Clinical/Basic Science Research Article

OPEN

Predictors of nonunion for transverse femoral shaft fractures treated with intramedullary nailing: a SIGN database study

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Abstract

Introduction: Nonunion is a common postfracture complication resulting in decreased quality of life for patients in resource-limited settings. This study aims to determine how age, sex, injury mechanism, and surgical intervention affect the rate of nonunion in transverse femur fractures treated with a SIGN intramedullary nail (IMN).

Methods: A retrospective study was conducted using the SIGN online surgical database. All patients older than 16 years with simple transverse (<30 degrees), open or closed, femur fractures treated using a SIGN IMN between 2007 and 2021 were included. Our primary outcome of nonunion was measured with the modified Radiographic Union Scale for Tibial fractures (mRUST); scores ≤9 of 16 defined nonunion. The secondary outcome was squat depth. Outcomes were evaluated at follow-up appointments between 240 and 365 days postoperatively. Univariate and multivariate analysis were used for statistical comparison.

Results: Inclusion criteria were met for 182 patients. The overall radiographic union rate was 61.0%, and a high proportion (84.4%) of patients could squat with their hips at or below the level of their knees. Older age, retrograde approach, and fracture distraction were associated with nonunion, but sex, injury mechanism, and other surgical variables were not.

Conclusion: Poor reduction with fracture distraction was associated with a higher rate of nonunion. Loss of follow-up may have contributed to our overall union rate; however, we observed high rates of functional healing using the SIGN IMN.

Level of evidence: IV.

Keywords: nonunion, transverse femur fracture, global health, trauma

1. Introduction

Traumatic injuries are a significant cause of morbidity and mortality in low- and middle-income countries (LMICs).[1] These injuries are commonly due to high-energy mechanisms such as road traffic accidents and often result in long bone fractures.[2] Of these long bone fractures, femur fractures have a worldwide incidence between 15 and 44.8 per 100,000 per year mostly occurring because of motor vehicle accidents.[3–5]

In LMICs, traumatic injuries are common and access to surgical resources is often limited, resulting in delays to surgical care and increased complication rates.[6] To mitigate these disparities in surgical care, SIGN Fracture Care International has developed an intramedullary nail (IMN) to be used in LMICs without the need for fluoroscopy.[7,8] The SIGN IMNs are donated to LMICs worldwide, with the expectation that local surgeons will record patient demographics and surgical outcomes to be used for quality improvement and data analysis.[9]

Nonunion after femoral shaft fractures has been cited to be as high as 6% in the United States.[10] In the experience of the senior author (L.Z.), transverse fractures have a higher risk of nonunion compared with other patterns after treatment with the SIGN IMN, although few studies have evaluated this association. Slow healing in transverse fractures has been attributed to increased disruption of the periosteum and decreased surface area of contact.[11] Previous studies have not specifically examined risk factors for nonunion among patients with this injury pattern. We hypothesized there would be modifiable treatment factors for nonunion that are unique to the transverse pattern such as surgical approach, nail length, diameter, canal fill, and reduction quality.

This study aims to identify which patient, injury, and treatment factors contribute to nonunion of transverse femur fractures treated with a SIGN intramedullary nail.

L. Zirkle is the President of the Board of Directors of SIGN Fracture Care International. D. Shearer is the Vice President of Board of Directors of SIGN Fracture Care International (unpaid). T. Smith is an Engineering Manager at SIGN Fracture Care International. For the remaining authors, no conflict of interests was declared. There was no funding involved for the research and production of this manuscript.

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OTAI (2023) e281

Received: 28 September 2022 / Received in final form: 25 May 2023 / Accepted: 14 June 2023
Published online 25 July 2023

http://dx.doi.org/10.1097/OI9.0000000000000281

2. Methods

2.1. Study Design and Ethical Approval

The SIGN Online Surgical Database (SOSD), a global orthopaedic trauma database, was used for a retrospective study of patients sustaining isolated transverse femur fractures (OTA/AO Fracture and Dislocation Classification 32-A3) treated with a SIGN IMN. This work was conducted with ethical approval obtained by the University of California San Francisco Human Subjects Research Internal Review Board (IRB# 20-31140).

