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Association between open or closed reduction and avascular necrosis in developmental dysplasia of the hip

A PRISMA-compliant meta-analysis of observational studies

Ya-Jie Wang, MS[a], Fan Yang, MS[a], Qi-Jun Wu, PhD[b], Shi-Nong Pan, MD, PhD[a,*], Lian-Yong Li, PhD[c,*]

Abstract

Background: The risk of avascular necrosis of the femoral head (AVN) after treatment of developmental dysplasia of the hip is associated with the method of reduction. Some authors have suggested that open reduction is a risk factor for AVN; however, this is controversial. To our knowledge, a quantitative comparison of the incidence of AVN between closed and open reduction has not been conducted.

Methods: Published studies were identified by searching PubMed, EMBASE, and the Cochrane Library up to May, 2015, focusing on the incidence of AVN after closed or open reduction for developmental dysplasia of the hip in children aged <3 years. Patients were age-matched who were treated by either closed or open reduction, but without pelvic or femoral osteotomy. Two authors independently assessed eligibility and abstracted data. Discrepancies were discussed and resolved by consensus. We pooled the odds ratios (ORs) and 95% confidence intervals (95%CIs) from individual studies using a random-effects model and evaluated heterogeneity and publication bias.

Results: Nine retrospective studies were included in this analysis. The pooled OR for comparing open reduction with closed reduction for all grades of AVN was 2.26 (95%CI = 1.21–4.22), with moderate heterogeneity ($I^2 = 44.7\%$, $P = 0.107$). The pooled OR for grades II to IV AVN was 2.46 (95%CI = 0.93–6.51), with high heterogeneity ($I^2 = 69.6\%$, $P = 0.003$). A significant association was also found for the further surgery between open and closed reduction, with a pooled OR of 0.30 (95%CI = 0.15–0.60) and moderate heterogeneity ($I^2 = 46.4\%$, $P = 0.133$). No evidence of publication bias or significant heterogeneity between subgroups was detected by meta-regression analyses.

Conclusion: Findings from this meta-analysis suggest that open reduction is a risk factor for the development of AVN compared with closed treatment. Future studies are warranted to investigate how open reduction combined with pelvis and/or femoral osteotomy affects the incidence of AVN.

Abbreviations: AVN = avascular necrosis of the femoral head, CI = confidence interval, DDH = developmental dysplasia of the hip, OR = odds ratio.

Keywords: avascular necrosis, developmental dysplasia of the hip, meta-analysis, open reduction

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SNP and LYL have contributed equally to the article.

Authors' contributions: YJW and LYL independently extracted the information from the eligible studies. Besides, YJW participated in the design of the study and performed the statistical analysis. FY participated in the quality assessment. QJW conceived of the study and participated in its design. SNP helped to draft the manuscript. All authors read and approved the final manuscript.

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[a] Department of Radiology, [b] Department of Clinical Epidemiology, [c] Department of Pediatric Orthopedics, Shengjing Hospital of China Medical University, Shenyang, China.

[*] Correspondence: Shi-Nong Pan, Shengjing Hospital of China Medical University, No. 36 Sanhao Street, Heping District, 110004 Shenyang, Liaoning, China (e-mail: cjr.panshinong@vip.163.com); Lian-Yong Li, Shengjing Hospital of China Medical University, No. 36 Sanhao Street, Heping District, 110004 Shenyang, Liaoning, China (e-mail: loyo_ldy@163.com)

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1. Introduction

Developmental dysplasia of the hip (DDH) is a spectrum of disorders in which the femoral head has an abnormal relationship to the acetabulum. This spectrum includes acetabular dysplasia without displacement, subluxation, and dislocation. DDH is the most common congenital joint disorder in the field of pediatric orthopedics, with an estimated incidence ranging from 1.4 to 35.0 per 1000 newborns.[1,2] DDH is influenced by many genetic and environmental factors, such as ligamentous laxity, breech position, family history, female sex, and racial predilection. It is well known that early diagnosis and treatment can provide the best possible functional outcome. Historically, ultrasound screening in combination with clinical examination was widely used for neonatal screening in most developed countries.[3,4] The Pavlik harness was subsequently applied in patients with DDH that was first diagnosed in infancy and achieved a success rate reaching 90%.[5,6] Despite efforts to recognize and treat all cases of DDH soon after birth, late presentations and failure of Pavlik harness treatment are unavoidable. Thus, further treatment such as closed or open reduction of the dislocated hip is necessary in these cases.[7–10]

Achieving a stable and concentric reduction of the hip while avoiding complications remains the primary goal in the management of DDH.[11,12] Avascular necrosis of the femoral head (AVN) following treatment of DDH is a serious complication and can lead to acetabular dysplasia, joint incongruity, limb-length discrepancy, and early osteoarthritis.[13–16] The reported incidence of AVN in recent years has varied widely from 6% to 48% and is affected by many factors, such as the previous treatment and immobilization, grade of dislocation, patient's age at surgery, and treatment method. With respect to the treatment method, controversy regarding open versus closed reduction has long existed.[17–22] Some researchers have found that closed reduction is a simple procedure and has the advantages of minimal invasion and fewer complications compared with open surgery.[1,16,23–30] However, many patients require further surgery for residual acetabular dysplasia and subluxation.[23] Other researchers have reported that open reduction allows for hip fixation within a shorter period of time and reduces the possibility of further surgical intervention; however, open reduction is associated with more surgical complications such as infection, stiffness of the hip joint, and an increased rate of AVN.[23,26,28,30] Conversely, some authors have found that open reduction is associated with a lower rate of AVN; they reported that the surgical release of soft tissues, removal of internal and external obstructing factors, and casting in a slightly abducted position effectively reduced the pressure between the femoral head and acetabulum.[25,31,32]

