

SYSTEMATIC REVIEW

Antegrade vs Retrograde Intra-Medullary Nailing in Femoral Shaft Fractures: A Systematic Review and Meta-Analysis

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Abstract

Objectives: Femoral shaft fractures are one of the most prevalent fractures found in clinical practice. Numerous operative and non-operative options are readily available for the treatment of such fractures with intra-medullary nailing being the gold standard. To date, no consensus has been reached favoring one approach over the other. Thus, this meta-analysis aims to compare the outcomes between an antegrade and retrograde intra-medullary nailing for the treatment of femoral shaft fractures.

Methods: PubMed, Cochrane, Google Scholar (page 1-20), and Embase were searched till January 2024. The clinical outcomes evaluated were the incidence of adverse events, reoperations, hip and knee pain, and surgery-related parameters.

Results: Higher rates of hip pain, and heterotopic ossification ($p=0.0003$, and $p=0.0002$ respectively) was observed with antegrade nailing. However, a higher rate of knee pain ($p=0.02$) was appreciated in retrograde nailing. There was no statistically significant difference in the remaining analyzed outcomes such as operative time, reoperation rate or other complications.

Conclusion: Despite a higher rate of heterotopic ossification using the antegrade nailing technique, both the antegrade and retrograde nailing techniques yield overall similar outcomes. Therefore, the decision to choose one or the other should be based on patient-related factors, and the surgeon's experience and preference.

Level of evidence: IV

Keywords: Antegrade, Femoral shaft fractures, Intra-medullary nail, Pseudoarthrosis, Retrograde

Introduction

Femoral fractures are considered as one of the most prevalent fractures in an orthopedic clinical practice. These fractures can include the proximal and distal femur, or the femoral shaft.¹⁻³ With a worldwide incidence ranging between 10 and 21 per 100,000 per year, femoral shaft fractures are among the most common fractures seen by orthopedic surgeons, with around 2% of those being open fractures.^{1,4} They often result from high-impact trauma mechanisms of injury and are usually seen in a polytraumatic setting associated with other serious injuries. Low-energy mechanisms are more frequently observed in the elderly population.^{5,6} Prompt recognition

and appropriate treatment are of paramount importance, as these fractures carry the risk of numerous complications and sequelae, mainly hemorrhage, limb shortening, and deformities.¹

Numerous operative and non-operative options are readily available for the treatment of femoral shaft fractures. These include external fixation or internal fixation such as plate osteosynthesis or intramedullary nailing with the latter remaining the gold standard of treatment.⁷ Intramedullary nailing can be further divided into both antegrade nailing (entry points being trochanteric, piriformis, etc.) or retrograde nailing (distal

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intercondylar or intra-articular entry point).⁸⁻¹⁰ while antegrade nailing is generally preferred in proximal femoral fractures, the more-recent retrograde technique has been usually utilized in distal fractures. However, both techniques have consistently yielded similar outcomes in shaft fractures when it comes to union and malunion rates.¹¹ To date, no consensus has been reached favoring one technique over the other for the treatment of femoral shaft fractures as several comparative studies showed comparable outcomes between the two techniques.¹²⁻¹⁵

Therefore, the goal of this meta-analysis is to compare these two intramedullary techniques in the treatment of patients with midshaft femoral fractures, in hopes of paving the way for a more standardized approach, better physician decision-making, and improved patient outcomes.

Materials and Methods

Search strategy

The PRISMA guidelines were followed. Searches were conducted in PubMed, Cochrane, Google Scholar (pages 1–20), and Embase up until January 2024. To find articles comparing the outcomes of antegrade versus retrograde intramedullary nailing in femoral shaft fractures, the following keywords and Boolean phrases were used: (((“Femor*”) OR (“Femur”)) AND (“antegrade”) OR (“retrograde”)) AND (“nail*”). Additionally, more studies were identified by manually reviewing reference lists and performing online searches. One author extracted the data, and another verified the article selection. The procedure is summarized in the PRISMA flowchart [Figure 1A].

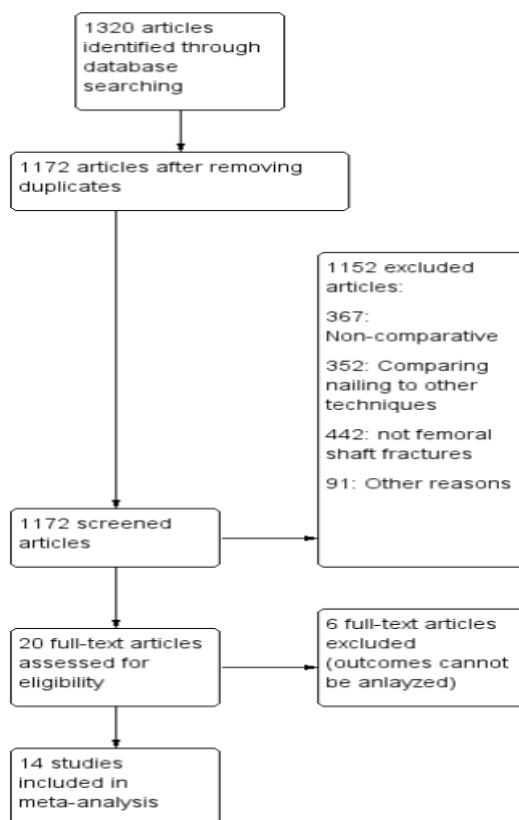


Figure 1. (A): PRISMA flowchart for article selection process. (B): Risk of bias item for each included study

