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ORIGINAL PAPER

Early versus late treatment of paediatric femoral neck fractures: a systematic review and meta-analysis

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Abstract

Purpose Femoral neck fractures in children represent less than 1% of all paediatric fractures. Osteonecrosis of the femoral head is one of the devastating complications of this fracture. Time to treatment is one of the most important predictors of this outcome with no clear consensus in the literature. The aim of this study was to determine whether early treatment (< 24 hours) of pediatric femoral neck fractures is associated with a lower rate of osteonecrosis of the femoral head compared to late treatment (> 24 hours).

Methods We searched several databases (PubMed, Embase, and Cochrane library), from January 1966 to November 2017 for any comparative studies that evaluated early (< 24 hours) versus late (> 24 hours) treatment of paediatric femoral neck fractures. We pooled the effect sizes using fixed effects model that compared the rate of osteonecrosis of the femoral head between children undergoing early versus late treatment, open versus closed reduction, displaced versus non-displaced and different Delbet type femoral neck fractures. Descriptive and qualitative data was also extracted.

Results Of the 391 articles identified, six studies (prospective and retrospective cohort studies) were eligible for the meta-analysis, with a total of 231 paediatric femoral neck fractures. The pooled odds ratio (OR) for osteonecrosis of the femoral head did not show any statistically significant difference between early (< 24 hours) versus late (> 24 hours) treatment (OR = 1.19, 95% CI 0.56, 2.51, $I^2 = 23.6\%$), nor between open versus closed reduction of paediatric femoral neck fractures (OR = 1.62, 95% CI 0.82, 3.22, $I^2 = 19.57\%$). Displaced and Delbet type I/II femoral neck fractures were 3.8 (OR = 3.81, 95% CI 1.49, 9.78, $I^2 = 0.00\%$) and 2.4 (OR = 2.43, 95% CI 1.28, 4.61, $I^2 = 0.57\%$) times more associated with osteonecrosis of the femoral head compared to non-displaced and Delbet type III/IV fractures respectively.

Conclusions The cumulative evidence at present does not indicate an association between the time to treatment or method of reduction of femoral neck fractures in children and the risk of osteonecrosis of the femoral head. However, initial expedient treatment of femoral neck fractures in children should always remain the rule especially for displaced and Delbet type I/II femoral neck fractures.

Level of evidence II/III

Keywords Hip fractures · Femur neck fractures · Pediatrics · Avascular necrosis · Osteonecrosis · Meta-anlysis

Introduction

Femoral neck fractures in children are rare and represent less than 1% of all paediatric fractures [1–4]. These fractures are usually caused by high energy trauma such as falling from a height or motor vehicle accidents. Although most paediatric fractures can be treated conservatively, this type of fracture requires a different approach as it has complications with devastating sequelae that may have lifelong adverse effects [5–7]. Common complications following paediatric femoral neck fractures include osteonecrosis of the femoral head, coxa vara, and premature physeal closure of the proximal femoral physis. Of these, osteonecrosis of the femoral head is the most troublesome complication and difficult to manage [1–8]. Once osteonecrosis of the femoral head occurs in children, there is no effective treatment and the outcome is poor. Hence, the best treatment is to prevent its occurrence.

The rate of osteonecrosis of the femoral head following femoral neck fractures in children varies between studies and has been reported to range from 0 to 92% [5, 6, 9].

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Functional outcome of these patients is mainly affected by the rate of osteonecrosis of the femoral head. Hence, it is important to recognize the risk factors of this complication [10]. Many variables that influence the development of osteonecrosis of the femoral head have been studied, including age, type of fracture, amount of fracture displacement, time to fracture treatment, method of reduction (open versus closed), and capsular decompression. However, there is no consensus on the extent of prediction of osteonecrosis concerning these factors [11, 12]. The Delbet classification system that was modified by Colonna is the most commonly used system to describe femoral neck fracture in children [9]. This classification scheme has been found to have prognostic significance with proximal fractures associated with a higher risk of osteonecrosis of the femoral head [1–5, 13–16]. The successful treatment of femoral neck fractures in children is mainly based on anatomical reduction and internal fixation as non-surgical management has been associated with high failure rates [10, 17].

