Intramedullary nailing vs sliding hip screw in trochanteric fracture management: the INSITE randomized clinical trial

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Intramedullary Nailing vs Sliding Hip Screw in Trochanteric Fracture Management
The INSITE Randomized Clinical Trial

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Abstract

IMPORTANCE Fractures of the hip have devastating effects on function and quality of life. Intramedullary nails (IMN) are the dominant implant choice for the treatment of trochanteric fractures of the hip. Higher costs of IMNs and inconclusive benefit in comparison with sliding hip screws (SHSs) convey the need for definitive evidence.

OBJECTIVE To compare 1-year outcomes of patients with trochanteric fractures treated with the IMN vs an SHS.

DESIGN, SETTING, AND PARTICIPANTS This randomized clinical trial was conducted at 25 international sites across 12 countries. Participants included ambulatory patients aged 18 years and older with low-energy trochanteric (AO Foundation and Orthopaedic Trauma Association [AO/OTA] type 31-A1 or 31-A2) fractures. Patient recruitment occurred between January 2012 and January 2016, and patients were followed up for 52 weeks (primary end point). Follow-up was completed in January 2017. The analysis was performed in July 2018 and confirmed in January 2022.

INTERVENTIONS Surgical fixation with a Gamma3 IMN or an SHS.

MAIN OUTCOMES AND MEASURES The primary outcome was health-related quality of life (HRQOL), measured by the EuroQol–5 Dimension (EQ5D) at 1-year postsurgery. Secondary outcomes included revision surgical procedure, fracture healing, adverse events, patient mobility (measured by the Parker mobility score), and hip function (measured by the Harris hip score).

RESULTS In this randomized clinical trial, 850 patients were randomized (mean [range] age, 78.5 [18-102] years; 549 [64.6% female) with trochanteric fractures to undergo fixation with either the IMN (n = 423) or an SHS (n = 427). A total of 621 patients completed follow-up at 1 year postsurgery (304 treated with the IMN [71.9%], 317 treated with an SHS [74.2%]). There were no significant differences between groups in EQ5D scores (mean difference, 0.02 points; 95% CI, −0.03 to 0.07 points; $P = .42$). Furthermore, after adjusting for relevant covariables, there were no between-group differences in EQ5D scores (regression coefficient, 0.00; 95% CI, −0.04 to 0.05; $P = .81$). There were no between-group differences for any secondary outcomes. There were also no significant interactions for fracture stability (β [SE] , 0.01 [0.05]; $P = .82$) or previous fracture (β [SE], 0.01 [0.10]; $P = .88$) and treatment group.

CONCLUSIONS AND RELEVANCE This randomized clinical trial found that IMNs for the treatment of trochanteric fractures had similar 1-year outcomes compared with SHSs. These results suggest that the SHS is an acceptable lower-cost alternative for trochanteric fractures of the hip.

(continued)

Key Points

Question Does fixation of trochanteric fractures with an intramedullary nail (IMN) lead to superior 1-year outcomes compared with a sliding hip screw (SHS)?

Findings In this large multicenter randomized clinical trial of 850 patients comparing IMN vs SHS fixation of trochanteric fractures, there was no significant between-group difference at 52 weeks in patient-reported health-related quality of life.

Meaning This study's results support increasing evidence that there is little benefit to using more costly IMN devices for the majority of patients with trochanteric hip fractures, and the increasing use of these implants is unwarranted.

+ Visual Abstract

+ Invited Commentary

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Abstract (continued)

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Introduction

Trochanteric hip fractures (also intertrochanteric or pertrochanteric fractures) are extracapsular, with the fracture line between the greater and lesser trochanters.[1] This fracture pattern accounts for approximately half of all hip fractures, and substantially affects patient health-related quality of life (HRQOL).[1-4] The mean annual cost attributed to trochanteric fractures is estimated at more than $50 000 per patient.[2]

Surgical treatment of trochanteric fractures consists of intramedullary nail (IMN) fixation or extramedullary fixation with a sliding hip screw (SHS); however, there is a lack of conclusive evidence supporting any one fixation type.[5] The Gamma nail (Stryker) is a well-established IMN device that has shown good clinical and radiographic outcomes following trochanteric fracture fixation and may be advantageous with certain fracture patterns.[6-8] Despite the paucity of high-quality evidence supporting intramedullary over extramedullary fixation, the use of IMNs has been increasing internationally.[9-13] This is concerning, as IMNs can cost up to 40% more than SHSs.[14] In fact, some postulate that the increasing use of IMNs may be related to higher reimbursement payments made to surgeons for IMN devices compared with SHSs.[9,15]