The PICO of this study included the following elements: P (Population): patients with femoral shaft fractures, I (Intervention): femoral nailing, C (Comparison): antegrade versus retrograde nailing, O (Outcomes): adverse events, reoperation rates, pain, and operative time. The inclusion criteria comprised comparative studies that evaluated outcomes and surgical variables in patients with femoral shaft fractures undergoing either antegrade or retrograde femoral nailing. The exclusion criteria ruled out non-comparative studies, and studies that reported non-relevant

outcomes (i.e., outcomes not assessed by any included study) or had missing data (e.g., missing mean values and standard deviations).

Data extraction

Two authors (M.D. and J.C.) independently assessed the eligibility of the studies. The extracted data primarily included adverse events (numbers and percentages) such as pseudoarthrosis, infection, malalignment, heterotopic ossification (HO), and overall complications; revision rates

(numbers and percentages); knee and hip pain (numbers and percentages); and operating room time (minutes).

Risk of bias assessment

Two authors (M.D. and J.C.) independently assessed the risk of bias in randomized controlled trials using the Cochrane risk-of-bias tool. They evaluated the trials based on several factors: random sequence generation, allocation concealment, blinding of participants and study staff to the research procedure, blinding of outcome assessment, incomplete outcome data, and selective reporting. A trial was considered to have a low risk of bias if it had a low risk of bias across all key domains. If a trial had a high risk of bias in more than one key domain, it was judged to have a high risk of bias. Trials were classified as having an unclear risk of bias if they did not meet either of these criteria. For non-randomized studies, the ROBINS-I tool was used in a similar fashion to assess risk of bias.¹⁶ Studies were assessed and graded as having low, moderate, or high risk of confounding bias, selection bias, classification bias, bias due to deviations from interventions, bias due to missing data, bias in the measurement of outcomes, and bias in the selection of reported results. Studies with a critical risk of bias were excluded. To evaluate publication bias, we examined the symmetry of the funnel plot for each outcome.

Statistical analysis

All statistical analyses were performed using Review Manager 5.4 (The Cochrane Collaboration, 2020). Odds ratios (OR) with 95% confidence intervals (CI) were calculated for dichotomous data, while mean differences (MD) with 95% CI were used for continuous data. To address heterogeneity, a random-effects model was implemented in all analyses.

Results

Characteristics of the included studies

Fourteen studies, (10 retrospective, 2 prospective, and 2 randomized controlled trials) were included in the meta-analysis [Table 1].^{11-15,17-25} The number of femoral fractures included was 1504 with 705 treated by an antegrade nail and 799 treated using retrograde nailing. The quality assessment of non-randomized studies showed that most of them had a moderate risk, but none of them had a high and critical risk of bias [Table 2]. As for randomized studies, they were shown to have low risks of bias in all of the bias categories assessed [Figure 1B]. Moreover, the symmetry observed in the funnel plots for each analyzed outcome indicated a minimal presence of publication bias.

Table 1. Characteristics of the included studies

Author	Methods	Type of fracture	Participants		Age (years)		Follow-up
			Antegrade	Retrograde	Antegrade	Retrograde	
Adesina et al. 2023	Retrospective	Diaphyseal femur fracture	84	154	35.4	39.6	3 months
Brewster et al. 2020	Retrospective	Diaphyseal femur fracture	43	71	49.7	45.7	96 months
Daglar et al. 2009	Prospective	Diaphyseal femur fracture	17	13	34	44.1	44 months
Dougherty et al. 2013	Retrospective	Diaphyseal femur fracture	28	53	33.6	30.5	7 months
Durigan et al. 2019	Retrospective	Diaphyseal femur fracture	65	61	29		12 months
Herscovici et al. 2000	Retrospective	Diaphyseal femur fracture	69	56	28.2		18 months
Kim et al. 2018	Retrospective	Infra-isthmal femur fracture	38	22	36.2	36.7	29.5 months
Kuhn et al. 2013	Retrospective	Proximal third femur fracture	35	34	33	34.3	55 months
Murray et al. 2008	Retrospective	Diaphyseal femur fracture	19	14	34.5	37.1	46 months
Ostrum et al. 2000	Randomized controlled trial	Diaphyseal femur fracture	46	54	26.6	29.4	7 months
Ricci et al. 2001	Retrospective	Diaphyseal femur fracture	183	174	32	34	23 months
Salemet al. 2006	Retrospective	Distal femur fracture	20	21	44.5		14 months
Toluse et al. 2015	Prospective	Diaphyseal femur fracture	20	41	37		9 months
Tornetta et al. 2000	Randomized controlled trial	Diaphyseal femur fracture	38	31	31	33	12 months

Table 2. Bias assessment in non-randomized studies

Studies	Confounding bias	Selection bias	Classification bias	Bias due to deviation from interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of reported results	Results
Adesina et al. 2023	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Brewster et al. 2020	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Daglar et al. 2009	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Dougherty et al. 2013	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Moderate risk	Moderate risk
Durigan et al. 2019	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Herscovici et al. 2000	Low risk	Low risk	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Moderate risk
Kim et al. 2018	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Kuhn et al. 2013	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Murray et al. 2008	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Ricci et al. 2001	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Salem et al. 2006	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Toluse et al. 2015	Moderate risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk

Adverse events

Pseudoarthrosis

851 patients in 8 studies (408 with antegrade nails and 443 with retrograde nails) had a reported rate of pseudoarthrosis, showing no difference between the two groups (OR=1.17; 95% CI: 0.68-2.03, p=0.57, [Figure 2A]).

