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Pilot study of micromotion nailing for mechanical stimulation of tibial fracture healing

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Aims

The study objective was to prospectively assess clinical outcomes for a pilot cohort of tibial shaft fractures treated with a new tibial nailing system that produces controlled axial interfragmentary micromotion. The hypothesis was that axial micromotion enhances fracture healing compared to static interlocking.

Methods

Patients were treated in a single level I trauma centre over a 2.5-year period. Group allocation was not randomized; both the micromotion nail and standard-of-care static locking nails (control group) were commercially available and selected at the discretion of the treating surgeons. Injury risk levels were quantified using the Nonunion Risk Determination (NURD) score. Radiological healing was assessed until 24 weeks or clinical union. Low-dose CT scans were acquired at 12 weeks and virtual mechanical testing was performed to objectively assess structural bone healing.

Results

A total of 37 micromotion patients and 46 control patients were evaluated. There were no significant differences between groups in terms of age, sex, the proportion of open fractures, or NURD score. There were no nonunions (0%) in the micromotion group versus five (11%) in the control group. The proportion of fractures united was significantly higher in the micromotion group compared to control at 12 weeks (54% vs 30% united; p = 0.043), 18 weeks (81% vs 59%; p = 0.034), and 24 weeks (97% vs 74%; p = 0.005). Structural bone healing scores as assessed by CT scans tended to be higher with micromotion compared to control and this difference reached significance in patients who had biological comorbidities such as smoking.

Conclusion

In this pilot study, micromotion fixation was associated with improved healing compared to standard tibial nailing. Further prospective clinical studies will be needed to assess the strength and generalizability of any potential benefits of micromotion fixation.

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Keywords: Intramedullary nailing, Micromotion locking

Introduction

Tibial shaft fractures are a common orthopaedic trauma injury for which the gold-standard treatment is intramedullary (IM) nailing.[1] Since the introduction of locking nails of the 1970s, advancements in nailing have included titanium alloys, optimized screw trajectories, reamed insertion, and improved instrumentation, including the suprapatellar insertion approach. The third-generation nailing systems currently available have been associated with generally good clinical outcomes, but persistent problems with nonunions and delayed healing remain.[2] Data from the UK and Europe support a consensus tibial nonunion rate of 12% for reamed nailing based on recent reports.[3-5] Data from USA-managed care claims databases are similar, with 12% to 14% tibial nonunion rates.[6,7] Data from North American Level I trauma centres is the

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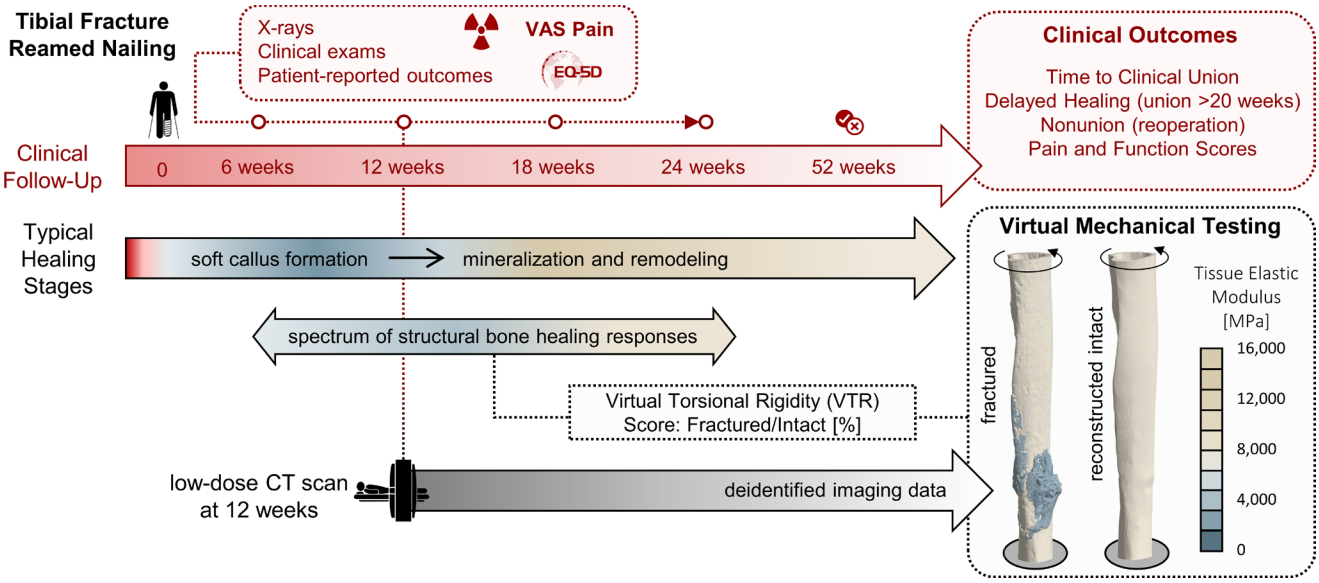

