■ FOOT AND ANKLE

Symptomatic treatment or cast immobilisation for avulsion fractures of the base of the fifth metatarsal

A PROSPECTIVE, RANDOMISED, SINGLE-BLINDED NON-INFERIORITY CONTROLLED TRIAL

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Aims

The purpose of this study was to compare symptomatic treatment of a fracture of the base of the fifth metatarsal with immobilisation in a cast.

Our null hypothesis was that immobilisation gave better patient reported outcome measures (PROMs). The alternative hypothesis was that symptomatic treatment was not inferior.

Patients and Methods

A total of 60 patients were randomised to receive four weeks of treatment, 36 in a double elasticated bandage (symptomatic treatment group) and 24 in a below-knee walking cast (immobilisation group). The primary outcome measure used was the validated Visual Analogue Scale Foot and Ankle (VAS-FA) Score. Data were analysed by a clinician, blinded to the form of treatment, at presentation and at four weeks, three months and six months after injury. Loss to follow-up was 43% at six months. Multiple imputations missing data analysis was performed.

Results

At four weeks and six months, symptomatic treatment proved non-inferior in terms of primary outcome.

Take home message: Immobilisation is no better than symptomatic treatment in the management of a fracture of the base of the fifth metatarsal when judged by PROMs. Significant loss to follow-up with this injury could be expected in longer term.

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Avulsion fractures of the base of the fifth metatarsal are common injuries in adulthood, and are considered to be relatively innocuous.[1-3] Their management, however, involves significant material and clinical resources. A number of non-operative forms of treatment have been studied which range from elasticated bandaging and wearing a hard-soled shoe through to immobilisation in a cast, focused rigidity casting or a walking boot.[2,4-14] Few authors recommend internal fixation.[3,15,16] Although some authors draw a distinction between the treatment of displaced and undisplaced fractures, others have noted no clear effect of the degree of comminution, the amount of displacement and the propagation of fracture into the fifth tarsometatarsal joint on the outcome of non-operative management.[3,9,17]

The limitations of previous studies, which compare non-operative treatments, include a lack of a comparative group; the inclusion of a heterogeneous group of metatarsal fractures; prospective randomised studies without power analyses and the use of non-validated outcome measures.[5-7,9]

The aim of this study was to carry out a prospective, randomised, non-inferiority, controlled study to compare symptomatic treatment in a double-layered elasticated bandage with immobilisation in a below-knee cast. The rationale for this design of study is that it may offer an advantage in terms of cost, availability and outcome compared to a reference form of treatment.

Our null hypothesis was that immobilisation in a below-knee cast gave significantly better patient reported outcome measures (PROMs). The alternative hypothesis was that symptomatic treatment was not inferior.

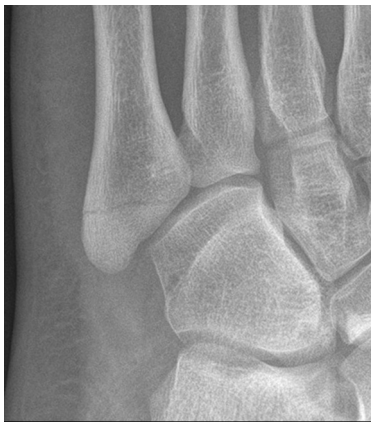

Fig. 1a

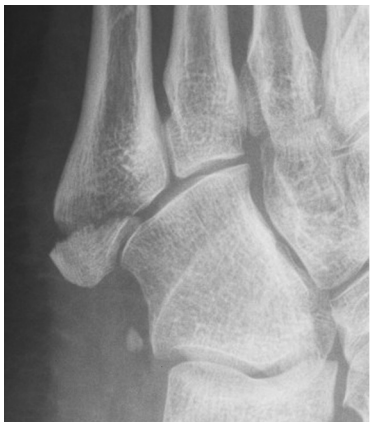

Fig. 1b

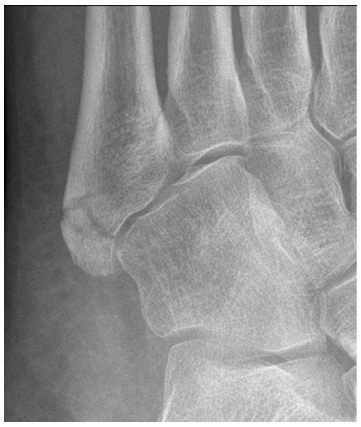

Fig. 1c

Radiographs showing various types of avulsion fracture of the base of the fifth metatarsal: a) undisplaced; b) displaced; c) comminuted avulsion fracture of the base of fifth metatarsal.

