OUTCOME OF DIFFERENT TREATMENT MODALITIES IN SEVERE LEGG–CALVÉ–PERTHES DISEASE: A SYSTEMATIC REVIEW AND META- ANALYSIS

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LIST OF ABBREVIATIONS AND SYMBOLS

LCPD	Legg–Calvé–Perthes Disease
FVO	Femoral Varus Osteotomy
SIO	Salter Innominate Osteotomy
Shelf	Shelf Acetabuloplasty
AD	Arthrodiastasis
Non-Op	Non-Operative
PROSPERO	International Prospective Register of Systematic Reviews
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
JBI	Joanna Briggs Institute
CI	Confidence interval
P	p-value
OR	Odds ratio
RevMan	Review manager
SD	Standard deviation
USA	United States of America
UK	United Kingdom
ARS	Abdul Razak Sulaiman
MAI	Md Asiful Islam

BPS	Belzinder Pal Singh
NA	Not applicable
NR	Not reported

ABSTRAK

Pengenalan

Penyakit Legg-Calvé-Perthes ialah nekrosis aseptik idiopatik kepala tulang peha sendi pinggul kanak-kanak. Rawatan Penyakit Legg-Calvé-Perthes melibatkan penahanan kepala tulang peha di dalam cawan sendi pinggul semasa fasa aktif penyakit. Pelbagai kaedah rawatan kini digunakan untuk mencapai pembendungan tersebut dengan hasil yang berbeza-beza. Kami melakukan semakan sistematik yang komprehensif dan meta-analisis untuk menganggarkan prevalens terkumpul mengikut pengkelasan *Stulberg* selepas rawatan berbeza di kanak-kanak berumur 6 tahun ke atas yang menghidap Penyakit Legg-Calvé-Perthes parah tanpa sekatan kangkangan yang diklasifikasikan sebagai *Catterall* III/IV dan/atau *Herring* B, B/C, C.

Kaedah Kajian

Pangkalan data *PubMed*, *Scopus* dan *Google Scholar* telah digunakan untuk mengenal pasti kajian yang diterbitkan sebelum 30 Jun 2021. Kami menggunakan model kesan rawak untuk menganggarkan *prevalens* terkumpul dengan 95% selang keyakinan (CI) pengkelasan *Stulberg* pada pesakit dengan LCPD parah. Hasil yang baik ditakrifkan sebagai Stulberg I dan II , hasil yang sederhana ditakrifkan sebagai Stulberg III dan hasil yang buruk ditakrifkan sebagai Stulberg IV dan V. Nisbah Kebarangkalian Terkumpul (OR) dengan 95% selang keyakinan (CI) dikira daripada kajian yang membandingkan dua modaliti rawatan yang berbeza. *Prevalens* terkumpul dan 95% selang keyakinan (CI) pengkelasan *Stulberg* selepas kaedah rawatan yang berbeza juga dianalisis. *Heterogenity* dinilai menggunakan statistik I^2 dan ujian Q *Cochran*. Kajian ini berdaftar dengan PROSPERO (CRD42021224676).

Keputusan

Kajian dikenalpasti adalah 1585 dengan 41 daripadanya (1517 pinggul) dimasukkan ke dalam meta-analisis ini. *Prevalens* terkumpul hasil baik (*Stulberg* I, II), sederhana (*Stulberg* III) dan buruk (*Stulberg* IV, V) pada kanak-kanak berumur 6 tahun atau lebih dengan LCPD parah tanpa mengira modaliti rawatan ialah 43.4% [95% CI: 38.3-48.4; I^2 = 73%], 36.6% [95% CI: 32.5-40.7; I^2 = 60%] dan 15.9% [95% CI: 12.8-18.9; I^2 = 60%] masing-masing. Analisis modaliti rawatan khusus menunjukkan prevalens hasil baik adalah tertinggi selepas *Salter Inominate Osteotomy*; 54.4% [95% CI: 43.8-65.1; I^2 = 68%]. *Prevalens* hasil buruk adalah tertinggi selepas *Arthrodiastasis* 22.0% [95% CI: 12.4-31.5; I^2 = 23%] dan tanpa pembedahan 20.8% [95% CI: 12.5-29.2; I^2 = 80%]. Kajian yang membandingkan hasil *Femoral Varus Osteotomy* berbanding tanpa pembedahan menunjukkan nisbah kebarangkalian terkumpul (OR) untuk hasil yang baik memihak kepada FVO pada 0.53 [95% CI: 0.35-0.81; p = 0.003; I^2 = 0%] dan kebarangkalian untuk hasil yang buruk adalah lebih tinggi selepas tanpa pembedahan pada 3.05 [95% CI: 1.71-5.42: p = 0.0002; I^2 = 0%]

