2-1-2017

Antegrade versus retrograde nailing techniques and trochanteric versus piriformis intramedullary nailing entry points for femoral shaft fractures: A systematic review and meta-Analysis

Nasir Hussain
Saint Michael's Hospital University of Toronto

Farrah Naz Hussain
Saint Michael's Hospital University of Toronto

Corey Sermer
University of Toronto Faculty of Medicine

Hera Kamdar
Dow University of Health Sciences Pakistan

Emil H. Schemitsch
Saint Michael's Hospital University of Toronto

See next page for additional authors

Authors
Nasir Hussain, Farrah Naz Hussain, Corey Sermer, Hera Kamdar, Emil H. Schemitsch, Amir Sternheim, and Paul Kuzyk

Antegrade versus retrograde nailing techniques and trochanteric versus piriformis intramedullary nailing entry points for femoral shaft fractures: a systematic review and meta-analysis

Nasir Hussain, MSc, MD
Farrah Naz Hussain, MD
Corey Sermer, MSc
Hera Kamdar, MD
Emil H. Schemitsch, MD
Amir Sternheim, MD
Paul Kuzyk, MASc, MD

Presented in part at the Canadian Orthopedic Association Annual Conference in Ottawa, Ont., 2012

Accepted Aug. 18, 2016; Early-released Dec. 1, 2016

Correspondence to:
N. Hussain
1280 East Campus Dr.
Mount Pleasant MI 48859 USA
hussa1n@cmich.edu

DOI: 10.1503/cjs.000616

Background: There are several different techniques commonly used to perform intramedullary (IM) nailing of the femur to fix femoral fractures. We sought to identify significant differences in outcomes of studies comparing 1) trochanteric and piriformis entry and 2) antegrade and retrograde entry in IM nailing of the femur.

Methods: We searched MEDLINE, Cochrane and Embase databases and the Orthopaedic Trauma Association and American Academy of Orthopaedic Surgeons websites for comparative studies published from inception to November 2015. Criteria used to select articles for detailed review included use of antegrade and retrograde entry point or use of trochanteric and piriformis entry point for IM nailing of the femur in adult patients. Functional and technical outcomes were extracted from accepted studies.

Results: We identified 483 potential studies, of which 52 were eligible. Of these, we included 13 publications and 2 abstracts (2 level I, 7 level II and 6 level III studies). Trochanteric entry significantly reduced operative duration by 14 min compared with piriformis entry ($p = 0.030$). Retrograde nailing had a greater risk of postoperative knee pain than antegrade nailing ($p = 0.05$). On the other hand, antegrade nailing had significantly more postoperative hip pain ($p = 0.003$) and heterotopic ossification ($p < 0.001$) than retrograde nailing. No significant differences in functional outcomes were observed.

Conclusion: Although some significant differences were found, the varying quality of studies made recommendation difficult. Our meta-analysis did not confirm superiority of either antegrade over retrograde or trochanteric over piriformis entry for IM nailing of the femur.

Level of evidence: Level III therapeutic.

Contexte : Plusieurs techniques différentes sont couramment utilisées pour l'enclouage intramédullaire (IM) du fémur afin d'immobiliser les fractures fémorales. Nous avons voulu dégager les différences significatives sur le plan des résultats d'études ayant comparé 1) l'entrée par le trochanter et par la fossette piriforme et 2) l'entrée par voies antérograde et rétrograde pour l'enclouage IM du fémur.

Méthodes : Nous avons interrogé les bases de données MEDLINE, Cochrane et EMBASE et les sites Web de l'Orthopaedic Trauma Association et de l'American Academy of Orthopaedic Surgeons pour recenser les études comparatives publiées depuis leur création et jusqu'en novembre 2015. Les critères utilisés pour la sélection des articles en vue d'un examen détaillé incluaient l'utilisation de points d'entrée antérograde et rétrograde ou du trochanter et de la fossette piriforme pour l'enclouage IM du fémur chez des patients adultes. Les résultats fonctionnels et techniques ont été dégagés des études retenues.

Résultats : Nous avons recensé 483 études potentielles, dont 52 se sont révélées admissibles. Parmi elles, nous avons inclus 13 publications et 2 résumés (2 études de niveau I, 7 de niveau II et 6 de niveau III). Le point d'entrée par le trochanter a significativement réduit la durée des interventions, soit de 14 min, comparativement à l'entrée par la fossette piriforme ($p = 0,030$). L'enclouage rétrograde a comporté un risque plus élevé de douleur postopératoire au genou comparativement à l'enclouage antérograde ($p = 0,05$). Par ailleurs, l'enclouage antérograde a donné lieu à significativement plus de douleur à la hanche ($p = 0,003$) et d'ossification hétérotopique ($p < 0,001$) postopératoires comparativement à l'enclouage rétrograde. Aucune différence significative n'a été observée sur le plan des résultats fonctionnels.

Conclusion : Même si nous avons noté quelques différences significatives, la qualité variable des études nous empêche de formuler des recommandations. Notre méta-analyse n'a pas confirmé la supériorité du point d'entrée antérograde plutôt que rétrograde ou par le trochanter plutôt que par la fossette piriforme pour l'enclouage IM du fémur.

Niveau de preuve : Niveau III thérapeutique.

Intramedullary (IM) nailing is a proven and effective method for the management of femoral shaft fractures.[1,2] The appropriate entry point can make nail insertion easier, affect fracture reduction, and may prevent complications.[1,3] Although both ends of the femur are suitable, there is debate in the literature concerning antegrade versus retrograde entry and, in antegrade nailing, the choice of the piriformis fossa versus greater trochanter as an entry point.[1,4] Antegrade nailing is useful for the treatment of proximal femoral fractures; however, studies have found it to result in damage to the hip abductors and sometimes the pudendal nerve if the patient is in the supine position on a fracture table.[5] Retrograde nailing is advantageous for patients with multiple injuries, patients sustaining ipsilateral femoral neck and shaft fractures and obese patients;[6] however, it may be accompanied by higher rates of knee pain and lower rates of union.[7] The entry point for antegrade nailing is also controversial, with advocates for both piriformis and trochanteric entry.[4,8,9] The piriformis fossa is colinear with the medullary canal, allowing for straight nails to be inserted easily. However, the piriformis is difficult to access in obese patients, leading to interest in the greater trochanter as an alternative antegrade entry point.[1] To our knowledge, a comprehensive systematic review or meta-analysis to summarize the effects of various entry points for IM nailing of the femur has not been performed.