Whether a difference exists in the incidence of AVN following treatment of DDH by open versus closed reduction has been a controversial point in recent years, and no meta-analyses regarding this association have been conducted. Therefore, the purpose of our study was to compare the incidence of AVN between open and closed reduction for the treatment of DDH in children aged <3 years by performing a meta-analysis.

2. Methods

2.1. Ethics statement and guidelines

This systematic review involved no animal experiments or direct human trials, and neither a special ethics review nor ethical approval was therefore necessary. Our study was performed in accordance with the preferred reporting items for systematic reviews and meta-analyses statement.[33]

2.2. Information sources and search

We performed a computerized search of PubMed, EMBASE, and the Cochrane Library up to May, 2015 for literature focusing on the incidence of AVN after closed or open reduction for DDH. The following search terms were used: "developmental dysplasia of the hip," "congenital hip dislocation," "hip dysplasia," "hip dislocation," "avascular necrosis," "osteonecrosis," "closed reduction," and "open reduction." The reference lists of selected articles, conference proceedings, and personal files for relevant citations were also screened to identify other eligible studies.

2.3. Eligibility criteria and study selection

The inclusion criteria were as follows: first, patients <3 years of age with DDH who had been treated by closed or open reduction after either failed treatment with the Pavlik harness or who had been first seen after the age of 6 months were eligible. Closed reduction was considered to have been achieved if the reduction was concentric and stable with a satisfactory safety zone (the arc between the angle of maximal achievable abduction [80°–90°] that can be attained comfortably and the angle that allows redislocation with the hip 90°–100° flexion: >30°).[34,35] When closed reduction failed or the hip was unstable, open reduction was performed. Open surgery included routine excision of the ligamentum teres, division of the inferior transverse ligament, and eversion of the limbus where necessary.[28] A hip spica cast was applied for 6 to 12 weeks after closed or open reduction, with a plaster change at several weeks. The hips were immobilized at 90° to 110° of flexion and 40° to 60° of abduction ("human" position). Thereafter, an abduction orthosis was applied for a period of time or until acetabular development was normalized. Second, AVN reported as an outcome and defined by radiographic criteria: either the Bucholz–Ogden system[36] or the Kalamchi–MacEwen system.[37] Comparison of the 2 systems has shown that Kalamchi–MacEwen grades I, II, and IV are identical to Bucholz–Ogden types I, II, and III, respectively.[38] Some authors do not regard grade I as real AVN[24,26,28,39] because it is relatively minor and can spontaneously resolve as the femoral head develops.[40,41] In grades II, III, and IV, there is additional damage to the growth plate resulting in coxa valga, coxa breva, or complete femoral head destruction, respectively. Thus, grades II through IV are considered to represent significant or severe AVN.[30] Third, evaluation of the incidence of AVN between open reduction (without pelvic osteotomy or femoral shortening) and closed reduction was performed. Lastly, the available data could be extracted for quantitative analysis.

Two reviewers (YJW and LYL) independently assessed the titles, abstracts, and full texts based on the inclusion criteria. At each stage, discrepancies were discussed and resolved by consensus.

2.4. Data collection and quality assessment

Selection of the literature, extraction of information, and evaluation of the methodological quality of the included studies were performed by 2 evaluators (YJW and LYL) independently, and differences were resolved through discussion. The information extracted from all included articles is summarized in Table 1. The extracted information included the author, country, year of

Table 1

Characteristics of included studies.