Older meta-analyses conclude that IMN fixation may be associated with a higher risk of complications; however, many of the trials included only patients with stable fracture patterns and did not investigate the potential effect modification of fracture stability on implant type.[16-23] This likely underestimated the risk of failure following SHS fixation for unstable fracture patterns. In addition, IMN design has improved, which possibly has reduced the risk of complications. Furthermore, many older randomized clinical trials (RCTs) included nonambulatory patients, which may minimize potential between-group differences. More recent meta-analyses of typically small, single-center RCTs found superior HRQOL and functional scores, as well as a potentially lower risk of complications in patients with unstable trochanteric fractures treated with IMN devices vs SHSs.[16,19,21,23-25]

The optimal device for surgical fixation of trochanteric fractures remains under debate. The primary objective of this RCT was to compare HRQOL between patients with trochanteric fractures treated with the Gamma3 IMN vs an SHS.

Methods

The INSITE trial was a multicenter, international parallel RCT in which we randomized 850 patients with trochanteric fractures across 25 sites to treatment with an IMN (n = 423) or SHS (n = 427) from January 2012 to January 2016. Of these, 621 patients completed the primary outcome at the 1-year follow-up. We prospectively registered the trial on ClinicalTrials.gov (NCT01380444). The institutional review board at each site approved the protocol (Supplement 1), and all participants provided written informed consent. This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.

Participants

We included ambulatory patients aged 18 years or older with low-energy trochanteric (AO Foundation and Orthopaedic Trauma Association [AO/OTA] type 31-A1 or 31-A2) fractures requiring fixation who received surgery within 7 days of the fracture. We present participant exclusion criteria in eAppendix 1 in Supplement 2.

Randomization

We randomized participants using a 24-hour digital randomization system (Empower Health Research).[26] We used an allocation ratio of 1:1 and stratified randomization by (1) center, (2) fracture stability (stable [single fracture line with no displacement] vs unstable [multiple fracture lines with displacement]), and (3) patient age (18-50 years vs >50 years). The analyst for the primary hypothesis was blinded to study allocation, however, surgeon investigators and participants were unable to be blinded to study allocation. In addition, due to an issue with the statistical files received from the Electronic Data-Capture program during analysis, the data analyst was unblinded for analysis of the secondary outcomes.

Interventions

Patients in the IMN group received either a long or short nail through a closed technique.[27,28] Patients in the SHS group received any commercially available SHS, inserted per the manufacturers' guidelines. eAppendix 1 in Supplement 2 outlines more details surrounding the interventions, participating surgeon expertise, and perioperative and postoperative care.

Outcomes

Our primary outcome was HRQOL via the validated EuroQol-5 Dimension (EQ5D) at 52 weeks' postoperative.[29] Our primary hypothesis was that patients treated with the IMN would report superior HRQOL compared with those treated with an SHS. Secondary outcomes included revision surgery, mortality, fracture healing, fracture-related adverse events, mobility via the validated Parker mobility score and hip function and disability via the validated Harris hip score.[30,31] eAppendix 1 in Supplement 2 outlines the ranges and minimum clinically important differences for patient-reported outcomes.

Assessments

We assessed patients at baseline (except the Harris hip score, which is unable to be completed by patients at baseline), 13 weeks, 26 weeks, and 52 weeks. The first 150 enrolled patients were approached at 104 weeks for a separate exploratory analysis (not reported). Investigators reviewed their patients' radiographs pre- and postoperatively within 3 days, as well as at 13 weeks' and 52 weeks' postoperative. The final study participant completed data collection in January 2017.

Sample Size

To detect a minimum clinically important difference of 0.04 in mean EQ5D scores at 52 weeks with a standard deviation of 0.18, we calculated that we would require 736 patients (allowing a 10% dropout rate). A blinded interim analysis when 50% of the patients were enrolled suggested a higher-than-expected dropout rate, and the steering committee made the decision to enroll an additional 114 patients to maintain the planned sample size for analysis.