Fig. 1

Clinical follow-ups were scheduled at six, 12, 18, and 24 weeks postoperatively, with a final case review after one year. Clinical outcome measures included time to clinical union, a categorical designation of union/delayed healing/nonunion, and patient-reported pain and function scores. Low-dose CT scans were acquired at 12 weeks postoperatively and captured a wide spectrum of structural bone healing responses. The deidentified imaging data were used to perform virtual mechanical testing. The resulting objective healing score – virtual torsional rigidity (VTR) – was reported as a percentage relative to each patient's intact tibia. VAS, visual analogue scale.

most variable, with a reported range of 7% to 22% for nonunion and reoperation.[8-12]

Tibial nailing is also associated with a significant proportion of slow-healing fractures. A recent UK-based single-centre review of over 1,000 tibial fractures treated by reamed IM nailing found the 75th percentile union time to be 20 weeks.[3] Similarly, a study from 41 Italian trauma centres reported that only 74% of nailed tibiae healed in less than six months,[5] while a large Belgian single-centre study reported an average healing time of 6.1 months for tibial fractures that did not require secondary interventions.[4]

Of course, not all tibial fractures are created equal, nor do all patients with similar injuries share the same baseline health risks. Nonunion and delayed healing are multifactorial problems with contributing factors including: fracture pattern, open injury, infection, compartment syndrome, age, sex, smoking and other substance use, chronic and systemic diseases (e.g. diabetes, hepatitis C), fixation instability, poor cortical continuity, and vascular disruption.[3,4,6,8,10,13-15] In addition to biology, vascularity, and physiological state, the diamond concept of fracture healing describes the mechanical microenvironment as a fourth essential ingredient for successful union.[16]

Evidence for the benefits of axial mechanical stimulation in accelerating fracture union was first presented in ovine models with external fixators.[17-19] Subsequently, clinical investigations conducted in the UK reported a 25% reduction in time to union in patients with micromotion stimulation compared to rigid external fixation.[18,20]

More recently, a concept for micromotion-enabled tibial nailing was introduced to combine the purported benefits of mechanical stimulation while retaining the biomechanical and procedural advantages of IM nailing.[21,22] Micromotion tibial nails are now commercially available in the form of the Apex Tibial Nailing System (OrthoXel, DAC; Ireland). The objective of this prospective pilot study was to provide a report of clinical outcomes in the first implantation series of the Apex Tibial Nail used in micromotion locking mode. The hypothesis was that micromotion fixation enhances healing compared to static fixation.

Methods

A total of 101 primary tibial fractures were treated by reamed intramedullary (IM) nailing in a single Level I trauma centre from 1 July 2017 to 31 December 2019. Of these, 62 patients were treated with TRIGEN META-NAIL Tibial Nails (Smith & Nephew; UK) in standard static locking mode with at least two proximal and two distal locking screws (control group). The other 39 patients were treated with Apex Tibial Nails (OrthoXel, DAC; Ireland) in micromotion locking mode with at least two proximal and two distal locking screws (micromotion group). All implantations were done using reamed insertion with a standard infrapatellar or parapatellar approach. Implant type was not randomized and was selected at the discretion of the treating physician. During the study, multiple consultant orthopaedic surgeons and specialist registrars completed implantations for patients across both groups. Treatment was not blinded.