Author, year, and country	Mean age at reduction (mo) (range)	Mean follow-up (y) (range)	Diagnostic criteria of AVN	Open reduction		Closed reduction		Quality score
				Rate (%)	Number	Rate	Number	
All grades of AVN								
Pospischill,[39] 2012, Austria	CR 4 (1.2–10.4); OS 3.6 (0.7–7.9)	6.8 (3.2–11.5)	B–O	20	15	28	46	9
Firth,[30] 2010, South Africa	CR 15 (2–65); OS 24 (6–117)	10.8 (4–26.3)	K–M	66	56	35	77	8
Clarke,[28] 2005, UK	11.5 (4–16)	≥3 (n/a)	K–M	50	22	18	28	7
Segal,[27] 1999, USA	CR 6 (3–9); OS 6 (2–11)	5 (0.8–15)	B–O	29	17	34	38	7
Luhmann,[26] 1998, USA	11 (1–24)	7 (n/a)	B–O	12	41	4	112	8
Mardam,[23] 1982, USA	30 (n/a)	14.7 (n/a)	K–M	45	22	24	59	5
Significant AVN								
Pospischill,[39] 2012, Austria	CR 4 (1.2–10.4) OS 3.6 (0.7–7.9)	6.8 (3.2–11.5)	B–O	7	15	20	46	9
Bolland,[43] 2010, UK	CR 21 (n/a) OS 33 (n/a)	9 (n/a)	K–M	10	134	11	104	6
Firth,[30] 2010, South Africa	CR 15 (2–65) OS 24 (6–117)	10.8 (4–26.3)	K–M	57	56	12	77	8
Jain,[29] 2007, UK	13 (n/a)	≥1.5 (n/a)	K–M	27	56	8	40	5
Clarke,[28] 2005, UK	11.5 (4–16)	≥3 (n/a)	K–M	14	22	7	28	7
Luhmann,[26] 1998, USA	11 (1–24)	7 (n/a)	B–O	5	41	3	112	8
Camp,[24] 1994, USA	11 (2–30)	4.3 (2–14)	B–O	11	28	2	55	6
Further surgery								
Pospischill,[39] 2012, Austria	CR 4 (1.2–10.4) OS 3.6 (0.7–7.9)	6.8 (3.2–11.5)	B–O	13	15	15	46	9
Bolland,[43] 2010, UK	CR 21 (n/a) OS 33 (n/a)	9 (n/a)	K–M	18	134	57	104	6
Clarke,[28] 2005, UK	11.5 (4–16)	≥3 (n/a)	K–M	41	22	57	28	7
Mardam,[23] 1982, USA	30 (n/a)	14.7 (n/a)	K–M	42	24	71	82	8

AVN = avascular necrosis of the femoral head, B–O = Bucholz–Ogden classification, CR = closed reduction, K–M = Kalamchi–MacEwen classification, n/a = not available, OS = open surgery or open reduction.

publication, mean patient age, mean number of follow-up years, diagnostic criteria, incidence of AVN after open or closed reduction, and quality assessment score. Quality assessments were performed according to the Newcastle–Ottawa Scale for observational studies,[42] which includes 3 aspects (total of 9 points): selection of the study groups (4 points), comparability of the study groups (2 points), and assessment of outcomes (3 points). The highest possible score was 9, and a high-quality study was defined as a study with a quality score of ≥7. We also evaluated whether the studies were adequately adjusted for potential confounders.

2.5. Data synthesis and analysis

Two-by-two tables were constructed using the data of the included studies. Odds ratios (ORs) and their 95% confidence intervals (95%CIs) were calculated from these tables. A random-effects model was used for all analyses.

Subgroup analyses were carried out on grades I to IV AVN and grades II to IV AVN based on the patients' age at the time of reduction (<18 vs >18 months), the mean follow-up duration (<7 vs >7 years), the classification criteria used (Bucholz–Ogden vs Kalamchi–MacEwen classification), total sample size (<100 vs >100 cases), and country (United States vs others). A meta-regression was performed to evaluate the heterogeneity among subgroups. A P value of <0.05 for the meta-regression indicated a statistically significant difference between subgroups.

Sensitivity analysis was performed by sequentially removing 1 study at a time and reanalyzing the data to determine whether any 1 study influenced the results. Heterogeneity was evaluated by the I^2 statistic. An I^2 value of >50% was considered to indicate significant heterogeneity. Begg funnel plots were created and Egger regression asymmetry tests were performed to investigate publication bias. STATA statistical software (version 12.0; StataCorp, College Station, TX) was used for the meta-analysis. All P values were two-sided with a significance level of 0.05.

3. Results

3.1. Search and study selection

In total, 108 studies were retrieved from the 3 databases: 67 articles from PubMed, 38 from EMBASE, and 3 from the Cochrane Library. A flowchart of the study selection process is shown in Fig. 1. Nine studies were included in the analysis.[23,24,26–30,39,43]

3.2. Study characteristics and quality assessment

All 9 studies were retrospective studies and included 391 hips treated by open reduction and 559 hips treated by closed reduction in patients <3 years old. AVN was classified with the Bucholz–Ogden system in 4 studies[24,26,27,39] and with the Kalamchi–MacEwen system in 5.[23,28–30,39] All grades (grades I–IV AVN) were considered in 6 studies.[23,26–28,30,39] Seven studies did not regard grade I AVN as real AVN[24,26,28–30,39,43]; the authors instead considered grades II to IV AVN as severe AVN. Four studies described the performance of further surgery due to redislocation or residual acetabular dysplasia after successful reduction.[23,28,39,43]

Study-specific quality scores are summarized in Supplemental table S1, http://links.lww.com/MD/B131. The quality scores ranged from 5 to 9 with a median score of 7. Because standard criteria have not been established, we considered the included studies to be of adequate quality for the analysis.