Statistical Analysis

We used the intention-to-treat method for this trial. We calculated descriptive statistics for patient demographics and outcomes, and we used independent *t* tests and Mann-Whitney *U* tests to compare unadjusted continuous outcomes between groups. We used a generalized linear mixed model to compare EQ5D index scores between groups while adjusting for age, fracture stability, prefracture living and functional status, and American Society of Anesthesiologists class. We included random effects in the model to account for clustering at the center level. We used Fisher exact and χ^2 tests to compare categorical outcomes between groups. We used Kaplan-Meier survival curves to compare mortality and fracture-related adverse event rates, and a composite outcome of mortality or fracture-related adverse events between groups. For revision surgery, we calculated absolute risk for both groups, as well as the risk reduction, absolute risk reduction, relative risk reduction, and number needed to treat with IMNs. For all secondary analyses, we included only patients with

complete data at each time point. All fractures were assessed as healed at 52 weeks; therefore, we performed a post hoc comparison of fracture healing between groups at 13 weeks. We included patients who died between baseline and 1-year follow-up in the primary analysis with a health utility value (EQ5D score) of 0. We performed sensitivity analyses to examine the robustness of our primary analysis by (1) excluding patients who died within 1 year and (2) using multiple imputation (assuming the data was missing at random with 25 imputed data sets) to impute missing health utility values (EQ5D scores) at 52 weeks (eAppendix 2 in Supplement 2). We planned a priori to test for interaction terms to determine if the treatment effect was modified by fracture stability or whether the patient had a previous hip fracture on the contralateral side. To apply more robust estimates for *P* values and confidence limits, we performed bootstrap analyses with 1000 samples for *t* tests of the primary outcome (the EQ5D), Parker mobility score, and Harris hip score (eAppendix 2 in Supplement 2). All statistical tests were 2-tailed with an α of .05 and 80% power; however, due to the multiple secondary outcomes and thus potential for type I error, findings for the analyses of the secondary end points should be interpreted as exploratory. Analysis deviations from the protocol are outlined at the end of Supplement 1. We used SAS version 9.3 (SAS Institute) for all analyses. The analysis was performed in July 2018 and confirmed in January 2022.

Results

We randomized 850 patients (mean [range] age, 78.5 [18-102] years; 549 (64.6% female) from 25 sites in 12 countries between January 2012 and January 2016: 423 to the IMN group, and 427 to the SHS group. Of these, 621 patients (304 treated with IMN [71.9%]; 317 treated with SHS [74.2%]) completed the primary outcome at the 1-year follow-up. The number of patients who dropped out and reasons for dropout were similar between groups (**Figure 1**). Similarly, baseline demographics and characteristics were balanced between groups. Among 418 patients in the IMN group with complete baseline data, 265 (63.4 %) were female; the mean (range) age was 78.2 (26-102) years. Among 415 patients included in the SHS group with complete baseline data, 277 (66.8%) were female; the mean (range) age was 78.8 (18-100) years (**Table 1**).

EQ5D Index Scores

We found no between-group differences in EQ5D scores at 52 weeks (including patients who died with a quality of life of 0; IMN: 358 patients vs SHS: 370 patients; mean difference, 0.02 points; 95% CI, −0.03 to 0.07 points; *P* = .42). We found no significant between-group differences in EQ5D scores following adjustment for relevant covariables (regression coefficient, 0.00; 95% CI, −0.04 to 0.05; *P* = .81) (eAppendix 2 in Supplement 2). We also found no mean between-group differences in EQ5D scores at 13 weeks (0.01 points; 95% CI, −0.02 to 0.05 points; *P* = .40) or 26 weeks (0.00 points; 95% CI, −0.04 to 0.04 points; *P* = .99) (**Figure 2**A; eAppendix 2 in Supplement 2).

Revision Surgery

At 52 weeks, we found no between-group difference in revision surgical procedures at 1-year postsurgery (IMN: 15 patients [3.6%] vs SHS: 22 patients [5.2%]; odds ratio [OR], 0.68; 95% CI, 0.35 to 1.32; *P* = .25) (**Table 2**; eAppendix 2 in Supplement 2). Two patients in the IMN group (0.5% of 417 with data available) underwent revision surgery prior to week 13, compared with 3 in the SHS group (0.7% of 411 with data available).

Fracture Healing

At 13 weeks, 441 patients had complete fracture healing data (221 with IMN, 220 with SHS). In the IMN group, 23 patients (10.4%) had unhealed fractures, compared with 35 patients (15.9%) in the SHS group (OR, 0.61; 95% CI, 0.35-1.08; *P* = .09). The median (range) time to fracture healing in days was similar in both groups (IMN: 93.8 [70.8-743.8] days; SHS: 93.8 [43.8-734.8] days; *P* = .99).