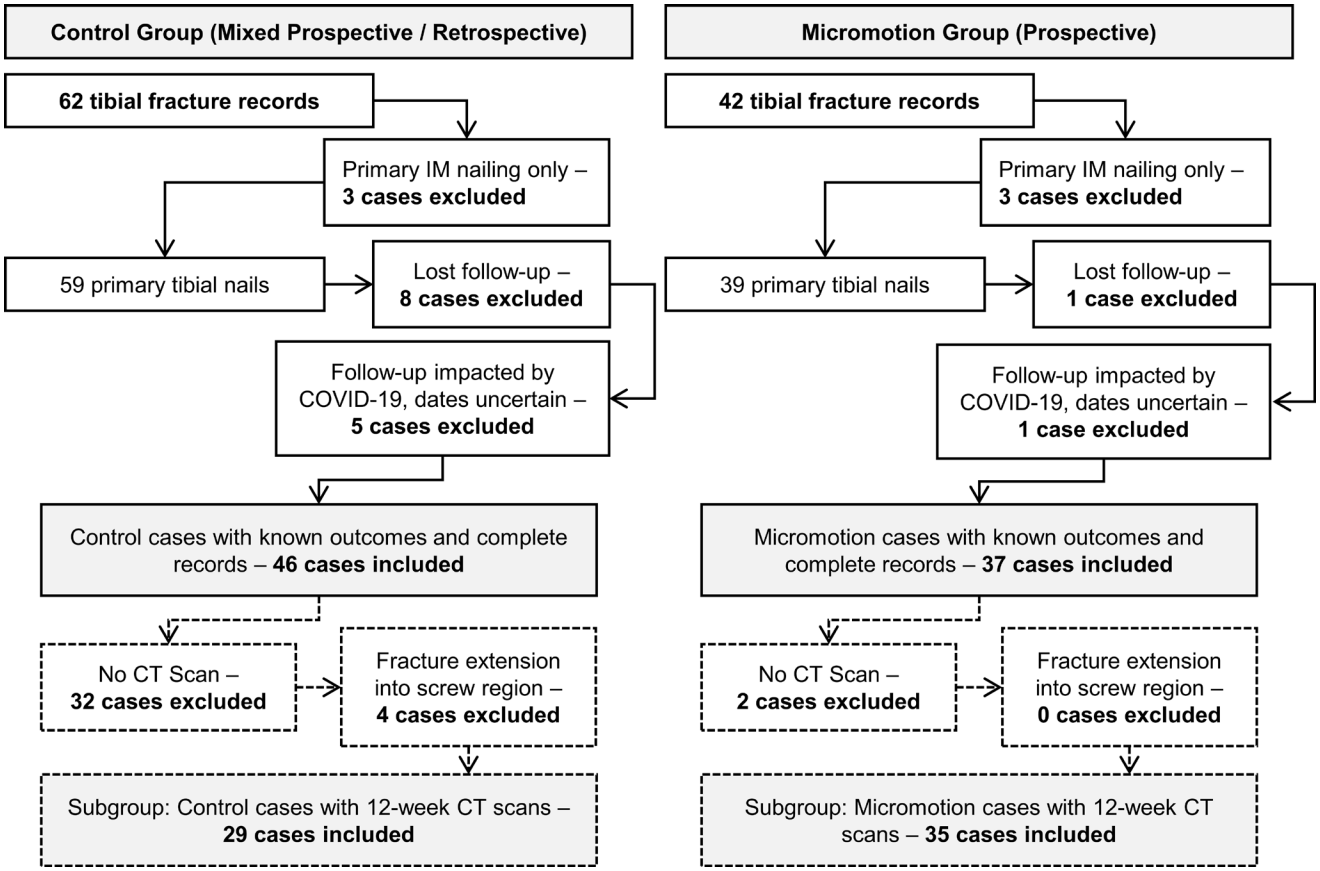

Fig. 2

Flowchart of case evaluation and application of inclusion/exclusion criteria for the control and micromotion groups. IM, intramedullary.

The protocol for this observational study was reviewed and approved by the local Ethics Committee and is summarized in Figure 1. All included patients provided written informed consent to participate. Study inclusion criteria was as follows: age 18 years or older with a diaphyseal or extraarticular proximal/distal tibia fracture (OTA/AO 41-A2/3, 42-A/B/C, or 43A) deemed appropriate for treatment by reamed nailing. Pain relief was not dictated by the study protocol and was almost exclusively non-narcotic. All micromotion patients were prospectively recruited. The control group had a mixed design, with some patients being prospectively recruited and some cases retrospectively reviewed to ensure that all tibial nails implanted in the centre during the study period were accounted for.

Patient demographic details, injury characteristics, and baseline health information were recorded. Nonunion Risk Determination (NURD) scores were calculated following a published formula.[8] Fracture reduction was quantified to compute NURD scores by recording the percentage of cortical continuity (≤ 25/50/75/100%) and these data were analyzed separately. Clinical assessments with biplanar radiographs were conducted at six, 12, 18, and 24 weeks or as needed until clinical union, which was defined as pain-free weight-bearing with a minimum of three bridged cortices. Patients were contacted for final follow-up at 52 weeks and all case records were reviewed at least 12 months after injury to exclude late-presenting complications. Delayed healing was defined as clinical union after 20 weeks, corresponding to the 75th percentile time to union in a recent large cohort study.[3] Nonunion was defined as a clinically symptomatic fracture at least six months postoperatively with failure to progress on serial radiographs for at least three months.