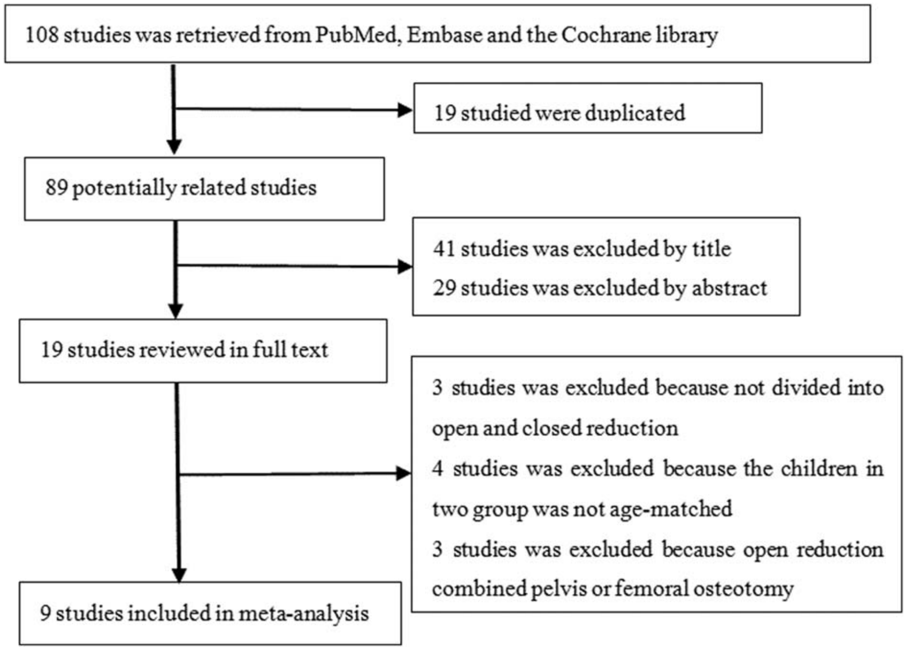

Figure 1. Flowchart of the study selection process.

3.3. Synthesis of results and additional analysis

3.3.1. Grades I to IV AVN.

The prevalence of all grades of AVN in the open reduction cohorts ranged from 12% to 66% in the 6 included studies and from 4% to 35% in the closed reduction cohorts. Analysis of the 6 studies showed a significant effect (OR = 2.26, 95%CI = 1.21–4.22) when comparing 73 cases of AVN (36%) in the open reduction group with 80 (21%) in the closed group, with moderate heterogeneity ($I^2 = 44.7\%$; $P = 0.107$) (Fig. 2).

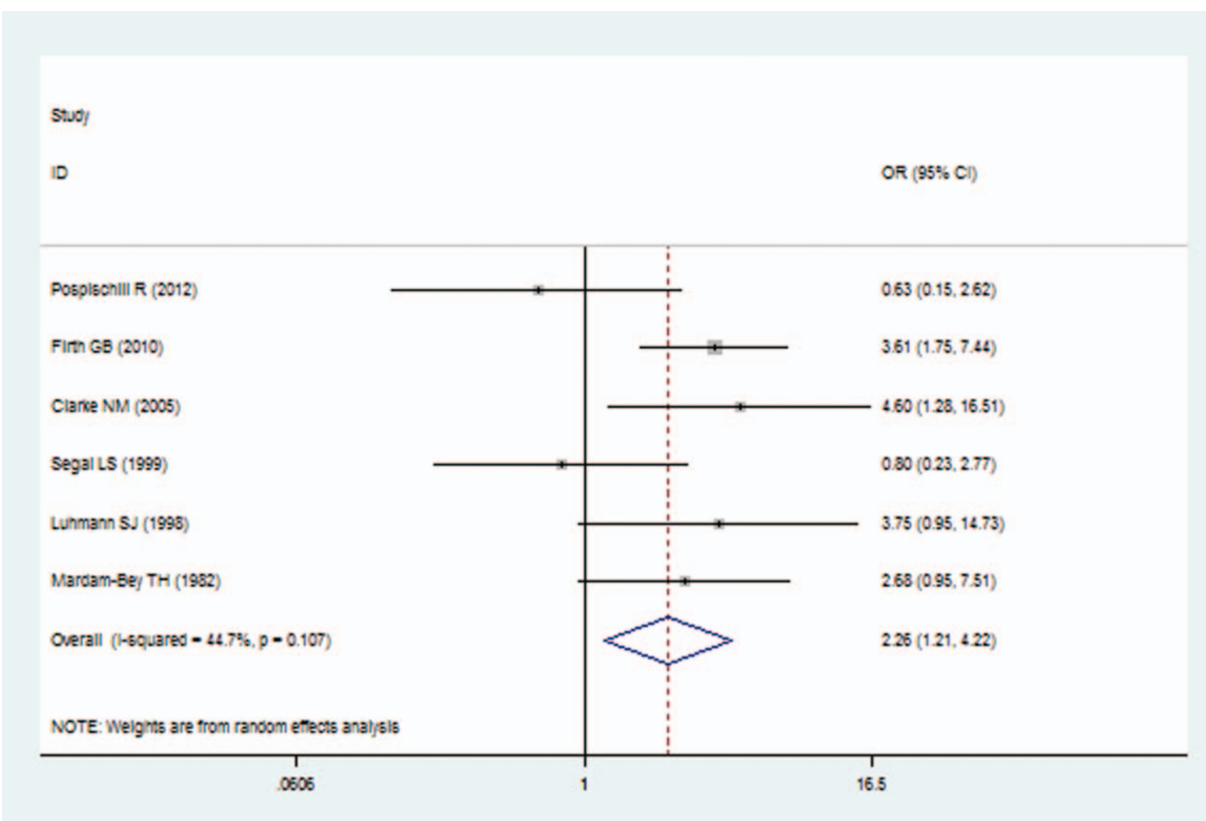

Figure 2. Forest plot (random-effects model) of the incidence of avascular necrosis of the femoral head grades I to IV between open and closed reduction. Squares indicate study-specific odds ratio (size of the square reflects the study-specific statistical weight); horizontal lines indicate 95%CIs; diamond indicates the summary relative risk estimate with its 95%CI. CI = confidence interval, OR = odds ratio.

