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Fixation using Alternative Implants for the Treatment of Hip Fractures (FAITH-2): The Clinical Outcomes of a Multi-Centre 2x2 Factorial Randomized Controlled Pilot Trial in Young Femoral Neck Fracture Patients

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ABSTRACT

Objective: To assess whether fixation method and vitamin D supplementation impact the risk of patient important outcomes within 12 months of injury in non-geriatric femoral neck fracture patients.

Design: Pilot factorial randomized controlled trial.

Setting: 15 North American clinical sites.

Participants: 91 adults aged 18-60 years with a femoral neck fracture requiring surgical fixation.

Intervention: Participants were randomized to a surgical intervention (sliding hip screw or cancellous screws) and a vitamin D intervention (vitamin D_3 4,000 IU daily versus placebo for 6 months).

Main Outcome Measurements: The primary clinical outcome was a composite of patient important complications (re-operation, femoral head osteonecrosis, severe femoral neck malunion, nonunion). Secondary outcomes included fracture healing complications and radiographic fracture healing.

Results: 86 participants with a mean age of 41 years were included. We found no statistically significant difference in the risk of patient important outcomes between the surgical treatment arms (hazard ratio (HR) 0.90, 95% CI 0.40-2.02, p=0.80) and vitamin D supplementation treatment arms (HR 0.96, 95% CI 0.42- 2.18, p=0.92).

Conclusions: These pilot trial results continue to describe the results of current fixation implants, inform the challenges of improving outcomes in this fracture population, and may guide future vitamin D trials to improve healing outcomes in young fracture populations. Although the pilot trial was not adequately powered to detect treatment effects, publishing these results may facilitate future meta-analyses on this topic.

Level of Evidence: Therapeutic Level II

Keywords: clinical protocols; femoral neck fractures; fracture fixation, internal; vitamin D; randomized controlled trial

INTRODUCTION

Femoral neck fractures in non-geriatric adults represent a distinct and challenging hip fracture population. The differences in physiology, injury characteristics, and activity level warrant a different treatment pathway compared to elderly fracture patients.[1–3] Internal fixation methods, using either cancellous screws (CS) or a sliding hip screw (SHS), are used to manage most femoral neck fractures in patients ≤60 years.[3] Despite internal fixation being the standard of care for treating younger adults with femoral neck fractures, there is no conclusive clinical evidence to determine if the CS or the SHS is the best device to use in this patient population.[4]

In addition to the lack of consensus for the optimal fixation device, it is plausible that non-surgical treatments could also improve fracture healing outcomes. Vitamin D is an essential nutrient for bone health and experimental animal studies suggest it may also play an important role in fracture healing.[5–9] Numerous observational studies have reported that nearly 75% of healthy adult fracture patients between the ages of 18-50 have vitamin D deficiency or insufficiency[5,6] Moreover, circulating vitamin D levels have been reported to acutely decrease following a fracture.[6,7,10–13] Therefore, vitamin D supplementation for young femoral neck fracture patients may be an effective non-surgical adjuvant therapy to improve healing outcomes.[6,14,15]

Recognizing the controversies surrounding implant selection and the unknown effect of vitamin D supplementation for young femoral neck fracture patients, we conducted the Fixation using Alternative Implants for the Treatment of Hip Fractures (FAITH-2) pilot trial. The primary clinical research objective of the FAITH-2 pilot trial was to determine whether fixation with a SHS and supplementation with vitamin D independently lowered the risk of patient important complications during the 12-month post-injury follow-up period in young adults (ages 18-60) with femoral neck fractures. Details of the feasibility and vitamin D supplementation adherence of the FAITH-2 pilot trial are reported separately.[16] Since these analyses demonstrated a multicenter definitive trial was not feasible, we present the clinical outcomes data for the pilot trial. We considered all clinical analyses of the pilot trial data as exploratory.

MATERIALS AND METHODS

Trial Design

FAITH-2 was a pilot trial conducted to determine the feasibility of a definitive 2x2 factorial design randomized controlled trial (RCT) comparing the two surgical implants plus vitamin D supplementation versus placebo for the treatment of femoral neck fractures in young adult patients (ages 18-60). A previously published protocol manuscript details the trial objectives and methods.[2] The trial was registered with ClinicalTrials.gov, number NCT01908751, and it was approved by the Hamilton Integrated Research Ethics Board (#13-807) and by all participating clinical sites' research ethics boards/institutional review boards.