Prospectively recruited patients were scheduled for low-dose CT scanning at 12 weeks postoperatively. Virtual mechanical testing was performed on each fracture using a published method to objectively assess virtual torsional rigidity (VTR).[23] VTR is expressed as a percentage where 0% indicates that no healing has occurred and 100% indicates structural equivalence with the patient's intact tibia. Virtual mechanical testing was carried out using de-identified scans and no patient data, and the results were not provided for clinical review until all patients had been discharged from clinical care.

Prospectively recruited patients also completed the following patient-reported assessments at six, 12, 18, and 24 weeks postoperatively: EuroQol multi-dimension

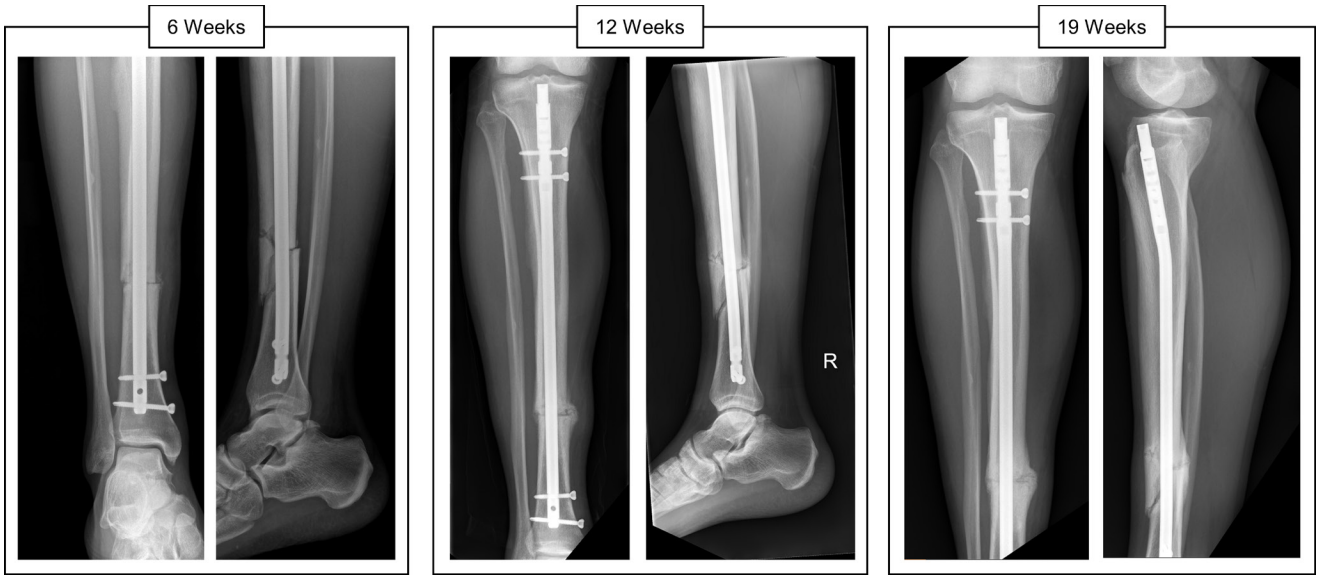

Fig. 3

Case example of a micromotion patient with anteroposterior and lateral radiographs shown at six, 12, and 19 weeks. This 25-year-old male with a sports-related closed fracture (closed, OTA/AO 42-B3) reported full return to activity with no pain at 12 weeks.

Table I. Open fractures in each group by Gustilo-Anderson grade.

Grade	Control	Micromotion
I	3	0
II	0	3
IIIa	3	3
IIIb	3	1
IIIc	1	0
Total	10	7

Table II. Clinical outcomes by category with percentages as a proportion of the number of patients in each group.

Outcome category	Control, n (%)	Micromotion, n (%)
Union (< 20 wks)	28 (61)	32 (86)
Delayed union (≥ 20 wks)	13 (28)	5 (14%
Nonunion	5 (11)	0 (0)
Total	46	37

health assessments (EQ-5D-5L)[24] and numeric rating scale (NRS) pain scores.

Statistical analysis. Statistical analysis was carried out in SPSS Statistics 25 (IBM, USA). All tests were run with a 95% confidence interval (significance level of 0.05). Shapiro-Wilk testing was used to test for violations of normality. Due to data distributions, descriptive statistics are reported as medians and interquartile ranges (IQRs). Individual statistical tests chosen for between-groups comparisons are presented with justifications in the results. Post-hoc power analysis was also performed using G*Power (ver. 3.1.9.7).

