.33, and other costs were £451.6 vs. £566.27 for the ICBG and BMP-7 groups, respectively. The average cost of treatment with BMP-7 was 6.78% higher (P=0.1) than with ICBG, and most of this (41.1%) was related to the actual price of the BMP-7. In addition to the satisfactory efficacy and safety of BMP-7 in comparison to the gold standard of ICBG, as documented in multiple studies, its cost effectiveness is advocated favourably in this analysis.

Résumé La paramètre des finances joue un rôle dominant en ce qui concerne l' usage de tout matériel médical contemporain. On présente une étude perspective, comparative et pas randomisée, du coût médical immédiat, pendant le premier effort du traitement des pseudarthroses aseptiques de tibia, avec l' usage d' autogreffe par la crête iliaque (ACI) où`a l' usage de protéines inductrices osseuses (BMP-7). Vingt-sept patients successifs qui ont été guéris avec succès par des fractures de pseudarthroses ont été divisés a deux groupes. Pour le premier groupe (12 patients) a été utilisé d'autogreffe par la crête iliaque. Pour le deuxième groupe (15 patients) a été utilisé BMP-7. Toutes ces pseudarthroses ont été guéries avec succès et l' analyse des finances présentée, prouve le meilleur scénario possible. Trois sur douze des patients du groupe ACI et seulement un sur quinze du groupe BMP-7 ont eu besoin de répéter l' opération chirurgicale. La comparaison entre le premier (ACI) et le deuxième (BMP-7) groupe a montré. La durée moyenne d' hospitalisation était 10,66 contre 8,66

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jours. La durée du traitement était 6,9 contre 5,5 mois. Les dépenses pour l' hôpital étaient 2133,6 £ contre 1733,33 £. Les dépenses chirurgicales étaient 2413,3 £ contre 906,67 £. Le coût des BMP-7 était 3002,2 £. Le coût des matières pour la fixation était 696,4 £ contre 592,3 £. Les dépenses radiologiques étaient 570 £ contre 270 £. Les dépenses après l'opération étaient 495,8 £ contre 223,33 £. Autres dépenses médicales étaient 451,6 £ contre 566,27 £. Le coût moyen du traitement avec BMP-7 était de 6,78% plus haut (P=0,1) et la plus grande partie de ce coût (41,1%) était relative au prix actuel de BMP-7. En dehors de l' efficacité satisfaisante et la sûreté de BMP-7 en relation avec "le standard d'or "d'autogreffe: comme tout ça est démontré par plusieurs études, le coût de son usage est prouvé avantageux par l' étude présente.

Introduction

It is estimated that approximately 5–10% of the 6.2 million fractures occurring annually in the United States are associated with impaired healing including delayed union or nonunion. Impaired fracture healing, leading to delayed union or nonunion, is associated with a number of risk factors including compromised biology secondary to a soft tissue injury, extensive bone loss, fracture instability, infection, and a poor general medical condition of the patient [4].

Fracture nonunions represent a difficult challenge for the surgeon, the patient, the health system, and the social services supporting them. Their average treatment management requires large assets and long-lasting therapies with frequent unrewarding results. Patients could undergo a number of surgical procedures requiring multiple hospital admissions [7, 18].

The accepted current treatment approaches for tibial fracture nonunions include excision of the fibrous tissue at the nonunion site, revision of the fixation using various forms of internal or external skeletal fixation devices (to achieve mechanical stability) and, not infrequently, the application of autologous bone graft [19, 20].

Autologous bone grafting is currently the gold standard for bone grafting procedures, as it possesses the essential properties of osteogenesis, osteoconduction, osteoinduction, and osteointegration [20]. The iliac crest remains a common site for harvesting autologous bone. However, considerable morbidity is associated with autologous bone harvesting procedures, including blood loss, nerve and muscle injury, chronic pain at the donor site, and local infection. Exclusive of complications, up to 49% of patients complain of ICBG-related pain, which is often persistent for several years after graft harvest. Furthermore, the available size, shape, and quantity of autologous bone graft represent relative limiting factors [26].

As an alternative, allografts such as those with demineralised bone matrix are more readily available, but lack osteogenic properties, may provoke a host immune reaction, and are associated with a risk of pathogen transmission. In order to provide solutions to the limitations of allografts, and the high morbidity and volume restrictions associated with the use of autologous bone grafting, research has focussed into developing biologically-based strategies that enhance the healing of acute fractures and improve the treatment of delayed unions and nonunions. These strategies include the use of exogenous growth and differentiation factors, mesenchymal stem cells, and gene therapy. Current evidence suggests that among the different factors that have been investigated to date, BMPs appear to have the most osteoinductive potential [13, 16, 17, 19, 22, 27].