Patients and Methods

Trial design. We studied Lawrence and Botte[2] type I avulsion fractures of the fifth metatarsal. In order to clarify the most commonly used form of treatment for these fractures, a preliminary survey of 29 foot and ankle surgeons was conducted. They were asked which form of treatment they commonly advised for this injury and for how long. As a result, four weeks in a below-knee walking cast was chosen to be the reference treatment arm. The symptomatic treatment selected was a double-layered elasticated bandage. We designed a prospective, randomised, non-inferiority controlled trial to compare two treatment arms. No amendments to the design occurred after the start of the trial. Having obtained ethical approval (YH - 107 - 0297), the study was conducted at our hospital (Sheffield Teaching Hospitals NHS Foundation Trust) between July 2012 and January 2014.

Patients. Adult patients over the age of 16 years who presented within seven days of injury with a closed Type I avulsion fracture of the tuberosity of the fifth metatarsal were considered for inclusion. The degree of displacement or comminution, or the propagation of fracture into the fifth tarsometatarsal joint did not preclude recruitment into the trial (Fig. 1). Exclusion criteria included diabetes; inflammatory joint disease; previous ipsilateral foot surgery or fracture; presentation more than seven days after the injury and an inability to understand written English. An information sheet about the study was given to potential participants either in the Emergency Department or in the fracture clinic, which allowed at least 24 hours, during which the patients could agree to participate. Recruitment into the study with a further explanation and informed consent was carried out in the clinic.

In all, 36 patients were allocated to wear a double-layered elasticated bandage applied by nursing staff inside their normal footwear (the symptomatic treatment group) and 24 patients were given a lightweight, below-knee walking cast applied by accredited casting technicians (the immobilisation group). Both types of treatment were for four weeks. This reference form of treatment was the same as in previous reports.[7,13] The use of elbow crutches was permitted in both groups and patients were encouraged to bear weight as soon as they could tolerate it. Those in the immobilisation group had the cast removed four weeks later in the clinic. Patients in this group were evaluated for the risk of venous thromboembolism and offered prophylaxis according to our Trust guidelines.

The non-inferiority hypothesis was tested for the primary outcome measure using the validated Visual Analogue Scale Foot and Ankle (VAS-FA) score.[18] This score ranges from 0 to 100 points: higher scores indicate a better functional outcome. This is the same primary outcome measure used in a previously published prospective report.[13]

The EuroQol-5D visual analogue scale (EQ-5D VAS) score was used as a secondary outcome measure: this ranges from 0 to 100.[19] Baseline data were collected at the time of enrolment in the clinic. Further data were collected at four weeks follow-up. Questionnaires and pre-paid envelopes were sent to the patients three months and six months after enrolment. Additional outcomes such as unexpected returns, change of treatment, further injury of the same foot and complications of treatment were noted.

Power analysis. The VAS-FA score was also used as the primary end-point to determine sample size. Since there is no universally established minimal clinically important difference (MCID) for this score, ten points (out of 100) was considered as a reasonable value for the MCID. Thus, with the α adjusted to 0.02 for multiple testing and power set at 90% for a MCID of ten points, the sample size calculation showed that we needed a minimum sample size of 12 patients in each arm to demonstrate non-inferiority. However, pragmatically, we anticipated a loss to follow-up of over 30% as had been seen in other studies.[6] We therefore proposed to recruit 30 patients in each arm in an attempt to generate useful data.