Results

After applying inclusion/exclusion criteria and excluding cases with incomplete records, there were 46 control cases and 37 micromotion cases for outcomes analysis (Figure 2). There were no instances of loss of fixation, no nail failures, and no deep infections in any implant. Radiographs from an example micromotion case are shown in Figure 3.

The control group had 32 males and 14 females (70% male) and the micromotion group had 26 males and 11 females (70% male). A chi-squared test of proportions confirmed there was no difference in the proportion of males between groups (asymptotic significance; p = 0.945). Median patient age was 40 years (IQR 27 to 54) in the control group and 35 years (IQR 26 to 54) in the micromotion group. Patient age was non-normally distributed in the control group (p = 0.019), so a Mann-Whitney U test was run and there was no difference in age between the two groups (p = 0.996).

Within the control group, there were 36 closed and ten open fractures (78%/22%). Within the micromotion group, there were 30 closed and seven open fractures (81%/19%). A chi-squared test of proportions confirmed there was no difference in the proportion of open fractures between groups (asymptotic significance; p = 0.752). The Gustilo-Anderson classifications for all open fractures in each group are recorded in Table I. There was one bilateral tibial fracture in the control group and none in the micromotion group.

The quality of fracture reduction was compared between the control and micromotion groups using a chi-squared test of homogeneity on the cortical continuity score data. The control group had 12 fractures (26%) with 100% cortical continuity, 27 fractures (59%)

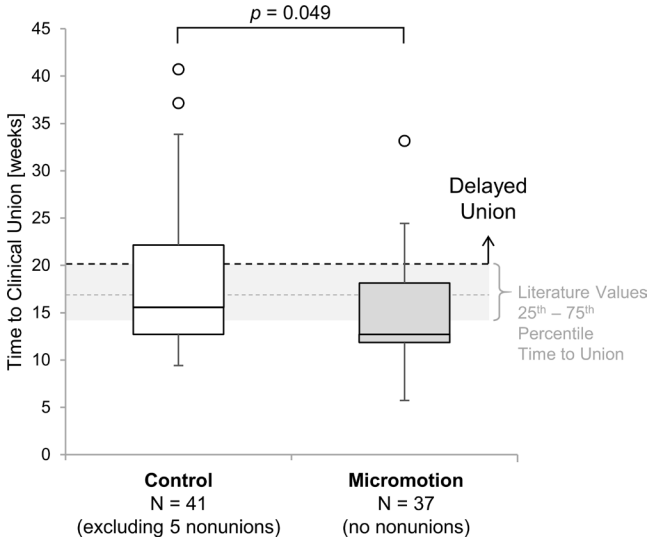

Fig. 4

Time to clinical union in the control and micromotion groups. Analysis considers only cases that achieved union without additional surgery; five nonunions in the control group were neglected. Literature reference data for union time with reamed tibial nailing is based on the distribution reported in a recent large-cohort study from an independent centre.[3]

Table III. Time to clinical union in weeks.

Time, wks	Control* (n = 41)	Micromotion (n = 37)
Median (IQR)	16 (13 to 22)	13 (12 to 18)

*Excluding five nonunion cases in control group; zero nonunions in micromotion group
IQR, interquartile range.

with 75% continuity, seven fractures (15%) with 50% continuity, and no fractures with 25% or lower continuity scores. The micromotion group had 11 fractures (30%) with 100% cortical continuity, 20 fractures (54%) with 75% continuity, six fractures (16%) with 50% continuity, and no fractures with 25% or lower continuity scores. There was no difference between the two multinomial probability distributions of cortical continuity scores between the control and micromotion groups (asymptotic significance; p = 0.910).

Clinical outcomes were tabulated by category in each group and are reported in Table II. Due to small cell counts (zero nonunions in the micromotion group), Fisher's exact test was run to compare the proportion of nonunions between groups. The difference in nonunion proportion was significantly higher in the control group (one-sided exact significance; p = 0.047). The proportion of patients in each group experiencing compromised healing (delayed healing and nonunion together) was also compared. There were 18 patients (39%) in the control group who experienced healing difficulties versus five patients (14%) in the micromotion group. A chi-squared test of proportions showed this difference was significant (asymptotic significance; p = 0.010).

Table IV. Proportion of fractures united at each follow-up, up to one year postperatively.

Evaluation timepoint, wks	Control, n (%)	Micromotion, n (%)	p-value
12	14/46 (30)	20/37 (54)	0.030*
18	27/46 (59)	30/37 (81)	0.029*
24	34/46 (74)	36/37 (97)	0.004*
52	41/46 (89)	37/37 (100)	0.047†
Nonunions	5/46 (11)	0/37 (0)	0.047†

*Chi-squared test of proportions, asymptotic significance.
†Fisher's exact test, one-sided exact significance (due to small cell counts).

