

# Assessment of clinical and radiographic outcomes following retrograde versus antegrade nailing of infraisthmic femoral shaft fractures without the use of intraoperative fluoroscopy in Tanzania

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**Objectives:** To compare clinical and radiographic outcomes following antegrade versus retrograde intramedullary nailing of infraisthmic femoral shaft fractures.

**Design:** Secondary analysis of prospective cohort study.

**Setting:** Tertiary hospital in Tanzania.

**Participants:** Adult patients with infraisthmic diaphyseal femur fractures.

**Intervention:** Antegrade or retrograde SIGN intramedullary nail.

**Outcomes:** Health-related quality of life (HRQOL), radiographic healing, knee range of motion, pain, and alignment (defined as less than or equal to 5 degrees of angular deformity in both coronal and sagittal planes) assessed at 6, 12, 24, and 52 weeks postoperatively.

**Results:** Of 160 included patients, 141 (88.1%) had 1-year follow-up and were included in analyses: 42 (29.8%) antegrade, 99 (70.2%) retrograde. Antegrade-nailed patients had more loss of coronal alignment ( $P = .026$ ), but less knee pain at 6 months ( $P = .017$ ) and increased knee flexion at 6 weeks ( $P = .021$ ). There were no significant differences in reoperations, HRQOL, hip pain, knee extension, radiographic healing, or sagittal alignment.

**Conclusions:** Antegrade nailing of infraisthmic femur fractures had higher incidence of alignment loss, but no detectable differences in HRQOL, pain, radiographic healing, or reoperation. Retrograde nailing was associated with increased knee pain and decreased knee range of motion at early time points, but this dissipated by 1 year. To our knowledge, this is the first study to prospectively compare outcomes over 1 year in patients treated with antegrade versus retrograde SIGN intramedullary nailing of infraisthmic femur fractures.

Level of Evidence: III

**Keywords:** antegrade, developing countries, infraisthmic femur fracture, intramedullary nail, orthopaedic surgery, retrograde, trauma

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## 1. Introduction

The global burden of femoral shaft fractures is high with up to 2.9 million fractures per year.<sup>[1]</sup> Low- and middle-income countries (LMICs) are disproportionately affected,<sup>[1]</sup> such as in Tanzania where the annual incidence of femoral shaft fractures is as many as 18.4 per 100,000.<sup>[2]</sup> The gold standard treatment for femoral shaft fractures is intramedullary nailing (IMN),<sup>[3,4]</sup> which can be done via antegrade or retrograde techniques. Two recent meta-analyses concluded that both techniques produce equivalent outcomes and lead to high union rates.<sup>[5,6]</sup> While previous prospective trials have broadly addressed antegrade versus retrograde nailing in femoral shaft fractures,<sup>[7]</sup> lack of consensus remains regarding best practices for fixation technique for infraisthmus femoral shaft fractures, warranting further exploration.

Of particular interest in distal fractures are infraisthmus fractures, defined as occurring below the femoral isthmus and above the femoral condyles.<sup>[8]</sup> Infraisthmus fractures show increased risk of nonunion,<sup>[9]</sup> which may be compounded in those treated with antegrade nailing due to mechanical instability in the distal segment and loss of alignment. Comparatively, retrograde nailing may decrease the risk of malalignment in infraisthmus femur fractures due to a longer functional length in fracture fragments, thereby providing an additional point of fixation for the intramedullary nail to engage the distal femur.<sup>[8,10]</sup> To our knowledge, only 1 study has been performed to compare antegrade and retrograde nailing of infraisthmus femur fractures.<sup>[11]</sup> This study showed no difference in malalignment between techniques, but conclusions were limited by short follow-up, few outcome measures, and relatively small sample size.<sup>[11]</sup>

The risk of malalignment in infraisthmus femur fractures is of particular concern in LMICs where intraoperative imaging may not be available. As a result, IMN is often done without the use of intraoperative fluoroscopy,<sup>[12]</sup> complicating fracture care in numerous ways, including hindering assessment of reduction quality and preventing conventional intramedullary nail interlocking techniques. Surgeons in LMICs may rely on implants, such as the SIGN intramedullary nail, that are designed to address these challenges. The SIGN intramedullary nail allows for insertion without image intensifiers by utilizing an external jig with a targeting arm for interlocking screw placement<sup>[12]</sup> though unlike current retrograde femoral nail designs used in HICs, the SIGN nail interlocking screws are limited to 2 proximal and 2 distal screws, all oriented in a single plane (lateral to medial) (Fig. 1A, B). Though widely used in LMICs<sup>[13]</sup> with high union rates,<sup>[12]</sup> the relative merits of antegrade versus retrograde techniques using the SIGN nail in infraisthmus fractures are unknown. Achieving adequate distal fixation of infraisthmus femur fractures nailed using an antegrade technique may be more difficult, a problem that is exacerbated in the absence of fluoroscopy to ensure maximal nail length in the distal fragment.