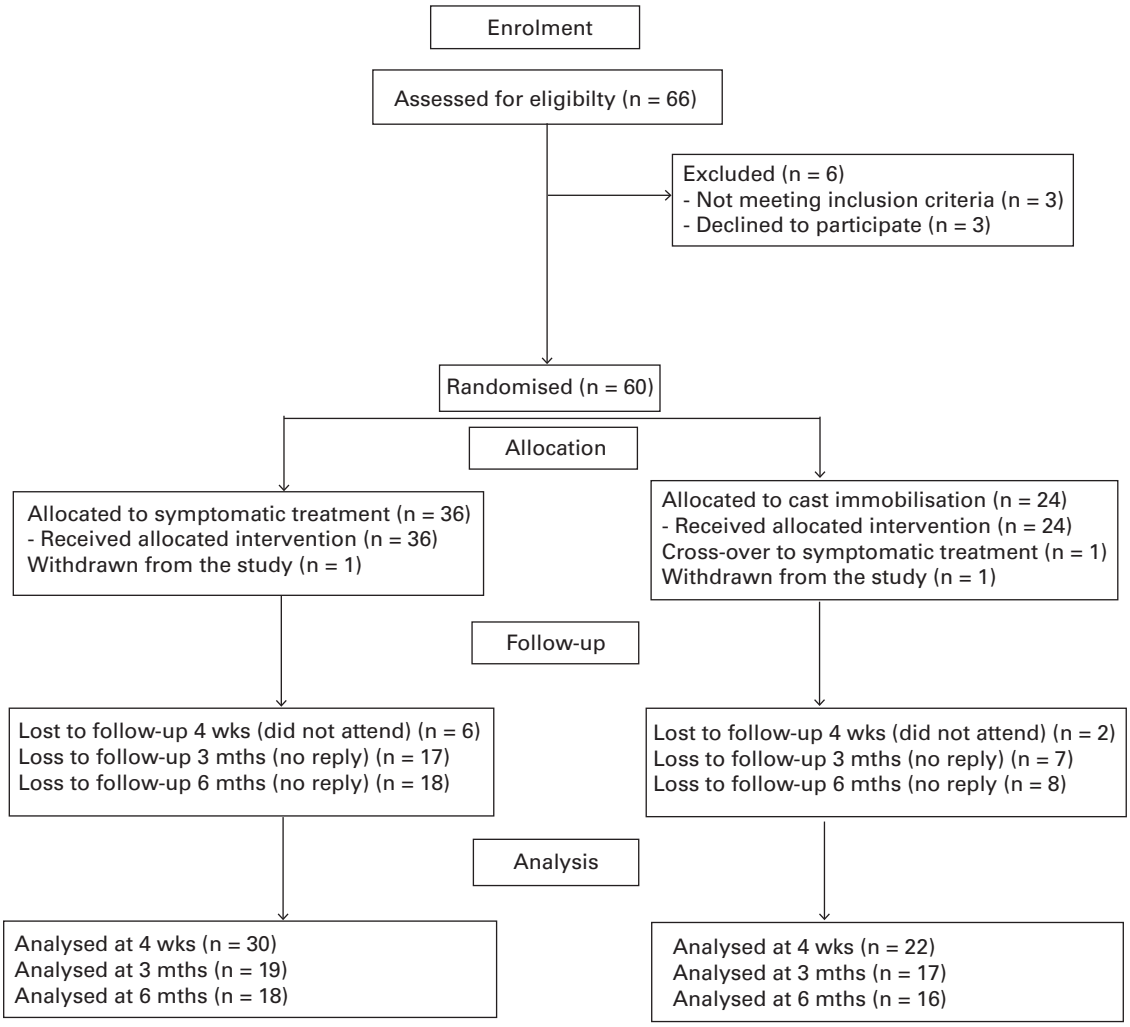

Fig. 2

Consolidated Standards of Reporting Trials (CONSORT) diagram showing the flow of patients through the trial.

Patients were allocated to a treatment group using an electronic random number generator. The generation of an even number randomised the participant to a below-knee walking cast, and an odd number to a double-layered elasticated bandage.

Statistical analysis. This is a non-inferiority study using a one-sided confidence interval for the difference between the two groups. The p-value was Bonferroni adjusted due to multiple testing: 0.02 was considered significant for the primary outcome and this was achieved using a 96% confidence interval. In order to accommodate the skew in the data, the Hodges-Lehman confidence interval for the median difference was calculated using a value of -10 as a non-inferiority boundary for the VAS-FA and EQ-5D VAS.