Moon and Mehlman [13] conducted a meta-analysis on 20 studies (levels IV and V) and reported that the only predictors for osteonecrosis of the femoral head following femoral neck fracture in children were age and fracture type. More recently, a meta-analysis by Yeranosian et al. [14] published in 2013 with 30 studies (27 level IV and 3 level III) demonstrated that osteonecrosis of the femoral head following femoral neck fracture in children is intrinsic to the type of fracture and time to reduction.

The literature is vastly discordant especially with regards to the time to treatment and risk of osteonecrosis of the femoral head [13–20]. Recent prospective and retrospective cohort studies have been published since the last meta-analysis and report conflicting results that time to treatment does not influence osteonecrosis rate, and other variables may be more important such as method of reduction (open versus closed), fracture type and displacement [21–25].

The aim of our study was to systematically review the literature that compares early (<24 hours from the time of injury) versus late (>24 hours from the time of injury) treatment of femoral neck fracture in children. The primary outcome analysis involved the rate of osteonecrosis of the femoral head. We also investigated the effect of reduction method (open versus closed), fracture displacement, and Delbet fracture type on our primary outcome.

Materials and methods

We used the PRISMA statement criteria in reporting our meta-analysis [26].

Search strategy

A systematic search was performed of MEDLINE using PubMed through January 1966 to November 2017 to retrieve all published studies comparing the outcomes of early (< 24 hours) versus late (> 24 hours) treatment of femoral neck fractures in children. The search terms were (fem* neck OR hip) AND (fracture) AND (paediatric* OR paediatric*), as words in the title or abstract. The search was limited to human subjects and English language. Supplementary searches were performed using Embase and Cochrane library using similar search terms. Furthermore, we performed a manual search using reference lists of original research and review articles.

Selection of studies

After retrieving publications from our search, two phases of selection were carried out according to the eligibility criteria in our meta-analysis, including comparative studies whether prospective or retrospective, that analyzed femoral neck fractures and reported the rate of osteonecrosis of the femoral head among children (under 18 years of age) undergoing early and late treatment for femoral neck fractures, method of reduction (open versus closed), whether they had displaced or non-displaced fractures and the Delbet type of fracture (Delbet I/II versus Delbet III/IV). Early treatment was defined as less than 24 h elapsed from the time of injury, whereas late treatment referred to those treated after 24 hours from the time of injury.

Data extraction

Two independent authors (N.A. and M.Y.) extracted the data including where each study was conducted, year of publication, number of patients and events, demographic characteristics of the study population, methodology, and details of outcomes reported. In the event of any difference in opinion, the conflict was discussed with the senior investigator and resolved by consensus.

Outcomes

The primary outcome in our meta-analysis was osteonecrosis of the femoral head, identified according to the radiographic criteria reported in each of the included studies. With respect to the time of femoral neck fracture treatment, early was defined as < 24 hours from the time of injury compared to late defined as > 24 hours from the time of the injury. In the secondary analyses, we investigated the effect of reduction method (open vs closed), fracture displacement (displaced vs non-displaced), and fracture type (Delbet I/II versus Delbet III/IV) on the rate of osteonecrosis of the femoral head.

Quality assessment

Quality assessment of the eligible studies was performed using the Newcastle–Ottawa scale [27] for non-randomized cohort studies; each study was judged on eight items, categorized into three domains: the selection of the study groups (4 stars), the comparability of the groups (2 stars), and the ascertainment of outcome of interest (3 stars). Stars were awarded such that the highest quality studies were awarded up to a maximum of nine stars.