To our knowledge, no prior studies have compared the antegrade and retrograde technique specifically in infraisthmus fractures treated with the SIGN nail. Further, existing studies of non-SIGN implants often followed patients for less than 1 year and did not use validated instruments. There is a need for additional research to address this gap in the literature, particularly in LMIC settings, where both the burden of femur fractures is high<sup>[2]</sup> and the use of SIGN nails is common.<sup>[12,13]</sup>

The purpose of this study was to conduct a secondary analysis of prospectively collected data to evaluate loss of alignment after antegrade compared with retrograde nailing of infraisthmus femoral shaft fractures without the use of intraoperative fluoroscopy in Tanzania.

## 2. Patients and methods

A prospective cohort study was conducted at a high-volume tertiary referral hospital in Dar es Salaam, Tanzania,<sup>[14]</sup> from July 2012 to July 2013. Institutional review board approval was obtained from the National Institute for Medical Research (NIMR) in Tanzania and the Committee for Human research at the partnering US institution, and the study was registered at ClinicalTrials.gov (NCT01548456).<sup>[14]</sup> Skeletally mature patients with diaphyseal femoral fractures (OTA/AO type 32)<sup>[15]</sup> were screened and enrolled postoperatively.

The comparison between antegrade and retrograde nailing was an unplanned secondary analysis of prospectively collected data. Patients were included if they had an infraisthmus femoral shaft fracture, were treated with intramedullary nailing, and had follow-up at 1 year (Table 1). Fractures were determined to be infraisthmus if they occurred in the distal half of the femur,<sup>[8]</sup> and only shaft fractures were included. AO/OTA type 33 fractures were not included (Fig. 1C). Data collected at enrollment included age, gender, smoking status, BMI, and fracture location. Surgical fixation was conducted without the use of fluoroscopy for the placement of either the SIGN Standard Nail (SIGN Fracture Care International, Richland, WA) or SIGN Fin Nail.<sup>[16]</sup> While both nails use an external jig for placement of interlocking screws close to the start site, fixation remote from the starting point of the nail is achieved through placement of interlocking screws using an external jig for the Standard nail and through interference fit for the Fin nail.<sup>[12]</sup> Antegrade or retrograde technique, nail type, diameter, and length, and number of proximal and distal interlocking screws were at the discretion of the treating surgeon.

Follow-up visits were conducted at 6, 12, 24, and 52 weeks postoperatively. Secondary outcomes of the prospective cohort study were evaluated, including pain, health-related quality of life (HRQOL), radiographic healing, alignment, and knee range of motion (ROM). All patients were allowed to bear weight as tolerated postoperatively. Physiotherapy was not routinely available.

### 2.1. Patient-reported outcomes

HRQOL was evaluated using the Euro-Qol group EQ-5D-3L index<sup>[17]</sup> which was administered in the validated Swahili version. Baseline HRQOL was established at enrollment with the validated method<sup>[18]</sup> of using the EQ-5D to help patients recall their preinjury health state. Overall pain level was evaluated using the Euro-Qol Visual Analogue Scale (VAS) score, and patients were asked to indicate the location of reported pain.

### 2.2. Radiographic healing and alignment

Orthogonal radiographs were obtained preoperatively, postoperatively, and at all follow-up visits. Coronal and sagittal plane angulation was evaluated for all postoperative radiographs. Adequate alignment was defined as less than or equal to 5 degrees of angular deformity, measured separately in coronal and sagittal planes. Loss of alignment was defined as transitioning from satisfactory reduction to greater than 5 degrees angular deformity in either the coronal or sagittal plane at any follow-up time point. Translation was not included in assessment of alignment. Degree of radiographic healing was determined using the Radiographic Union Scale in Tibia fractures (RUST) score,<sup>[19-21]</sup> a validated tool for both tibia and femur fractures.