Parker Mobility Scores

We found no between-group difference in Parker mobility score at 52 weeks' postsurgery (mean difference, 0.37 points; 95% CI, −0.04 to 0.79 points; *P* = .08). We found statistically significantly higher Parker mobility score in the IMN group at 13 weeks (mean difference, 0.45 points; 95% CI, 0.09 to 0.80 points; *P* = .01) and 26 weeks (mean difference, 0.47 points, 95% CI, 0.09 to 0.86 points; *P* = .01) compared with the SHS group (Figure 2B); however, these differences did not reach the Parker mobility score minimum clinically important difference of 1 point.[32]

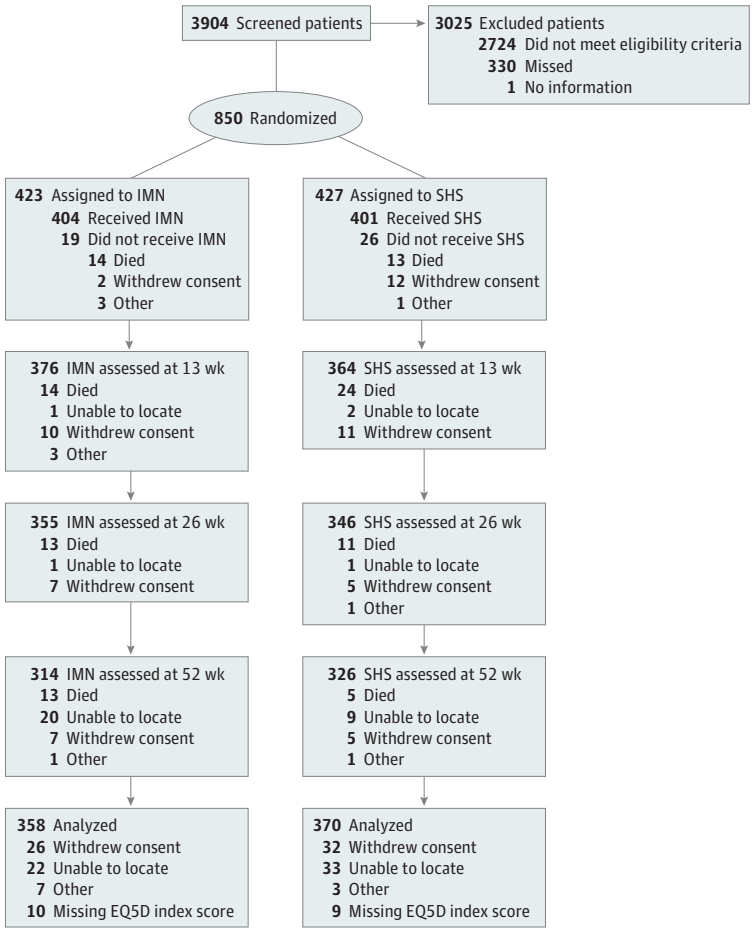
Harris Hip Scores

We found no between-group difference in Harris hip score at 52 weeks' postsurgery (mean difference, 1.24 points; 95% CI, −2.59 to 5.06 points; *P* = .53). We found a statistically significantly higher Harris hip score in the IMN group at 13 weeks (mean difference, 3.94 points: 95% CI, 0.72 to 7.17 points; *P* = .02), and 26 weeks (mean difference, 4.55 points; 95% CI, 1.00 to 8.11 points; *P* = .01) compared with the SHS group (Figure 2C); however, these did not reach the threshold for being clinically meaningful.[33,34]

Mortality and Adverse Events

We found no between-group difference in mortality (IMN: 63 patients [15.1%] vs SHS: 61 patients [14.6%]; OR, 0.97; 95% CI, 0.66-1.42), or fracture-related adverse events at 1-year postsurgery (IMN: 28 patients [6.6%] vs SHS: 33 patients [7.7%]; OR, 0.85; 95% CI, 0.50-1.42; *P* = .53) (**Table 3**).

Figure 1. Study Flow Diagram



EQ5D indicates EuroQol-5 Dimension.