Infections

605 patients in 4 studies (242 with antegrade nails and 363 with retrograde nails) had a reported rate of infection, showing no difference between the two groups (OR=0.63; 95% CI: 0.16-2.43, p=0.50, [Figure 2B]).

Malalignment

338 patients in 4 studies (169 with antegrade nails and 169

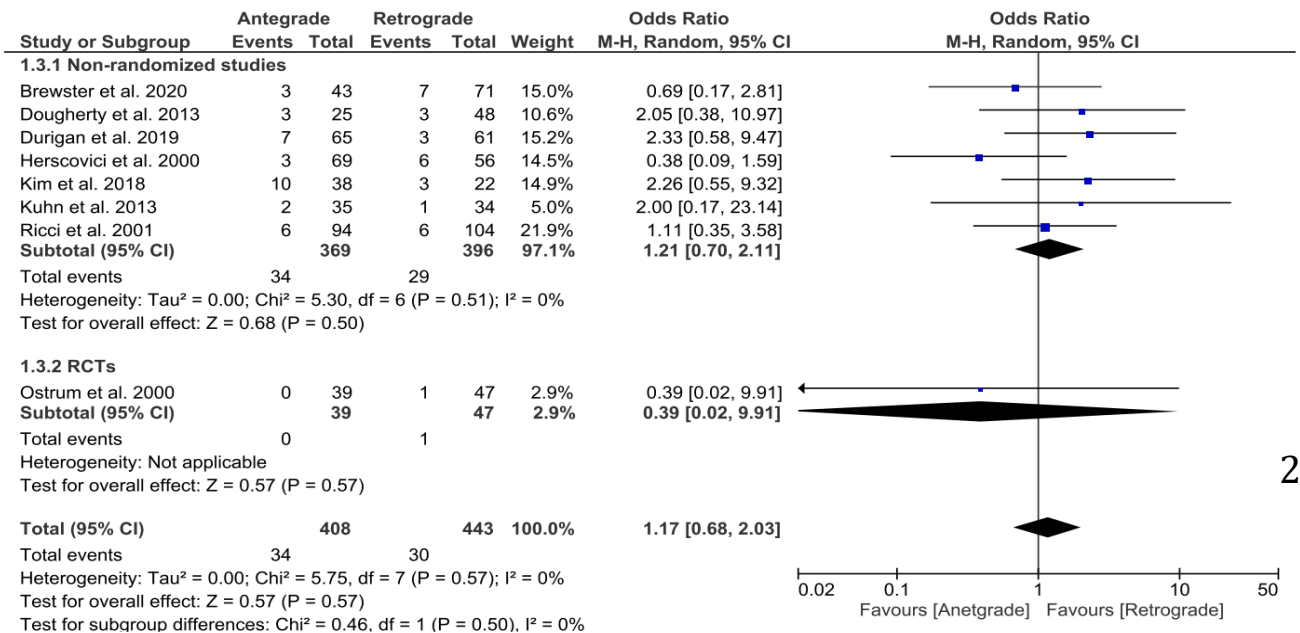
with retrograde nails) had a reported rate of malalignment, showing no difference between the two groups (OR=0.87; 95% CI: 0.45-1.69, p=0.69, [Figure 2C]).