Participants

We randomized patients with a femoral neck fracture requiring fracture fixation across 15 clinical centers in the USA and Canada. Eligible patients were adult men and women aged 18 to 60 years with a femoral neck fracture. All fracture patterns (subcapital, midcervical, or basicervical) amenable to both surgical treatments (SHS and CS) were eligible. Patients with osteoporosis or other bone metabolism disorders were excluded. Ipsilateral femoral shaft fractures treated with retrograde nailing or plating were eligible for inclusion, as well as patients with multiple trauma.

Surgical Procedures

Participants allocated to the CS group received multiple cancellous screws with a minimum diameter of 6.5 mm. Participants allocated to the SHS group received a single

larger diameter partially threaded screw affixed to the proximal femur with a side-plate. Surgeons were permitted to use any fixed-angle plate construct which included a large diameter screw or blade that could slide within the plate. Surgeons were also allowed to use additional derotation screws and buttress plates.

Procedures for Vitamin D Supplementation

Vitamin D supplementation was administered upon hospital discharge or within two weeks of the participant's femoral neck surgery, whichever came first. Participants allocated to the vitamin D group received a bottle of 2,000 IU vitamin D drops (Ddrops®, Ddrops Company) and were instructed to take two drops daily for six months, for a total daily dose of 4,000 IU. Participants in the placebo group received an identical bottle of placebo drops with no active ingredient.

Follow-up Schedule

Participant follow-up visits occurred post-operatively, and at 6 weeks, 3 months, 6 months, 9 months, and 12 months post-fracture.

Primary Clinical Outcome

The primary clinical outcome for the pilot trial was a composite of patient important outcomes that occurred within the 12 months from the index surgery. A participant was classified as having the primary clinical outcome if they experienced one or more of the following patient important outcomes: 1) re-operation, defined as any unplanned surgery related to the treatment of the femoral neck fracture; 2) femoral head osteonecrosis as

reported on any follow-up medical imaging study 3) severe femoral neck malunion, defined as shortening of >10mm in any plane on follow-up x-rays; or, 4) nonunion, defined as the failure of the fracture to progress towards healing defined as a Radiographic Union Score for Hip (RUSH) below 18, at 6 months or greater post-injury.[17] The individual complications within the composite outcome were chosen to balance a feasible one-year follow-up timeline and the likelihood of a clinically important event. For example, asymptomatic or "pre-collapse" femoral head osteonecrosis was included because many of these cases will not progress to full collapse or reoperation until more than 12-months post-injury.

Secondary Clinical Outcomes

The secondary outcomes for the pilot trial included fracture healing complications and radiographic fracture healing. Fracture healing complications included wound healing problems, infection (superficial and deep), hardware failure, hardware breakage, painful hardware, and peri-prosthetic fracture.

Adjudication Procedures and Blinding

An orthopaedic surgeon with prior adjudication experience independently adjudicated participant eligibility and study outcomes. Surgeons, research personnel, participants, and the adjudicator could not be blinded to the treatment allocation of the surgical interventions (SHS versus CS), but the data analyst, Steering Committee, and those interpreting the trial results were blinded to the surgical treatment allocation. The

complete blinding of the supplement was achieved by using vitamin D_3 and placebo liquid products that were indistinguishable.

Statistical Analysis

Sample Size

The planned sample size for the definitive RCT was 898 patients. Based on our feasibility objectives for this pilot trial, we sought to enroll a minimum of 60 patients within a 12-month recruitment period.