Table 1. Patient Characteristics at Baseline[a]

Characteristic	Patients, No. (%)	
	IMN (N = 418)	SHS (N = 415)
Age, mean (range), y	78.2 (26-102)	78.8 (18-100)
Sex		
Male	153 (36.6)	138 (33.3)
Female	265 (63.4)	277 (66.8)
BMI, mean (SD)	23.4 (4.2)	23.6 (4.4)
Comorbidities		
Bleeding disorder	33 (7.9)	42 (10.1)
Back pain	55 (13.2)	73 (17.6)
Cancer	56 (13.4)	54 (13.0)
Depression	52 (12.3)	57 (13.4)
Diabetes	77 (18.4)	84 (20.2)
Heart disease	181 (43.3)	186 (44.8)
Hypertension	265 (63.4)	273 (65.8)
Stroke history	58 (13.9)	51 (12.3)
Kidney disease	48 (11.5)	47 (11.3)
Leg pain	42 (10.1)	47 (11.3)
Leg pain when walking	55 (13.2)	60 (14.5)
Liver disease	21 (5.0)	25 (6.0)
Lung disease	71 (17.0)	68 (16.4)
Nervous system disorder	35 (8.4)	40 (9.6)
Osteoporosis	100 (23.9)	107 (25.8)
Thyroid disease	48 (11.5)	44 (10.6)
Psychological disorder	59 (14.1)	60 (14.5)
Rheumatic disease	14 (3.4)	19 (4.6)
Gastrointestinal disorder	73 (17.5)	75 (18.1)
Other	109 (26.1)	105 (25.3)
Medications		
Bisphosphonates	9 (2.2)	25 (6.0)
Hypertensive	232 (55.5)	242 (58.3)
Cardiac	139 (33.3)	137 (33.0)
Pulmonary	47 (11.2)	41 (9.9)
Osteoporosis	50 (12.0)	63 (15.2)
Steroids	21 (5.0)	21 (5.1)
NSAIDS	49 (11.7)	41 (9.9)
Opioids	33 (7.9)	40 (9.6)
Place of residence		
Home	310 (74.2)	316 (76.1)
Home with care	48 (11.5)	44 (10.6)
Institution	60 (14.4)	55 (13.3)
Mechanism of injury		
Fall	407 (97.1)	405 (97.6)
Spontaneous	8 (1.9)	8 (1.9)
Other	4 (1.0)	2 (0.5)
Additional injuries	36 (8.6)	37 (8.9)
Fracture stability		
Stable	223 (53.4)	223 (53.7)
Unstable	195 (46.7)	192 (46.3)

(continued)

Table 1. Patient Characteristics at Baseline[a] (continued)

Characteristic	Patients, No. (%)	
	IMN (N = 418)	SHS (N = 415)
Fracture type		
A1.1	95 (22.8)	91 (21.9)
A1.2	101 (24.2)	104 (25.1)
A1.3	14 (3.4)	21 (5.1)
A2.1	68 (16.3)	74 (17.8)
A2.2	95 (22.8)	91 (21.9)
A2.3	44 (10.6)	33 (8.2)
Missing	1 (0.2)	
Prefracture mobility		
No assistance	272 (65.1)	230 (55.4)
Crutches/cane	76 (18.2)	102 (24.6)
Walker	69 (16.5)	81 (19.5)
Other	1 (0.2)	2 (0.5)
ASA Class		
I	33 (7.9)	33 (8.0)
II	175 (42.1)	144 (35.0)
III	182 (43.8)	215 (52.2)
IV	26 (6.3)	20 (4.9)
Missing	2 (0.4)	3 (0.7)
Operative time, mean (SD), min	59 (27)	64 (23)
Blood loss, mean (SD), mL	137.0 (156.6)	170.2 (183.4)

Abbreviations: IMN, intramedullary nail; SHS, sliding hip screw; BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; NSAIDS, nonsteroidal anti-inflammatory drugs; ASA, American Society of Anesthesiologists.

[a] Baseline data were not collected for 5 patients in the IMN group, and 12 in the SHS group due to death (IMN: 3; SHS: 2), withdrawal of consent (IMN: 1; SHS: 9), and other reasons for dropout (IMN: 1; SHS: 1).

eAppendix 2 in Supplement 2 outlines the survival analyses for mortality and fracture-related adverse events.

Sensitivity Analyses

Our sensitivity analyses resulted in no relevant deviation from the original analysis (eAppendix 2 in Supplement 2), and we found no statistically significant interaction term between treatment group and fracture stability (β [SE], 0.01 [0.05]; $P = .82$) or previous contralateral side fracture (β [SE], 0.01 [0.10]; $P = .88$) (eAppendix 2 in Supplement 2).