Statistical analysis

We performed the meta-analysis using the OpenMeta-Analyst software (Center for Clinical Evidence Synthesis, Tufts Medical Center Boston, MA, USA) [28], using odds ratio (OR) as an effect measure, with a 95% confidence interval. The analysis was performed using the fixed effects model when there was no significant heterogeneity. We repeated the analysis using the random effects model to ensure that our results were robust. Heterogeneity was assessed using I^2, where a value of $> 50\%$ was considered significant and Cochrane Q statistics. Publication bias was explored using funnel plot and the Egger test [29, 30].

Results

The systematic and manual search identified 391 studies published between January 1966 and November 2017. After two phases of selection, six prospective and retrospective cohort studies evaluating the rate of osteonecrosis of the femoral head following early and late treatment of pediatric femoral neck fractures were considered for inclusion in our meta-analysis. Figure 1 summarizes the process of identifying the eligible studies. Twenty-five studies were excluded because they were not comparative studies (i.e., systemic reviews or case series), seven of the excluded studies did not report the primary outcome of interest (osteonecrosis of the femoral head) and three studies recorded the timing of treatment in a different time format that we could not specify the 24hour limit for early and late treatment.

Characteristics of included studies

Table 1 summarizes the characteristics of the six studies included in our primary analysis. All included studies reported the events of osteonecrosis of the femoral head with sufficient details to define the timing of treatment. The sample size ranged from 22 to 70 children. The total number of patients included was 230 children, with 231 femoral neck fractures, of which 142 fractures were treated within the first 24 hours of injury, and 89 fractures treated after 24 hours. All the patients were of paediatric age group (less than 18 years of age). The mean age of patients in both groups was 11.4 years, ranging from two to 18 years. Falling from height followed by motor vehicle accidents were the most reported mechanisms of injury for the femoral neck fractures in the children, 41% and 35% respectively, while sport injuries were responsible for 19% of femoral neck fractures. All studies described femoral neck fractures using the Delbet classification system [9], with Delbet type II fractures being the most prevalent, comprising more than 50% of all the femoral neck fractures. Of the included studies, all reported the details of displacement with 179 displaced femoral neck fractures, whereas 52 were non-displaced fractures. However, Panigrahi et al. [22] did not report the number of osteonecrosis of the femoral head in the displaced and non-displaced fractures. Furthermore, 76 of the femoral neck fractures required an open reduction in comparison to 126 fractures treated with closed reduction. Panigrahi et al. [22] did not specify the method of reduction of the fractures. Various methods of treatment were described in the eligible studies, either closed reduction and hip spica casting, closed reduction with internal fixation by Kirschner wires or percutaneous screws, or open reduction and internal fixation. Patients were followed up for at least one year and ranged from one to 26 years.

Quality assessment

Table 2 summarizes the results for the different domains of study quality adapted from the Newcastle–Ottawa scale for cohort studies [27]. The assessment of the included cohort studies suggests that two studies (Stone et al. [24] and Panigrahi et al. [22]) had unbalanced prognostic factors of the children in their cohorts, as they did not match patients in the design, nor did they adjust for important confounding factors, in contrast to the remaining cohort studies. In addition, the studies of Panigrahi et al. [22] and Baysal et al. [25] did not have adequate follow-up with more than 20% of their children lost to follow-up. In summary, three of the six included studies scored 8 out of 9 stars on the Newcaslte–Ottawa scale (Inan et al. [23], Spence et al. [12], and Riley et al. [21]), while two studies (Stone et al. [24] and Baysal et al. [25]) scored 7 out of 9, and one study (Panigrahi et al. [22] scored 6 only.

Quantitative data synthesis

The fixed effects model for pooling the odds ratios was used due to the minimal values of I^2, indicating mild heterogeneity in the retrieved data. We repeated the analysis using the random effects model to ensure the robustness of our approach. The comparative effect of early (< 24 h) treatment of paediatric femoral neck fractures showed no significant difference in the rate of osteonecrosis of the femoral head, compared to late (> 24 h) treatment (OR = 1.19, 95% CI 0.56, 2.51, I^2 =