Statistical Analysis of Outcomes

We adopted the CONSORT extension to pilot trials in reporting the results of this pilot trial.[18] The baseline characteristics, fracture and injury characteristics, surgical details, and peri-operative care data were summarized using descriptive statistics. We considered the clinical analyses of the pilot trial data as exploratory; therefore, we did not adjust for multiple testing, nor did the analyses seek to make definitive conclusions.[19] The first analysis of clinical outcomes was a Cox proportional hazards regression with main effects for implant type and supplementation, and the interaction between the two. In this analysis, we used 377 days post-fracture as the time of censoring, which was the time of the last reported event within the composite, and within 2-weeks of the 12-month follow-up date. We conducted additional sensitivity analyses censoring at 365 days, which did not change our study results. All analyses were adjusted for 1) femoral neck fracture displacement, 2) presence of an ipsilateral femoral shaft fracture, and 3) geographic region of the recruiting center (Canada versus the United States). The test of interaction

between the surgical implant and vitamin D supplement interventions was not significant, and therefore their treatment effects were analyzed separately. Hazard ratios with 95% confidence intervals (CI) were reported for each model. All outcome analyses adhered to the intention-to-treat principle. We used SPSS Version 25 to perform all analyses.

RESULTS

Enrollment

Between February 2015 and March 2018, 91 patients were randomized from 15 North American hospitals into the FAITH-2 pilot trial. 86 patients were deemed eligible and included in the analyses (**Figure 1 and Table, Supplemental Digital Content 1, http://links.lww.com/JOT/B21**). Of the 86 participants, 43 were allocated to receive a sliding hip screw and 43 were allocated to receive CS. Concomitantly, 45 were allocated to receive vitamin D, and 41 were allocated to receive placebo (see **Figure, Supplemental Digital Content 2, http://links.lww.com/JOT/B22**). 12-month follow-up was achieved for 67 patients (77.9%).

Participant Demographics and Fracture Characteristics

Typical participants were men (73.3%) of white/Caucasian ethnicity (79.1%) with a mean age of 41.1 (SD 12.2). The majority of fractures were displaced (71%), with 44% of the fractures being a vertical Pauwels Type III pattern (**Table 1**). Of the 86 eligible participants, 15 (17.4%) also sustained an ipsilateral femoral shaft fracture **(see Table, Supplemental Digital Content 3, http://links.lww.com/JOT/B23)**.

Surgical Details

The mean time from injury to surgery was similar across all treatment groups (median: 21.2 hours, interquartile range: 18.1 hours). An open reduction was used in the majority of participants (55.8%). The remainder of key surgical details are summarized in **Table 2**.

Vitamin D Supplementation Adherence

The proportion of participants taking a minimum of 75% of their prescribed daily supplements decreased significantly with time. At 6 weeks post-fracture, 72.1% reported acceptable adherence; at 3-months the proportion decreased to 60.5%; at 6-months, only 54.7% of participants were taking at least 75% of their daily doses. Overall, only 33% of participants reported full daily adherence for the first three months.

Primary Clinical Outcome

Eleven participants in the SHS group (25.6%) and 13 participants in the CS group (30.2%) experienced the composite complication outcome (HR 0.90, 95% CI 0.40 – 2.02). Re-operations accounted for nine SHS events and six CS events (**Table 3**). There were three conversions to total hip arthroplasty (THA) in the SHS group and one conversion to THA in the CS group (**Table 4**). There was one case in the SHS group and five cases in the CS group of femoral neck osteonecrosis that did not result in a re-operation within the 12-month trial period. There was one case in the SHS group and two cases in the CS group of isolated femoral neck shortening >1 cm that was not also associated with femoral head osteonecrosis or a re-operation. All seven nonunion cases

were treated with a re-operation: four cases in the SHS group and three cases in the CS group.

With respect to the vitamin D supplement comparison, the composite complication outcome occurred in 11 participants (24.4%) in the vitamin D group and 13 participants (31.7%) in the placebo group (HR 0.96, 95% CI 0.42 – 2.18). There were seven reoperations in the vitamin D group and eight reoperations in the placebo group. There were two conversions to THA in each treatment group. Breakdowns of the primary clinical endpoint composite by treatment group and re-operation by treatment group are displayed in **Tables 3 and 4**, respectively.

Secondary Clinical Outcomes

Fracture Healing Complications

All fracture healing complications were either treated with re-operation or captured under the primary composite outcome, except for one case. One participant in the CS surgical treatment group experienced painful hardware at the final 12-month follow-up visit that was not treated with re-operation.

Ipsilateral Shaft Fractures

Of the 86 eligible participants, 15 (17.4%) also sustained an ipsilateral femoral shaft fracture. The majority of these fractures were closed (64.7%) and located in the middle (76.5%) of the femoral shaft. Three participants in the CS group and none in the SHS group underwent a re-operation to treat non-union or delayed healing.