Discussion

To our knowledge, the INSITE trial is the first large, international multicenter RCT comparing trochanteric fracture fixation with the IMN vs an SHS. We found no significant between-group differences in HRQOL, function, mobility, or revision surgery at 1-year postsurgery.

A 2022 Cochrane review of 76 primarily single-center RCTs comparing IMNs vs extramedullary implants for extracapsular hip fractures found very low-quality evidence that patients treated with the IMN may report statistically significantly better postoperative mobility, but this difference is unlikely to be clinically meaningful.[27,35-41] In contrast, there was moderate-quality evidence suggesting that patients treated with the IMN device had a significantly higher risk of periprosthetic fracture. The authors noted high levels of heterogeneity, and a lack of patient-relevant outcomes, but found no significant, between-group differences in reoperations, pain, or mortality, and no subgroup differences for fracture stability or nail length. Furthermore, more than half the included studies were conducted before 2010, and likely involved older, inferior generations of IMN devices. Interestingly, the authors found no statistical evidence of differences between studies published before or after 2010, however, this was an arbitrary cutoff. The authors further noted that the number of overall

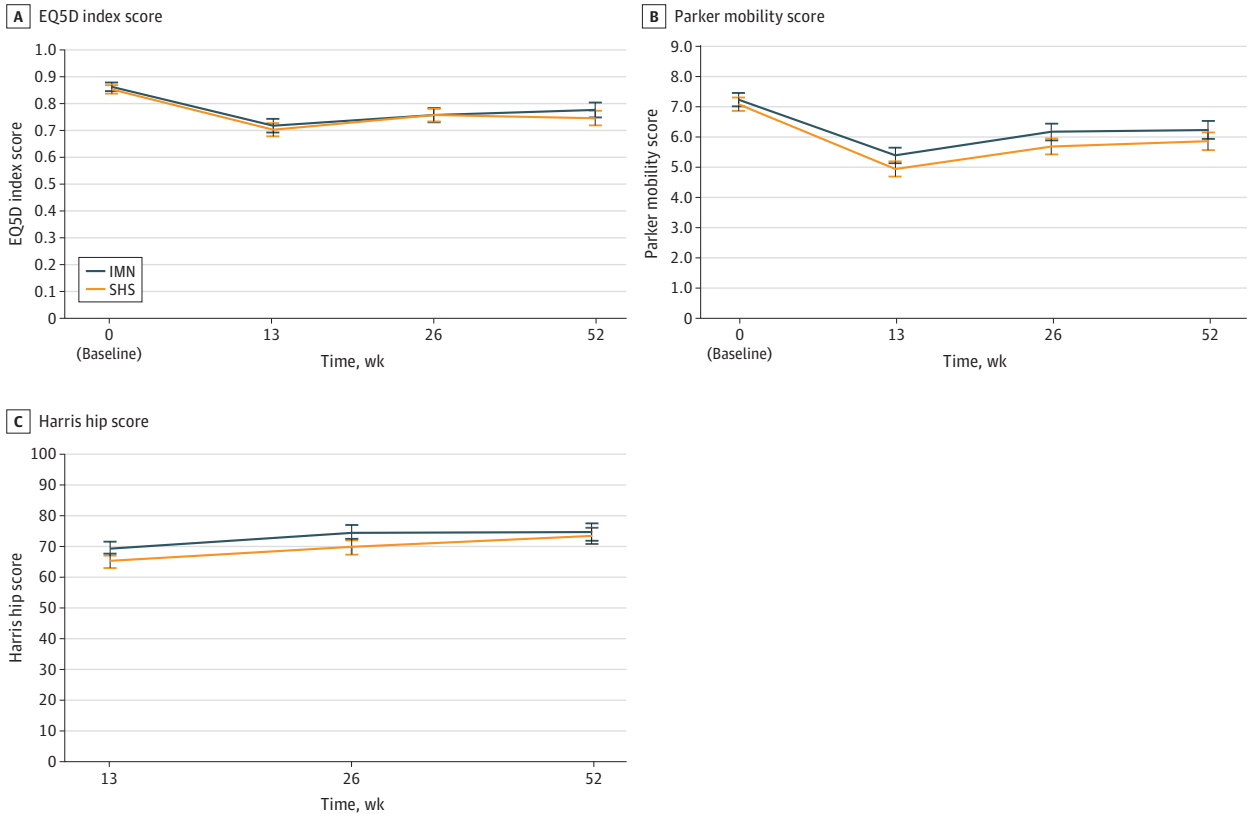
adverse events was low, and a larger sample is required to properly evaluate temporal improvements in implant design.