Kesimpulan

Pada kanak-kanak 6 tahun ke atas yang meghidap penyakit Legg-Calvé-Perthes parah tanpa sekatan kangkangan, semua kaedah rawatan pembedahan kecuali *arthrodiastasis* mempunyai hasil yang lebih baik berbanding dengan rawatan tanpa pembedahan. *Prevalens* tertinggi hasil keputusan yang baik dalam Penyakit Legg-Calvé-Perthes parah serta dalam Penyakit Legg-Calvé-Perthes paling parah (*Herring* C & *Catterall* IV) ditunjukkan oleh *Salter Inominate Osteotomy*.

Kata Kunci:

LCPD; Perthes: rawatan; Femoral Varus Osteotomy; Salter innominate osteotomy; Arthrodiastasis; Shelf; semakan sistematik; meta-analisis

ABSTRACT

Introduction

Legg–Calvé–Perthes disease (LCPD) is an idiopathic aseptic necrosis of the femoral head in children. Management of LCPD centres around containment of the femoral head within the acetabulum during the active phase of the disease. Multiple modalities are currently used to achieve said containment with varying results. We conducted a comprehensive systematic review and meta-analysis to estimate the overall pooled prevalence of Stulberg outcome in severe LCPD classified as Catterall III/IV and/or Herring lateral pillar classification B, B/C, C in children 6 years and older without hinge abduction after different treatment modalities.

Materials and methods

PubMed, Scopus, and Google Scholar databases were searched to identify studies published before 30th June 2021. We used random-effects model to estimate the pooled prevalence with 95% confidence intervals (CIs) of Stulberg outcome. Stulberg class I, II were defined as good outcome, Stulberg class III as fair outcome and Stulberg class IV, V were defined as poor outcome. Pooled Odds ratio (OR) with 95% confidence intervals (CIs) was calculated from studies comparing two different treatment modalities. As subgroups, pooled prevalence and 95% confidence intervals (CIs) of Stulberg outcome classifications in patients with severe LCPD after different treatment modalities was analysed. Heterogeneity was assessed using the I^2 statistic and Cochran's Q test. This study is registered with PROSPERO (CRD42021224676).

Results

We identified 1585 studies, of which 41 studies (1517 hips) were included in the meta-analysis. Overall, the pooled prevalence of good (Stulberg I, II), fair (Stulberg III) and bad (Stulberg IV, V) outcome in children 6 years or older with severe LCPD regardless of the treatment modality was 43.4% [95% CI: 38.3-48.4; I^2 = 73%], 36.6% [95% CI: 32.5-40.7; I^2 = 60%] and 15.9% [95% CI: 12.8-18.9; I^2 = 60%] respectively. In terms of outcome after specific treatment modality, prevalence of good outcome was highest after Salter Innominate Osteotomy (SIO) at 54.4% [95% CI: 43.8-65.1; I^2 = 68%]. Prevalence of bad outcome was highest after Arthrodiastasis 22.0% [95% CI: 12.4-31.5; I^2 = 23%] and Non-operative 20.8% [95% CI: 12.5-29.2; I^2 = 80%]. Studies comparing outcomes of Femoral Varus Osteotomy (FVO) versus non-operative showed a pooled Odds ratio (OR) for good outcome favouring FVO at 0.53 [95% CI: 0.35-0.81; p = 0.003; I^2 = 0%] and pooled OR for bad outcome was higher in non-operative at 3.05 [95% CI: 1.71-5.42: p = 0.0002; I^2 = 0%].