Bone morphogenetic protein-7 (BMP-7), also known as human osteogenic protein-1 (OP-1), is a member of the transforming growth factor-beta (TGF-β) super-family. It is produced by osteoprogenitor and mesenchymal cells, osteoblasts, and chondrocytes, and it possess great osteoinductive properties. It induces the migration and proliferation of mesenchymal cells and their differentiation into bone-forming cells [24, 25]. The role of recombinant human bone morphogenetic protein-7 (BMP-7) in stimulating bone healing has been evaluated extensively in preclinical studies [6], and its efficacy has been assessed in the treatment of different long bone fracture nonunions with encouraging results [9, 10, 16, 25].

The economic aspect of treatment of nonunions includes many components [18]. Medical resources are among the major cost components and include hospitalisation, medical equipment, medical implants, diagnostic tests, outpatient follow-ups, therapies, and drugs. However, the literature says little about the health economics of application of autologous iliac crest bone grafting or BMPs for the treatment of tibial fracture nonunions [7, 18].

Current practice suggests that orthopaedic surgeons consider the use of BMPs in the treatment of nonunions only after other treatment options have been exhausted, and this practice may be partly influenced by its high cost. It may be perceived that the use of autologous iliac crest bone grafting remains a safer and cheaper option when compared with the use of biologically based treatments such as BMP-7.

The aim of this study therefore was to estimate and compare the direct medical cost implications of the first successful attempt to treat tibial fracture nonunions with either autologous iliac crest bone grafting or BMP-7.

Patients and methods

Adult patients who were successfully treated for tibial fracture nonunions between January 2004 and December

2006 in our institution were eligible to be enrolled in this study. Nonunion was defined as the clinical and radiological failure of the fracture to progress to union after a period of nine months from the time of the initial fracture stabilisation. Patients who received either autologous iliac crest bone graft (ICBG) or BMP-7 in order to enhance the local biological substrate during their first treatment episode following the declaration of tibial fracture nonunion were included. Exclusion criteria included a diagnosis of an infected nonunion, children, or patients that had malignancy, chronic debilitating disease, or at least one attempt for the treatment of their nonunion.

Two groups of patients were formed. Group 1 received autologous iliac crest bone grafting and group 2 received BMP-7. The decision to use BMP-7 or autologous bone graft was guided purely by the surgeon's preference, as also was the decision of the mode of fixation and the implant used. All patients received three doses of prophylactic intravenous Cefuroxime. Following discharge from the hospital, according to our unit's protocol all patients were followed up at four-week intervals in the outpatient clinic for clinical and radiological assessment until fracture union and restoration of function. Treatment end point was defined as painless full weight bearing (clinical union) and radiological evidence of bridging callus of all cortices in the two standard planes (radiological union).

Details including patient age, sex, initial injury, hospital stay, surgical procedures performed, the method of fracture stabilisation or limb immobilisation, postoperative complications, rehabilitation requirements (e.g. physiotherapy and occupational therapy), outpatient reviews, investigations, and blood transfusion requirements were recorded and entered into a computerised database. Whilst there was prospective documentation of data in a specifically developed nonunion database, all data collected were analysed in a retrospective manner. Where insufficient information was available, the hospital clinical charts were reviewed and the desired clinical data were retrieved.

Cost estimation and analysis methods

All the associated costs of treatment of each patient were analysed and calculated. The costs covered the actual treatment each patient received and included costs of hospital stay per day (trauma wards, high dependency unit, and intensive therapy unit), theatre sessions, use of orthopaedic equipment, orthopaedic implants, drug administration, investigations (haematological, microbiological, and radiological), transport, outpatient attendances, and physiotherapy treatments (Table 1). The total cost of treatment was then determined. The cost of each individual entry was obtained from the appropriate department (e.g. trauma and orthopaedics finance department, services agreement department, pharmacy department cost, inter-provider tariff list, implant provider reference costs, theatre financial records, and the 'Unit Costs of Health and Social Care 2001' document).