Table 2

Summary risk estimates of comparing the incidence of AVN between open and closed reduction.

	All grades of AVN					Significant AVN				
	No. of studies	Summary OR (95%CIs)	I^2 (%)	P1	P2	No. of studies	Summary OR (95%CIs)	I^2 (%)	P1	P2
Overall	6	2.28 (1.24–4.22)	44.7	0.107		7	2.46 (0.93–6.51)	69.6	0.003	
Subgroup analysis										
Age at reduction					0.961					0.867
<18 months	4	1.73 (0.64–4.72)	56.4	0.076		4	1.62 (0.51–5.17)	23.8	0.268	
≥18 months	2	2.26 (1.21–4.22)	0	0.644		3	3.50 (0.76–16.19)	86.2	0.001	
Mean follow-up					0.59					0.742
<7 years	3	1.35 (0.39–4.62)	62.3	0.071		4	2.24 (0.65–7.74)	43.6	0.15	
≥7 years	3	3.34 (1.94–5.76)	0	0.884		3	2.72 (0.51–14.58)	86.2	0.001	
Classification standard					0.383					0.848
B–O	3	1.23 (0.42–3.61)	48.1	0.145		3	1.49 (0.28–7.93)	48	0.146	
K–M	3	3.47 (2.03–5.95)	0	0.803		4	3.16 (0.90–11.08)	79.6	0.002	
Sample size					0.801					0.742
<100	4	1.65 (0.67–4.05)	52.7	0.096		4	2.24 (0.65–7.93)	43.6	0.15	
≥100	2	3.64 (1.92–6.90)	0	0.96		3	2.72 (0.51–14.58)	86.2	0.001	
Country					0.703					0.513
USA	3	2.00 (0.83–4.83)	37.9	0.2		2	3.01 (0.72–12.61)	0	0.405	
Others	3	2.42 (0.85–6.91)	62	0.072		5	2.22 (0.65–7.58)	79	0.001	

AVN = avascular necrosis of the femoral head, B–O = Bucholz–Ogden classification, CIs = confidence intervals, K–M = Kalamchi–MacEwen classification, OR = odds ratio, P1 = value for heterogeneity within each subgroup, P2 = value for heterogeneity between subgroups with meta-regression analysis.

Publication bias was not seen in the symmetrical funnel plots and was not indicated with Begg's test ($P = 0.260$) or Egger's test ($P = 0.319$). Sensitivity analysis was carried out by excluding 1 study at a time and reanalyzing the others. The 6 study-specific ORs ranged from a minimum of 1.93 (95%CI = 1.62–4.79) after omission of the study by Firth et al[30] to a maximum of 2.79 (95%CI = 1.57–4.96) after omission of the study by Segal et al.[27] In the subgroup analysis, all strata showed positive associations, and there was no evidence of significant heterogeneity between subgroups in the meta-regression analysis (Table 2).

3.3.2. Grades II to IV AVN. Similarly, the incidence of grades II to IV AVN ranged from 5% to 57% for open reduction versus 2% to 20% for closed reduction. The meta-analysis of the 7 studies indicated that 70 patients (20%) in the open reduction cohort developed AVN compared with 38 (8%) in the closed cohort, with a significant difference (OR = 2.46, 95%CI = 0.93–6.51) and high heterogeneity ($I^2 = 69.6\%$; $P = 0.003$) (Fig. 3). There was no indication of publication bias according to Egger's test ($P = 0.710$). Sensitivity analysis similarly indicated that the 7 study-specific ORs ranged from a minimum of 1.71 (95%CI = 0.78–3.75) after omission of the study by Firth et al[30] to a maximum of 3.20 (95%CI = 1.20–8.48) after omission of the study by Bolland et al.[43] In the subgroup analysis, although the direction of all strata was consistent, none of them showed statistical significance in the meta-regression analysis (Table 2).

3.4. Further surgery

There was a statistically significant difference in the rate of further surgery between the open and closed reduction groups (OR = 0.30, 95%CI = 0.15–0.60), with moderate heterogeneity ($I^2 = 46.4\%$, $P = 0.133$) (Fig. 4). There was no indication of publication bias with Egger's test ($P = 0.734$) or Begg's test ($P = 0.355$).