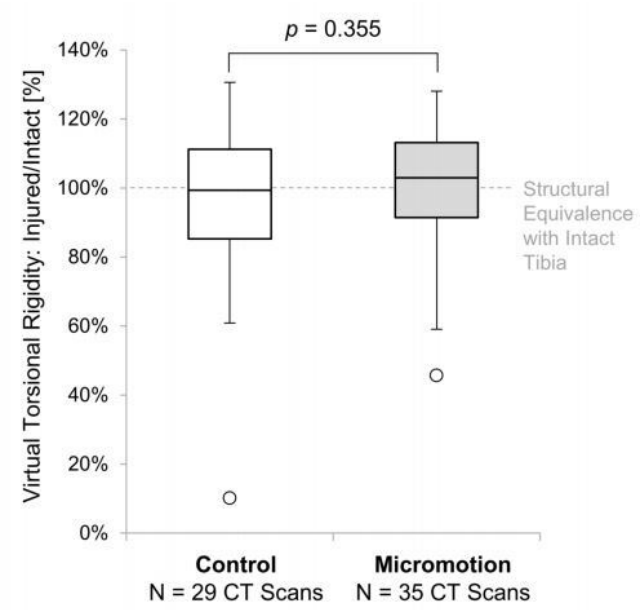

Fig. 5

Virtual torsion test results for all patients with CT analysis, including all fracture types (open and closed) and patients with and without comorbidities.

Time to clinical union was examined for patients who achieved union without additional surgeries: 41 out of 46 patients in the control group and all 37 patients in the micromotion group. Summary statistics for time to clinical union are presented in Table III and distributions are plotted in Figure 4. Union time was non-normally distributed in both groups (p ≤ 0.003), so a Mann-Whitney U test was run: it showed that median time to union for the micromotion patients was significantly lower (18% faster healing based on medians) compared to the control group (p = 0.049). A post-hoc power analysis was performed on the time to union data (group means, standard deviations, and sample sizes), for a one-tailed Mann-Whitney U test with an effect size $d = 0.483$ at a significance level of 0.05. The post-hoc achieved power for the significant difference reported in Figure 4 was 66%.

Starting at 12 weeks, the proportion of patients in each group that were united was calculated for each follow-up timepoint and is reported in Table IV. Chi-squared tests