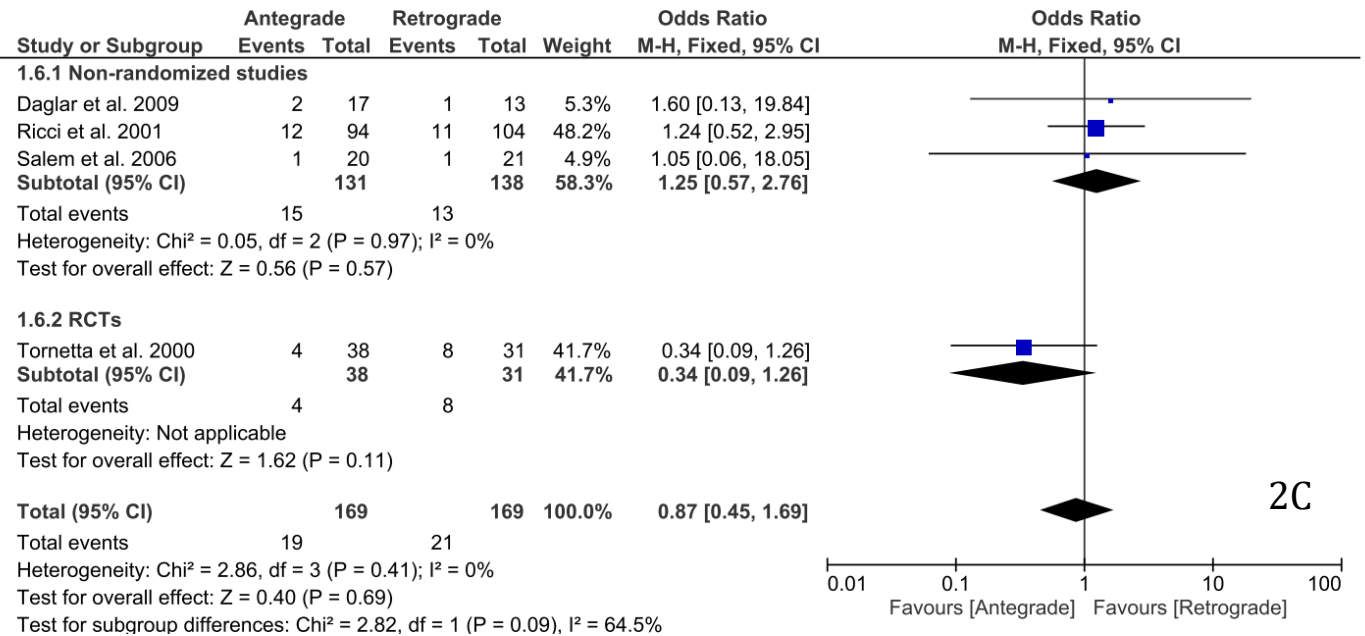
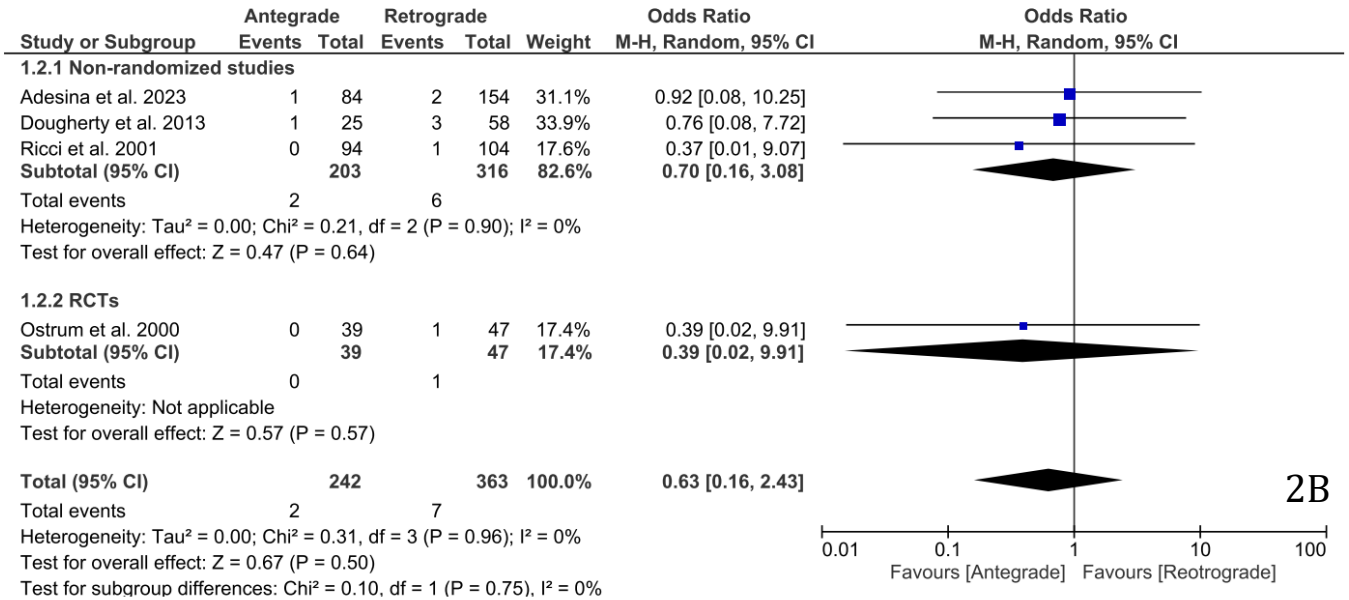
HO

336 patients in 3 studies (167 with antegrade nails and 169 with retrograde nails) had a reported rate of HO, showing a higher rate with antegrade nailing (OR=24.68; 95% CI: 4.63-131.44, p=0.0002, [Figure 2D]).

Overall Complications

1198 patients in 13 studies (537 with antegrade nails and 661 with retrograde nails) had a reported rate of complications, showing no difference between the two groups (OR=1.05; 95% CI: 0.68-1.64, p=0.82, [Figure 2E]).