2.2. Patient Selection

All data from the SOSD from 2007 to 2021 were manually filtered for transverse femur fractures and extracted using Metabase v0.41.4 (Metabase, Inc v0.41.4, San Francisco, CA). This filter was established based on the OTA/AO Fracture and Dislocation Classification, and all simple, transverse (<30 degrees), diaphyseal femur fractures (Classification 32-A3) were included; fractures that did not meet these characteristics, such as oblique or multifragmentary fractures, were not included. Using Metabase, a search query identified 1066 patients who were deemed eligible for review based on their surgical records of having transverse femoral fractures treated with either the standard or fin SIGN IMN. The SIGN fin nail is similar to the SIGN standard intramedullary nail, except it does not require distal interlocking screws. To achieve distal fixation, the fin nail has an enlarged, fluted distal end aimed to achieve interference fit without the need for interlocking screw placement.[12] Exclusion criteria were patients younger than 16 years and with hip fractures. Cases were considered incomplete and excluded from the analysis if there was no follow-up between 240 and 365 days postoperatively, uninterpretable radiographs, and incomplete charts (ie, missing radiographs, missing patient demographic information) (Fig. 1).

Case information regarding patient age, sex, injury details, implant dimensions as well as surgical approach and fracture location were entered by treating surgeons. Complications including infection and implant breakage were also self-reported by the treating surgeons prospectively.

2.3. Evaluation of Radiological and Clinical Healing

This study evaluated fracture healing based on radiographic review using the modified Radiographic Union Scale for Tibial fractures (mRUST) (Fig. 2). This methodology has a high interobserver reliability and was previously established as an effective measure to assess union and bridging callus formation in long bone femur fractures treated with IMN or plate fixation.[7,13,14] The cases and respective radiographs used in this study were assessed by 4 reviewers (B.C., B.J., K.P., T.S.).

Based on previous work, we dichotomized fracture healing using mRUST scores into 2 groups: scores ≤9 were considered "nonunion," and scores >9 were considered "union."[7,14,15] The Food and Drug Administration's (FDA) definition of nonunion is a fracture that persists for a minimum of 9 months without signs of healing for 3 months.[16] Thus, radiographs were evaluated using the mRUST methodology at patient's follow-up appointments no earlier than 240 days postoperation and no later than 365 days postoperation (Fig. 2).

Patient radiographs were further evaluated based on the quality of surgical reduction and IMN implantation at the patient's initial follow-up after surgery. Two independent reviewers (B.C., B.J.) evaluated surgical reduction quality by scoring the radiograph at the fracture site and determining whether the fracture showed evidence of "distraction" or "no distraction" at the fracture line (Fig. 3). Distraction at the fracture line was determined by using the width of the interlocking screws (4.5 mm) viewed in the radiograph. Each reviewer labeled the radiograph as "distracted" if the width between the proximal and distal femoral cortex was wider than approximately half the width of the interlocking screw (2.25 mm) used in either the lateral or anterior-posterior views (Fig. 3). Similarly, 2 independent reviewers (B.C., B.J.) also assessed IMN canal fill by evaluating the space between the nail and adjacent cortical bone at the fracture site in lateral and anterior-posterior views. Canal fill scores were structured as follows: 0 = visible canal space in 2 views; 1 = visible canal space in 1 view; 2 = both views show a tight-fitting nail with little to no space between the nail and canal wall. For distraction and canal fill assessments, interrater reliability was assessed for absolute agreement between each reviewer; corresponding Kappa coefficients for each rating system were 0.86 and 0.82, respectively. Discordant evaluations were resolved by consensus and updated for final analysis.