4. Discussion

4.1. Summary of evidence

To our knowledge, this is the first meta-analysis to evaluate the association between the treatment method for DDH and the risk of developing AVN. The findings from this meta-analysis suggest that open reduction as a risk factor for an increased incidence of AVN (both grades I–IV and grades II–IV) compared with closed reduction when restricted to <3-year-old age-matched patients with DDH. An additional analysis indicated that the rate of further surgery in the form of open reduction was much lower than the rate of closed reduction.

Although the results of the meta-regression revealed no evidence of significant heterogeneity between subgroups by age at reduction, certain differences were noted. We also found that the rates of the different AVN grades among children aged <18 months was almost half that among children aged >18 months. Meanwhile, some studies have considered that age at the time of reduction is also a risk factor for AVN. This could be partly explained by age-related aggravation of the morphologic changes of the acetabulum, femoral head, and joint capsule of DDH[44–46] and the fact that maximal spontaneous remolding of the dysplastic hip occurs during the first year of life.[28,39,43] Moreover, DDH detected later in life is more likely to be treated with open reduction and lead to a higher rate of AVN. Many studies have reported that age at the time of reduction had no effect on the incidence of AVN.[27,30,47–49] However, considering that our analysis included few studies, further research is needed to confirm whether age at the time of reduction is a risk factor for AVN.

Similarly, in the subgroup analysis of the follow-up time, we found that the OR when the follow-up time was <7 years was lower than that when the follow-up was >7 years. This was also true for the subgroup analysis of sample size. This may be explained by the fact that the development of AVN is a dynamic process. Several investigators have emphasized that certain radiographic signs of AVN may not be detected until the patient is ≥12 years of age.[41,50] Akilapa[51] found that studies with longer follow-up periods reported higher AVN rates than did studies with shorter follow-up periods. Therefore, we suppose that a follow-up of <7 years is not long enough to evaluate the development of AVN. The 2 studies involving larger sample sizes had longer follow-up times, which may explain the disappearance of heterogeneity and the increase in the OR. These results

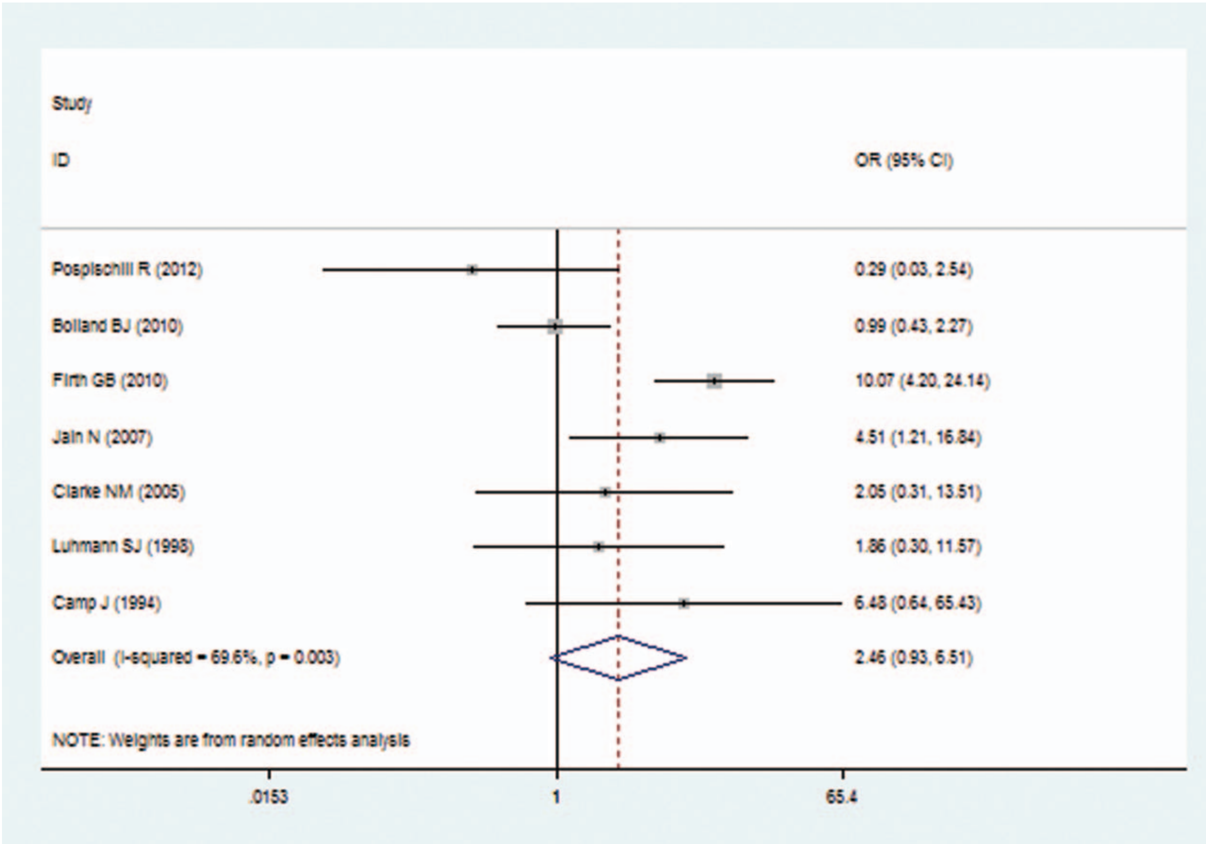

Figure 3. Forest plot (random-effects model) of the incidence of avascular necrosis of the femoral head grades II to IV between open and closed reduction. Squares indicate study-specific odds ratio (size of the square reflects the study-specific statistical weight); horizontal lines indicate 95%CIs; diamond indicates the summary relative risk estimate with its 95%CI. CI = confidence interval, OR = odds ratio.

should be interpreted cautiously because of the limited number of studies.