We were able to confirm radiographic healing of the ipsilateral femoral shaft fracture in 10 participants (66.7%). The average time to radiographic healing for ipsilateral femoral shaft fractures was 11.1 months (SD 3.8 months) for those who did achieve radiographic healing and did not differ between the surgical treatment groups (p=0.75) nor the vitamin D supplementation treatment groups (p=0.52).

DISCUSSION

The FAITH-2 pilot trial successfully enrolled 86 young femoral neck fracture patients across 15 North American trauma centers. This pilot trial sought to demonstrate the feasibility of proceeding to a larger 898-patient definitive trial comparing the sliding hip screw (SHS) versus cancellous screws (CS) and supplementation with vitamin D_3 versus placebo to independently reduce the risk of patient-important complications within 12-months post-injury. Secondarily, the pilot trial sought to add to the sparse clinical outcomes data in this challenging fracture population.

The slow recruitment and regulatory challenges of administering vitamin D outside of North America have led to the conclusion that the larger trial is not feasible. As expected, the preliminary clinical results do not approach statistical significance within the pilot sample size; however, the point estimates for each treatment comparison are in the hypothesized direction. The hazard ratio for complications was 0.90 for the SHS relative to CS (p=0.80), and 0.96 for vitamin D supplementation relative to placebo (p=0.92).

Despite the pilot nature, the clinical results of this trial are important exploratory comparisons. The previous literature comparing surgical implants for young femoral neck fracture patients remains sparse. A similar 30 patient RCT comparing CS and the SHS

reported CS led to decreased operative time, superior functional outcomes, and fewer complications; however, key data were missing from the report to support the author's conclusions. Moreover, this trial was conducted in a developing country 30 years ago, and its generalizability to current practice remains unclear. These potential concerns have been further highlighted by conflicting retrospective studies suggesting superior outcomes with fixed angle devices.[20,21] More recently, a fifty-eight patient RCT reported a larger proportion of CS patients lost >5° of coronal alignment reduction within 6 months of injury, and all were treated with a valgus intertrochanteric osteotomy (18% vs 0%, $p<0.001$).[22] There were no differences detected in the incidence of osteonecrosis, and the authors did not report the incidence of nonunion.

With respect to our findings for the potential effectiveness of vitamin D supplementation, we are unaware of any previous results from other young femoral neck fracture populations. Even within other non-osteoporotic fracture populations, there have been few studies that have examined the effectiveness of vitamin D supplementation to improve fracture healing outcomes. Previous authors have shown that post-fracture vitamin D supplementation can increase serum 25(OH)D levels in the adult fracture population.[23–25] Naturally, the increase in serum levels is dependent on patient adherence, which also seems to vary between populations. Andres et al. reported 82% of their adult fracture patients were adherent to a daily 1,600 IU vitamin D dose;[25] this is much higher than the 33% of participants that reported taking their supplement daily in our trial. Regardless, the evidence for the clinical effectiveness of vitamin D supplementation to reduce fracture complications remains lacking.[26,27] Similarly, a recent meta-analysis has suggested no benefit to vitamin D supplementation in most potential

clinical indications.[27] Despite the lack of efficacy data to suggest vitamin D supplementation improves fracture healing, some authors continue to recommend its routine use because it is an inexpensive intervention with a wide safety profile.[28]

Our clinical results highlight ongoing uncertainty within surgical treatment and vitamin D supplement choices, and these results must be further considered within the limitations of the pilot trial. Since the sample size of the FAITH-2 pilot trial was chosen to test trial feasibility, it was underpowered to detect treatment effects and support definitive clinical comparisons. Despite this limitation, we decided to report the clinical results of FAITH-2 as per the recommendation of Conn et al.[29] Not only is it unethical to not report results of a conducted trial, but in making these results available, it allows for their inclusion in future meta-analyses.[29] Other challenges of the FAITH-2 pilot trial included relatively low participant adherence to taking the daily vitamin D supplement and maintaining >80% 1-year follow-up.[16] This is not surprising compared to other hip fracture trials, given the higher proportion of young male participants and individuals with multiple injuries that were recruited. Finally, it is important to recognize that the 1-year duration of follow-up may underestimate the occurrence of several important complications. For example, femoral head osteonecrosis is known to present later than 1-year post-injury, and population-level data suggest the median time to conversion to total hip arthroplasty after a young femoral neck fracture is 16 months.[30]