Results

The flow of patients through the trial is shown in Figure 2. A total of 66 patients were evaluated for eligibility. Three did not meet the inclusion criteria, and three declined to participate. Thus, 60 patients were included in the study: 36 were randomised to the symptomatic group and 24 to the immobilisation group. All patients received the allocated treatment. One patient in the immobilisation group opted to have symptomatic treatment after two weeks and one in each group subsequently withdrew from the study.

The loss to follow-up was eight patients (13%) at four weeks, 24 (40%) at three months and 26 (43%) at six months. In both groups, patients who were lost to follow-up failed to complete all the questionnaires. In an attempt to increase the size of the sample, reminder telephone calls were made and additional sets of questionnaires were posted to all non-responders at each time point. In total, in the symptomatic group, outcome data were recorded and analysed for 30 patients (83%) at four weeks, 19 (53%) at three months, and 18 (50%) at six months. In the immobilisation group, data were analysed for 22 patients (92%) at four weeks, 17 (71%) at three months, and 16 (67%) at six months. The data for all patients were analysed on an intention-to-treat basis by an investigator (PIA) blinded to the type of treatment.

Table I. The demographic data of the patients

Characteristic	Symptomatic treatment group (n = 36)	Cast immobilisation group (n = 24)	p-value*
Mean age (yrs) (SD) range	42 (17) 19 to 68	44 (20) 16 to 79	p = 0.62
Male:female	11:25	6:18	p = 0.64
Right:left	16:20	12:12	

* unpaired student's *t*-test

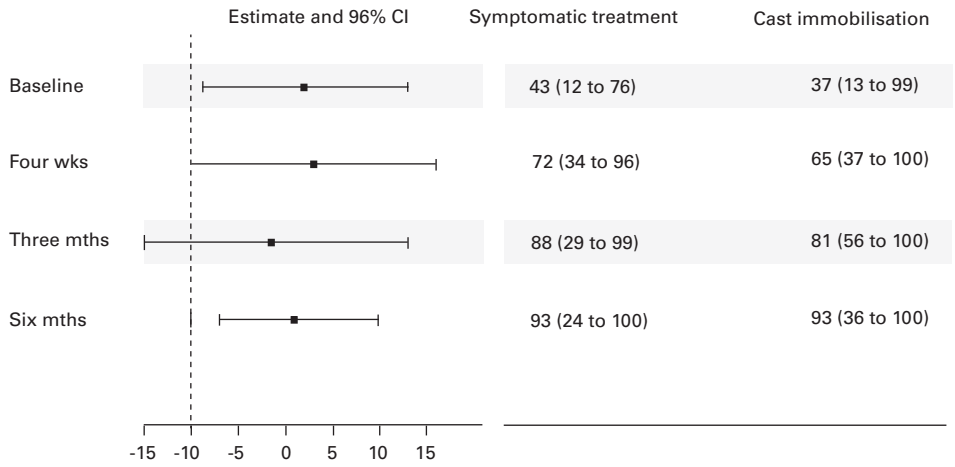

Fig. 3

Diagram showing the primary outcome: the Visual Analogue Scale Foot and Ankle (VAS-FA) Score (CI, confidence interval).

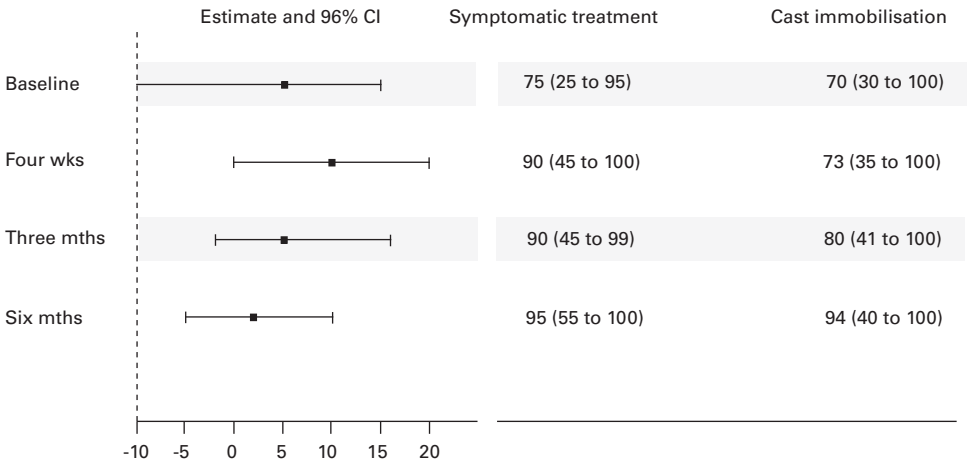

Fig. 4

Diagram showing the secondary outcome: EuroQol 5D visual analogue scale (EQ-5D VAS) score. (CI, confidence interval).