Indeed, studies that include newer generations of IMNs show significantly lower incidences of secondary fracture around the device compared with older generations.[22,42] We found a similar proportion of complications (including femoral shaft fractures) in the patients treated with the IMN vs an SHS, further suggesting that newer generation IMN devices have resolved some of the earlier issues that led to the increased risk of periprosthetic fractures.

We found no between-group differences at 1-year in patient HRQOL, mobility, or function; however, patients in the IMN group reported statistically significantly higher mobility and functional scores at 13 weeks and 26 weeks. While these exploratory results did not reach the threshold to be clinically meaningful, they still suggest that IMN fixation may offer faster functional recovery compared with SHS fixation. This aligns with the 2022 Cochrane review that concluded there was very low-quality evidence that treatment with the IMN (vs extramedullary) device may lead to more patients who report independent mobility at 4-months' postoperative.[27]

Similar to our results, the majority of previously published RCTs were unable to discern any differences in functional outcomes at 1-year postoperative between patients with trochanteric fractures treated with the IMN vs an SHS.[17] Nevertheless, some argue that IMN fixation may be superior in higher-functioning patients, and including lower functioning or nonambulatory patients may minimize potential between-group differences.[43,44] To our knowledge, no studies compare outcomes in only higher-functioning patients treated with IMN vs SHS fixation of trochanteric fractures. Two studies of patients with trochanteric fracture treated with other IMN devices vs an SHS suggest subgroups of patients with higher prefracture functional mobility or independence

Figure 2. EuroQol–5 Dimension (EQ5D) Index Scores, Parker Mobility Scores, and Harris Hip Scores Over Time



A, EQ5D index scores were used to measure health-related quality of life, ranging from 0 (death) to 1 (perfect health). B, Parker mobility scores range from 0 to 9, with higher scores indicating more mobility. C, Harris hip scores range from 0 to 100, with higher scores indicating better hip function. Harris hip scores were not measured at baseline.

appear to regain superior mobility following IMN fixation.[43,44] However, it is unclear whether these differences were clinically meaningful, and likely that the subgroup analyses were underpowered.

While we excluded nonambulatory patients, 40% of our patients used a walking aid prior to their fracture. Our primary hypothesis was that all ambulatory patients with trochanteric fractures treated with the IMN device would report significantly higher EQ5D scores at 1-year postoperative.

Table 2. Subsequent Surgical Procedures

	Procedures, No.	
Surgical procedure	IMN	SHS
Irrigation and debridement	1	0
Implant removal	11	11
Wound closure	1	0
Revision fixation	8	11
Arthroplasty	3	4
Bone graft	1	1
Other	1	2

Abbreviations: IMN, intramedullary nail; SHS, sliding hip screw.

Table 3. Fracture-Related Adverse Events

	Events, No.	
Adverse event	IMN	SHS
Avascular necrosis	0	3
Collapse of fracture	1	1
Collapse of fracture and migration of hardware	0	1
Screw cut out	5	3
Cut out and screw breakage	0	1
Deep infection	0	2
Deep intraoperative wound infection[a]	0	1
Distal fissure of bone	0	1
Distal locking screw dislocation	0	1
Femoral mononeuropathy	0	1
Femoral shaft fracture	1	1
Greater trochanter fracture	0	1
Hip pain	7	1
Implant dislocation	0	1
Implant dislocation (lag screw)	1	1
Intraoperative intertrochanteric fracture	0	1
Lag screw positioning	1	0
Lateral wall fracture	0	1
Loss of reduction	0	3
Massive heterotopic ossification	1	0
Misdrilling	2	0
Nonunion	1	0
Other pain	0	1
Pseudarthrosis	1	0
Screw breakage	2	5
Screw protrusion	3	2
Shortening	1	4
Shortening and back pain	1	0
Superficial infection	1	0
Superficial (hematoma)	0	1
Superficial intraoperative wound infection	0	1

Abbreviations: IMN, intramedullary nail; SHS, sliding hip screw.

[a] An intraoperative wound swab showed a germ colonization with *Staphylococcus lungdunensis* and was treated with antibiotics with success.