The purpose of this study was to identify significant differences in outcomes of studies comparing 1) trochanteric and piriformis entry and 2) antegrade and retrograde entry in IM nailing of femoral shaft fractures. We conducted a systematic review and meta-analysis using randomized controlled trials (RCTs) and prospective and retrospective comparative studies assessing rates of reoperation, dynamization, union, malalignment, nonunion, delayed union, pain, complications, mortality, operative duration, blood loss and functional outcomes in patients with femoral shaft fractures.

Methods

Eligibility criteria

Three authors (F.N.H., A.S. and P.K.) reviewed each article independently and determined their eligibility based on the following preset inclusion criteria: use of antegrade, retrograde, trochanteric entry or piriformis entry for IM nailing of the femur in adult (age > 18 yr) patients. Based on the search strategy developed, 3 authors (F.N.H., A.S. and P.K.) independently screened the results based on title and abstract alone and then screened all potentially eligible articles via full text. Disagreements were resolved by a consensus meeting.

Search strategy

Comparative studies in English were identified through a systematic search of MEDLINE, Embase, and Cochrane databases from inception to November 2015. The database search strategy was "femur AND fracture AND nail AND (antegrade OR retrograde)." The search strategy used was broad in order to encompass all potentially relevant articles. We examined the bibliographies of retrieved studies. We also searched the Orthopaedic Trauma Association (OTA) and American Academy for Orthopaedic Surgeons (AAOS) websites.

Assessment of study quality

Eligible studies were read in full by 3 authors (F.N.H., A.S. and P.K.). Each author independently assessed the methodological quality of included studies using the Cochrane Bone, Joint and Muscle Trauma Group reporting quality assessment tool.[10] This 12-item questionnaire assesses the methodological quality of reports of RCTs. The final reported scores for each study were determined by consensus.

Data abstraction

The relevant data were extracted from each study and recorded in a database. Information on the manufacturer and type of IM nails; number of patients and femoral shaft fractures; patient sex, age and body mass index (BMI); follow-up rate; functional outcome measures; operative duration; presence of pain; and rates of nonunion, malunion, reoperation, dynamization and femoral shortening was included.

Evaluation of agreement

Agreement among the 3 reviewers (F.N.H., A.S. and P.K.) on scoring the studies was evaluated using the κ statistic, with a score of 0 indicating chance agreement and a score of 1 indicating perfect agreement among the raters.[11]

Statistical analysis

We calculated the mean difference for operative duration and used the standard deviation (SD) to estimate the variance. If the SD was not available, it was calculated using standard error derived from a *p* value. If *p* values were unavailable, the SD was estimated using the range. All calculations were made according to methodology in the Cochrane Handbook.[10] The values obtained may be imprecise because the imputation methods used make assumptions about unknown data.[10]

We calculated risk ratios (RR) and 95% confidence intervals (CI) for the following dichotomous outcomes: union, nonunion/delayed union, malalignment (varus–valgus, longitudinal angular and rotational), femoral shortening, knee pain, hip/thigh pain, dynamization, heterotopic ossification and reoperations. A random-effects model was used to pool the relative risk estimates from these studies.[12]

Two-tailed tests of significance for treatment effects were used. We considered results to be significant at $p < 0.05$. RevMan software version 5.0 (The Nordic Cochrane Centre) was used to statistically analyze all pooled outcomes.

Evaluation of heterogeneity

To evaluate the extent to which the results of the subgroups differed from one another, stratified analyses and a statistical test of interaction were performed.[13] The I^2 statistic was used to quantify heterogeneity among studies, with an I^2 value of 0%–40% representing low heterogeneity and values greater than 40% representing moderate to high heterogeneity.[10] As a result, we evaluated heterogeneity on the basis of study design and overall study quality when I^2 was above 40%.

RESULTS

We identified 483 potential studies. We eliminated 431 studies after reviewing their titles and abstracts, leaving 52 studies for full text screening. Following full text screening, we included a total of 13 publications and 2 abstracts, 4 of which compared greater trochanter with piriformis entry, and 11 of which compared antegrade with retrograde entry (Fig. 1). Our assessment of study quality is summarized in Table 1. Studies were excluded for several reasons, including a lack of an adequate compartor group and a lack of live human participants. Our review includes articles reporting on a total of 1140 femoral shaft fractures treated with antegrade or retrograde nailing and 267 femoral shaft fractures treated with antegrade nailing from the greater trochanter or piriformis fossa (Table 2 and Table 3).

Sample demographics

Overall, the population sampled was similar among studies and was representative of the typical femoral shaft fracture population. The mean age of patients ranged from 21.75 to 52.15 years. The percentage of male patients ranged from 55% to 91%. The BMI ranged from 24 to 29. Except for 1 study in each comparison, the studies followed patients for longer than 12 months. The follow-up rate, when reported, was 14%–100% (Table 2 and Table 3).

Among the studies comparing antegrade with retrograde entry, 5 reported a greater number of distal femoral fractures in the retrograde group[14,16–18,25] (Table 2). Although not significant, the reported BMI tended to be greater in patients assigned to trochanteric entry over piriformis entry[4,8] (Table 3).