The baseline demographic data are shown in Table I. There were no significant differences between the groups in terms of age and gender. Demographically, these patients were similar to those in other series investigating metatarsal fractures in adults.[5,6,9,13]

The VAS-FA scores are shown in Figure 3. In the symptomatic group, the non-inferiority boundary of -10 was not crossed at the baseline, four weeks or six months indicating that symptomatic treatment was not inferior. At three months, the confidence intervals for the median difference in the two groups was smaller than the MCID, making the results inconclusive.

The secondary outcome scores are shown in Figure 4. The non- inferiority boundary of -10 was not crossed at any time point indicating that symptomatic treatment was not inferior. No patients in either arm of the study reported any complications.

Due to the considerable but anticipated loss to follow-up, analysis of the missing data was performed using a multiple imputations method. The pattern of these data was found to be missing at random. Data were imputed based on complete data for age and gender as well as partial data for VAS-FA and EQ-5D VAS at each time point. For VAS-

FA, out of ten imputed datasets which were re-analysed, none estimated the lower limit of the Hodges –Lehman confidence interval for the median to be less than -10. At four weeks a mean estimate was 2.7 and the minimum lower level was -9. At three months and six months the mean points were zero and 0.48, and minimum lower limits were -8 and -7, respectively. Similarly, for EQ-5D VAS, out of ten imputed datasets which were re-analysed, at no time point was the lower limit of confidence interval less than -10. Thus, the non-inferiority of symptomatic treatment specifically was further supported by the data for both outcomes.

Discussion

There are many descriptions of the types of fracture that affect the proximal end of the fifth metatarsal, but it seems clear that, with the exception of a true Jones fracture, the type of fracture has no influence on functional outcome.[9,17,20-22] Most unite within eight weeks: those that do not are often asymptomatic.[23] Vorlat, Achtergael and Haentjens[22] reported that the most significant predictor of a poor functional outcome after these injuries was a prolonged period of non-weight-bearing. Despite a general acceptance that non-operative treatment gives a high rate of patient satisfaction, evidence about the best form of non-operative treatment is scant.[13,20]

Several authors have studied the non-operative treatment of fractures which just involve the base or tuberosity of the fifth metatarsal.[5,6,9,13] The demographic data from these reports reveal that these fractures occur more commonly in women than men (1.7:1 ratio) at a mean age of 42.9 years (15 to 82). The baseline data in our study are similar in both respects. The authors who included a mixture of proximal fifth metatarsal fractures, including Jones fractures, have reported different demographic characteristics, with a mean age of 23.0 years (17 to 41), in a predominantly male population (4.1:1).[8,24,25] Therefore, conclusions about the management of avulsion fractures cannot be drawn from studies which include Jones fractures.

Previously, some authors have argued that non-operative treatment is inappropriate for patients with a displaced or comminuted fracture of the tuberosity of the fifth metatarsal.[3,15,16,24] There is, however, no evidence that this is so.[9,17,20-22] Many authors, in fact, suggest that non-operative management gives an acceptable outcome and return to function.[3,12,13] The problem with some studies which advocate non-operative treatment is the lack of a comparative treatment group.[9,11] Seven previous reports have compared the outcomes of two forms of non-operative treatment.[4-8,12,13] Of these, two were conducted without any of the rigours of modern designs of study with patients poorly allocated to the two treatment arms.[4,8] One prospective randomised study treated a heterogeneous group of injuries which included fractures of the neck and shaft of the fifth metatarsal and fractures of the shaft of the second and third metatarsals.[7] Another prospective study compared the functional outcome of treatment in a short-leg walking cast with that of immobilisation in a walking boot and found that the levels of pain and function were significantly better in those patients treated in a walking boot at nine weeks post-injury.[13] Unfortunately, without randomisation, this study suffered from bias and drew conclusions about the effect of an elasticated bandage beyond the scope of their study.[13] Of the remaining three prospective randomised studies, none included a power analysis and all used non-validated outcome measures.[5,6,12]