**Figure 1.** SIGN nail and representative infraisthmic fracture radiographs. Panel A shows a SIGN Standard intramedullary nail. Panel B shows a SIGN Fin nail. Source: SIGN Fracture Care International Technique Manual (2012). Panel C shows a representative radiograph of an infraisthmic femoral shaft fracture. Panel D shows a representative radiograph of an antegrade nailed infraisthmic femoral shaft fracture. Panel E shows a representative radiograph of a retrograde nailed infraisthmic femoral shaft fracture. Position of interlocks (proximal or distal) are noted relative to the femur regardless of direction of nail insertion, as indicated in panels D and E.

**2.3. Knee range of motion testing**

Knee ROM was assessed clinically by local providers without the use of a goniometer at each follow-up time point.

**2.4. Data management and statistical analysis**

Study data were collected and managed using Research Electronic Data Capture (REDCap, Nashville, TN), a secure,

<b>Table 1</b>	
<b>Inclusion and exclusion criteria</b>	
<b>Inclusion criteria</b>	<b>Exclusion criteria</b>
1. Skeletally mature patients (>18 years old)	1. OTA Type 33 fracture (based on the rule of squares)
2. Diaphyseal femur fracture (OTA type 32) located in distal half of femur	2. Radiographic or intraoperative evidence of pathologic fracture
3. Treated with intramedullary nailing	3. Prior surgery of affected femur
	4. Delayed presentation (>6 weeks postinjury)
	5. Clinical signs of surgical site infection prior to or during surgery
	6. Severe brain injury (GCS<12)
	7. Severe burns (>10% TBSA or >5% TBSA with full thickness or circumferential injury)
	8. Unlikely to complete follow-up (patient or treating surgeon's discretion)

GCS = Glasgow Coma Scale; OTA = Orthopaedic Trauma Association; TBSA = total body surface area.

web-based software platform designed to support data capture for research studies.<sup>[22,23]</sup> Analyses were performed using Stata statistical software (StataCorp, College Station, TX). Comparisons were made in HRQOL, radiographic healing, knee ROM, pain, and fracture alignment between patients treated with antegrade versus retrograde nailing. Means were compared using unpaired Student *t* test and proportions were compared using Fisher exact test. Significance threshold was  $P < 0.05$ .

### 3. Results

Of 331 patients with diaphyseal femur fractures screened for fracture location, 160 (48.3%) had infraisthmic fractures. Of the patients identified with infraisthmic fractures, 141 (88.1%) were treated via antegrade or retrograde nailing and had follow-up at 1 year, so were included in final analysis. The majority of participants were young, nonsmoking, healthy men with isolated femoral shaft fractures from road traffic injuries (Table 2). Forty-two patients (30%) were treated with antegrade nailing (Antegrade Group) using the Standard SIGN Nail and 99 patients (70%) were treated with retrograde nailing (Retrograde Group). In the Retrograde Group, 33 (34%) were treated with the SIGN

Fin Nail and 65 (66%) with the SIGN Standard Nail (Table 2). There were no significant demographic differences between the Antegrade Group and Retrograde Group (Table 2). Fractures were more proximal in the Antegrade Group than in the Retrograde Group ( $P < .001$ ). When comparing fractures treated with the SIGN Standard Nail, significantly fewer proximal interlocking screws were used in the Antegrade Group compared with the Retrograde Group ( $P < .001$ ) (Table 2).

#### 3.1. Immediate postoperative alignment and subsequent loss of alignment

Adequate postoperative coronal and sagittal angular alignment was achieved in the vast majority of both Antegrade and Retrograde Groups: 93% of all patients had adequate alignment in the coronal plane, and 83% and 92% of Antegrade and Retrograde Group patients had adequate alignment in the sagittal plane, respectively. There was no difference between Antegrade and Retrograde Groups in percent of patients with loss of sagittal alignment within 1 year after surgery ( $P = 1.000$ ). In the Retrograde Group, 1% of patients lost coronal alignment within 1 year after surgery, while 10% of patients in the Antegrade Group lost coronal alignment within 1 year after surgery ( $P = .026$ ). Fracture location was not independently associated with loss of coronal alignment ( $P = .096$ ). Stratified analysis based on fracture location demonstrated that, when considering only the proximal subset of infraisthmic fractures, the Antegrade Group still had significantly increased loss of coronal alignment compared with the Retrograde Group. At 1 year after surgery, 8% ( $n = 8$ ) of the Retrograde Group and 17% ( $n = 7$ ) of the Antegrade group were malaligned in the coronal plane, either immediately postoperatively or at 1 or more follow-up time point, though this difference did not reach statistical significance ( $P = .105$ ). Of these, 60% ( $n = 9$ ) had varus and 40% ( $n = 6$ ) valgus malalignment, without difference between Antegrade and Retrograde groups ( $P = .315$ ).