Images of patients in an active knee range-of-motion squat (Squat and Smile or S&S) has been previously established as an effective method in determining bone healing and clinical weight-bearing in patients undergoing IMN of the femur.[17] We assessed S&S images of patients at the same follow-up appointment in which mRUST was measured and scored each patient's ability to squat below their knee line. Scoring of active knee range-of-motion images was performed by 2 independent reviewers (B.C., B.J.). Each image was scored on a 2-part scale: Patients were considered "functionally healed" if they could squat at or below their knee level, and patients were considered "not functionally healed" if their squat level was above their knee level.

2.4. Statistical Analysis

Analysis included descriptive statistical analysis, chi-squared, and two-sample t-tests to examine the injury and treatment factors that influence healing of transverse femur fractures. A multivariate logistic regression model was used to control for confounding variables after predictor variables were identified through univariate analysis. The regression model's goodness of fit was tested using Hosmer-Lameshow chi-squared tests. All statistical analyses were completed using SPSS software version 28.0 (SPSS Inc., Chicago, IL).

3. Results

3.1. General Outcomes and Demographics

Nine hundred twenty-two patients (922) were initially included based on the eligibility criteria, but only 182 patients had adequate follow-up and met radiographic requirements. The total follow-up rate was 19.7%. These 182 patients were then included in our final analysis. The average number of follow-ups was 4.67, and the mRUST and S&S tests were assessed at an average of 300 days postoperatively (Table 1). Most of the patients were male (75.8%) with a mean age of 31. Transverse femur fractures of the middle third of the femur

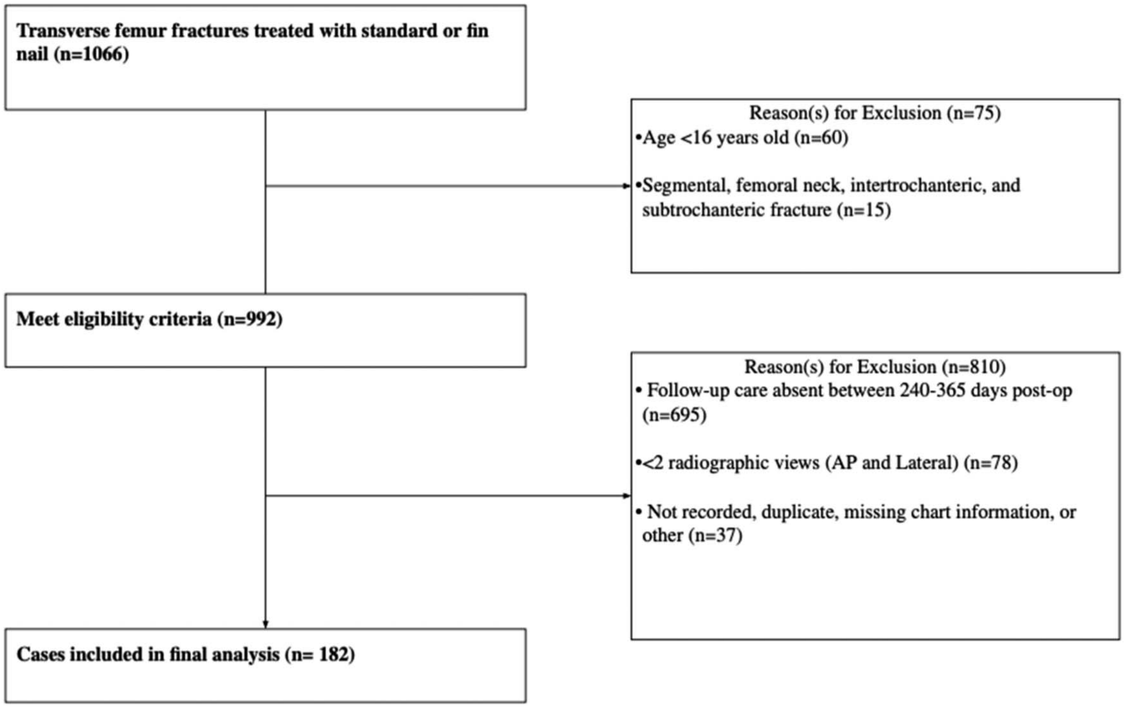

Figure 1. CONSORT diagram. Flowchart demonstrating methodology of selection and chart review of eligible patients. AP = anteroposterior.