Conclusion

In children 6 years and older diagnosed with severe LCPD without hinge abduction**,** all operative treatment modalities except for arthrodiastasis had better outcome compared to non-operative treatment. Salter Innominate Osteotomy (SIO) had the highest prevalence of good outcome results in severe LCPD hips as well as in the subgroup of Herring C & Catterall IV hips.

Keywords:

LCPD; Perthes: treatment; FVO; SIO; Arthrodiastasis; Shelf; systematic review; meta-analysis

CHAPTER 1: INTRODUCTION

Introduction

Legg–Calvé–Perthes disease (LCPD) is an idiopathic aseptic necrosis of the femoral head in children (1). The disease was first described nearly simultaneously in 1909 and 1910 by Arthur Legg(Boston), Jacques Calvé (France) and Georg Perthes (Germany). It affects about 1 in 10000 children with the most common age of presentation being between the ages of 4 to 8.

It is self-limiting in nature with 4 distinct stages namely necrosis, fragmentation, revascularization and remodelling (1-4). The necrotic femoral epiphysis is weakened and is unable to withstand the load applied to it during weight bearing leading to femoral head deformation. This is worsened during the revascularization phase as vascular invasion and osteoclastic resorption of necrotic bone further compromise the mechanical strength of the femoral head (5).

The aim of management of LCPD is containment of the femoral head within the acetabulum during the active phase of the disease while necrotic bone is resorbed and replaced with living bone (6, 7). The ultimate goal of such containment is to prevent femoral head deformation by using the acetabulum as a mould, thus preventing secondary degenerative arthritis of the hip joint.

Multiple modalities are currently used in the management of LCPD ranging from conservative techniques such as weight relief, abduction splints/casts and range of motion physiotherapy to surgical techniques such as femoral and pelvic osteotomies either as a single or combined procedure, augmentation acetabuloplasties as well as hinged distraction of the hip joint (7-13). There is no consensus on which treatment modality is the best and global differences exist as shown by a recent literature review of 123 studies which showed non operative treatment was used more

commonly in the European and North American continent while operative treatment was more common in all the other continents (14).

Patients with less severe LCPD such as those with Catterall classification I/II or Herring Lateral Pillar Classification A are usually managed non operatively and have a good prognosis (8). The same applies to children who present with LCPD at a younger age and hence have a longer time for remodelling to correct the femoral head deformity. However, in older children or those with more severe LCPD, there are conflicting results after different treatment modalities in the literature.

Therefore, the aim of this study was to determine if there is a difference in outcome of severe LCPD classified as Catterall III/IV and/or Herring lateral pillar classification B, B/C, C in children 6 years and older after different treatment modalities.

Literature review

In patients with severe LCPD (Catterall III/IV, Herring Lateral Pillar B, B/C, C) or those with a later age on onset, there is a significant variability in terms of outcome in the literature.

Wiig et al. 2008 in their prospective nationwide study found that in children older than 6 years old with Catterall III/IV hips, the prevalence of good outcome was 35% (15). Osman et al. 2009 carried out a retrospective study of 44 hips treated with four different treatment modalities in children older than 8 years old and found that the prevalence of good outcome was only 19% (11). In a nationwide Japanese study done in 2006, Kim et al. found the prevalence of good outcome in children 8 years and older with Herring B, C and Catterall III, IV hips to be 52% (16).

The literature is also varied on outcome after different treatment modalities. A retrospective study which included 371 patients older than 8 years old found no difference in head sphericity at maturity between operative and non-operative groups (17). A large multicentre prospective study on the other hand found that surgical treatment improved outcomes in children older than 8 years old with Herring B, B/C hips (8). Kamegaya et al. 2004, published results of a paired study on Perthes disease comparing conservative and surgical treatment in which 36 children were paired with matching of gender, body mass index, age at onset, stage at the first visit, necrotic area and radiological at-risk signs (18). They concluded that frequency of good outcome was higher in the surgical group.