#### 3.2. Reoperation, health-related quality of life, radiographic healing, knee ROM

At 1 year, there was no difference in the rate of reoperation ( $P = 1.000$ ), with 1 (2%) reoperation in the Antegrade Group and 4 (4%) reoperations in the Retrograde Group. There were no differences in EQ-5D score (Fig. 2A), RUST score (Fig. 2B), or maximum knee extension (Fig. 2C) between Antegrade and Retrograde Groups at any postoperative time point (Supplementary Table 1, <http://links.lww.com/OTAI/A16>). By 1 year follow-up, the average RUST score in both groups surpassed threshold for bony union, as defined by RUST score of greater than 9<sup>[24]</sup> (Fig. 2B) with 65% ( $n = 11$ ) of the Antegrade Group and 77% ( $n = 33$ ) of the Retrograde Group achieving bony union. Patients in the Antegrade Group achieved increased knee flexion ( $P = .021$ ) compared with patients in the Retrograde Group at 6 weeks after surgery, but not at 12, 24, or 52 weeks (Fig. 2D).

#### 3.3. Pain

Between Antegrade and Retrograde Groups, there were no differences at any time point in percent of patients reporting pain (Fig. 3A), overall pain scores (Fig. 3B), or hip or thigh pain (Fig. 3C). Patients in the Retrograde Group reported more knee pain at 6 months postoperatively compared with the Antegrade Group ( $P = 0.017$ ) (Fig. 3D).

**Table 2**

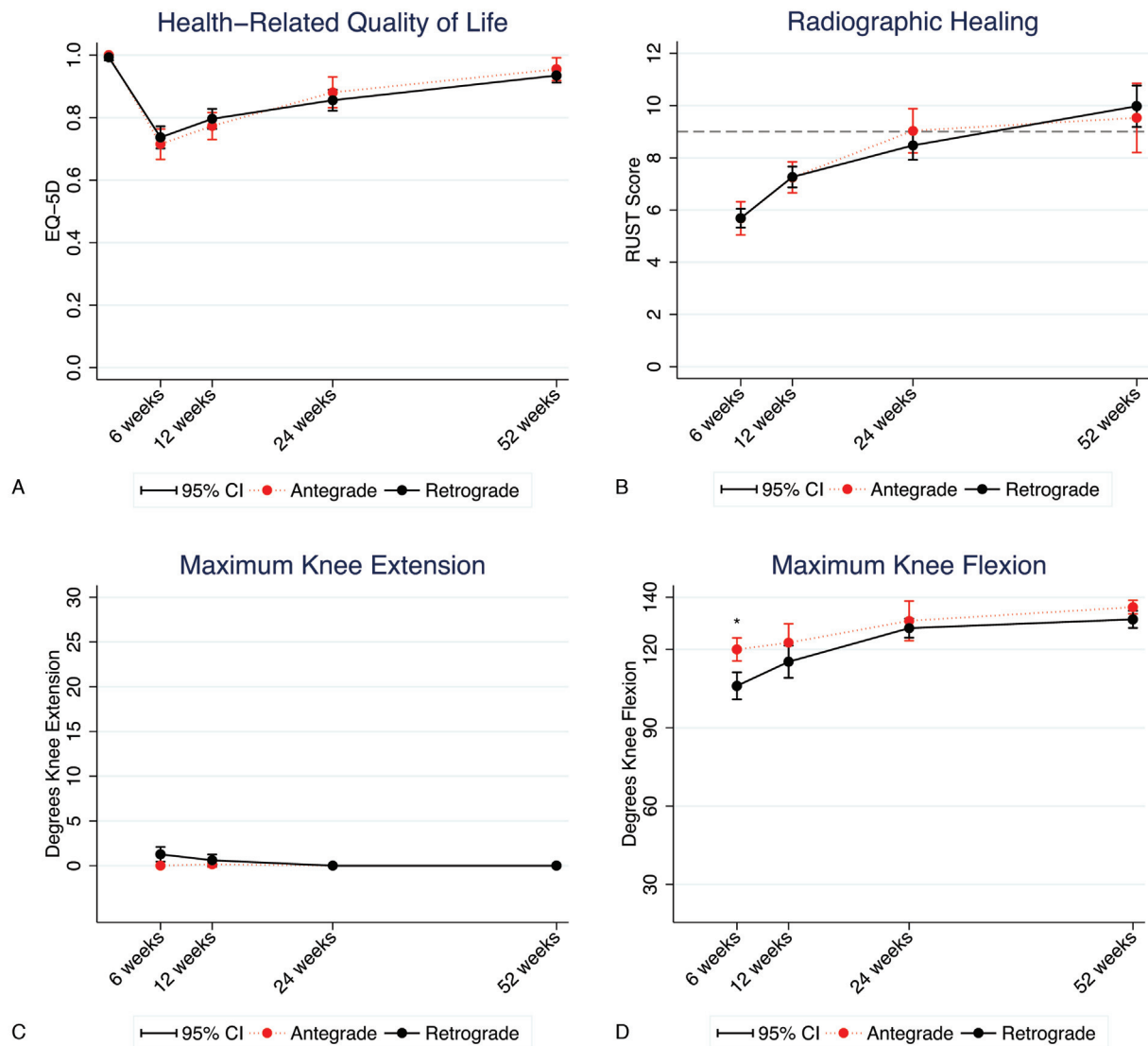
**Patient demographics and implant details**