were the most common (62.6%). Road traffic accidents were the most common mechanism of injury (89.6%) (Table 1). Transverse fractures were treated most often with an antegrade (62.1%) SIGN standard IMN (86.8%) (Table 2). Postoperatively, there were 3 reported infections documented (1.6%), and 2 patients had broken distal screws found during the postoperative period requiring revision (1.1%).

Within our follow-up period, 111 of 182 patients (61%) were considered healed by mRUST scores. Patients who did not heal during our follow-up period were tracked retrospectively to determine the time of healing. Of the remaining 39% of patients (n = 71) who had mRUST scores ≤9, only 16.9% of these patients (n = 12) returned for follow-up appointments until their fractures were healed, which took an average of 737 days. Using the S&S test to assess functional healing, 15.5% of patients (n = 14) who were unable to squat during our follow-up period took an average of 401 days to squat with only 21.4% of these (n = 3) patients following up until they were able to adequately squat. In addition, there was significant correlation between the mRUST score and the S&S test ($P = 0.008$).

In univariate analysis of patient factors, only older age was associated with nonunion ($P = 0.034$). There was no significant difference in the likelihood of nonunion based on sex ($P = 0.767$), mechanism of injury ($P = 0.818$), or fracture type ($P = 0.121$). Squat depth did not differ based on any factor including sex ($P = 0.767$), mechanism of injury ($P = 0.818$), or fracture type ($P = 0.121$).

Among treatment factors, retrograde nail insertion ($P = 0.01$) and fracture distraction ($P < 0.001$) were associated with nonunion. There was no significant difference in risk of nonunion for method of fracture reduction (open vs. closed, $P = 0.792$), nail type (fin vs. standard nail, $P = 0.871$), nail length ($P = 0.661$), nail diameter ($P = 0.10$), or canal fill ($P = 0.584$). Overall, initial reduction quality was identified as "no distraction" between fracture segments in 92.3% of patient cases, and fracture segments with "distraction" were found in 7.7% of cases. When analyzing squat depth between groups, shorter nails and retrograde approach were associated with a higher rate of inability to squat ($P = 0.047$, $P = 0.030$). There was no significant relationship in the ability to squat and reduction type ($P = 0.594$), nail type ($P = 0.181$), nail length ($P = 0.279$), nail diameter ($P = 0.679$), reduction quality ($P = 0.594$), or canal fill ($P = 0.912$) (Table 3).

To control for confounding, a multivariate logistic regression model determined the factors most strongly associated with radiographic nonunion were retrograde surgical approach and fracture distraction at first postoperative follow an odds ratio of 2.2 (95% confidence interval [CI], 1.13–4.38) and 23.7 (95% CI, 5.27–106.1) (Table 4).

4. Discussion

This study aimed to identify risk factors of nonunion among patients with transverse femur fractures treated using the SIGN IMN. We found nonunion was associated with older age, fracture distraction, and retrograde nail insertion. Overall, a large proportion of patients experienced nonunion (39.0%), although many were considered functionally healed with regard to squat depth.