In our study, we pragmatically included all types of avulsion fracture of the base or tuberosity of the fifth metatarsal: no distinction was made between the degree of displacement, comminution or intra-articular extension. The intention was that our findings would be applicable to all types of avulsion fracture which involve the tuberosity. We saw the universal availability and inexpensive properties of the double-layered elasticated support bandage as a simple and attractive form of symptomatic treatment. Unlike traditional superiority trials, our aim was to show that patients with an avulsion fracture of the base of the fifth metatarsal treated symptomatically, did no worse than those treated with immobilisation in terms of validated PROMs. This was the rationale for choosing a non-inferiority design. Accordingly, we used an appropriate validated primary outcome tool, the MCID, as a discriminator and confidence intervals with median differences and range to demonstrate such non-inferiority.

In general terms, the MCID is a difficult value to establish in terms of functional outcome. With regards to pain, however, Farrar et al[26] in their study of over 2700 patients in ten placebo-controlled trials, reported that a 30% reduction in pain in a given range is a sensitive cut-off value in PROMs. We used a much smaller value of 10% as the MCID of a validated score where pain is a significant component, and believe that it provided sufficient sensitivity to demonstrate the non-inferiority of symptomatic treatment. We found that symptomatically treated patients did no worse in terms of validated PROMs in both the short and long term. Our data were inconclusive about the primary outcome at three months. Specifically, the lower limit of confidence interval for the median difference between the groups was smaller than the MCID. At the same time, the confidence interval was well balanced around zero. The most likely explanation for this is the significant loss to follow-up of patients in both groups. We acknowledge that, although at all time points the number of patients available for analysis remained well above the required minimum, the substantial increase in loss to follow-up, which reached 43% at six months, could potentially be a significant limitation of our study. It is well known that loss to follow-up is a difficult problem when studying patients who have suffered injury. In separate studies, failure to attend follow-up after non-operative cast treatment of distal radial fractures in 37 patients, and splinting of metacarpal fractures in 335 patients was noted as 30.9% and 29.7% respectively.[27,28] There is more recent evidence that even in surgically-treated

trauma patients, loss to follow-up can reach 67% (215 patients out of 307) by six months after the injury.[29] In order to address this issue, we carried out multiple data imputations, which is a recognised method of analysing missing data and further supports our findings.[30] Specifically we could not see any pattern in the missing data between the groups and therefore data were assumed to be missing at random. With the assumption of 'worst case scenario' in both groups, we used ten datasets for both outcomes with the recommended minimum of five based on available variables for the age and gender of the missing patients. The non-inferiority of symptomatic treatment was further confirmed by this method. One possible explanation for failure to attend follow-up in this study may be that avulsion fractures of the base of the fifth metatarsal are benign injuries and most patients recover function and become free of pain between four and twelve weeks after injury. Alternatively, there may have been a difference in sociological groups between the attenders and non-attenders for follow-up that was not accounted for in the design of the study.[27] Furthermore, in hindsight we think that using block randomisation could have potentially made the size of the groups equal, which may or may not have affected the results. Lastly, as with any study which compares explicit forms of treatment, it was not possible to double blind it.

Given these limitations, this is the first methodologically robust prospective randomised trial, to our knowledge, which shows that cast immobilisation of avulsion fractures of the base of the fifth metatarsal in adults provides no benefit over symptomatic treatment in the short and longer term. A significant loss to follow-up could be expected with these injuries in the longer term.

Author contributions:
P. I. Akimau: Conceived the idea, Designed the trial, Obtained REC approval, Analysed data, Wrote the article.
K. L. Cawthron: Recruited and followed up patients.
W. M. Dakin: Recruited and followed up patients.
C. Chadwick: Recruited patients, Analysed and revised paper.
C. M. Blundell: Recruited patients, Supervised the study, Analysed and revised paper.
M. B. Davies: Recruited patients, Supervised the study, Analysed and revised paper.

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