Description of surgical techniques used for placement of IM nails

Two surgical methods were used for placement of IM nails. In studies comparing trochanteric with piriformis entry, 2 used a fracture table for both groups (Table 3). In studies comparing antegrade with retrograde entry, 3 used

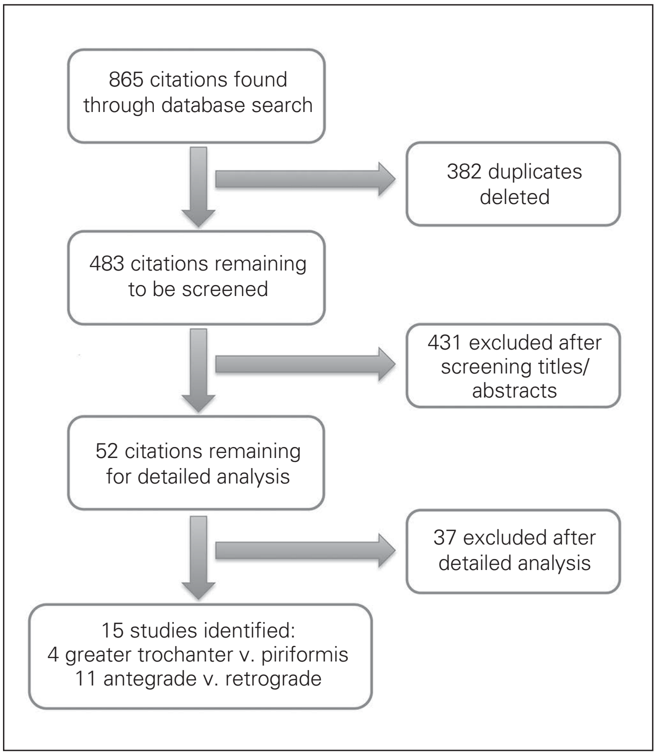

Fig. 1. Identification of trials comparing greater trochanter with piriformis entry, and antegrade with retrograde entry in intramedullary nailing of the femoral shaft.

a radiolucent table in both groups, 3 used a fracture table for antegrade nailing and a radiolucent table for retrograde nailing, and 1 used both methods for antegrade nailing and a radiolucent table for retrograde nailing (Table 2).

Operative duration and blood loss

Six studies comparing antegrade with retrograde entry in 396 fractures reported operative duration[14,15,20–22,25] (Table 4). Two studies[14,22] did not report an SD, *p* values or ranges, so the mean difference could not be estimated; however, these 2 studies reported no significant difference in operative duration. Therefore, 4 studies[15,20,21,25] reporting on 242 fractures were included in this analysis. There was no significant difference in operative duration between the 2 groups in this analysis (95% CI –21.31 to 15.61, $p = 0.76$, $I^2 = 85\%$; Fig. 2). Two studies comparing trochanteric with piriformis entry in 125 fractures reported operative duration[4,8] (Table 5). Operative duration was 14 min shorter when trochanteric entry was used than when piriformis entry was used, and this difference was sigificant (95%CI –26.67 to –1.34, $p = 0.030$, $I^2 = 0$). Heterogeneity was not successfully resolved when the results were categorized by study design. Further exploration on the basis of overall study quality also did not resolve heterogeneity.

Four studies[14,19,22,25] estimated blood loss in patients treated with either antegrade or retrograde nailing (Table 4). The results could not be pooled owing to unreported *p* values and/or ranges. Ricci and colleagues[25] reported significantly higher levels of blood loss in patients treated with antegrade nailing, while Ostrum and colleagues,[14] Tornetta and Tiburzi,[19] and Dougherty and colleagues[22] found no significant differences.

Union

Four studies[4,8,9,24] reported rates of union and delayed/nonunion in patients treated with trochanteric or piriformis nailing (Table 5). One study[21] did not indicate the number of patients allocated to each treatment arm and was excluded from this analysis. Therefore, 3 studies[4,8,9] reporting on 233 fractures were included. There was no significant difference between the 2 treatment groups.

Six studies[14,19,20,22,23,25] examining 576 fractures reported rates of union and delayed/nonunion in patients treated with either antegrade or retrograde IM nailing (Table 4). There were no significant differences found among the studies between the 2 treatment groups.

Malalignment and femoral shortening

We defined malalignment as ≥ 5° of deformity in any plane.[26–28] Two studies[4,8] examining 125 fractures treated with either trochanteric or piriformis nailing reported rates of malalignment (Table 5). There was no significant difference between the 2 treatment groups (RR 2.3, 95% CI 0.57–9.34, $p = 0.24$, $I^2 = 0\%$). Six studies[14–16,18–20] examining 693 fractures treated with either antegrade or retrograde nailing reported rates of malalignment (Table 4). There was no significant difference between the 2 treatment groups (RR 0.9, 95% CI 0.57–1.56, $p = 0.82$, $I^2 = 42\%$). Heterogeneity was not successfully resolved when the results were categorized by study design. Further exploration on the basis of overall study quality also did not resolve heterogeneity. Reported rates of

Table 1. Quality of the 13 comparitive studies assessed using the Cochrane Bone, Joint and Muscle Trauma Group reporting quality assessment tool

Question	κ (no. valid cases)*	Asymptomatic SE†	Approx. *t*‡	*p* value
Was the assigned treatment adequately concealed before allocation?	0.27 (10)	0.11	1.16	0.25
Were the outcomes of participatins who withdrew described and included in the analysis (intention to treat)?	0.09 (13)	0.09	0.74	0.46
Were the outcome assessors blinded to treatment status?	0.40 (13)	0.35	1.39	0.17
Were the treatment and control group comparable at entry? (likely confounders may be age, activity level)	0.22 (13)	0.23	1.08	0.28
Were the participants blind to assignment status after allocation?	1.00 (13)			
Were treatment providers blind to assignment status?	1.00 (13)			
Were care programmes, other than the trial options, identical?	0.22 (13)	0.20	1.11	0.27
Were inclusion and exclusion criteria clearly defined?	0.56 (13)	0.21	2.55	0.010
Were the interventions clearly defined?	0.40 (13)	0.35	1.39	0.17
Were the outcome measures used clearly defined (by outcome)?	0.40 (13)	0.35	1.39	0.17
Were diagnostic tests used in outcome assessment clinically useful (by outcome)?	1.00 (13)			
Was the surveillance active, and of clinically appropriate duration?	0.40 (13)	0.35	1.39	0.17

SE = standard error.
*The κ values are reported for the 3 reviewers (F.N.H, A.S. and P.K.).
†Not assuming the null hypothesis.
‡Using the asymptotic standard error assuming the null hypothesis.

varus–valgus, longitudinal and rotational malalignment or deformity did not differ significantly between the 2 groups.