There are also discrepancies in outcome after operative management of severe LCPD using different treatment modalities. Worldwide, Femoral Varus Osteotomy(FVO) is the commonest surgery done to achieve containment of the femoral head followed by pelvic Salter Innominate Osteotomy (SIO) [14]. Wiig et al. (15) in their prospective nationwide study found that in children 6 years and older with Catterall III/IV hips, the prevalence of good outcome after femoral varus osteotomy(FVO) was 43%. Kaneko et al. 2019 published the findings of their study comparing Salter Innominate Osteotomy(SIO) with Non-Operative management in children older than 6 years with severe LCPD and found the prevalence of good outcome after SIO to be 74% (19). Herring et al in 2004 published results of their prospective multicentre study on effect of treatment on outcome of LCPD (8). They compared Non-operative treatment to FVO and SIO. In patient older than 6 years with severe LCPD, the prevalence of good outcome after specific surgical treatment was FVO (65%) and SIO (56%).

In the past two to three decades, newer surgical techniques have been also used to manage severe LCPD such as Shelf acetabuloplasty, Arthrodiastasis and Combined FVO&SIO (7, 10, 13). The outcome after these treatment modalities is also varied and yet to be comprehensively compared to the more commonly performed FVO/SIO.

CHAPTER 2: OBJECTIVES

General Objective

To study the outcome of severe LCPD classified as Catterall III, IV and Herring B, B/C, C without hinge abduction in children equal to or older than 6 years old using systematic review and meta-analysis methodology

Specific Objective

1. To study the outcome of severe LCPD classified as Catterall III, IV and Herring B, B/C, C without hinge abduction in children equal to or older than 6 years old after different treatment modalities
2. To study the outcome of the most severe LCPD classified as Catterall IV and Herring C without hinge abduction in children equal to or older than 6 years old after different treatment modalities

CHAPTER 3: MANUSCRIPT

OUTCOME OF DIFFERENT TREATMENT MODALITIES IN SEVERE LEGG–CALVÉ–PERTHES DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction

Legg–Calvé–Perthes disease (LCPD) is an idiopathic aseptic necrosis of the femoral head in children (1). It is self-limiting in nature with 4 distinct stages namely necrosis, fragmentation, revascularization and remodelling (1-4). The necrotic femoral epiphysis is weakened and is unable to withstand the load applied to it during weight bearing leading to femoral head deformation. This is worsened during the revascularization phase as angiogenesis and new blood vessel formation brings with it osteoclastic resorption of necrotic bone which further weakens the mechanical strength of the femoral head (5).

The aim of management of LCPD is containment of the femoral head within the acetabulum during the active phase of the disease while necrotic bone is resorbed and replaced with living bone (6, 7). The ultimate goal of such containment is to avert femoral head damage and deformation by using the acetabulum as a mould, thus preventing future osteoarthritis of the hip joint. Multiple modalities are currently used in the management of LCPD ranging from conservative techniques such as weight relief, abduction splints/casts and range of motion physiotherapy to surgical techniques such as femoral and pelvic osteotomies either as a single or combined procedure, augmentation acetabuloplasties as well as joint distraction of the hip (7-13). There is no clear evidence suggesting which treatment modality is the best. Global differences also exist as shown by a recent literature review of 123 studies which showed non operative treatment was used more commonly in the European and North American continent while operative treatment was more common in all the other continents in the management of severe LCPD. (14).

Children with less severe LCPD such as those with Catterall classification I/II or Herring Lateral Pillar Classification A are usually managed non operatively and have a good prognosis (8). The same applies to children who present with LCPD at a younger age and hence have a longer time for remodelling to correct the femoral head deformity. However, in older children or those with more severe LCPD, there are conflicting results after different treatment modalities in the literature.

A retrospective study which included 371 patients older than 8 years old found no difference in head sphericity at maturity between operative and non-operative groups (17). However, a large multicentre prospective study found that surgical treatment improved outcomes in children older than 8 years old with Herring B, B/C hips (8). The study by Wiig et al. (15) found better results in children older than 6 years old with Catterall III/IV hips undergoing FVO when compared to non-operative treatment.

Therefore, this study was designed with the goal of determining if there is a difference in outcome of severe LCPD classified as Catterall III/IV and/or Herring B, B/C, C in children 6 years and older without hinge abduction after different treatment modalities. The treatment modalities that were compared included Non-operative, Femoral varus osteotomy (FVO), Salter innominate osteotomy (SIO), Shelf acetabuloplasty, Arthrodiastasis and Combined FVO&SIO.