Despite the inability of this pilot data to guide strong clinical recommendations, the FAITH-2 trial is an incremental step towards improving clinical research within this challenging fracture population. The 2x2 factorial randomization allowed for novel efficiencies to compare two surgical interventions and vitamin D supplements in a single

trial. The multi-center recruitment helped increase the sample size and ensure the results are generalizable beyond a single center. The vitamin D intervention was placebo controlled and double-blinded, which removes multiple potential sources of treatment and assessment biases. Although the surgical interventions could not be blinded, a single independent orthopaedic surgeon adjudicated all trial outcomes to minimize any local site or investigator biases.

There are several important over-arching conclusions to be drawn from the FAITH-2 trial. First, the complication rate of internal fixation for young femoral neck fractures remains >20%. Second, despite the apparent need to improve treatment outcomes, it is unlikely to be feasible to conduct a large multi-center trial in this fracture population. Third, the superiority of a surgical implant to decrease the risk of nonunion remains to be proven in both young and elderly femoral neck fractures; however, the complication profile of the SHS and CS continues to be consistent. It was the implant specific complications that were the primary determinant of differences in the risk for reoperation among the displaced elderly femoral neck fractures in the FAITH trial (HR 0.57, p=0.04). CS fail with varus fracture collapse and lateral screw prominence; the SHS fails with superior screw cutout. Therefore, the relevant clinical question may not be, "*Which implant is better?"* but rather, "*Which complication profile is most acceptable for each individual patient?*" Finally, when considering whether to add vitamin D supplementation to the post-operative treatments of young femoral neck fracture patients, surgeons should not expect daily adherence to a supplement prescription.

The FAITH-2 program will not proceed to a definitive trial, but these pilot trial results continue to describe the results of current fixation implants, inform the challenges of improving outcomes in this fracture population, and may guide future vitamin D trials to improve healing outcomes in young fracture populations. Although the pilot trial was not adequately powered to detect treatment effects, publishing these results may facilitate future meta-analyses on this topic.

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Table 1: Participant Demographics