Femoral shortening was defined as inequality in limb length ≥ 10 mm. Data from 3 studies[16,19,20] comparing

Table 2. Characteristics of included trials comparing antegrade with retrograde intramedullary nailing of the femoral shaft

Study	Study design	Functional measurement	Treatment groups	No. femurs	Nailing technique	Mean age, yr	% male	BMI	ISS	% follow-up	Mean follow-up (range), mo
Daglar et al.[20]	Level II quasi-randomized	Lysholm knee score	Antegrade (piriformis)	41	Radiolucent table	34	69		15.2	43	44 (25–80)
			Retrograde	30	Radiolucent table	44.1			14.3	43	
Ostrum et al.[14]	Level II quasi-randomized		Antegrade (piriformis) (10 mm titanium cannulated nail, Synthes)	46	Fracture table, radiolucent table	26.6	61	24.6		85	7.28 (2.5–14.83)
			Retrograde (titanium femoral nail, Biomet)	54	Radiolucent table	29.4	63	26.4		87	
Tornetta and Tiburzi[19]	Level II quasi-randomized		Antegrade (piriformis)	38	Fracture table	31			12.4 (4–42)	92	
			Retrograde	31	Radiolucent table	33			12.5 (4–42)	97	
Toluse et al.[21]	Level II prospective cohort		Antegrade	20							
			Retrograde	41							
Herscovici et al.[15]	Level II prospective cohort		Antegrade (femoral nail, Synthes)	69		28.2	72			76	18.3 (12–59)
			Retrograde (femoral nail, Synthes)	56							
Dougherty et al.[22]	Level III retrospective		Antegrade	25	Fracture table	33.6	91			89	26 (3–112)
			Retrograde	43	Radiolucent table	30.5	86			81	41 (3–148)
Kuhn et al.[23]	Level III retrospective		Antegrade	35	Radiolucent table	33.0	80	26.0			12.87 (3–38)
			Retrograde	34	Radiucent table	34.3	59	33.1			15.42 (3.5–68.25)
Ricci et al.[8]	Level III retrospective		Antegrade	134		32	69			70	23 (5–64)
			Retrograde	147		34	73			71	23 (6–66)
Salem et al.[16]	Level III retrospective	Merle d'Aubigne and Postel, Tegner and Lysholm score	Antegrade (piriformis) (UFN, Synthes; RFN, Synthes)	29	Radiolucent table					69	14.4 (4.4–24)
			Retrograde (DFN, Synthes: IMSC Nail, Smith & Nephew)	33	Radiolucent table					64	13 (2.4–32.4)
Ricci et al.[18]	Level III retrospective		Antegrade	183	Fracture table	31				100	
			Retrograde	172	Radiolucent table	33				100	
Murray et al.[17]	Level III retrospective	KOOS, HOOS	Antegrade	19		34.5			15.21 ±12.40	14	56.8
			Retrograde	14		37.1			16.36 ±10.40		36.5

BMI = body mass index; DFN = distal femoral nail; HOOS = hip dysfunction and osteoarthritis outcome score; IMSC = intramedullary supracondylar; ISS = injury severity score; KOOS = knee injury and osteoarthritis outcome score; RFN/UFN = reamed/unreamed femoral nail.

antegrade with retrograde nailing in 140 fractures yielded no significant difference (RR = 0.6, 95% CI 0.16–1.98, p = 0.38, I^2 = 35%).

Pain

Rates of postoperative pain in the knee and hip/thigh were pooled from studies comparing antegrade with retrograde nailing. Three studies[14,19,25] examining 291 fractures reported knee pain (Table 4). The results were significantly in favour of antegrade nailing (RR 0.4, 95% CI 0.25–0.61, p < 0.001, I^2 = 15%; Fig. 3). Two studies[14,25] examining 256 fractures reported hip/thigh pain (Fig. 2). The risk of having hip/thigh pain was significantly greater in those receiving antegrade nailing than in those receiving retrograde nailing (RR 4.3, 95% CI 1.66–11.10, p = 0.003, I^2 = 0; Fig. 4). No studies examining trochanteric versus piriformis entry reported rates of postoperative pain.

Reoperations and dynamization

There were no significant differences in rates of reoperation (RR 1.0, 95% CI 0.57–1.72, p = 0.98, I^2 = 5%) or dynamization (RR 0.6, 95% CI 0.19–1.65, p = 0.30, I^2 = 12%) in studies comparing antegrade with retrograde nailing (Table 4).

Functional outcomes

The studies that reported functional outcomes used different tools for assessment. Therefore, the results could not be pooled. Three studies[4,8,9] comparing trochanteric with piriformis nailing reported postoperative functionality (Table 5). None of the studies found significant differences. Archdeacon and colleagues[24] reported significant differences in hip range of motion (ROM; p = 0.025) favouring trochanteric nailing. Three studies[16,17,20] that examined outcomes after antegrade or retrograde IM nailing reported postoperative functional outcomes (Table 4). Murray and colleagues[17] reported that the Knee Injury and Osteoarthritis Outcome Scores were significantly worse (p = 0.005) in the retrograde group (Table 4).

Mortality and complications

Reported deaths in both comparisons were found to be nonsignificant (Table 4 and Table 5).

Radiographic evidence of heterotopic ossification (HO) around the hip was reported in 3 studies[19,23,25] comparing antegrade and retrograde nailing (Table 4). There was a significantly greater risk of HO with antegrade nailing than with retrograde nailing (RR 19.51, 95% CI 3.80–100.20, p < 0.001, I^2 = 0%) favouring retrograde nailing (Fig. 5); however, only 1 study[23] reported on symptomolgy associated with HO. Of the 10 patients who had radiographic evidence of HO, only 1 had associated symptoms.