Our results did not support this hypothesis; however, we found prior use of an ambulatory aid and institutionalized living were significantly associated with EQ5D scores at 1 year.

Some authors suggest that SHS fixation of unstable trochanteric fractures may be associated with a high risk of failure, and the inclusion of primarily stable fracture patterns in previous studies has underestimated this.[39-41] However, there is no universal method for classifying the stability of trochanteric fractures. Unfortunately, the interrater reliability of the 2 primary classification systems (the Jensen-modified Evans and AO/OTA classifications), as well as the more general classification of stable vs unstable, is relatively poor.[45-49] Previous studies use a combination of these systems to classify trochanteric fracture stability, and even those that use the same classification system include different subtypes in their unstable group.[35,40,50] These discrepancies complicate between-study comparisons and contribute to the lack of consensus surrounding the treatment of these injuries. Indeed, while the authors of the 2022 Cochrane review comparing IMNs with extramedullary devices for trochanteric fractures found no significant subgroup differences based on fracture stability, they suggest "researchers focus on the unstable fracture subpopulation in future studies."[27]

Our sensitivity analyses indicated no effect modification between fracture stability and treatment type. It is possible that we were underpowered for this analysis, or our definition of unstable fracture (multiple fracture lines [comminution] with displacement) did not accurately classify fracture stability. With the poor reliability of currently used classification systems, future research should identify specific instability criteria to better preoperatively classify these injuries.

Moreover, it is possible that effect modification between fracture stability and treatment type may be observed only in patients who are functionally independent. Additional research may determine if IMN devices offer superior results (or shorter recovery times) compared with SHSs in sub-groups of patients, such as those with unstable fractures who are high-functioning and not using ambulatory aids prior to their fracture. However, most evidence to date suggests no significant difference between intramedullary vs extramedullary fixation for trochanteric fractures. To our knowledge, the INSITE trial is the first well-powered multicenter RCT comparing IMN with SHS fixation of trochanteric hip fractures in ambulatory patients, and our results lend support to this suggestion. Given that IMN implants cost up to 40% more than SHSs, and implants are the second highest driver of inpatient costs for these patients, there may be an economic benefit to choosing an SHS instead of the IMN.[14,51,52]

Limitations

Limitations of this study include the high proportion of patients lost to follow-up. While we used strategies to reduce patient attrition, this can be difficult with a patient population consisting of primarily advanced ages and substantial comorbidities. However, we accounted for this in our sample size calculation and examined the robustness of our results via sensitivity analyses. Despite this, patients we were unable to contact may have had adverse events or revision surgical procedures without our knowledge. Patients in the INSITE trial reported relatively higher EQ5D scores at 13 weeks compared with other studies of patients with hip fractures, which may be related to our exclusion of nonambulatory patients or those with dementia. As such, our results should be interpreted in consideration of this population. Moreover, while all patients in the IMN group were treated with a Gamma3 nail, the SHS group was not standardized. Although it is possible this may have led to a performance difference between devices, it contributes to the generalizability of our results. An apparent conflict of interest may be perceived as a limitation given the study sponsor is the manufacturer of the IMN. However, the sponsor was not involved in the design and drafting of the manuscript, or the decision to publish the findings. The negative results presented further support independence of the writing team from any potential sponsor influence.

Strengths of this study include the large sample size, and the inclusion of several international sites, increasing the statistical power and generalizability. Our stratified randomization ensured an appropriate between-group balance of several prognostic factors. Additionally, we performed several sensitivity and interaction term analyses that strengthen our interpretations.

Conclusion

In this randomized clinical trial of patients with trochanteric hip fracture, we found no significant differences in HRQOL, revision surgical procedures, fracture healing rate, or adverse events at 1-year postoperative between patients treated with the IMN or an SHS for trochanteric fractures. Although IMN fixation may offer some benefits surrounding earlier mobility over SHS fixation for certain subgroups of patients (ie, those who are high-functioning with unstable fracture types), these data suggest this is not the case for most patients, and that the recent increase in more costly IMN fixation is unwarranted.

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SUPPLEMENT 1.
Trial Protocol and Analysis Deviations From Protocol

SUPPLEMENT 2.
eAppendix 1. Supplemental Methods
eAppendix 2. Additional Analyses and Information

SUPPLEMENT 3.
Nonauthor Collaborators

SUPPLEMENT 4.
Data Sharing Statement