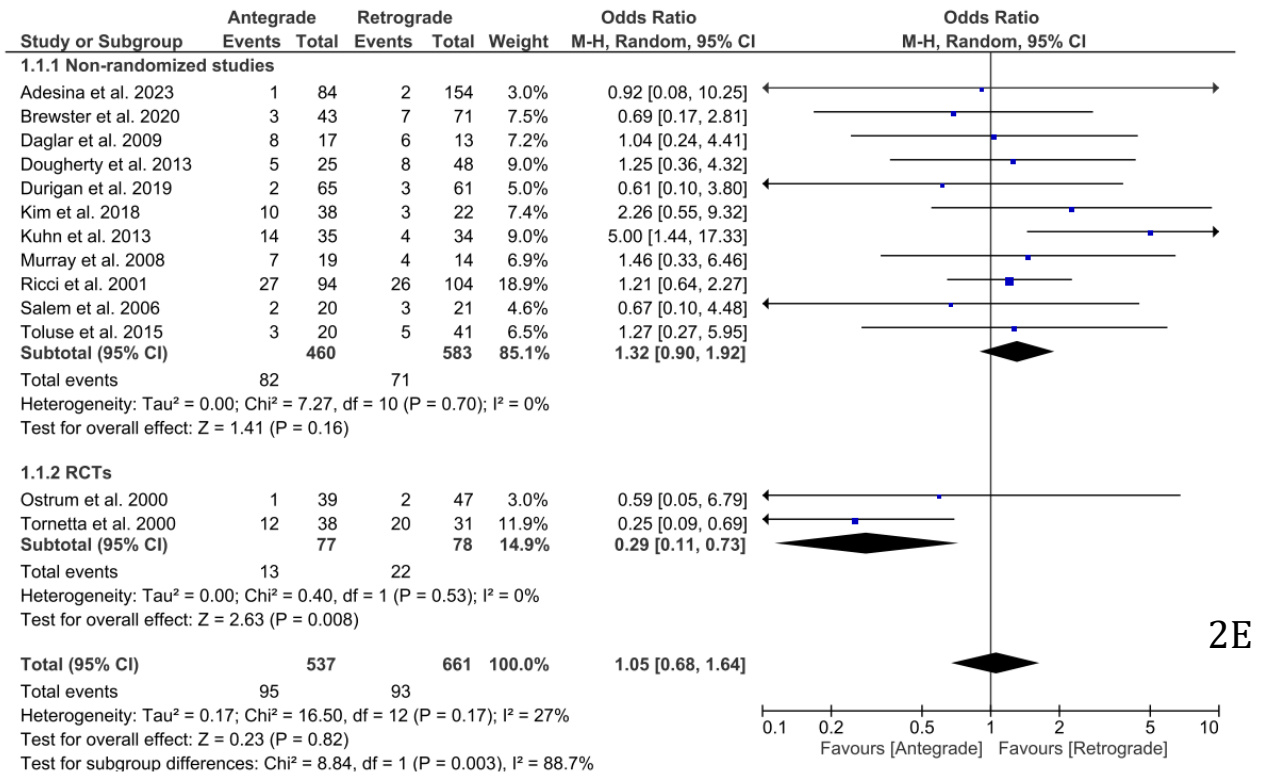
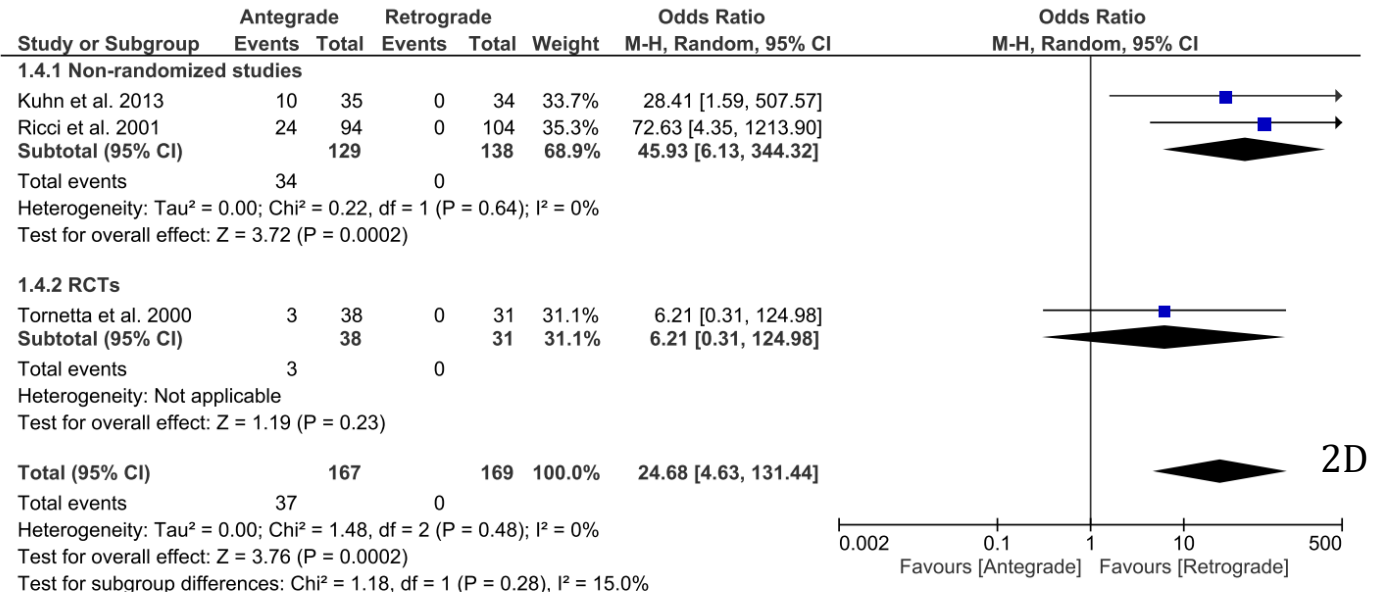