For the remainder of the complications, each study reported different outcomes, which could not be statistically pooled. Within the studies comparing antegrade with retrograde nailing, Ostrum and colleagues[14] reported that a Trendelenburg gait was present in all 39 patients treated

Table 3. Characteristics of the 4 included trials comparing greater trochanter with piriformis entry in intramedullary nailing of the femoral shaft

Study	Study design	Functional measurement	Treatment groups	No. femurs	Nailing technique	Mean age, yr	% male	BMI	ISS	% follow-up	Mean follow-up (range), mo
Stannard at al.[9]	Level I randomized	WOMAC	Trochanteric	59							
			Piriformis	55							
Archdeacon et al.[24]	Level I randomized		Trochanteric	47							
			Piriformis*								
Ricci et al.[8]	Level II prospective cohort	Lower extremity measure	Greater trochanter (Trigen TAN, Smith-Nephew)	38	Fracture table	28 (16–88)	66	24 (10–80)		84	10 (7–25)
			Piriformis (Trigen FAN, Smith-Nephew)	53	Fracture table	29 (16–79)	55	24 (18–45)			
Starr et al.[4]	Level II quasi-randomized	Harris hip score	Trochanteric (Long Gamma Nail version 2, Howmedica)	17	Fracture table	37 (19–50)		29 (20–55)	15 (9–48)	76	16 (12–29)
			Piriformis (Russel-Taylor Recon Nail, Smith-Nephew)	17	Fracture table	32 (19–45)		26 (19–56)	15 (9–29)	88	15 (12–28)

BMI = body mass index; FAN = femoral antegrade nail; ISS = injury severity score; TAN = trochanteric antegrade nail; WOMAC = Western Ontario and McMaster Universities Arthritis Index.
*Not reported.

Table 4. Summary of outcome measures for antegrade versus retrograde studies

Measure	Herscovici et al.[15] Level II prospective cohort	Ostrum et al.[14] Level II randomized	Tornetta and Tiburzi [19] Level II quasirandomized	Daglar et al.[20] Level II quasirandomized	Toluse et al.[21] Level II prospective cohort	Dougherty et al.[22] Level III retrospective	Kuhn et al.[23] Level III retrospective	Salem et al.[16] Level III retrospective	Ricci et al.[25] Level III retrospective	Ricci et al.[18] Level III retrospecitve	Murray et al.[17] Level III retrospective
Operative duration		NS	$p < 0.05$‡	$p = 0.029$§	NS	NS			$p < 0.01$ (unreamed)§		
Estimated blood loss		NS	NS			NS			$p < 0.01$ (unreamed)§		
Malalignment	NS	$p = 0.05$	$p < 0.05$‡	$p = 0.44$				NS		NS	
Union		NS	NS	NS					NS		
Delayed union		NS		$p = 0.59$		NS			NS		
Nonunion		NS				NS	NS		NS		
Malunion							NS	NS	NS		
Deaths		NS									
Functional outcome measure*				$p = 0.70$				NS			$p < 0.05$ (KOOS)‡ NS (HOOS)
Hip ROM			NS								NS
Knee ROM		NS	NS								$p < 0.05$‡
Hip pain		$p = 0.0108$§							$p < 0.05$§		
Knee pain		NS	$p < 0.05$‡						$p < 0.001$‡		
Dynamization		$p = 0.10$§									
Femoral shortening			$p < 0.05$‡	$p = 0.32$				NS			
Reoperations				$p = 0.47$					NS		$p < 0.05$‡
Heterotopic ossification around the hip			NS				$p < 0.001$‡		$p < 0.001$§		
Pudendal nerve injury									NS		
Trendelenburg gait		$p < 0.05$§									
Other medical complications†	NS	NS				NS	NS		NS		NS

HOOS = hip dysfunction and osteoarthritis outcome score; KOOS = knee injury and osteoarthritis outcome score; NS = not significant; ROM = range of motion.
*Functional outcome measures include lower extremity measure, Harris hip score, Lysholm score, Lysholm and Tegner score, Western Ontario and McMaster Universities Arthritis Index, Merle d'Aubigne and Postel, KOOS and HOOS.
†Other medical complications include: pulmonary embolism, fat embolus syndrome, deep venous thrombosis, postoperative hematoma, haemarthrosis, infection, hyperbilirubinemia, and pneumonia.
‡Favours antegrade nailing.
§Favours retrograde nailing.

with antegrade nailing and absent in the 35 patients treated with retrograde nailing. Differences between antegrade and retrograde treatment groups in other reported complications were not significant[14,15,17,22,23,25] (Table 4).

In studies examining trochanteric versus piriformis nailing, Stannard and colleagues[9] reported greater HO of the hip in the piriformis group. This difference was not significant ($p = 0.10$; Table 5).

Discussion

The results of this systematic review and meta-analysis suggest that retrograde nailing is favourable over antegrade nailing in terms of hip pain and HO of the hip. However, the results also are in favour of antegrade nailing with respect to knee pain. Moreover, there was level-II[14] evidence showing Trendelenburg gait, favouring retrograde nailing, and level-III[17] evidence showing significant differences in knee function and ROM, favouring antegrade nailing. The only significant difference in the trochanteric versus piriformis pooled data was operative duration, which favoured trochanteric entry. There was also level-I evidence showing significant differences in hip ROM, favouring trochanteric nailing.