There is not currently a well agreed on criteria for nonunion. While nonunion can be assessed for radiographic, clinical, or functional healing, this study focused primarily on radiographic and functional healing.[14,17,18] Radiographic union and nonunion have been reliably assessed using the mRUST score.[13–15,19] This study found the union rate for transverse femur fractures to be 61.0% based on mRUST score at a minimum of 9-month follow-up. Previous

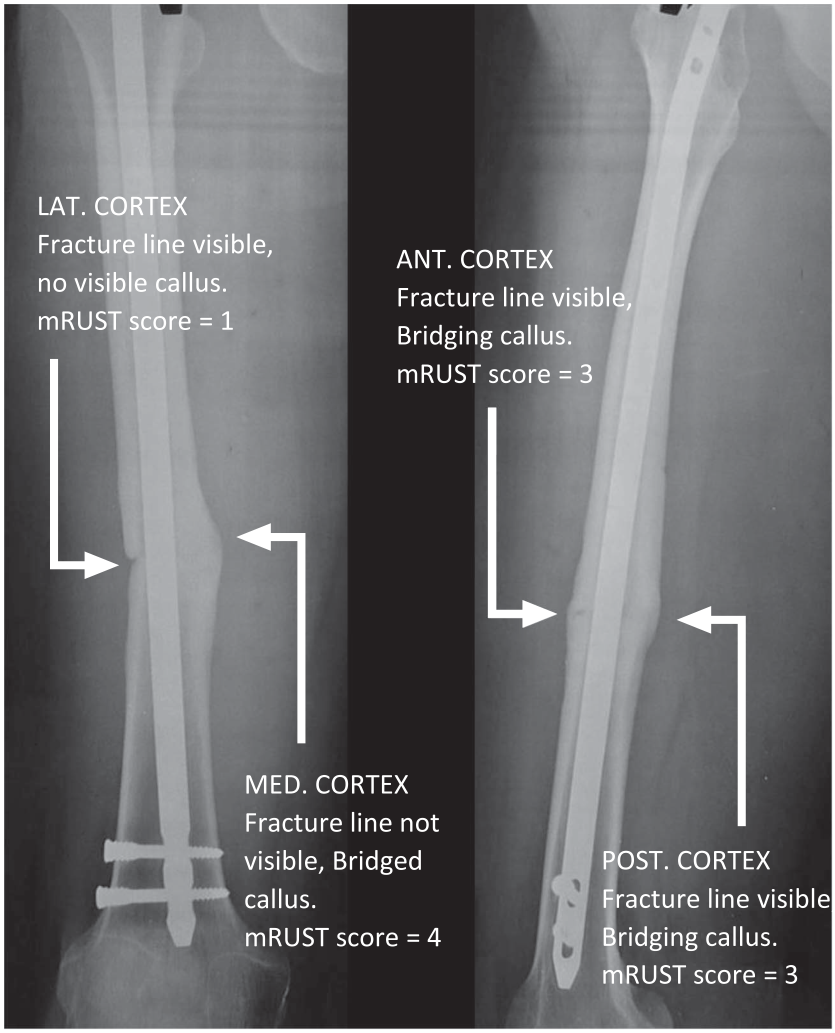

Figure 2. mRUST scoring breakdown. Anteroposterior (Left) and lateral (Right) radiographs of femur with SIGN IMN detailing mRUST scoring breakdown. Arrows and text refer to different stages of callus formation and their subsequent mRUST score.

investigations using the SIGN IMN in long bone fractures found union rates, defined clinically or radiographically, to be 69%–99%.[20–24] Although we anticipated a high nonunion rate in this cohort of patients with transverse fractures, we suspect this is primarily explained by a strong selection bias, whereby patients who are experiencing pain or other complications are more likely to return for later follow-up. Furthermore, owing to our specific follow-up period, we did not include 171 patients who were considered radiographically healed using mRUST before 240 days postoperation. The inclusion of these patients to our 182-patient cohort would have increased our union rate to 79.9% of the new total of 353 patients.