Figure 2. (A): Forest plot showing the difference in the rate of pseudoarthrosis (B): Forest plot showing the difference in the rate of infection. (C): Forest plot showing the difference in the rate of malalignment. (D): Forest plot showing the difference in the rate of heterotopic ossification. (E): Forest plot showing the difference in the rate of overall complications

Re-operations

964 patients in 11 studies (500 with antegrade nails and 464 with retrograde nails) had a reported rate of

reoperations, showing no difference between the two groups (OR=0.68; 95% CI: 0.44–1.04, p=0.08, [Figure 3]).

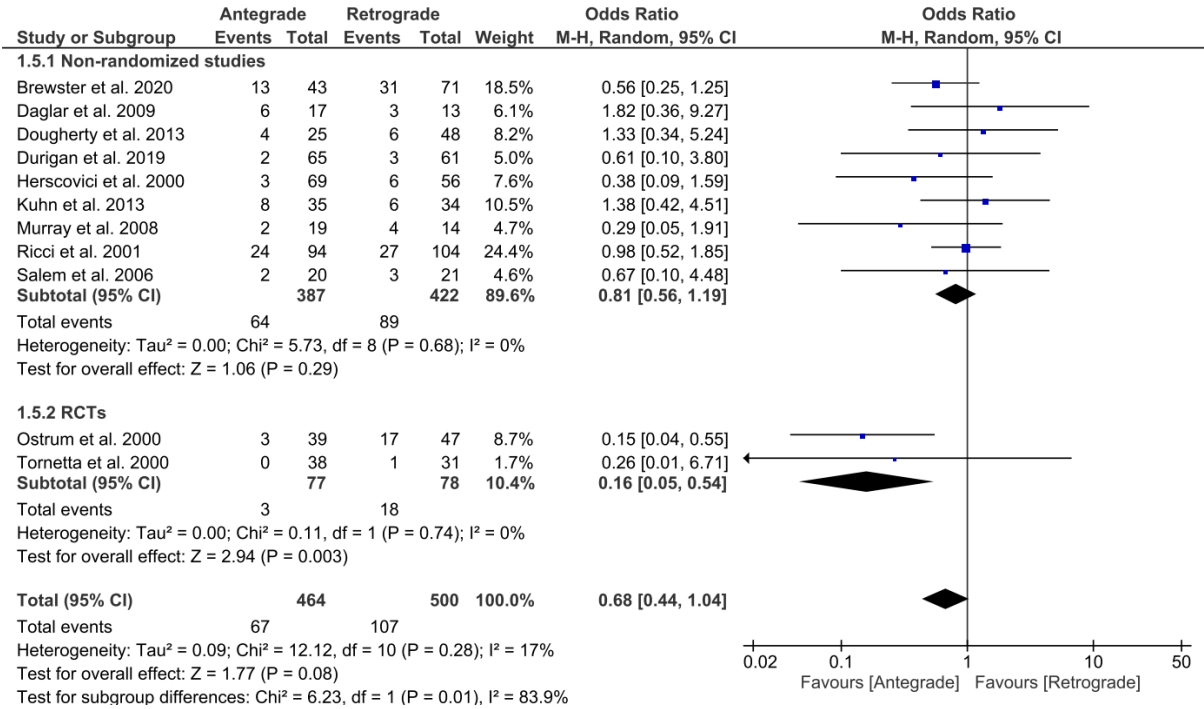


Figure 3. Forest plot showing the difference in the rate of reoperations

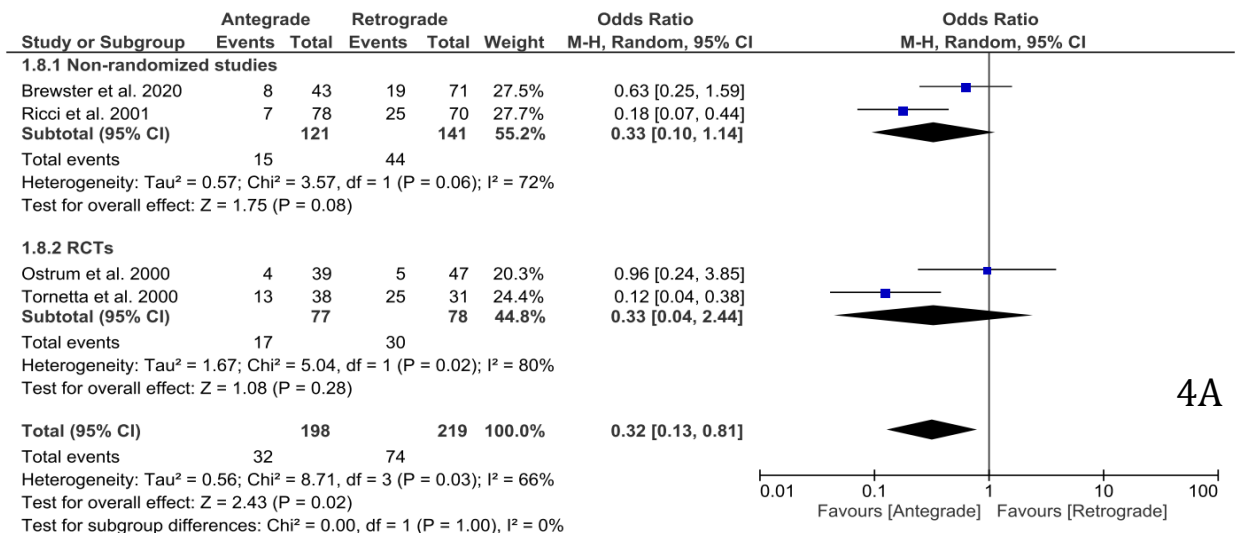
Pain

Knee Pain