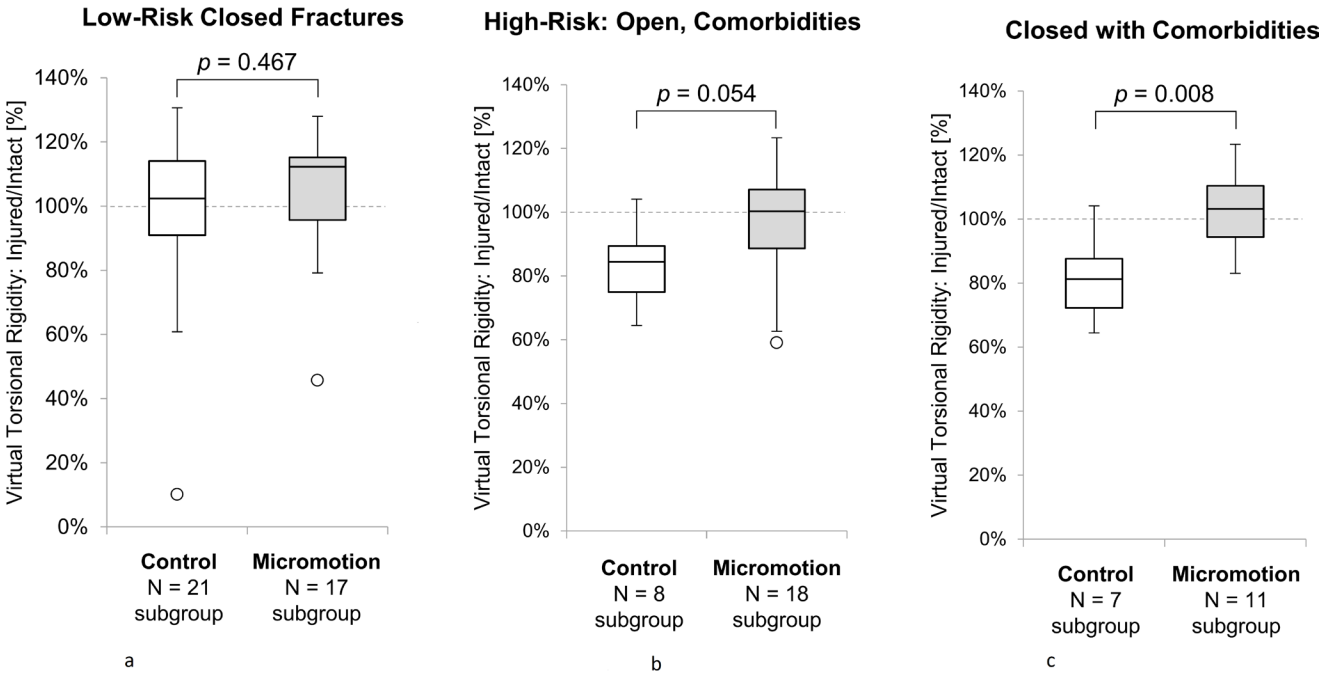

Fig. 6

Virtual torsion test results for patients in three subgroups: a) low-risk injuries (closed and Gustilo I) in patients with no comorbidities, b) high-risk injuries (Gustilo II and above) and all patients with comorbidities regardless of injury severity, and c) low-risk (closed and Gustilo I) injuries in patients with comorbidities.

of proportions showed that the proportion of patients united was significantly higher in the micromotion group compared to control at 12, 18, and 24 weeks. The post-hoc achieved power for the significant differences in the proportion of united fractures at 12, 18, and 24 weeks was 72%, 71%, and 92%, respectively. At 52 weeks, all micromotion fractures were united. The remaining five nonunited fractures in the control were all diagnosed as nonunions. Four were reoperated (exchange nail) at 90, 73, 39, and 38 weeks from their initial surgery date. All revised nonunions ultimately united without additional surgeries. The final nonunion in the control group was not revised, with the patient refusing surgery due to COVID-19 concerns.

A subset of patients from both groups had CT scans available for virtual mechanical testing: 29 control and 35 micromotion (see Figure 2). All patients with CT scans healed without secondary interventions (i.e. no nonunions were scanned at 12 weeks). None of the control group nonunions were scanned at 12 weeks for a variety of reasons including: primary treatment occurred outside the prospective study period, patient not screened for enrolment, late consent after 12 weeks, and one missed scan appointment. The key outcome measure from the CT analysis, virtual torsional rigidity (VTR), was non-normally distributed in both the control and micromotion groups ($p \leq 0.011$), so Mann-Whitney U-tests were run to determine if there were differences in VTR between control and micromotion patients overall and for three subgroups of interest: a) low-risk patients – closed and low-severity open fractures (Gustilo-Anderson grade I) with no biological comorbidities (e.g. smoking, diabetes, systemic disease, etc.); b) high-risk patients – high-severity open fractures (Gustilo-Anderson grade II and above) and all patients with biological comorbidities, regardless of injury type; and c) biological comorbidities patients – closed and low-severity open fractures (Gustilo-Anderson grade I) with biological comorbidities.

Considering all patients with CT analysis, there was not a significant difference in VTR between the control and micromotion groups ($p = 0.355$; see Figure 5). Comparisons of VTR for control and Apex patients in the subgroups described above can be found in Figure 6. For the low-risk subgroup (Figure 6a), there was not a difference between groups based on the 12-week CT ($p = 0.467$). For the mixed high-risk subgroup (high-grade open fractures and patients with comorbidities; Figure 6b), VTR clearly tended to be higher in the micromotion group, but the difference was not significant ($p = 0.054$). Considering patients who had low-risk injuries coupled with biological comorbidities (Figure 6c), the median VTR in the micromotion group was 103% (IQR 94% to 110%) versus 81% (IQR 72% to 88%) in the control, which was a statistically significant difference ($p = 0.008$). A post-hoc power analysis on the comorbidities subgroup VTR data showed that for a one-tailed Mann-Whitney U test with an effect size $d = 1.76$ at a significance level of 0.05, the achieved power for the significant

difference between control and micromotion fixation was 96%.

Complete patient-reported outcomes measures (PROMs) results are included in the Supplementary Material. All PROMs were non-normally distributed, so between-groups testing at each timepoint was conducted using Mann-Whitney U tests. There were no significant differences between the control and micromotion groups for any component score at any timepoint, although the component scores for mobility, self-care, and usual activities tended to be lower (indicating less difficulty) in the micromotion group at all timepoints.