Methods

Systematic Review Protocol

This study's protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database with the following number: CRD42021224676. The systematic review and meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline (20) to study the outcome of severe LCPD after different treatment modalities.

Eligibility Criteria

The aim was to identify research published on management of severe LCPD classified as Herring B, B/C, C and Catterall III, IV using different treatment modalities worldwide. The study design was not limited but we focused on observational studies (cross sectional, cohort, case control) for inclusion. Studies by the same authors or facilities were only considered if the study population was different. Review articles, editorials, case reports, other meta-analysis, letters, erratum and comments were excluded.

In terms of specific inclusion criteria, only data from participants equal to or older than 6 years old with pre-treatment classification of either Herring B, B/C, C or Catterall III, IV with no hinge abduction was recorded. Data from the included studies failing to meet these inclusion criteria was not recorded. Studies which did not published the Stulberg classification after treatment were excluded.

Search Strategy

Google Scholar, PubMed and Scopus databases were searched to identify only studies published before 30th June 2021 without any language limitations. The following terms were used during the search: Legg–Calvé–Perthes Disease, Perthes, LCPD, LCP, Osteochondritis deforman, Osteochondritis deformans, Coxa Plana, Acetabuloplasty, Acetabuloplasties, Shelf procedure, Arthrodiastasis, Hinged distraction, External Fixator, Osteotomy, Osteotomies, Non-operative, Conservative. Two themes of Medical Subject Headings (MeSH) terms and associated keywords were included in the electronic search, which were further merged with Boolean operators ('AND' and 'OR') utilising the 'Advanced' and 'Expert' search options. Detailed information of our search strategy is depicted in Table S1. References of eligible studies were also reviewed and articles of interest were retrieved to achieve a more extensive search procedure. EndNote X8 software was utilized to identify and filter out duplicate studies.

Study Selection

Titles and abstract of articles identified from the search were screened to identify eligible studies. Full text of potential articles was then reviewed for inclusion. Two author (BPS and MAI) worked independently on this process. Disagreements over inclusion were explored and resolved by discussion with the third author (ARS).

Data Extraction

Data extraction process was carried out separately by two authors (BPS and MAI). It was then ratified by the third author (ARS). Prior to data extraction, research written in languages other than English were translated into English using Google Translate and confirmed by a native speaker. Duplicate data was dealt with by excluding the study with incomplete data or smaller sample size. We then extracted into a pre-defined Excel spreadsheet the following information from each included study: last name of first author, publication year, country study conducted in, data collection period, treatment modality used, onset and operative ages of the participants, total number of hips, number of hips subdivided by Herring (21) and Catterall (22) classifications and Stulberg class at maturity (23).

Study Quality Assessment

The Joanna Briggs Institute (JBI) critical appraisal tools for cohort studies (24) was used to assess the quality of included studies. Two authors (BPS & MAI) independently carried out the quality assessment and the results were validated by the third author (ARS). If the overall score of the quality assessment was less than 50%, the study was classed as low quality (high risk of bias), moderate quality if it scored between 50% to 70% and high quality (low risk of bias) if the overall score was greater than 70%. For assessment of publication bias, we produced funnel plots presenting prevalence estimate against the standard error and Egger's test was used to confirm the asymmetry of the funnel plots.

Data Analyses

The pooled prevalence and 95% confidence intervals (CIs) of Stulberg outcome in patients with severe LCPD was calculated using a random-effects model. Stulberg class I, II were defined as good outcome, Stulberg class III was defined as fair outcome and Stulberg class IV, V were defined as poor outcome. We also identified included studies which analysed outcome after 2 different treatment modalities and a pooled Odds ratio (OR) with 95% confidence intervals (CIs) of good, fair and bad outcome was calculated. The I^2 statistic was used to quantify heterogeneity between studies ($I^2 < 50\%$ was classed as low heterogeneity, I^2 between 50% to 75% classed as moderate heterogeneity and $I^2 > 75$ percent classed as high heterogeneity). The significance of heterogeneity was subsequently determined using Cochran's Q test. Additionally, we constructed a Galbraith plot to identify the outlier studies and the sources of heterogeneity. RevMan (version 5.4) and metaprop codes in meta (version 4.19-0) and metafor (version 3.0-2) packages of R (version 3.6.3) in RStudio (version 1.4.1106) software were used to create all the analyses and generating plots (RStudio, Inc., Boston, MA, USA) (25).