Table 1 Costs of treatments, investigations, and support services

Category	Item	Cost (£)
Drugs/Blood	BMP 7 (Osigraft) /vial	3,002.2
	Cefuroxime/750 mg	2.34
	Cefuroxime/1.5 g	4.7
	Blood transfusion /unit	140
Hospitalisation/day	Adult HDU	900
	Adult ITU	2,000
	Trauma ward	200
	Outpatient clinic (new)	50
	Outpatient clinic (follow-up)	50
	Theatre session	800
Support services	Physiotherapy/15 min session	24
Investigations	Electrocardiogram (ECG)	60
	Echocardiography	60
Radiology	X-ray	59.5
	CT scan	450
	MRI	550
Plaster	Plaster of Paris application	90
Blood tests	Urea/electrolytes	4
	Liver enzymes	4
	Full blood count	3
	Coagulation screen	4
	Calcium (bone profile)	4
Microbiology	MRSA screen	14
	Urine microscopy and culture	8
	Wound swab	14
	Blood cultures	17
	Antibiotic assay	16
	Fluid microbiology	16

HDU high dependency unit, *ITU* intensive therapy unit, *MRI* magnetic resonance imaging, *MRSA* methicillin-resistant *Staphylococcus aureus*

Recombinant human bone morphogenetic protein-7 (BMP-7)

Recombinant human bone morphogenetic protein-7 (rhOP-1) was supplied by Stryker Biotech (Berkshire, UK). Each sterile package (vial) contained 3.5 mg of the rhOP-1 mixed with 1 gram of type I bovine-derived collagen (the total reconstituted volume was approximately 4 ml per vial).

Data analysis

The significance of the differences between treatment costs was analysed using a statistical package (Astute, The University of Leeds). Independent samples *t*-test was used to test the significance of the difference between the two

groups in terms of the cost per patient. Differences were considered statistically significant at $p<0.05$.

Results

Out of 63 consecutive patients treated in our institution for established nonunion, 27 patients met the inclusion criteria. Group 1 consisted of 12 patients who received iliac crest bone grafting whereas group 2 consisted of 15 patients that received BMP-7. The two groups were comparable in terms of age, sex, and ratio of open to closed fractures (Table 2).

In group 1, two of the open fractures were Gustilo grade II, one was grade IIIA, and one was grade IIIB. In group 2, two of the open fractures were Gustilo grade II and two were grade IIIB. All patients in both groups progressed to clinical and radiological union. Patients in group 2 united within a mean time of 5.5 months (range 4.7–6.2) compared to a mean time of 6.9 months (range 6.1–7.6) for patients in group 1 ($P<0.001$). On average, patients in group 2 were discharged two days earlier than patients in group 1 (Table 2) ($P=0.061$).

In group 1, wound drains inserted at the harvesting site (iliac crest) were used in nine out of 12 patients. These drains were removed within 24–48 hours following surgery. Infection was well documented in one patient in group 1 who required two admissions in order to treat an abscess at the donor site. In group 2, one superficial wound infection settled down with a seven-day course of oral antibiotics without any need for surgical intervention.

All patients in group 1 underwent unilateral harvesting of bone graft from the ipsilateral iliac crest to the site of tibial nonunion, except for one patient, who underwent bilateral ICBG for a previously highly comminuted fracture.

Six patients received ICBG without any revision of fixation in group 1. The remaining six patients underwent revision of fixation as well as ICBG. Three patients in group 1 required subsequent revision surgery following ICBG. Two patients, primarily treated with intramedullary nailing following their injury (prior to ICBG), underwent exchange intramedullary nailing without the need for further ICBG. One patient, who also received ICBG only as the initial treatment of tibial nonunion, required dynamisation of the intramedullary nail in order to achieve bony union (Table 3).

In group 2, eight patients underwent revision of fixation in addition to application of BMP-7. The remaining seven patients received BMP-7 alone at the site of nonunion. Only one patient required subsequent revision surgery following BMP-7 application in the form of dynamisation of the intramedullary nail in order to achieve bony union (Table 4). Four patients in group 1 and five patients in group 2 were re-admitted to hospital for removal of metalwork.

All patients in both groups received paracetamol and codeine as regular analgesia. Four patients in group 1, but none in group 2, required supplementary patient-controlled opiate analgesia (PCA) to manage donor site pain postoperatively.