Discussion

All micromotion patients united without additional interventions (i.e. there were zero nonunions). By comparison, the 11% nonunion rate in the control group is consistent with expectations for the current standard of care from the clinical literature. One limitation of this finding is that the sample sizes in this study are small, especially given the complex aetiology of nonunion. In a larger sample of micromotion patients, it would be unsurprising to have a non-zero nonunion rate.

Patients treated with micromotion appeared to heal significantly faster compared to the control group, based on union time and the proportion united at each follow-up. The incidence of delayed union was also significantly lower with micromotion. One key limitation of this finding is that time to union is a subjective measure that is determined considering both radiological signs (callus bridging) and clinical signs (patient-reported pain and mobility). Timing of recall examinations can vary, with patients occasionally missing exams due to non-clinical factors. Even with these potential sources of uncertainty, it is reasonable to assume that patients who are experiencing healing difficulties are likely to follow up for longer if they are in discomfort due to lack of bone consolidation.

Diagnosis of nonunion is also challenging, with acknowledged inconsistency in the timing and criteria used to make this decision.[25,26] The five nonunions that occurred in the control group were reoperated at a minimum of 38 weeks (about nine months), which represents a conservative waiting period consistent with widespread clinical practice to exclude the possibility of spontaneous union. For fractures that united without intervention, the union times recorded for the control group are also entirely consistent with union times reported in a recent large cohort study.[3]

Considering the objective measurements obtained from the CT scans, most low-risk patients had good structural bone healing by 12 weeks with no apparent difference between implant groups. For high-risk patients including high-grade open fractures and patients with comorbidities (Figure 6b), there was a trend toward higher VTR in the micromotion group. This difference was not significant and the implications are limited due to the heterogeneity of the patients with open fractures. In contrast, the effect of comorbidities on healing was clearly demonstrated in VTR testing. Considering only the control group, patients with comorbidities lagged behind low-risk patients in their structural bone healing. More than 75% of control patients with comorbidities had VTR scores below 90%, compared to the 75% of low-risk control patients who had VTR scores above 90% at the same timepoint. Notably, micromotion patients with comorbidities had significantly higher VTR scores compared to controls with comorbidities (Figure 6c) and they exhibited structural healing on par with both low-risk control and low-risk micromotion patients.

One significant limitation of this study is its non-randomized design. Both implant systems studied were commercially available in the hospital during the period of investigation. The choice of implant for each case was completely at the discretion of the treating surgeon on call and this was not controlled in the study design. These choices may have been influenced by factors unrelated to implant mechanics, such as familiarity with instrumentation and personal preference. To assess the impact of non-randomization on the data reported here, we made sure to account for every tibial nail implanted during the study period, then to compare patient demographic details, injury characteristics, nonunion risk (NURD score), and fracture reduction quality between the implant groups. We found no differences between the control and micromotion patients based on any of these measures.

An additional limitation of this study is that CT scans were only obtained at one timepoint (12 weeks). At this timepoint, for patients without significant injury risks or comorbidities, the majority achieved a normalized VTR score of 90% or higher, regardless of the implant used (Figure 6a). In interpreting this finding, it is critical to note that the VTR test cannot be used to date a union and cannot distinguish between a recently bridged fracture and one that has more advanced remodelling. The use of two low-dose CT scans may have been more effective at distinguishing between faster and slower healers, particularly within the low-risk groups.

This study was also under-powered to detect differences in PROMs. The largest difference was for the EQ-5D mobility component score at six weeks, with a mean difference of -0.5 for micromotion (mean 2.7) compared to control (mean 3.2). A post-hoc power calculation suggests that the minimum sample size in each group to detect this difference at 80% power and a significance level of 0.05 would have been 77 patients. All other component scores had smaller mean

differences and would therefore require even larger sample sizes to detect significant differences.

In conclusion, this pilot study found no concerns with safety or efficacy associated with micromotion tibial nailing. Clinical outcomes with micromotion fixation were equivalent to and in some instances superior to the current standard of care, static interlocked IM nailing. The findings suggest that potential benefits of micromotion could include an accelerated time to union and reduced incidence of nonunion. These findings are limited by the small samples and non-randomized study design in this pilot series, but they suggest that designing a controlled trial to test hypotheses pertaining to faster healing and reduced nonunions with micromotion fixation would be appropriate and substantially supported by these initial findings.

Take home message

- Delayed healing and nonunion remain persistent problems in tibial nailing. In this pilot study, mechanical stimulation through controlled micromotion fixation promoted faster healing, particularly in at-risk patients, and merits further clinical investigation.

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Supplementary material

Complete results of patient-reported outcomes (EuroQol five-dimension five-level scores) at all study timepoints.

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