Characteristic	CS N=43	SHS N=43	Vitamin D N=45	Placebo N=41	Total N=86
Age in years, mean (SD)	39.2 (13.2)	43.0 (11.4)	40.6 (12.0)	41.6 (13.0)	41.1 (12.4)
Sex, n (%)					
Male	33 (76.7)	30 (69.8)	33 (73.3)	30 (73.2)	63 (73.3)
Female	10 (23.3)	13 (30.2)	12 (26.7)	11 (26.8)	23 (26.7)
Ethnicity, n (%)					
Native/Aboriginal	0 (0.0)	1 (2.3)	0 (0.0)	1 (2.4)	1 (1.2)
South Asian	1 (2.3)	1 (2.3)	1 (2.2)	1 (2.4)	2 (2.3)
East Asian	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)
Southeast Asian (Filipino)	0 (0.0)	1 (2.3)	0 (0.0)	1 (2.4)	1 (1.2)
Hispanic/Latino	1 (2.3)	1 (2.3)	1 (2.2)	1 (2.4)	2 (2.3)
White/Caucasian	36 (83.7)	32 (74.4)	33 (73.3)	35 (85.4)	68 (79.1)
Black (African/Caribbean)	4 (9.3)	5 (11.6)	7 (15.6)	2 (4.9)	9 (10.5)
Mixed (Black & White)	0 (0.0)	1 (2.3)	1 (2.2)	0 (0.0)	1 (1.2)
Middle Eastern	1 (2.3)	1 (2.3)	2 (4.4)	0 (0.0)	2 (2.3)
Work Related Injury, n (%)	4 (9.3)	8 (18.6)	8 (17.8)	4 (26.7)	12 (14.1)
History of Smoking, n (%)					
Yes	17 (39.5)	15 (34.9)	11 (24.4)	21 (52.5)	32 (37.2)
Previously smoked but quit	3 (7.0)	13 (30.2)	12 (26.7)	4 (10.0)	16 (18.6)
No	22 (51.2)	15 (34.9)	22 (48.9)	15 (37.5)	37 (43.0)
Unknown	1 (2.3)	0	0	1 (2.4)	1 (1.2)
Consumption of Alcohol, n (%)	29 (67.4)	24 (55.8)	32 (71.1)	21 (51.2)	53 (61.6)
Current Medications, n (%)					
None	33 (78.6)	29 (90.7)	32 (71.1)	30 (73.2)	62 (72.0)
NSAID	4 (9.3)	4 (9.3)	4 (8.9)	4 (9.8)	8 (9.3)
Steroid Medications	1 (2.3)	1 (2.3)	1 (2.2)	1 (2.4)	2 (2.3)
Calcium	3 (7.0)	7 (16.3)	8 (17.8)	2 (4.9)	10 (11.6)
Vitamin D	4 (9.3)	8 (18.6)	8 (17.8)	4 (9.8)	12 (14.0)
Number of Major Co-Morbidities, n (%)	23 (53.5)	14 (32.6)	19 (42.2)	18 (44.0)	37 (43.0)
None	10 (50.0)	15 (51.7)	14 (53.8)	11 (47.8)	25 (51.0)
One	5 (25.0)	6 (20.7)	6 (23.1)	5 (21.7)	11 (22.4)
Two	3 (15.0)	7 (24.1)	5 (24.1)	5 (21.7)	10 (20.4)
Three	1 (5.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (2.0)
Four	1 (5.0)	1 (3.4)	1 (3.8)	1 (4.3)	2 (4.1)
Level of the Fracture Line, n (%)					
Subcapital	11 (25.6)	13 (30.2)	11 (24.4)	13 (31.7)	24 (27.9)
Midcervical	13 (30.2)	15 (34.9)	13 (28.9)	15 (36.6)	28 (32.6)
Basal	18 (41.9)	15 (34.9)	21 (46.7)	12 (29.3)	33 (38.4)
Unable to Assess	1 (2.3)	0 (0.0)	0 (0.0)	1 (2.4)	1 (1.2)
Garden Classification, n (%)					
Garden I (undisplaced)	5 (11.6)	9 (20.9)	7 (15.6)	7 (17.1)	14 (16.3)
Garden II (undisplaced)	6 (14.0)	3 (7.0)	5 (11.1)	4 (9.8)	9 (10.5)
Garden III (displaced)	14 (32.6)	13 (30.2)	16 (35.6)	11 (26.8)	27 (31.4)
Garden IV (displaced)	17 (39.5)	17 (39.5)	16 (35.6)	18 (43.9)	34 (39.5)
Unable to Assess	1 (2.3)	1 (2.3)	1 (2.2)	1 (2.4)	2 (2.3)
Pauwels' Classification, n (%)					
Type I	3 (7.0)	9 (20.9)	5 (11.1)	7 (17.1)	12 (14.0)
Type II	16 (37.2)	19 (44.2)	19 (42.2)	16 (39.0)	35 (40.7)
Type III	23 (53.5)	15 (34.9)	21 (46.7)	17 (41.5)	38 (44.2)
Unable to Assess	1 (2.3)	0 (0.0)	0 (0.0)	1 (2.4)	1 (1.2)