Studies show that the incidence of postoperative knee pain after retrograde nailing can be as high as 70%.[7,29] Our

	Antegrade			Retrograde				Mean difference
Study	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random (95% CI)
Dagler et al.[20]	122	16.509	17	108	16.509	13	27.5%	14.00 (2.08 to 25.92)
Ricci et al.[25]	102.58	24.02	59	88.78	10.91	23	29.5%	13.80 (6.22 to 21.38)
Toluse et al.[21]	137.4	32.69	20	157.07	46.07	41	22.7%	–19.67 (–39.77 to 0.43)
Tornetta and Tiburzi[19]	116	40	38	147	58	31	20.3%	–31.00 (–55.05 to –6.95)
Total (95% CI)			**134**			**108**	**100.0%**	**–2.85 (–21.31 to 15.61)**

Heterogeneity: Tau^2 = 285.81; Chi^2 = 20.59, df = 3 ($p = 0.0001$); I^2 = 85%

Test for overall effect: $z = 0.30$ ($p = 0.76$)

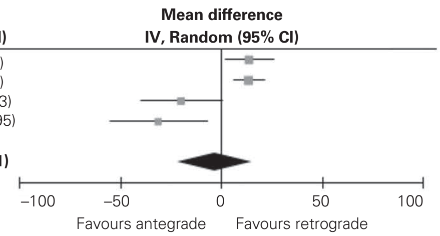

Fig. 2. Trials comparing operative duration in patients treated with antegrade or retrograde nailing of the femur. CI = confidence interval; SD = standard deviation.

Table 5: Summary of outcome measures for trochanteric versus piriformis studies

Measure	Archdeacon et al.[24] Level I randomized	Stannard et al.[9] Level I randomized	Starr et al.[4] Level II quasirandomized	Ricci et al.[8] Level II prospective cohort
Operative duration			$p = 0.26$	$p = 0.08$
Estimated blood loss			$p = 0.15$	
Malalignment			$p = 0.3$	NS
Union	NS	NS	NS	NS
Delayed union		NS	NS	NS
Nonunion		NS	NS	
Malunion				
Deaths			NS	
Functional outcome measure*		NS	$p = 0.60$	NS
Hip ROM	$p = 0.025$‡		NS	
Knee ROM			$p = 0.13$	
Hip pain				
Knee pain				
Dynamization				
Femoral shortening				
Reoperations				
Heterotopic ossification around the hip		NS		
Pudendal nerve injury				
Trendelenburg gait				
Other medical complications†				NS

NS = nonsignificant; ROM = range of motion.

*Functional outcome measures include lower extremity measure, Harris hip score, Lysholm score, Lysholm and Tegner score, Western Ontario and McMaster Universities Arthritis Index, Merle d'Aubigne and Postel, knee injury and osteoarthritis outcome score and hip dysfunction and osteoarthritis outcome score.

†Other medical complications include pulmonary embolism, fat embolus syndrome, deep venous thrombosis, postoperative hematoma, hemarthrosis, infection, hyperbilirubinemia and pneumonia.

‡Favours greater trochanteric nailing.

study revealed that a statistically greater number of patients undergoing retrograde nailing than antegrade nailing experienced knee pain. The etiology of this pain has been attributed to events such as concomitant patellar or ligamentous injury from the initial trauma, sepsis of the knee joint, distal locking screws, quadriceps atrophy, or protruding nails.[7,25,29,30] This may also explain the finding of Murray and colleagues,[17] who showed that both knee function and ROM were significantly lower in patients treated with retrograde nailing. None of the studies had long enough follow-up to show an increased incidence of knee osteoarthritis (OA) with retrograde nailing. In the absence of a prominent nail within the knee joint or septic arthritis, the risk of knee OA is likely minimal; however, the long-term incidence of OA following retrograde nailing remains unknown. It is important to note that none of the studies reviewed in this meta-analysis reported any occurrence of septic arthritis.

Whereas Ostrum and colleagues[14] and Tornetta and Tiburzi[19] reported no significant differences between antegrade and retrograde nailing in terms of blood loss, Ricci and colleagues[25] found levels of estimated blood loss to be significantly lower in patients treated with retrograde than antegrade nails. They attributed this finding to the use of a tourniquet during retrograde nail insertion; however, tourniquet usage was not mentioned in the other included

Study	Antegrade Events	Antegrade Total	Retrograde Events	Retrograde Total	Weight	Risk ratio M-H, Random (95% CI)
Ostrum et al.[14]	4	39	5	35	12.2%	0.72 (0.21–2.46)
Ricci et al.[25]	7	78	25	70	28.1%	0.25 (0.12–0.54)
Tornetta and Tiburzi[19]	13	38	25	31	59.7%	0.42 (0.26–0.68)
Total (95% CI)		**155**		**136**	**100.0%**	**0.39 (0.25–0.61)**
Total events	24		55			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 2.37$, df = 2 ($p = 0.31$); $I^2 = 15\%$

Test for overall effect: $z = 4.14$ ($p = 0.0001$)

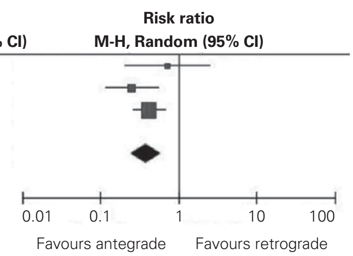

Fig. 3. Trials comparing knee pain in patients treated with antegrade or retrograde nailing of the femur. CI = confidence interval; M-H = Mantel-Haenszel.

Study	Antegrade Events	Antegrade Total	Retrograde Events	Retrograde Total	Weight	Risk ratio M-H, Random (95% CI)
Ostrum et al.[14]	10	39	2	47	42.6%	6.03 (1.40–25.88)
Ricci et al.[25]	10	85	3	85	57.4%	3.33 (0.95–11.69)
Total (95% CI)		**124**		**132**	**100.0%**	**4.29 (1.66–11.10)**
Total events	20		5			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.36$, df = 1 ($p = 0.55$); $I^2 = 0\%$

Test for overall effect: $z = 3.00$ ($p = 0.003$)

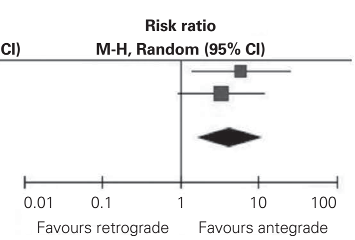

Fig. 4. Trials comparing hip/thigh pain in patients treated with antegrade or retrograde nailing of the femur. CI = confidence interval; M-H = Mantel-Haenszel.