	Antegrade	Retrograde	P value
N	42	99	
Age, mean (SD)	31.30 (10.58)	32.68 (11.47)	0.510
Gender: male	35 (83%)	82 (83%)	1.000
Smoking status			0.948
Current	5 (12%)	10 (10%)	
Former	4 (10%)	11 (11%)	
Never	33 (79%)	76 (78%)	
BMI, mean (SD)	23.66 (3.19)	23.72 (3.42)	0.920
Mechanism of injury			0.475
Motor vehicle crash	21 (52%)	46 (48%)	
Motorcycle crash	14 (35%)	38 (40%)	
Pedestrian versus auto	0 (0%)	2 (2%)	
Fall from height	5 (12%)	6 (6%)	
Other	0 (0%)	4 (4%)	
Fracture location <sup>†</sup> , mean (SD)	57.86 (7.75)	63.84 (8.75)	<0.001*
Nail type			<0.001*
FIN nail	0 (0%)	33 (34%)	
SIGN nail	42 (100%)	65 (66%)	
Number of proximal screws			<0.001*
0	1 (2%)	0 (0%)	
1	17 (40%)	12 (12%)	
2	24 (57%)	86 (88%)	
Number of distal screws			0.111
0	1 (2%)	0 (0%)	
1	17 (40%)	37 (57%)	
2	24 (57%)	28 (43%)	
Nail diameter			0.199
8 mm	6 (15%)	7 (7%)	
9 mm	18 (45%)	33 (35%)	
10 mm	12 (30%)	34 (36%)	
11 mm	3 (8%)	9 (9%)	
12 mm	1 (2%)	12 (13%)	
Reamed	42 (100%)	95 (99%)	1.000
Coronal alignment immediately postop <sup>‡</sup>	37 (92%)	89 (93%)	1.000
Sagittal alignment immediately postop <sup>‡</sup>	21 (88%)	30 (91%)	0.690

\*  $P < .05$ .

<sup>†</sup> Fracture location reported as 0 to 100 from proximal to distal along the length of femur.

<sup>‡</sup> Reported as number of patients with adequate alignment.



**Figure 2.** Health-related quality of life, radiographic healing, and knee range of motion over time. Panel A shows the health-related quality of life, as measured by EuroQuol-5D-3L (EQ-5D) at each time point after surgery. Panel B shows the progression of radiographic healing as measured by the Radiographic Union Scale of Tibial fractures (RUST) score at each time point after surgery. The gray dashed line denotes the minimum RUST score that indicates radiographic union. Panel C shows the maximum knee extension at each time point after surgery, where 0° indicates full extension. Panel D shows the maximum degree of knee flexion at each time point after surgery. 95% CI=95% confidence interval. \**P* < .05. Data are tabulated in Supplementary Table 1, <http://links.lww.com/OTA/A16>.