In the subgroup analysis of classification criteria, we found no significant heterogeneity by meta-regression; however, certain differences were found. The studies that used the Bucholz–Ogden classification system had younger patients, a shorter follow-up time, and a smaller sample size, which may explain the weaker association between the method and the development of AVN. However, the discrepancy between these 2 classification criteria should be further studied.

In this study, we concluded that open reduction is a risk factor for AVN compared with closed reduction in younger children. Disturbance of the blood supply of the femoral head affects the quality of hip development and maturation, leading to reduced perfusion, lack of development, ossification, and finally AVN.[52] The excessive pressure on the femoral head and ischemic injury to the capital femoral epiphysis during hip reduction may lead to a reduced blood supply; both of these factors are considered to be involved in the developmental mechanism of AVN.[46,53] Therefore, we can explain the cause of AVN in open reduction based on these 2 mechanisms. First, open reduction is invasive. The medial femoral circumflex artery is the main blood supply to the femoral head. It lies between the adductor and iliopsoas muscles and traverses the anteromedial capsule of the hip. This artery needs to been ligatured during open surgery or may be injured during capsulotomy.[54–56] During capsulotomy, the acetabular labrum, ligamentum teres, and other soft tissues may be separated intraoperatively, leading to tightness of the posterosuperior capsule, contracture of the external rotators, increased pressure of the joint cavity, and increased pressure on the femoral head.[43] Because extrinsic compression of the blood vessels and excessive pressure on the femoral head may occur during joint reduction, patients who undergo repeated reduction attempts for recurrent dislocation are believed to have a higher risk of AVN.[39,53] In 1 study, most patients treated by open surgery underwent failed or unstable closed reduction or severe dislocation before treatment with open reduction[29]; this may increase the incidence of AVN and the poor prognosis to different degrees.

The current consensus is that DDH in children aged <18 months is best treated by closed reduction. However, the present analysis results show that children <3 years old who underwent closed reduction had a lower risk of development of AVN than did those who underwent open reduction. In fact, controversy regarding the treatment decision in patients aged >18 months has existed for decades. Our subgroup analysis of age at the time of reduction indicated a growing tendency of the risk of AVN in children aged >18 months. Considering the limited number of included studies, however, this finding should be interpreted with caution. Future studies need to clarify with greater confidence whether open reduction increases the development of AVN. In addition, considering the matched age between the 2 groups and the comparability of our analyses, only patients <3 years old were included because the most frequent age at which open or closed reduction is performed is <3 years. In patients >3 years old, open reduction is usually used in combination with pelvic or