Study	Antegrade Events	Antegrade Total	Retrograde Events	Retrograde Total	Weight	Risk ratio M-H, Random (95% CI)
Kuhn et al.[23]	10	35	0	34	34.2%	20.42 (1.24–335.28)
Ricci et al.[25]	24	94	0	104	34.5%	54.16 (3.34–878.37)
Tornetta and Tiburzi[19]	3	35	0	30	31.3%	6.03 (0.32–112.21)
Total (95% CI)		**164**		**168**	**100.0%**	**19.51 (3.80–100.20)**
Total events	37		0			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.25$, df = 2 ($p = 0.53$); $I^2 = 0\%$

Test for overall effect: $z = 3.56$ ($p = 0.0004$)

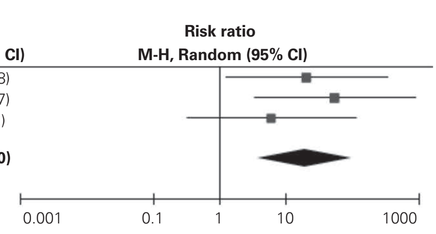

Fig. 5. Trials comparing heterotopic ossification around the hip in patients treated with antegrade or retrograde nailing of the femur. CI = confidence interval; M-H = Mantel-Haenszel.

studies. Additional studies have also shown retrograde nailing to be associated with minimal blood loss,[31] which may be a result of reduced operative duration and soft tissue dissection. Another important finding among studies in this comparison was the greater presence of HO around the hip in patients treated with antegrade than retrograde nailing. This has been attributed to the requirements of additional muscle dissection and reamings from the femoral canal deposited in the soft tissues around the hip.[5,6,32] However, only 1 study reported on symptoms caused by the HO, and none of the studies reported that patients required excision of HO. Therefore, the increase in HO with antegrade femoral nailing is not likely to be clinically significant. Furthermore, antegrade nailing frequently causes injury to the gluteus medius and minimus muscles and the superior gluteal nerve, causing abduction weakness.[33] Weak abductors may be easily fatigued when challenged, consequently resulting in pain and a Trendelenburg gait.[33,34] This is a possible explanation for the statistically greater numbers of patients experiencing hip pain in the antegrade than the retrograde nailing group and the finding of a Trendelenburg gait in all patients treated with antegrade nails in the study by Ostrum and colleagues.[14]

No differences in union, delayed/nonunion, malalignment or femoral shortening were observed between antegrade and retrograde nailing. Previous studies evaluating retrograde nailing also shown rates of healing that were comparable to those of anterade nailing.[29,30] Differences in other complications were found not to be significant. However, this could be attributed to the small sample size and the fact that not all authors reported the same complications.

Our analysis showed differences in operative duration between trochanteric and piriformis nailing treatment groups, and 1 level-I study[24] showed significant differences in hip ROM, favouring trochanteric nailing. Cadaver studies have shown that nailing through the piriformis fossa penetrated muscles and tendons of the hip abductors and external rotators, including the gluteus medius muscle.[35,36] Replacement of these contractile fibres in living patients can have consequences for muscle function, and choosing a more lateral entry point, such as the greater trochanter, may be beneficial both for hip function and ease of access for the surgeon.[35,36]

Limitations

Our study had several limitations. In order to reduce bias and heterogeneity in the results, it would have been best to use only level-I studies or RCTs. However, there is a paucity of such trials examining viable entry points for femoral nailing, perhaps owing to the difficulty in performing these studies in acute orthopaedic trauma patients. Although several of the included studies were randomized, blinding or randomization was often inadequate and included a relatively small number of patients. Combining the results of RCTs and lower level studies, as presented here, greatly reduces the external validity of the pooled analysis. Moreover, the studies examined different outcomes of interest and often reported these outcomes differently, which made it difficult to statistically pool data and decreased the available sample size for each outcome. There was also variation among studies in terms of surgical technique, which may have contributed to heterogeneity and bias. Finally, 8 of the 15 studies had a loss to follow-up greater than 10%. Despite these pitfalls, we were able to elucidate some key findings from the included studies, which may be a helpful starting point for more methodologically rigourous studies.

Conclusion

Our meta-analysis did not confirm superiority of either antegrade over retrograde nailing, or trochanteric over piriformis entry in IM nailing of the femur. The 15 included studies varied in quality and outcomes reported, and thus higher-quality studies are required to clearly establish any recommendations. We suggest that surgeons use their best judgment as to the choice of entry point based on surgeon comfort with the technique and on patient and fracture characteristics.

Affiliations: From the Department of Orthopaedics, St. Michael's Hospital, University of Toronto, Toronto, Ont. (Hussain, Naz Hussain, Schemitsch); the Wayne State University School of Medicine, Detroit, Michigan (Naz Hussain); the Division of Orthopaedic Surgery, Mount Sinai Hospital, University of Toronto, Toronto, Ont. (Sermer, Sternheim, Kuzyk); ans the Dow University of Health Sciences, Karachi, Pakistan (Kamdar).

Competing interests: E. Schemitsch has been a paid consultant with Stryker, Smith and Nephew and Zimmer for work unrelated to the products mentioned in this article. No other competing interests declared.

Contributors: N. Hussain, E. Schemitsch, A. Sternheim and P. Kuzyk designed the study. N. Hussain, F. Hussain, C. Sermer and P. Kuzyk acquired the data, which all authors analyzed. N. Hussain, F. Hussain, C. Sermer, H. Kamdar and P. Kuzyk wrote the article, which all authors reviewed and approved for publication.

References

1. Charopoulos I, Giannoudis PV. Ideal entry point in antegrade femoral nailing: controversies and innovations. *Injury* 2009;40:791-4.
2. Winquist RA, Hansen ST Jr, Clawson DK. Closed intramedullary nailing of femoral fractures. A report of five hundred and twenty cases. *J Bone Joint Surg Am* 1984;66:529-39.
3. Kale SP, Patil N, Pilankar S, et al. Correct anatomical location of entry point for antegrade femoral nailing. *Injury* 2006;37:990-3.
4. Starr AJ, Hay MT, Reinert CM, et al. Cephalomedullary nails in the treatment of high-energy proximal femur fractures in young patients: a prospective, randomized comparison of trochanteric versus piriformis fossa entry portal. *J Orthop Trauma* 2006;20:240-6.
5. Kao JT, Burton D, Comstock C, et al. Pudendal nerve palsy after femoral intramedullary nailing. *J Orthop Trauma* 1993;7:58-63.