In prospectively collected data in clinical studies, the union rate is much higher.[24] Functional healing has been assessed using the S&S test, the patient's ability to perform an unassisted active knee range-of-motion squat, which we have shown to indicate earlier healing compared with radiographic evaluation, but its utility as a measure of healing is controversial.[17,20,25,26] Of the 84 patients in our cohort who had an S&S test, 83.3% of them were considered functionally healed which is similar to Scuito et al[17] who found 80.2% of their 89 patient cohort with femoral fractures were able to pass the S&S test at 24 weeks. Our findings comparing S&S with radiographic healing showed a significant correlation between the 2 tests which may add validity to the S&S examination. Further research is needed to compare the efficacy in replacing standard radiographs for postoperative management as substituting S&S testing for radiographic evaluation in regard to femur fracture healing maybe helpful to limit financial burden in resource-limited settings.

Despite fracture healing being a multifactorial biomechanical process, surgeons and their choice of technique and equipment have been shown to affect the course of fracture healing.[27] Our findings are similar to the investigation by Serrano et al[28] in which they assessed femur fractures and found no relationship between femur nonunion and canal fill, nail length, or nail diameter. In contrast to our findings, Serrano et al[28] observed significant differences in nonunion rates based on initial femoral fracture locations: Proximal femur fractures were 5.6 times more likely to develop nonunion than distal or midshaft fractures and found no

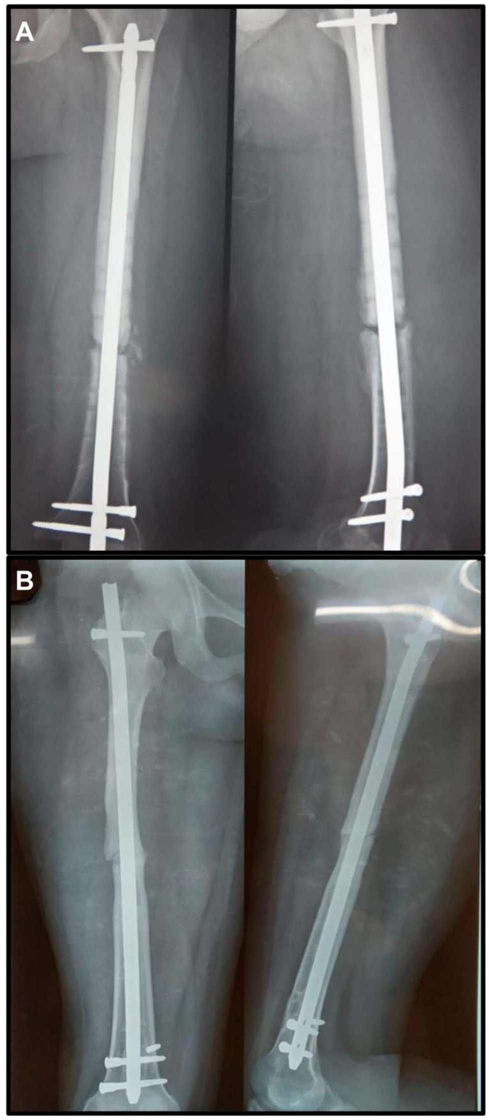

Figure 3. Scoring of postoperative IMN gapping. This figure displays examples of the dichotomized methodology used to determine fracture distraction: Image "A" comprised 2 radiographs depicting a "distracted" fracture (width between proximal and distal bone is more than half of the width of interlocking screws) in both the anteroposterior (top right) and lateral (top left) views, and image "B" are 2 radiographs depicting a "no distraction" fracture (width between proximal and distal bone is less than half of the width of interlocking screws) in both the anteroposterior (bottom left) and lateral views (bottom right).

significant relationship between nonunion and IMN insertion site. In a prospective study using SIGN IMN to treat femur fractures, proximal fracture location with varus malreduction was 8.2 times more likely to have reoperation due to nonunion; however, proximal femur fractures alone were not associated with reoperation.[24] Our study did not observe a relationship between fracture location and nonunion, but we did find an association between patients having retrograde IMN approach and nonunion. A prospective comparison of retrograde and antegrade IMN by Ostrum et al[29] also found that antegrade femurs healed faster than those treated with retrograde nailing ($P < 0.05$). However, the association of nonunion healing with specific nailing techniques has not been established.[10,30]