417 patients in 4 studies (219 with antegrade nails and 198 with retrograde nails) had a reported rate of Knee pain, showing a higher incidence of knee pain in the retrograde group (OR=0.32; 95% CI: 0.13–0.81, p=0.02, [Figure 4A]).

Hip Pain

389 patients in 3 studies (222 with antegrade nails and 167 with retrograde nails) had a reported rate of hip pain, showing a higher incidence of hip pain in the antegrade group (OR=7.66; 95% CI: 2.55–23.02, p=0.0003, [Figure 4B]).



4A

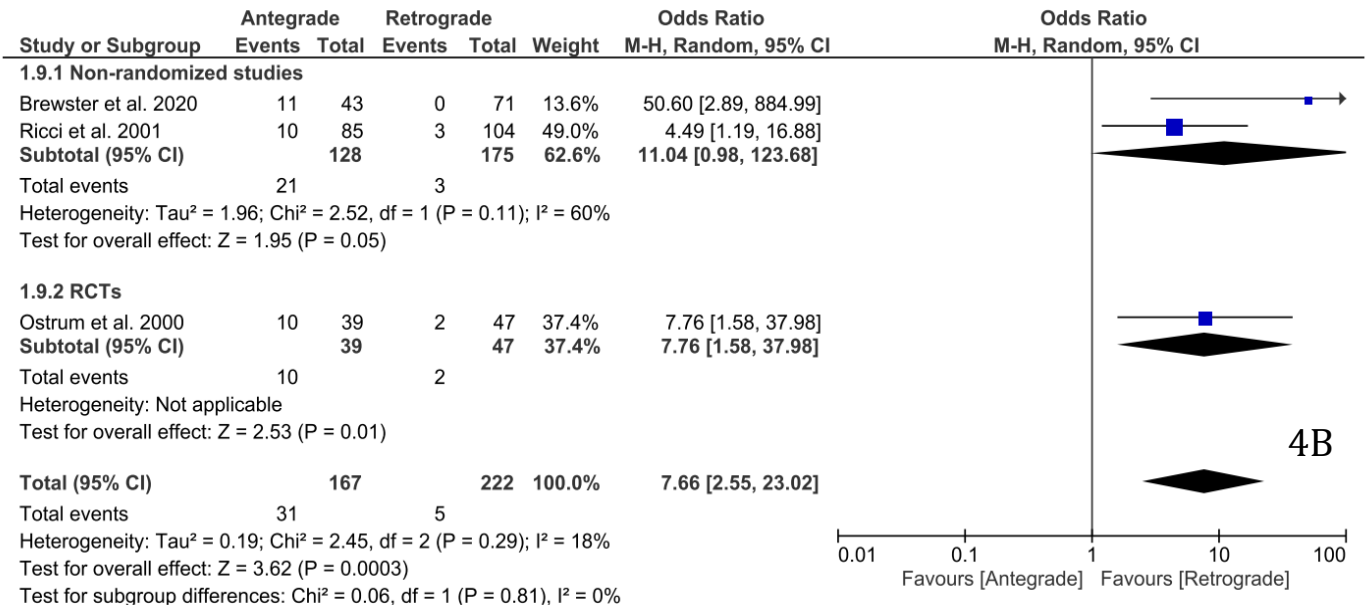


Figure 4. (A): Forest plot showing the difference in the rate of Knee pain (B): Forest plot showing the difference in the rate of Hip pain

Operative time

368 patients in 3 studies (142 with antegrade nails and 226 with retrograde nails) had a reported operative time,

showing no difference between the two groups (MD=-8.95; 95% CI: -43.56-25.66, p=0.61, [Figure 5]).