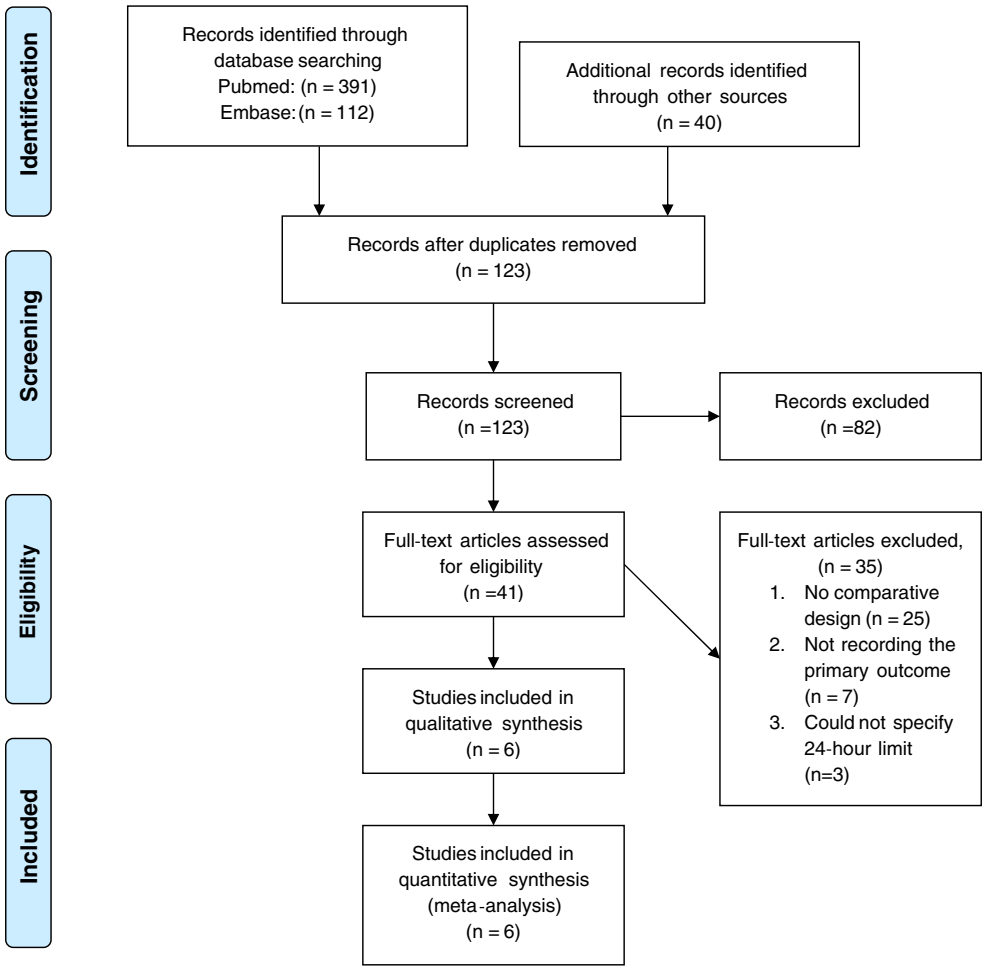

Fig. 1 Flow diagram of eligible studies

23.64%) (Fig. 2). Similarly, we failed to prove any statistical significance for the method of reduction (open versus closed) on the rate of osteonecrosis of the femoral head (OR = 1.62, 95% CI 0.82, 3.22, $I^2 = 19.57\%$) (Fig. 3).

There was a significant trend for increased osteonecrosis of the femoral head when treating pediatric displaced femoral neck fractures compared to non-displaced fractures (OR = 3.81, 95% CI 1.49, 9.78, $I^2 = 0.00\%$) (Fig. 4). Furthermore, osteonecrosis of the femoral head was more associated with Delbet type I/II fractures in comparison to Delbet type III/IV fractures (OR = 2.43, 95% CI 1.28, 4.61, $I^2 = 0.57\%$) (Fig. 5).

Publication bias was assessed using funnel plots and Egger tests, which did not show patterns for significant bias in terms of any measured outcomes.