Primary prevention of femur nonunion has been clinically established and includes infection control, precise surgical hardware that provides stability and matches patient's anatomy, and compliance to postoperative protocols. Operative techniques such as the backslap technique has also been found to be effective in correcting fracture diastasis and promoting fracture union during the index operation.[31] Exchange nails, dynamization, and plating techniques are secondary surgical interventions that can help treat nonunion fractures after IMN.[32–34]

The results of our study should be considered in the context of its limitations. One of the major drawbacks in this study is the loss to follow-up. Only patients who had radiographs and follow-up care between 240 and 365 days postoperatively were included. This likely resulted in selection bias because patients who healed clinically or radiographically before 240 days may not have returned for follow-up care likely influencing our nonunion rate. Whereas patients with pain or other functional limitations are more likely to return, particularly in lower resource settings. Our follow-up rate of 19.7% can be contrasted to another study assessing fracture

TABLE 1

Cohort demographics

	Total n = 182	Healed (mRUST >9) n = 111	Nonunion (mRUST ≤9) n = 71	*P**
Mean age (SD)	31.0 (11.7)	29.7 (12.1)	32.9 (10.9)	0.034†
Sex				0.767
Male	138	85 (61.6%)	53 (38.4%)	
Female	44	26 (59.1%)	18 (40.9%)	
Injury cause				0.818
Road traffic accident	163	100 (61.3%)	63 (38.7%)	
Fall	13	7 (53.8%)	6 (46.2%)	
Gunshot	1	1 (100%)	0 (0%)	
Other	5	3 (60%)	2 (40%)	
Transverse fracture location				0.121
Distal	40	20 (50%)	20 (50%)	
Middle third of femur	114	76 (66.7%)	38 (33.3%)	
Proximal	28	15 (53.6%)	13 (46.4%)	
Number of follow-ups (mean, SD)	4.67	4.59 (2.1)	4.77 (2.0)	0.566†
Average days postoperatively of mRUST/S&S assessment (SD)	300.0	302.0 (35.9)	295.1 (35.2)	0.208†
Injury to admission days	45.4	48.4	40.8	0.368

* Analysis completed using chi-square tests unless otherwise stated.
† Student t test used for analysis.

care in 331 patients using SIGN IMNs in LMICs which had a follow-up rate of 82.2% after 1-year postoperation.[24] The latter was a prospective study that actively enrolled and followed patients during the study's timeline of 1 year. However, many other studies of this population in LMICs have struggled with follow-up.[35] Poor follow-up was exacerbated by missing or poor quality radiographs, which further limit sample size and may introduce bias. Second, the OTA/AO Fracture Classification for long bone fractures to our knowledge have not specifically evaluated the reliability of the

TABLE 2

Treatment factors assessed using mRUST

	Total n = 182	Healed (mRUST >9) n = 111 (61.0%)	Nonunion (mRUST ≤9) n = 71 (39.0%)	*P**
Surgical approach				0.01
Antegrade	113	77 (68.1%)	36 (31.9%)	
Retrograde	69	34 (49.3%)	35 (50.7%)	
SIGN nail used				0.871
Fin nail	24	15 (62.5%)	9 (37.5%)	
Standard nail	158	96 (60.8%)	62 (39.2%)	
Infection				0.322
Yes	3	1 (33.3%)	2 (66.7%)	
No	179	110 (61.5%)	69 (38.5%)	
Fracture reduction				0.792
Closed	14	9 (64.3%)	5 (35.7%)	
Open	168	102 (60.7%)	66 (39.3%)	
Nail length				0.661
240 mm–300 mm	20	12 (60%)	8 (40%)	
320 mm–360 mm	101	59 (58.4%)	42 (41.6%)	
380 mm–420 mm	61	40 (65.6%)	21 (34.4%)	
Nail diameter				0.10
8 mm	18	7 (38.9%)	11 (61.1%)	
9 mm	72	52 (46.8%)	20 (27.8%)	
10 mm	70	36 (51.4%)	34 (48.6%)	
11 mm	16	13 (81.3%)	3 (18.7%)	
12 mm	6	3 (50%)	3 (50%)	
Reduction quality at first preoperative follow-up				<0.001
No distraction	168	110 (65.5%)	58 (34.5%)	
Distraction	14	1 (7.1%)	13 (92.9%)	
Canal fill at first preoperative follow-up				0.584
No gaps	81	48 (59.3%)	33 (40.7%)	
Gap in 1 view	46	31 (67.4%)	15 (32.6%)	
Gap in 2 views	55	32 (58.2%)	23 (41.8%)	