Table 5 summarises the direct costs incurred during the treatment of patients in each group. The total cost of treatment of all patients in group 1 was £81,968.76 (£6,830.73 per patient) compared to a total cost of £109,411.5 in group 2 (£7,294.1 per patient). The costs are further broken down to the main components contributing to the total cost. There was evidence of a significant reduction in theatre costs, radiological investigations, and outpatient costs in group 2 compared with group 1. However, the total cost of treatment for patients in group 2 (£7,294.1) remained higher than that for patients in group 1 (£6,830.73). This accounted for a 6.78% increase in costs incurred for patients in group 2. Nonetheless, the total cost difference per patient between the two groups of patients was not statistically significantly higher ($P=0.1$).

Discussion

This study, as well as previous studies [18, 23], illustrates that the economic costs of treating nonunions to the National Health Service may be substantial. A full economic evaluation of any treatment method or of a

Table 2 Demographic details of patients in each group

Demographic	ICBG	BMP-7	*P* value
Number of patients (total $N=27$)	12	15	$P>0.05$
Male/female	9/3	10/5	$P>0.05$
Mean age (range)	41.4 years (16.1–63.9)	38.5 years (20.4–79.2)	$P>0.05$
Open/closed	4/8	4 /11	$P>0.05$
Mean hospital stay (range)	10.66 days (9–13)	8.66 days (7–11)	($P=0.061$)
Mean time to union (range)	6.9 months (6.1–7.6)	5.5 months (4.7–6.2)	($P<0.001$)
Follow-up (years)	2.84	2.4	

ICBG iliac-crest-bone-graft, *BMP-7* bone morphogenetic protein-7

Table 3 Summary of treatment in group 1

Site of tibial nonunion	*n*	Primary treatment after initial injury	First treatment after diagnosis of nonunion (*n*)	Subsequent revision surgery
Proximal	2	ORIF	Proximal Tibia ORIF + ICBG (1) ICBG alone (1)	(0)
Mid-shaft	7	IM nailing	Exchange IM nailing + ICBG (4) ICBG alone (3)	None (4) Exchange IM nailing (2) Dynamisation IM nail (1)
Distal	3	ORIF	Distal Tibia ORIF+ ICBG (1) ICBG alone (2)	(0)

ORIF open reduction internal fixation, *IM* intramedullary, *ICBG* iliac-crest-bone-graft, *BMP-7* bone morphogenetic protein-7

sickness requires an analysis of the direct monetary costs, as well as the indirect costs associated with the duration of therapy, the final functional outcome, and any disability payments of each patient [3].

The lengthier the treatment of nonunion, the higher is the risk of developing complications, and the greater the financial cost to the health care institution. In addition, the loss of productivity of patients during the period of postinjury disability will have indirect adverse effects on the economy. Furthermore, the impact on the well-being of the family members of patients suffering from fracture nonunion can be devastating (indirect costs and quality-of-life related costs) [21]. In general, the inpatient costs represent 87–94% of the direct medical costs and it is estimated that the indirect costs for musculoskeletal conditions represent about 80% of the total costs of these conditions [3].

Beaver et al. [2] investigated the actual costs of treatment of tibial nonunions and reported the cost of treatment to be in the region of $11,333. Kanakaris and Giannoudis [18], in their recent review on the existing evidence of the economic burden of long bone fracture nonunions, included a cost identification attempt on a "best-case" scenario. They estimated the direct and indirect medical costs at £15,566, £17,200 and £16,330 for humeral, femoral, and tibial nonunions, respectively. Heckman et al. [14] calculated the economics of treating tibial nonunions by using three models each with a defined management pathway. Their study estimated the cost of treating tibial nonunions between $23,246 and $58,525 depending on the method of treatment provided and showed that a reduced treatment and hospitalisation time could yield substantial cost savings.

Variations in the reported costs of the different health economics studies reflect the differences in currencies, the annual impact of inflation, the healing rates between different fracture sites and types, and mostly the inclusion of either direct, indirect, intangible, or combinations of these costs to each cost analysis. Direct comparisons and drawing of clear conclusions is difficult from the existing literature evidence, as is clearly denoted in a recent review analysis [18].