Discussion

The current study revealed no statistically significant difference in the observed rate of osteonecrosis of the femoral head following femoral neck fracture in children when comparing early (< 24 hours) versus late (> 24 hours) treatment. Moreover, a separate pooled analysis in our study for the method of reduction found no significant difference between open versus closed reduction of femoral neck fracture. However, there were significant associations between the displacement and Delbet type of the fracture with the rate of osteonecrosis of the femoral head, with pooled odds ratio of 3.8 and 2.4 times more in children with displaced and Delbet type I/II fractures. The results were consistent across different assumptions. The extent to which these statements reflect the true outcome of comparison requires an understanding of the limitations in the current literature and included studies and consideration of the conduct and interpretation of the results of our analyses. Although our study mainly assessed the effect of early treatment, there was varied reporting regarding the key determinants of pediatric femoral neck fractures known to influence the rate of osteonecrosis of the femoral head. Furthermore, none of the included studies reported effect estimates adjusted for these potential confounders.

Important factors that influence the rate of osteonecrosis of the femoral head in femoral neck fractures in children have been reported in the literature with no consensus among studies and no established causal relationships [13, 14]. Although several studies have shown a positive correlation between the time to treatment and the rate of osteonecrosis of the femoral

Table 1 Characteristics of the included studies in the meta-analysis

Study	Year	Country	Design	Level of evidence	Total patient/ fracture	Treatment < 24 h	Treatment > 24 h	Delbet classification	Method of reduction and type of fixation	Displaced/ non-displaced	Gender M/F	Mean age [years] (range)	Mean follow-up [years] (range)
Inan et al. [23]	2009	Turkey	Retrospective cohort	III	39/39	26	13	I: 0 II: 21 III: 14 IV: 4	ORIF: 5 CRIF: 32 CR and casting:2	31/8	22/17	11.1 (4–16)	3.4 (1–9.5)
Stone et al. [24]	2015	USA	Retrospective cohort	III	22/22	18	4	I: 0 II: 13 III: 8 IV: 1	ORIF: 6 CRIF: 16	22/0	13/9	11.5 (4.5–17.4)	2.1 (1–8.7)
Riley et al. [21]	2015	USA	Retrospective cohort	III	43/44	22	22	I: 4 II: 18 III: 12 IV: 10	ORIF: 13 CRIF: 25 CR and spica: 5 No reduction: 1	30/14	27/16	11.3 (0.9–17)	6.4 (1.0–26.2)
Panigrahi et al. [22]	2015	India	Prospective cohort	II	28/28	4	24	I: 0 II: 19 III: 9 IV: 0	NR	24/4	16/12	10.57 (4–15)	(2–6)*
Spence et al. [12]	2016	USA	Retrospective cohort	III	70/70	48	22	I: 5 II: 31 III: 29 IV: 5	ORIF: 38 CRIF: 31 CR and spica: 1	54/16	41/29	13.2 (2.6–18.1)	2.8(**)
Baysal et al. [25]	2016	Turkey	Retrospective cohort	III	28/28	24	4	I: 2 II: 16 III: 8 IV: 2	ORIF: 14 CRIF: 14	18/10	16/12	10.8 (2–16)	7.6 (1.25–18)

ORIF open reduction and internal fixation, *CRIF* closed reduction and internal fixation, *CR* closed reduction, *NR* not reported

*Mean not reported

**Range not reported

Table 2 Newcastle–Ottawa quality assessment of the included studies in the meta-analysis (maximum of 9 stars)