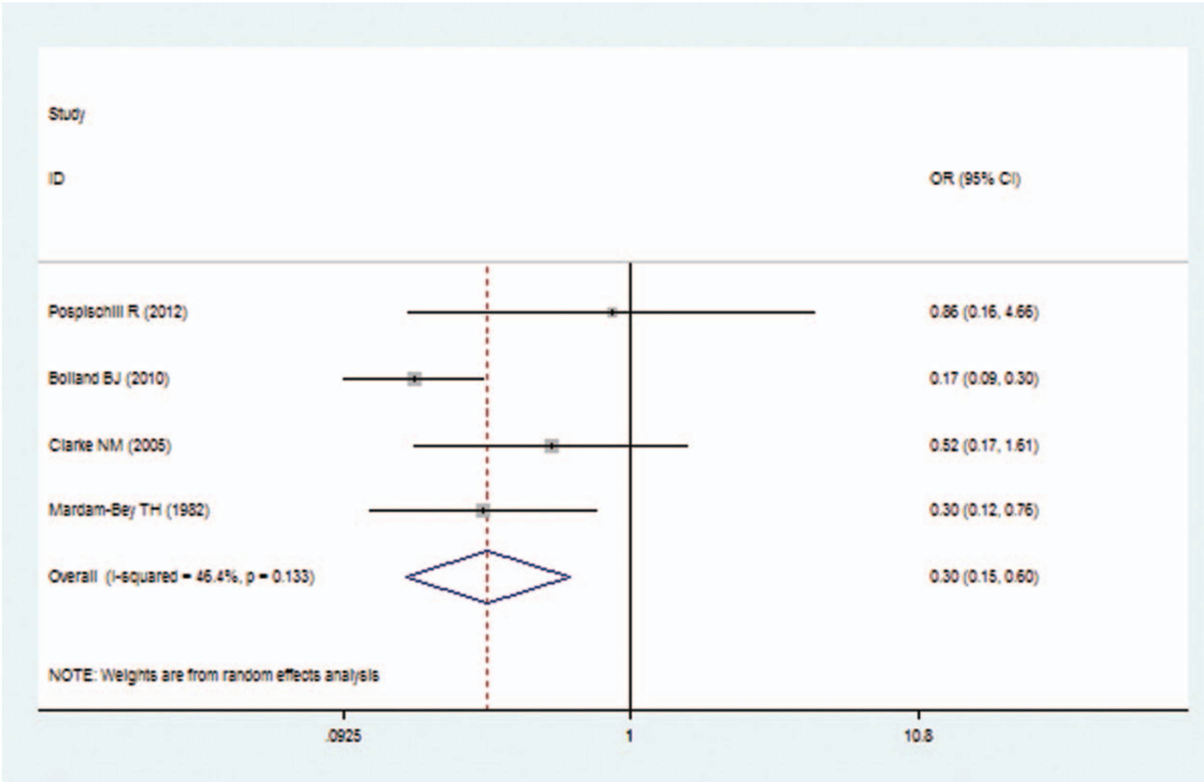

Figure 4. Forest plot (random-effects model) of the incidence of further surgery between open and closed reduction. Squares indicate study-specific odds ratio (size of the square reflects the study-specific statistical weight); horizontal lines indicate 95%CIs; diamond indicates the summary relative risk estimate with its 95% CI. CI = confidence interval, OR = odds ratio.

femoral osteotomy. Pospischill et al[39] concluded that open reduction with pelvic osteotomy increases the risk of AVN and that it would be relieved by femoral shortening owing to reduction of the pressure on the femoral head; this applies to older children. However, a study by Huang and Wang[25] showed that combined osteotomy resulted in a lower rate of AVN than did closed reduction. We did not analyze how open reduction combined with pelvic or femoral osteotomy affects the development of AVN; this requires further study.

The present study also found that the occurrence of further surgery after treatment by open reduction was much lower than that after treatment by closed reduction. A study by Pospischill et al[39] involving early reduction showed the smallest incidence of further surgery in the 4 included studies and similar rates for open reduction (13%) and closed reduction (15%). However, in 3 other studies,[2,26,43] the reduction was delayed because of the presence of an ossific nucleus or patient age of >13 months, and the rate of further surgery showed a greater increase than did early reduction[39] (Table 1). These findings could indicate that the delayed treatment resulted in insufficient reduction and development, which could lead to redislocation and residual hip dysplasia[26,43] and could increase the need for secondary reconstructive operations. In addition, patients who underwent failed closed reduction constituted the majority of the open surgery cohort, which may be the reason for the lower incidence of further surgery after open reduction. Moreover, open reduction removed intra-articular obstructive factors such as hypertrophic soft tissue, ligamentum teres, and labrum, making the reduced femoral head more stable.[25] Although open reduction reduced the rate of further surgery, it increased the risk of AVN in our analysis; this appears to be a contradiction. Notably, however, younger children had a lower risk of AVN and further surgery. This indicates that early diagnosis and reduction is particularly important. Finally, it is necessary for future studies to analyze the association between the surgical approach and the risk of AVN or further surgery, which was not addressed in our study.

4.2. Strengths and limitations

This study had several strengths. To the best of our knowledge, this is the first meta-analysis to compare the incidence of AVN between open and closed reduction for the treatment of DDH. Moreover, it included a total of 391 hips treated by open reduction and 559 hips treated by closed reduction, which should have increased the statistical power to detect these risk factors. In addition, we performed a number of subgroup analyses to detect potential sources of heterogeneity.

Our study also contained several limitations. First, the included studies were all retrospective cohort studies; therefore, the potential study biases inherent in the original studies could not be avoided compared with a prospective study, decreasing the quality of evidence. Second, although the results of the meta-regression analyses did not show significant differences between subgroups, differences in the results and unstable heterogeneity were still observed among the stratified analyses. This cannot be fully explained by the "limited studies"; we found no good explanation for the greater heterogeneity or the disappearance of heterogeneity. The development of AVN may be associated with several other factors such as the present of an ossific nucleus, previous treatment, the fixed angle, and combined osteotomy. However, many but not all studies adjusted for the potential confounding factors. Further studies of these factors are necessary to clearly define the occurrence of AVN. Third, significant heterogeneity and possible publication bias must be considered. There was significant heterogeneity in the pooled analysis of significant AVN ($I^2 = 69.6\%$, $P = 0.003$), but this may be at least partially explained by differences in the study quality, study design, exposure assessment, study population, and adjustment for potential confounders. Publication bias can be a problem in any meta-analysis, but we found no statistical evidence of such bias in our analysis.

5. Conclusion

In summary, this meta-analysis has demonstrated that compared with closed treatment, open reduction without osteotomy is associated with a higher risk of AVN. Especially in children <18 months of age, closed reduction should be employed as early as possible to minimize the risk of AVN. This analysis is limited to children aged <3 years, and we found that open reduction increased the risk of AVN but reduced the occurrence of further surgery. Thus, determination of which treatment method to use for children aged 18 to 36 months is unclear. This decision may be based on the degree of dislocation or intra-articular obstructive factors; further research is necessary. In addition, further studies should investigate how open reduction combined with pelvic or femoral osteotomy influences the development of AVN.

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