The iliac crest is a common site for harvesting autologous bone, which remains the gold standard for bone grafting procedures in fracture nonunion treatment. However, the considerable morbidity associated with this procedure as well as the reduced availability of autologous bone graft represent relative limiting factors for its use. In

Table 4 Summary of treatment in group 2

Site of tibial nonunion	*n*	Primary treatment after initial injury	First treatment after diagnosis of nonunion (*n*)	Subsequent revision surgery
Proximal	1	ORIF (1)	BMP-7 alone (1)	(0)
Mid-shaft	5	IM nailing (4)	Exchange IM nailing + BMP-7 (3) BMP-7 alone (1)	Dynamisation IM nail (1)
		Ilizarov (1)	BMP-7 alone (1)	(0)
Distal	9	ORIF (6)	ORIF + BMP-7 (3) Ilizarov + BMP-7 (1) BMP-7 alone (2)	(0)
		Ilizarov (3)	ORIF + BMP-7 (1) BMP-7 alone (2)	

ORIF open reduction internal fixation, *IM* intramedullary, *ICBG* iliac-crest-bone-graft, *BMP-7* bone morphogenetic protein-7

Table 5 Costs of treatment (£) per patient in each group

Treatment description	ICBG	BMP-7
Hospital	2,133.63	1,733.33
Theatre	2,413.3	906.67 ($p<0.00001$)
Implant	696.4	592.3
Radiology	570	270 ($p<0.01$)
Drains	70	-
Outpatient	495.8	223.33 ($p<0.02$)
BMP-7	-	3,002.2
Other costs	451.6	566.27
Total cost	6,830.73	7,294.1

ICBG iliac-crest-bone-graft, *BMP-7* bone morphogenetic protein-7

addition, the direct and indirect costs associated with autologous bone graft harvesting compared to synthetic grafting materials can be considerable [11, 26].

Although there is currently good evidence that supports the effectiveness and safety of BMP-7 in the treatment of recalcitrant nonunions of long bones, concerns are continuously raised about the cost implications associated with its use. The high cost of BMP-7 reflects its production using recombinant DNA technology. However, it has also been suggested that the financial burden to the health institution could be reduced by early BMP-7 administration when a complex or persistent fracture nonunion is present or anticipated [7].

In this study we aimed to investigate this hypothesis. Only direct medical costs have been assessed and it was found that the overall actual cost of treatment in the BMP-7 group (group 2) was higher by £463.37 compared to the overall cost incurred in group 1. However, it was interesting to find out that the cost differential was much less than the unit cost of BMP-7 (£3,000.2). The cost offsets were attributable to a reduced hospital stay, reduced operative costs, as well as reduced costs of outpatient attendances. A reduced hospital stay associated with the use of BMPs compared to ICBG has been reported by other authors [8]. The operative costs have been related to better use of theatre time, staff, and equipment in group 2. It may, however, be argued that theatre costs could be reduced if a surgical assistant is experienced enough to simultaneously take ICBG unsupervised, thus reducing operative time and, subsequently, cost. This however is unlikely to reduce the costs associated with using bone harvesting operative-sets during the procedure. Such a setup also presumes that the surgical assistant is either not needed at the main operative site or that a third assistant is available, which may further increase the overall operative costs. Furthermore, in the current climate of reduced working time directives, the availability of more than one surgical assistant cannot be guaranteed.

Patients have a direct and often clearly articulated interest in avoiding the complications associated with iliac crest bone harvesting. Other advantages of using BMP-7 include a decreased surgical time, faster postoperative rehabilitation, and less powerful pain relieving agents.

The literature is sparse with regards to comparative studies assessing the health economics between BMP-7 and ICBG for the treatment of long bone nonunions. In this study, we intended to estimate and compare the direct medical cost implications of the first attempt of treatment of tibial fracture nonunions. Previous studies that attempted to analyse the cost of treatment using BMP-7 have used an economic model analysis [15]. In one study, a comparison was made between the overall clinical efficacy and total costs in the treatment of tibial nonunions in the United Kingdom (UK) and Germany using an economic decision tree [5]. In this model, the data on efficacy was obtained from previous published clinical trials. Estimates on health care utilisation were based on questionnaires completed by seven orthopaedic surgeons. In the UK model, the study compared treatment using BMP-7 to autograft or the Ilizarov frame. It estimated a total cost per patient receiving BMP-7 of £8,797 compared to £9,084 for autograft, and £13,722 for the Ilizarov fixation technique. However, the authors concluded that cost-effectiveness ratios of all three treatments were comparable [5].