Domain	Item	Inan et al. [23]	Stone et al. [24]	Riley et al. [21]	Panigrahi et al. [22]	Spence et al. [12]	Baysal et al. [25]
Selection (maximum of 4 stars)	-Representativeness of the exposed cohort	*	*	*	*	*	*
	-Selection of the non-exposed cohort	*	*	*	*	*	*
	-Ascertainment of exposure	*	*	*	*	*	*
	-Demonstration that outcome of interest was not present at start of study	*	*	*	*	*	*
Comparability (maximum of 2 stars)	-Comparability of cohorts on the basis of the design or analysis	*	Nil	*	Nil	*	*
Outcomes (maximum of 3 stars)	-Assessment of outcome	*	*	*	*	*	*
	-Was follow-up long enough for outcomes to occur	*	*	*	*	*	*
	-Adequacy of follow-up of cohorts	*	*	*	Nil	*	Nil

head [14, 15], there is no prospective study evaluating the effect of early treatment on the rate of femoral head osteonecrosis following femoral neck fracture in children. The ability to detect a difference was further confounded by the relatively small sample size. More recent studies including level II evidence failed to detect a statistically significant correlation between time to treatment and the rate of osteonecrosis of the femoral head [21–25]. Damage to the blood supply is thought to take place at the time of initial trauma and some studies dispute that the severity of initial fracture displacement is more important than the timing of treatment [12, 25].

A meta-analysis by Moon and Mehlman [13] in 2006 with a total of 360 patients (including 20 studies) reported age and fracture type as the only significant predictors of femoral head osteonecrosis following pediatric femoral neck fracture. Using regression analysis, they concluded that older children had a 1.14 higher risk of developing osteonecrosis for each year of increasing age, and Delbet type I to III fractures were more likely to develop osteonecrosis compared to type IV fractures. However, this meta-analysis only included level IV studies and lacks a meaningful statistical analysis. A further meta-analysis by Yeranosian et al. [14] in 2013 compared various treatments and outcomes of femoral neck fractures in children and included 30 studies (27 level IV and 3 level III) with a total of 935 patients. This meta-analysis showed that the risk of osteonecrosis was intrinsic to the type of fracture and only affected by early treatment. The study reported the risk of osteonecrosis of the femoral head to be 22% higher in Delbet type I/II and an odds ratio of 4.2 when comparing time to reduction before versus after 24 h from the time of injury. However, this meta-analysis only analyzed the data of six studies that compared early versus late treatment, and all of the studies were level IV with only two studies statistically scrutinized. Other variables that influence the risk of osteonecrosis of the femoral head were investigated such as open versus closed reduction, operative versus non-operative intervention and capsular decompression, which showed that operative treatment and open reduction had a higher risk of osteonecrosis of the femoral head than closed reduction. However, this could be explained by selection bias with severe injuries requiring open reduction in Delbet type I/II fractures.

Our systematic review identified six cohort studies (level II/III) that compared the rate of osteonecrosis of the femoral head following femoral neck fractures in children who underwent early treatment (< 24 hours) with the corresponding rate in those who underwent late treatment (> 24 hours). All studies were of good methodological quality according to the Newcastle–Ottawa scale, with limitations in the

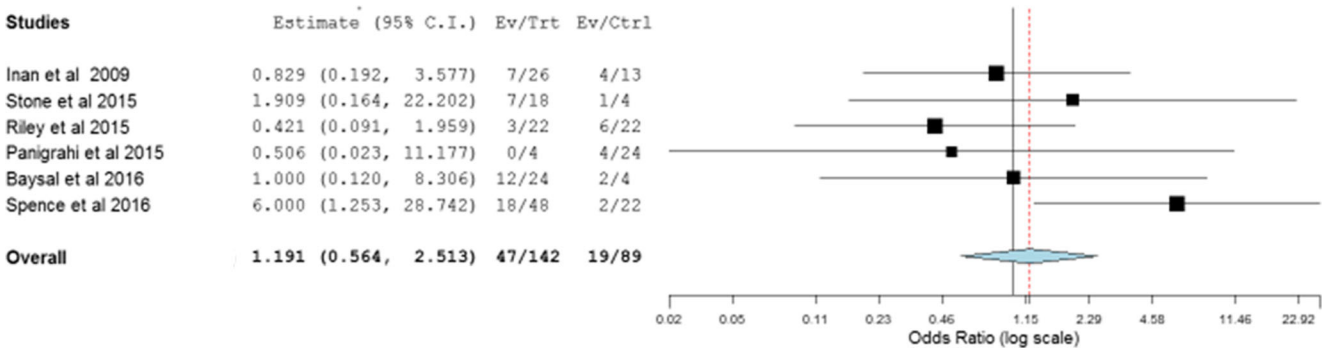

Fig. 2 Forest plot: pooled odds ratio (OR) for osteonecrosis in the early versus late treatment groups