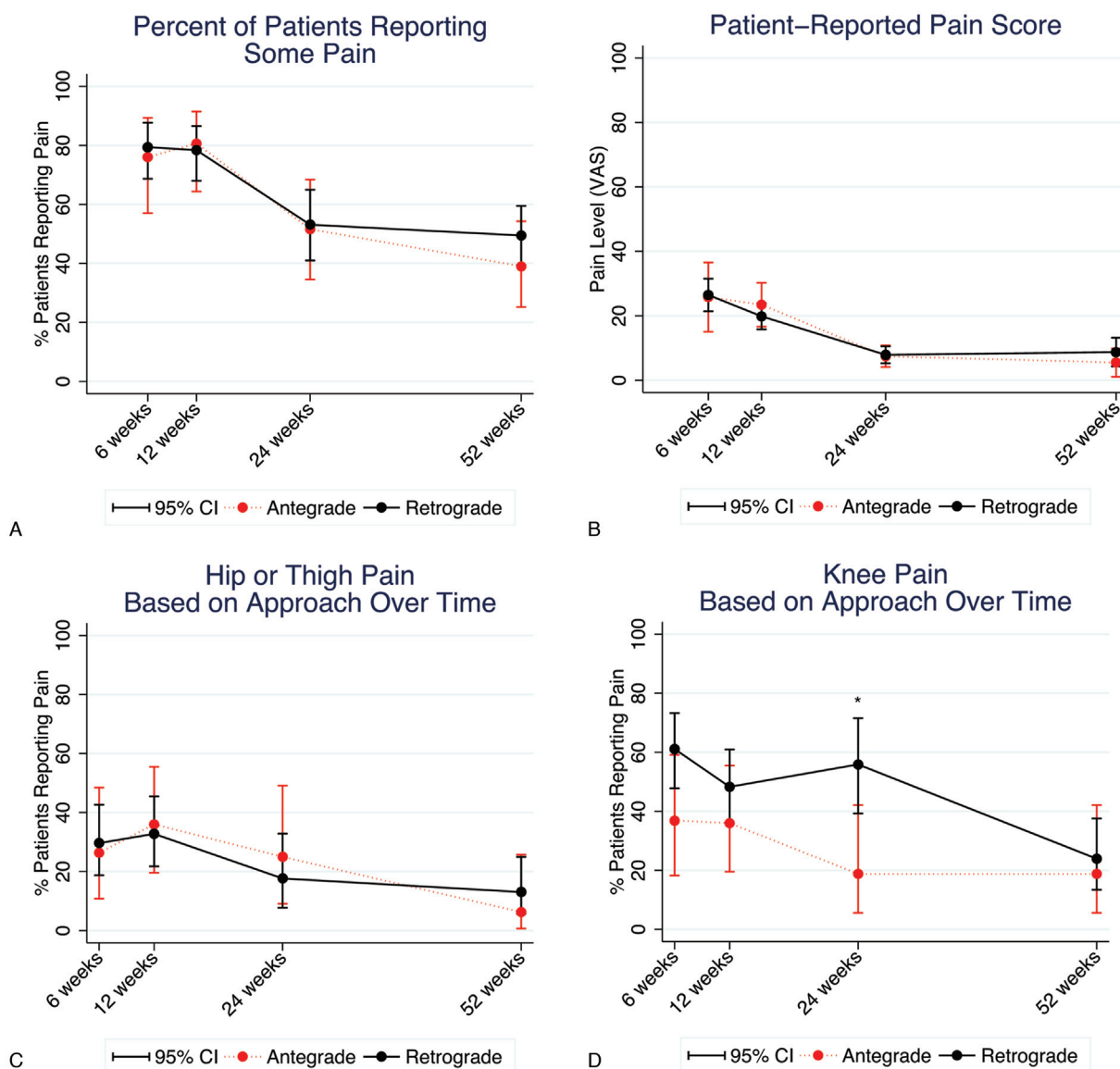
#### 4. Discussion

The aim of this study was to compare outcomes between patients with infraisthmic diaphyseal femur fractures treated via antegrade or retrograde technique with the SIGN intramedullary nail. Over 1-year follow-up, patients exhibited comparable immediate postoperative alignment, radiographic union via RUST score,<sup>[24]</sup> number of reoperations, HRQOL, knee extension, and hip pain. Patients treated with antegrade nailing had a higher rate of loss of coronal alignment over 1 year compared with those treated with retrograde nailing, but had improved knee range of motion at 6 weeks postoperatively and less knee pain at 6 months postoperatively.