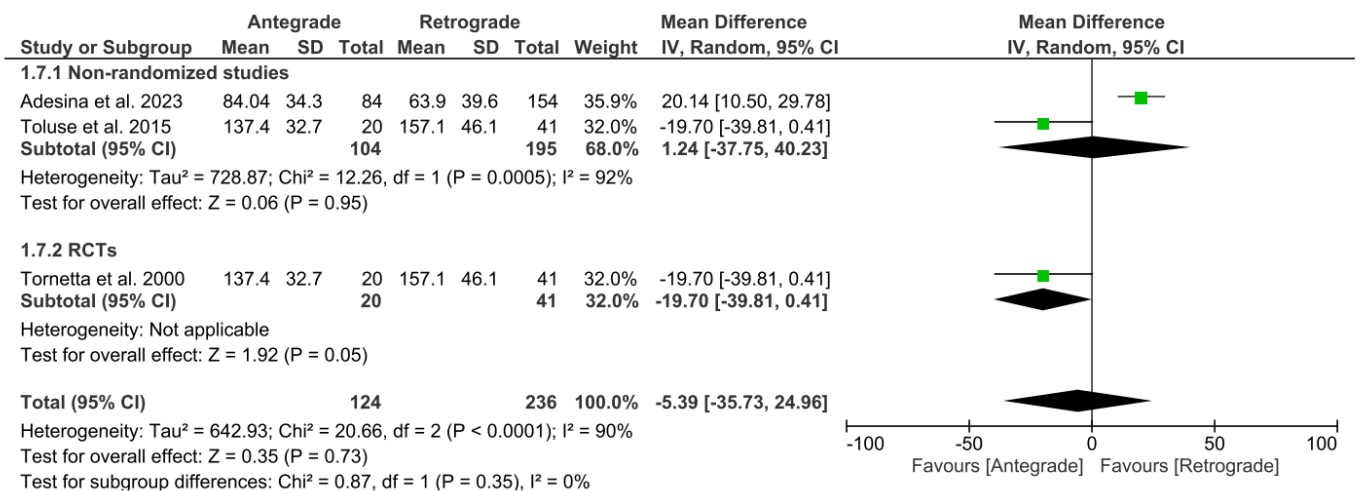


Figure 5. Forest plot showing the difference in operative time

Discussion

Femoral shaft fractures are among the most common fractures found in orthopedic clinical practice and intramedullary nailing constitutes the gold standard operative technique for these fractures. For the treatment of such fractures, two attitudes exist, an antegrade and retrograde nailing technique with no clear guidelines and information about whether or not they have similar outcomes. This meta-analysis compared these two different approaches and reported similar rates of pseudoarthrosis, infection, malalignment, overall complications, reoperation rates, and similar operative time. In comparison, a higher rate of heterotopic ossification, and hip pain was observed in patients undergoing antegrade nailing versus retrograde nailing, whereas a higher rate of knee pain was observed in the retrograde nailing groups.

In regarding to the remaining unspecified complications, when analyzed separately or combined, our study reported no difference in any of the reported complications. This could explain the reason why reoperation rates were shown to be similar between these two approaches. In regard to the operative time, there was no significant difference in operative time between the two groups. This could further explain the reported similarity in complications rates between both groups because increased operative time can be highly associated to an increase in adverse events.²⁶ In addition, an increased rate of heterotopic ossification as observed in the antegrade nailing technique group. This could be explained by the antegrade nailing surgical approach that involves more plane dissections around the hip requiring more muscle dissection and possible bone debris deposits within the soft tissues from the intramedullary canal femoral reaming.^{14,27} Furthermore, only one out of the three studies reporting HO rates discussed the symptoms related to HO, and none of the other studies mentioned additional interventions required for ossification excision. Therefore, despite the increases rate of HO in the antegrade nailing groups, this might only be a statistical finding with no clinical impact. Nevertheless, one way to reduce the rate of this complication would possibly be with extensive intraoperative lavage using pulse lavage which was proven to reduce the rate of heterotopic ossification formation.²⁸

Furthermore, a higher incidence of anterior knee pain was observed with retrograde femoral nailing, while a higher rate of hip pain was exhibited in antegrade nailing. The higher rate of knee pain could be explained by a concurrent traumatic patellar or tendinous injury caused by the surgical approach and dissections and also the utilization of distal locking screws over the ligamentous insertions with the possibility of also inducing quadriceps weakness and atrophy while involving the knee in the approach.^{11,29-31} This adds to the results presented by Murray et al. showing that patients receiving retrograde nailing had a lower knee range of motion and function.²¹ In regards to the increased rate of hip pain in antegrade nailing, this could also be possibly explained by the surgical approach and plane muscle dissection, or a higher risk of nerve injuries resulting in

lateral cutaneous sensory deficits as well as possible muscle abduction weakness.^{32,33}

Strengths and limitations

The main limitation of this study is the small number of studies for some of the analyzed parameters and the lack of patient-reported outcomes in most of the included studies. However, the study has several strengths: an extensive search strategy was employed, resulting in a substantial number of included studies. Additionally, only comparative studies were included, which reduces the risk of operative and matching bias.

Conclusion

When comparing antegrade and retrograde intramedullary nailing for the treatment of femoral shaft fracture. The antegrade group showed an increased risk of hip pain and an increase rate of heterotopic ossification. In contrast, the retrograde nailing group showed an increase in anterior knee pain however, no difference in reoperation rates or surgical time was reported between both groups. Therefore, with both approaches having an increased risk of joint pain based on their area of incision and plane dissection, the decision on whether to use either of the approaches should be taken based on patient-related factors and surgeon experience and ease.

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