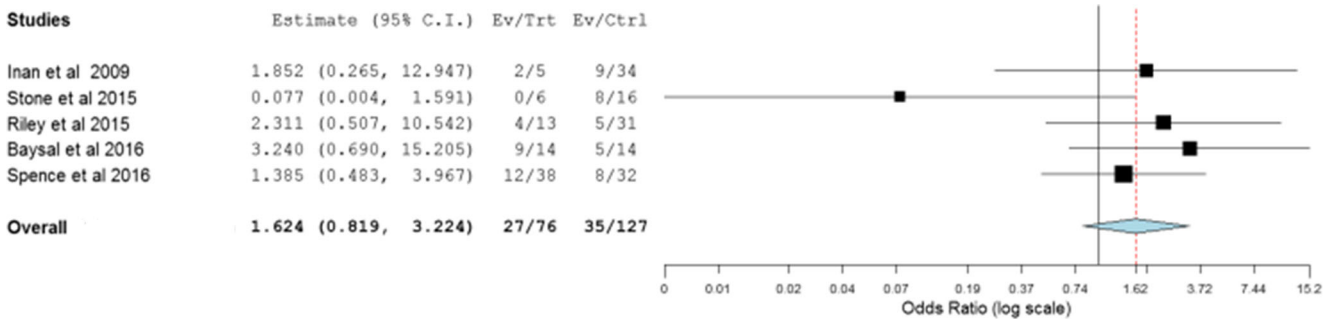

Fig. 3 Forest plot: pooled odds ratio (OR) for osteonecrosis in the open versus closed reduction groups

comparability domain. Because of the small number and type of included studies, we did not incorporate quality in our sensitivity analysis. The simplest approach is to judge studies on specific domains of quality that are most relevant to the control of bias for that particular study. Our findings are consistent with the literature, with an overall rate of osteonecrosis of 28.5% [13, 14]. Five of the six included studies in our meta-analysis showed that early treatment did not influence the rate of femoral head osteonecrosis [21–25]. On the other hand, other studies have reported a higher rate of osteonecrosis of the femoral head with delayed treatment. Dhar et al. [19] reported a rate of 60% for osteonecrosis of the femoral head after a mean delay of 7 days [19]. These findings were consistent with previous studies regarding the type of fracture and more proximal femoral neck fractures associated with a higher risk of osteonecrosis [5, 13–16]. Although initial displacement of the fracture has been recently considered as a critical predictor for osteonecrosis of the femoral head [12, 25], previous studies have not found a statistically significant correlation with osteonecrosis, which can be explained by inter-observer reliability, sample size or due to variation in displacement definitions [13].

Factors that may influence the rate of osteonecrosis of the femoral head after femoral neck fracture including age of the patient, quality of reduction, and capsular decompression could not be controlled for in this analysis, due to the paucity of individual-level data in the included studies and this requires further research. The limited number of studies addressing these factors permits limited conclusions for the current meta-analysis. Additionally, these factors will particularly vary from centre to centre, with disparity in clinical skills and patient assessment, and will further confound the results. The only outcome measure examined in this meta-analysis was the rate of osteonecrosis of the femoral head. This is a clinically relevant and important outcome, and it is the most troublesome and devastating complication following femoral neck fracture in children. Our study only assessed the effect of time to treatment, method of reduction, displacement and Delbet fracture type on the rate of osteonecrosis of the femoral head following femoral neck fracture in children, even though these are some of many factors that may influence osteonecrosis. Consequently, our analysis has a limitation due to the lack of studies addressing these pivotal issues. Furthermore, the various types of treatment cannot be analyzed due to lack of data in the included studies and inability to pool data for loss of reduction and/or implant failure. Although, there were only six eligible published studies with mild to moderate heterogeneity among the data of these studies, we chose to perform this meta-analysis to provide a more generalizable result on the effect estimate as this is the best available evidence in the literature.