Jones et al. [15] developed an economic model based on data from a clinical trial that had demonstrated improved clinical parameters (the rate of fracture healing, secondary interventions, infection rates) when 12 mg of recombinant human bone morphogenetic protein-2 (rhBMP-2) was used as an adjunct to intramedullary nailing in the treatment of open tibial fractures. Their study estimated the cost of treatment with BMP-2 to the hospital at $13,733 and to the patient at $16,734, assuming no BMP-2 reimbursement. They concluded that the clinical benefits of rhBMP-2 used in first line treatment of open tibial fractures translate into reductions in medical costs over a two-year period for hospitals and patients. Their estimates showed favourable total cost offsets (the proportion of the upfront rhBMP-2 price offset by other medical resource reductions) when 50% of the BMP-2 cost was reimbursed [15].

In a study of the peri-operative costs for patients treated with rhBMP-2 as compared with an ICBG in lumbar fusion surgery, the mean hospital cost was $24,736 for the rhBMP-2 group and $21,138 for the ICBG group [12]. The study included costs incurred up to three months after surgery. Costs associated with posthospital rehabilitation averaged $4,906 in the rhBMP-2 group vs. $6,820 in the ICBG group. Although the hospital incurred an increased cost in patients treated using rhBMP-2, the mean cost differential ($3,599) was less than the unit cost of rhBMP-2 itself ($5,000). This $1,401 difference was based on cost

offsets, partially attributable to fewer complications and decreased hospital length of stay.

This study included a cohort of patients who were successfully treated at the first attempt of addressing a tibial nonunion. We were interested in estimating the cost implications of the two treatment modalities. The study was not aimed at comparing the efficacy of BMP-7 vs. ICBG. We prospectively followed-up all patients to whom BMP-7 or ICBG was administered as part of the successful treatment of tibial nonunion. We aimed at covering most aspects of management of patients with established tibial nonunions. NHS institutions estimate the cost of each patient's treatment episode based on codes used to describe the type of treatment provided for that patient during that episode. This may be a feasible way of estimating gross average costs at NHS Trust levels where numbers are very high. However, it did not reflect the true costs of treatment for the cohort of patients analysed in our study.

This study provides a detailed and accurate collation of clinical data from which costs were derived. We have accounted for hospital stay, investigations, specific treatments including the type of surgery and implant used, and outpatient follow-up. However, some limitations should be considered in the interpretation of the results. The decision to use BMP-7 or ICBG was guided by the treating surgeon's preferred method of treatment. Secondly, the study has not examined costs related to unemployment and compensations secondary to the fractures, costs of occupational therapy modifications, travel to the hospital costs or resource consumption following discharge, which are difficult to assess accurately. Although the complications related to treatment were recorded, a direct correlation to cost implications was not attempted.

This study was not intended to provide a cost-utility analysis [1] in which the outcomes are adjusted for quality of life, for example, quality-adjusted life-years (QALYs). Such an analysis may be used to compare BMP-7 to autogenous bone graft, given the expected health-related 'quality of life' impact of eliminating complications associated with autogenous bone graft. Neither is this study intended as an analysis of clinical effectiveness or cost effectiveness. However, it has been postulated that considerable cost offsets may be achieved as the result of a decreased revision rate with rhBMP-7 [7]. Nevertheless, this study provides an up-to-date rational fair costing for the treatment of recalcitrant nonunions using BMP-7 or ICBG. A hypothetical decrease of the current price of a vial of BMP-7 by 15% (~£2,500) would make the total direct medical cost of its use lower than that of the gold standard ICBG. If we consider that its confirmed efficacy and safety equals at least those of the ICBG, as proven in numerous studies [9, 10, 16, 17, 25], that would eliminate any existing reluctance of its wider spread application in the difficult clinical setting of atrophic tibial nonunions as a first line treatment.

In conclusion, although the total cost of treatment of tibial nonunion using BMP-7 may be higher than that using ICBG, the cost differential is much less than the unit cost of BMP-7. The cost difference between the two groups of patients in our study was not statistically significant. Since this analysis represents a best case scenario (all successfully treated cases in the first grafting attempt), the financial implications of aseptic nonunions can only be higher in those cases where additional interventions and revision surgery is necessary.

This study therefore supports the view that the cost implications associated with the use of BMP-7 in the treatment of tibial nonunion are being offset by a reduction in other costs that can be incurred with iliac crest bone grafting. Further larger prospective randomised studies would provide further evidence with regard to the health economics issue of the utilisation of growth factors for the treatment of nonunions in the clinical setting.

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