Subgroup and Sensitivity Analyses

As subgroups, the pooled prevalence and 95% confidence intervals (CIs) of Stulberg outcome classifications in patients with severe LCPD after different treatment modalities was analysed. We then identified included studies which had published individual patient pre-treatment Herring/Catterall classification and post treatment Stulberg classification. Data of outcome in the most severe LCPD (Herring C/Catterall IV) children was recorded from these studies. The pooled

prevalence and 95% confidence intervals (CIs) of Stulberg outcome in the most severe LCPD (Herring C & Catterall IV) after different treatment modalities was also then analysed. Sensitivity analyses were carried out using the following methodologies to determine the source of heterogeneity and assess the results' robustness: i) exclusion of studies with small sample size (n=15); ii) exclusion of low-quality studies (high risk of bias); and iii) exclusion of outlier studies.

Results

Study selection

Our initial search yielded 1585 studies. 914 studies were then removed for the following reasons: i) review articles (n=8); ii) case reports (n=12); iii) duplicate studies (n=894). The titles and abstracts of 671 studies were then assessed for eligibility, with 539 studies being excluded because they were not relevant with our study objective. 132 full texts were then evaluated for inclusion, of which 91 were rejected for: i) not meeting the inclusion criteria of age or severity; ii) no Stulberg outcome results available; iii) used treatment modality not being analysed in our study; iv) included hips with hinged abduction in the study. Finally, 41 studies were included in this systematic review and meta-analysis (Fig. 1).