In conclusion, the cumulative evidence at present does not indicate an association between the timing of treatment and method of reduction with the rate of osteonecrosis of the femoral head following femoral neck fractures in children. However, this cumulative evidence does elucidate a positive association between initial fracture displacement and the proximity of femoral neck fractures with the rate of osteonecrosis of the femoral head. The results of our meta-analysis are based on observational studies; hence, multi-centre prospective

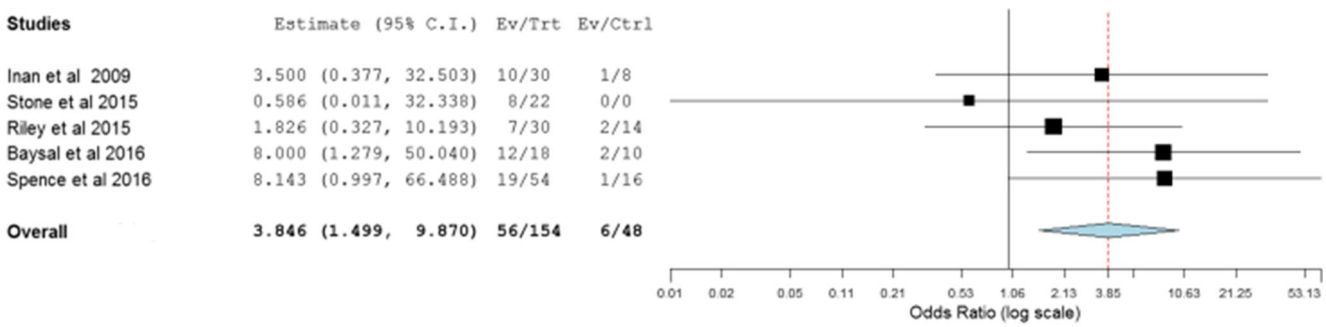

Fig. 4 Forest plot: pooled odds ratio (OR) for osteonecrosis in the displaced versus non-displaced pediatric femoral neck fractures

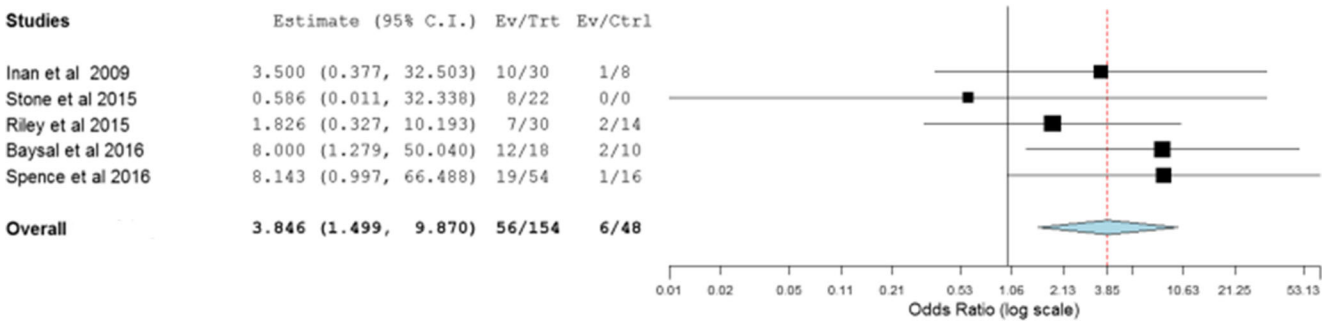

Fig. 5 Forest plot: pooled odds ratio (OR) for osteonecrosis in the Delbet type I/II versus Delbet type II I/IV pediatric femoral neck fractures

cohort studies are necessary to be able to answer questions with more certainty and a higher level of evidence.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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