Table 2: Surgical Details

Surgery Characteristic	CS N=43	SHS N=43	Vitamin D N=45	Placebo N=41	Total N=86
Time from Injury to Surgery in hours, mean (SD)	28.9 (24.3)	25.0 (16.2)	28.0 (23.4)	25.7 (17.5)	26.9 (20.6)
Type of Reduction Used, n (%)					
Closed	16 (37.2)	16 (37.2)	16 (35.6)	16 (39.0)	32 (37.2)
Open	23 (53.5)	25 (58.1)	25 (55.6)	23 (56.1)	48 (55.8)
None	4 (9.3)	2 (4.7)	4 (8.9)	2 (4.9)	6 (7.0)
Procedure Performed, n (%)					
CS	43 (100.0)	1 (2.3)	24 (53.3)	20 (48.8)	44 (51.2)
SHS	0 (0.0)	41 (95.3)	21 (46.7)	20 (48.8)	41 (47.7)
Cephalomedullary Nail (Protocol Deviation)	0 (0.0)	1 (2.3)	0 (0.0)	1 (2.4)	1 (1.2)
Other Procedures Performed During Same Operation as Femoral Neck Fracture Internal Fixation, n (%)	14 (32.6)	11 (25.6)	14 (31.1)	11 (26.8)	25 (29.1)
Number of Screws Used, n (%)					
Three	39 (88.6)				
Four	5 (11.4)				
Diameter of Screws, n (%)					
6.5 mm	12 (27.3)				
7.3 mm	30 (68.2)				
8.0 mm	2 (4.5)				
Formation of Screws (or Pins), n (%)					
Triangle (Apex at Top) (3 Screws)	6 (13.6)				
Inverted Triangle (Apex at Bottom) (3 Screws)	31 (70.5)				
Square (4 Screws)	2 (4.5)				
Diamond	1 (2.3)				
Pauwels	4 (9.1)				
Aiming of Screws (or Pins), n (%)					
Parallel	40 (90.9)				
Crossed	4 (9.1)				
Type of Sliding Fixed-Angle Plate Construct Used, n (%)					
Traditional Large Diameter Hip Screw		38 (92.7)			
Spiral/Helical Blade		3 (7.3)			
Implant Position in Head of Femur					
Centre-Centre Position, n (%)		22 (53.7)			
Superior Position		1 (2.4)			
Anterior Position		1 (2.4)			
Inferior Position		16 (39.0)			
Posterior Position		1 (2.4)			
Supplemental (Derotational) Screws Included in Fixation, n (%)		29 (67.4)			

Table 3: Primary Clinical Endpoint Composite by Treatment Group

Endpoint	Overall N=86	CS N=43	SHS N=43	Vitamin D N=45	Placebo N=41
Primary Clinical Endpoint*, n (%)	24 (27.9)	13 (30.2)	11 (25.6)	11 (24.4)	13 (31.7)
Individual Endpoints					
Re-operation,** n (%)	15 (17.4)	6 (14.0)	9 (20.9)	7 (15.2)	8 (19.5)
Femoral head osteonecrosis,*** n (%)	9 (10.5)	7 (16.3)	2 (4.7)	5 (10.9)	4 (10.0)
Severe femoral neck malunion,**** n (%)	8 (9.3)	6 (14.0)	2 (4.7)	5 (10.9)	3 (7.5)
Nonunion,***** n (%)	7 (8.2)	3 (7.0)	4 (9.3)	4 (8.7)	3 (7.5)

*For the primary clinical endpoint, one event per patient was counted

**3 patients underwent two, two, and three separate re-operations, respectively. Therefore, breakdown of re-operations totals to 19 instead of 15.

***3 patients with femoral head osteonecrosis also underwent a re-operation

****3 patients with severe femoral neck malunion also underwent a re-operation, 2 patients with severe femoral neck malunion also had femoral head osteonecrosis, and 1 patient with severe femoral neck malunion had a nonunion

*****All 7 patients with a nonunion also underwent a re-operation

Table 4: Re-Operation by Treatment Group

Endpoint	Overall N=86	CS N=43	SHS N=43	Vitamin D N=45	Placebo N=41
Primary Clinical Endpoint of Re-operation					
Re-operation*, n (%)	15 (17.4)	6 (14.0)	9 (20.9)	7 (15.2)	8 (19.5)
Conversation to Total Hip Arthroplasty, n (%)	4 (4.7)	1 (2.3)	3 (7.0)	2 (4.4)	2 (4.9)
Proximal Femur Osteotomy, n (%)	5 (5.8)	3 (7.0)	2 (4.7)	3 (6.7)	2 (4.9)
Implant Removal, n (%)	5 (5.8)	1 (2.3)	4 (9.3)	1 (2.2)	4 (10.0)
Irrigation and Debridement for Deep Infection, n (%)	3 (3.5)	0 (0.0)	3 (7.0)	3 (6.7)	0 (0.0)
Implant Exchange, n (%)	2 (2.3)	1 (2.3)	1 (2.3)	0 (0.0)	2 (4.9)

*For the primary clinical endpoint, one event per patient was counted
*3 patients underwent two, two, and three separate re-operations, respectively. Therefore, breakdown of re-operations totals to 19 instead of 15.

Figure 1: Flow Diagram – Surgical Treatment

*One patient withdrew their consent post-surgery