6. Starr AJ, Bucholz RW. Retrograde nailing of fractures of the femoral shaft. *Current Orthopaedics* 1999;13:237-41.
7. Papadokostakis G, Papakostidis C, Dimitriou R, et al. The role and efficacy of retrograding nailing for the treatment of diaphyseal and distal femoral fractures: a systematic review of the literature. *Injury* 2005;36:813-22.
8. Ricci WM, Schwappach J, Tucker M, et al. Trochanteric versus piriformis entry portal for the treatment of femoral shaft fractures. *J Orthop Trauma* 2006;20:663-7.
9. Stannard JP, Bankston LS, Jennings JK, et al. Piriformis vs trochanteric antegrade nailing of femoral fractures: a prospective randomized study. American Academy of Orthopaedic Surgeons (AAOS) 2009 Annual Meeting; 25-28 Feb; 2009.
10. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.0.2 ed.: The Cochrane Collaboration; 2009.
11. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. *Psychol Bull* 1979;86:420-8.
12. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177-88.
13. Altman DG, Bland JM. Interaction revisited: the difference between two estimates. *BMJ* 2003;326:219.
14. Ostrum RF, Agarwal A, Lakatos R, et al. Prospective comparison of retrograde and antegrade femoral intramedullary nailing. *J Orthop Trauma* 2000;14:496-501.
15. Herscovici D Jr, Ricci WM, McAndrews P, et al. Treatment of femoral shaft fracture using unreamed interlocked nails. *J Orthop Trauma* 2000;14:10-4.
16. Salem KH, Maier D, Keppler P, et al. Limb malalignment and functional outcome after antegrade versus retrograde intramedullary nailing in distal femoral fractures. *J Trauma* 2006;61:375-81.
17. Murray P, Bergin P, Labropoulos P, et al. Retrograde femoral nailing and knee function. *Orthopedics* 2008;31:e1-8.
18. Ricci WM, Bellabarba C, Lewis R, et al. Angular malalignment after intramedullary nailing of femoral shaft fractures. *J Orthop Trauma* 2001;15:90-5.
19. Tornetta P III, Tiburzi D. Antegrade or retrograde reamed femoral nailing. A prospective, randomised trial. *J Bone Joint Surg Br* 2000; 82:652-4.
20. Daglar B, Gungor E, Delialioglu OM, et al. Comparison of knee function after antegrade and retrograde intramedullary nailing for diaphyseal femoral fractures: results of isokinetic evaluation. *J Orthop Trauma* 2009;23:640-4.
21. Toluse AM, Ikem IC, Akinyoola AL, et al. Antegrade versus retrograde approach to interlocking nail fixation of the femoral diaphyseal fractures: Is there a different in time to union? *Niger Postgrad Med J* 2015;22:41-4.
22. Dougherty PJ, Gherebeh P, Zekaj M, et al. Retrograde versus antegrade intramedullary nailing of gunshot diaphyseal femur fractures. *Clin Orthop Relat Res* 2013;471:3974-80.
23. Kuhn KM, Ali A, Boudreau JA, et al. Antegrade vs retrograde intramedullary nailing of proximal third femur fractures. *J Surg Orthop Adv* 2013;22:263-9.
24. Archdeacon M, Hewett T, Wyrick J, et al. A prospective, randomized functional evaluation of hip function after piriformis versus trochanteric femoral nailing. Orthopaedic Trauma Association (OTA) 2006 Annual Meeting; 5-7 Oct; 2006.
25. Ricci WM, Bellabarba C, Evanoff B, et al. Retrograde versus antegrade nailing of femoral shaft fractures. *J Orthop Trauma* 2001;15:161-9.
26. Karpos PA, McFerran MA, Johnson KD. Intramedullary nailing of acute femoral shaft fractures using manual traction without a fracture table. *J Orthop Trauma* 1995;9:57-62.
27. Neher C, Ostrum RF. Treatment of subtrochanteric femur fractures using a submuscular fixed low-angle plate. *Am J Orthop* 2003;32(Suppl): 29-33.
28. Sanders R, Koval KJ, DiPasquale T, et al. Retrograde reamed femoral nailing. *J Orthop Trauma* 1993;7:293-302.
29. Acharya KN, Rao MR. Retrograde nailing for distal third femoral shaft fractures: a prospective study. *J Orthop Surg (Hong Kong)* 2006;14:253-8.
30. Clement H, Heidari N, Kosuge D, et al. Anatomical structures at risk with the proud retrograde femoral nail. *Arch Orthop Trauma Surg* 2011.
31. Moed BR, Watson JT. Retrograde intramedullary nailing, without reaming, of fractures of the femoral shaft in multiply injured patients. *J Bone Joint Surg Am* 1995;77:1520-7.
32. Brumback RJ, Wells JD, Lakatos R, et al. Heterotopic ossification about the hip after intramedullary nailing for fractures of the femur. *J Bone Joint Surg Am* 1990;72:1067-73.
33. Bain GI, Zacest AC, Paterson DC, et al. Abduction strength following intramedullary nailing of the femur. *J Orthop Trauma* 1997;11:93-7.
34. Bednar DA, Ali P. Intramedullary nailing of femoral shaft fractures: reoperation and return to work. *Can J Surg* 1993;36:464-6.
35. Ansari Moein CM, Verhofstad MH, Bleys RL, et al. Soft tissue anatomy around the hip and its implications for choice of entry point in antegrade femoral nailing. *Clin Anat* 2008;21:568-74.
36. Dora C, Leunig M, Beck M, et al. Entry point soft tissue damage in antegrade femoral nailing: a cadaver study. *J Orthop Trauma* 2001; 15:488-93.