The choice between antegrade and retrograde nailing depends on patient and fracture characteristics as well as surgeon preference.<sup>[5,7,25–28]</sup> While techniques for intramedullary fixation of femoral shaft fractures have been studied for decades,<sup>[8]</sup> this

study is unique in its focus on infraisthmic fractures treated with SIGN intramedullary nails. A previous study that evaluated alignment after surgical fixation of femur fractures with the SIGN nail reported no difference in alignment between antegrade and retrograde techniques.<sup>[29]</sup> However, that study was not restricted to the infraisthmic region and only included postoperative radiographs without additional outcomes.<sup>[29]</sup>

While fractures at the level of the isthmus typically achieve stable fixation after intramedullary nailing because of congruency of the nail and the femoral canal, the widening of the femoral canal as it approaches the distal metaphysis<sup>[8,30]</sup> makes infraisthmic fractures at risk for mechanical instability due to decreased contact between the implant and cortical bone.<sup>[10]</sup> Unlike IMNs used in HICs, SIGN nails were designed for placement in austere environments where intraoperative fluoroscopy may be unavailable. The significance of this is twofold:



**Figure 3.** Patient-reported pain over time. Panel A shows the percent of patients reporting any pain at each time point after surgery. Panel B shows the level of pain reported by patients using a visual analog score from 0 (no pain) to 100 (maximum pain). Panel C shows the percent of patients who reported hip or thigh pain. Panel D shows the percent of patients who reported knee pain. 95% CI=95% confidence interval. \**P* < .05.

SIGN nail interlocking screw trajectories are limited to a single plane (lateral to medial), and without fluoroscopy, placement of an antegrade nail deep into the distal femur is more difficult. These factors compound the challenge of achieving fixation in infraisthmus fractures using antegrade techniques, which likely contributes to the finding of increased loss of alignment with antegrade nailing.

Our analysis of secondary outcomes between antegrade and retrograde nailing of infraisthmus fractures was largely equivocal, with the majority of outcomes showing no significant differences at 1 year. One commonly cited advantage of antegrade nailing is avoiding violation of the knee joint, but the ability to achieve adequate fixation in more distal fractures may be compromised.<sup>[10,15,31]</sup> This was demonstrated in our study as retrograde-nailed fractures did demonstrate worse knee pain and motion at early time points; however, these did not persist at final follow-up.

#### 4.1. Limitations

This study has several limitations. This analysis was conceived as a secondary research question after the conclusion of the prospective cohort study. As such, it was not randomized, and more patients with infraisthmus fractures were treated with retrograde than antegrade nailing, yielding unequal cohorts and potentially confounding results. This reflects current practice, where retrograde nailing is more commonly used for distal femur fractures. Additionally, sample size was small, increasing the risk for type II error and limiting the ability to perform additional subgroup analyses to investigate the effects of surgeon choices including number of interlocks. Although loss to follow-up was low (90% retention at 1 year), not all patients had complete data at all time points, including follow-up radiographs, further constricting our sample size. In particular, although we did not identify a difference in radiographic healing or reoperation, it is conceivable that with larger numbers the loss of alignment after

antegrade nailing may be associated with higher rates of nonunion or implant failure. Knee ROM measurements were conducted without a goniometer by treating physicians. Although this is standard clinical practice in Tanzania, it is likely to be unreliable and potentially prone to bias. Finally, the duration of follow-up was limited to 1 year, while the clinically significant impacts of the primary outcome of malalignment may not become apparent until much later. While increased loss of alignment observed with antegrade nailing was not associated with quantifiable differences in pain or function in this study, patients with malaligned femurs may be at significant risk of earlier degenerative joint changes compared with those with adequate alignment.

Despite these limitations, this study adds relevant data to the ongoing discussion of the relative benefits of antegrade versus retrograde techniques, and is unique as it was conducted in an LMIC where IMN is routinely done without intraoperative fluoroscopy, focused on infraisthmic fractures of the femur, and measured fracture alignment and secondary outcomes out to 1 year.

## 5. Conclusions

SIGN intramedullary nailing using antegrade or retrograde techniques was associated with equivalent rates of union, quality of life, and reoperation at 1 year for patients with infraisthmic femoral shaft fractures. However, the antegrade technique led to an increased risk of loss of coronal alignment compared with retrograde nailing. This supports the notion that antegrade nailing provides less stable fixation compared with the retrograde technique for these fracture locations. Nonetheless, there were small but measurable advantages to antegrade nailing due to improved early knee ROM and pain.

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