* Analysis completed using chi-square tests unless otherwise stated.

TABLE 3

Treatment factors assessed using Squat and Smile

	Total n = 90	Squat and Smile at or below 90 degrees n = 76 (84.4%)	Squat and Smile above 90 degrees n = 14 (15.6%)	*P**
Surgical approach				0.030
Antegrade	61	55 (90.2%)	6 (9.8%)	
Retrograde	29	21 (72.4%)	8 (27.6%)	
SIGN nail used				0.181
Fin nail	10	7 (70%)	3 (30%)	
Standard nail	80	69 (86.3%)	11 (13.8%)	
Infection				0.666
Yes	1	1 (100%)	0 (0%)	
No	89	75 (84.3%)	14 (15.7%)	
Fracture reduction				0.440
Closed	8	6 (75%)	2 (25%)	
Open	82	70 (85.4%)	12 (14.6%)	
Nail length				0.047
240 mm–300 mm	13	8 (61.5%)	5 (38.5%)	
320 mm–360 mm	46	41 (89.1%)	5 (10.9%)	
380 mm–420 mm	31	27 (87.1%)	4 (12.9%)	
Nail diameter				0.679
8 mm	6	5 (83.3%)	1 (16.7%)	
9 mm	40	32 (80%)	8 (20%)	
10 mm	35	30 (85.7%)	5 (14.3%)	
11 mm	6	6 (100%)	0 (0%)	
12 mm	3	3 (100%)	0 (0%)	
Reduction quality at first preoperative follow-up				0.594
No distraction	86	73 (84.9%)	13 (15.1%)	
Distraction	4	3 (75%)	1 (25%)	
Canal fill at first preoperative follow-up				0.912
No gaps	40	34 (85%)	6 (15%)	
Gap in 1 view	28	23 (82.1%)	5 (17.9%)	
Gap in 2 views	22	19 (86.4%)	3 (13.6%)	

* Analysis completed using chi-square tests unless otherwise stated.

OTA/AO definition for transverse fractures compared with other types.[19,36] This may affect the reproducibility in future studies that assess transverse fractures.

Finally, the study team used a new, unvalidated method to assess fracture reduction and make other imaging assessments. To mitigate this issue, we used 2 independent reviewers and provided data on the interrater reliability of these assessments.

In conclusion, transverse femur fractures treated using the SIGN IM nail system in LMIC are associated with a higher risk of nonunion when compared with cohorts of mixed femur shaft fractures treated with standard reamed IM nails in the United States This risk was highest among older patients treated using the retrograde approach with distraction at the fracture site on immediate postoperative radiographs. Fracture distraction, specifically, was strongly associated with nonunion and is within the control of surgeons treating these injuries. Future studies with higher data quality are needed to validate these findings that could directly affect patient care.

TABLE 4

Logistic regression model for predictors of nonunion healing using mRUST

	Odds ratio	95% CI	*P*
Retrograde surgical approach	2.25	1.13–4.38	0.02
Fracture distraction	23.7	5.27–106.1	<0.001

ACKNOWLEDGMENTS

Special thanks to Frank Faultersack, Joel Gillard, and the rest of the SIGN engineers that assisted with this project.

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