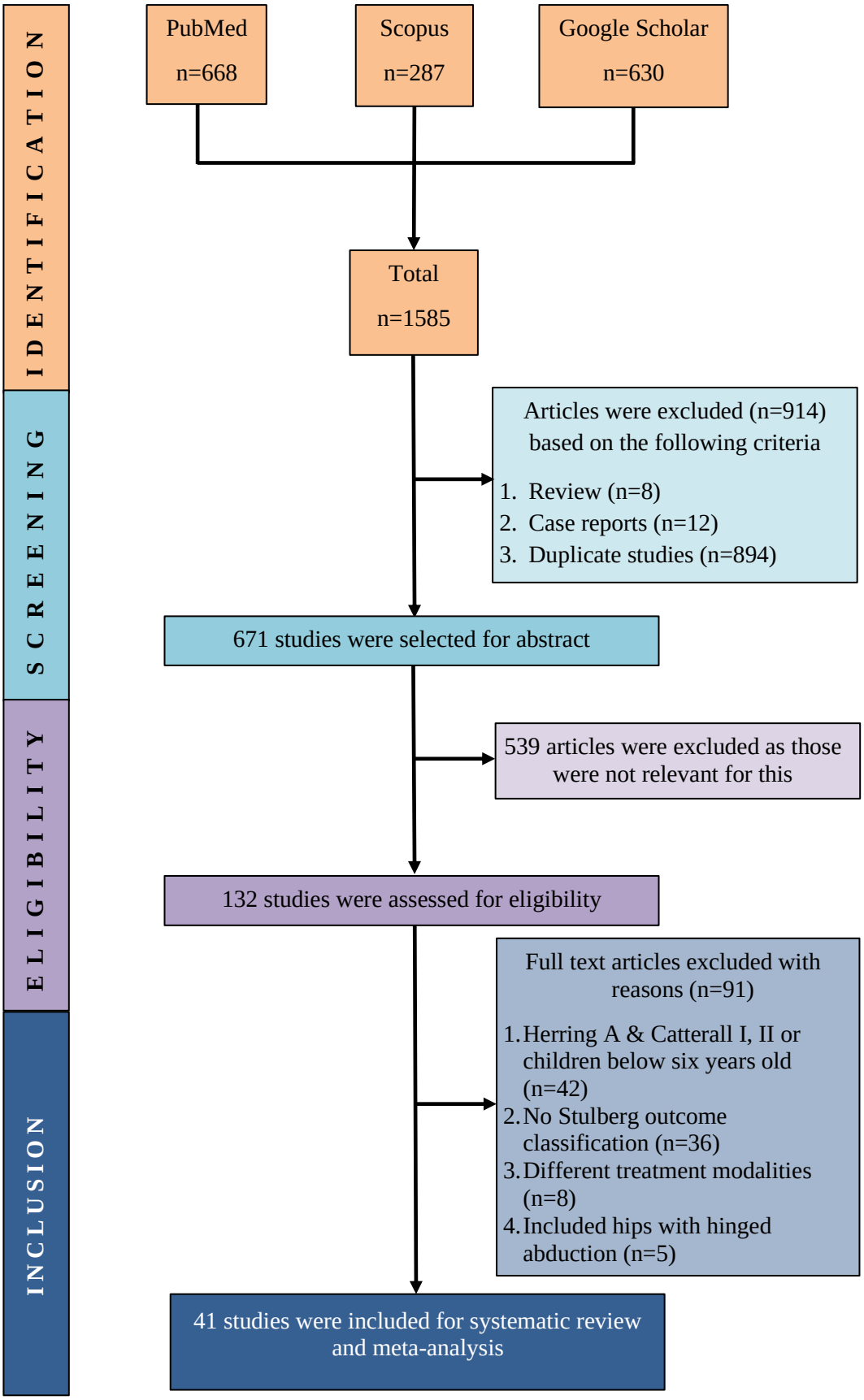

Figure 1: PRISMA flow diagram showing the process of selecting eligible studies.

Study characteristics

Detailed characteristics and references of the included studies are presented in Table 1. In total, 1517 hips with severe LCPD were studied in this meta-analysis. All of the patients in this meta-analysis were older than 6 years old with an age range of 6 to 15 years old. All children had Catterall III/IV and/or Herring B, B/C, C hips. The sample sizes of the studies that were included ranged from 7 to 340 children. Thirty-three studies reported on the specific Herring classification of included patients, of which 625 (49.8%) were Herring B, 180 (14.4%) Herring B/C, and 449 (35.8%) Herring C. Twenty-three studies reported on the Catterall classification of included patients of which 376 (59.8%) were Catterall III and 253 (40.2%) were Catterall IV. Of the 1517 hips studied, 482 (31.8%) were treated non operatively, 422(27.8%) underwent FVO, 265(17.5%) underwent SIO, 184(12.1%) underwent Shelf acetabuloplasty, 90(5.9%) underwent arthrodiastasis and 74(4.9%) underwent combined FVO&SIO. The follow up period in the included studies ranged from 1 to 25 years. Studies were from 6 continents and 15 countries namely USA, Canada, Brazil, Colombia, UK, Norway, France, Turkey, Egypt, India, Japan, Korea, Bangladesh, Thailand and China.

Table 1. Major characteristics of the included studies

No	Study ID	Country	Study Period	Treatment Modality	Age at presentation (years) (mean±SD / range)	Operative Age (years) (mean±SD / range)	No. of hips	Herring	Catterall
1	Aksoy 2005 (26)	Turkey	NR	FVO	7-11	NR	26	C: 26	NR
2	Alves 2005 (9)	Brazil	NR	Non-op	7.7±1.4	NA	17	B: 12; C: 5	III: 12; IV: 5
3	Aydin 2016 (6)	Turkey	1985-1994	FVO	6.0-12.0	9.3±2.4	17	B: 11; C: 6	NR
4	Bhuyan 2016 (7)	India	2005-2012	Combined (SIO+FVO)	6.9±0.8	7.5±0.8	14	B: 8; B/C: 2; C: 4	III: 11; IV: 3
5	Bowen 2011 (10)	USA	NR	Shelf	7.6±1.9	8.8±1.8	42	B: 23; C: 19	III: 22; IV: 20
6	Bulut 2014 (27)	Turkey	2004-2008	SIO	6.0-10.0	8.1±1.4	16	B: 4; B/C: 8; C: 4	NR
7	Carsi 2015 (28)	UK	1999-2010	Shelf	6.0-12.0	8.2±1.7	22	B/C: 9; C: 4	III: 14; IV: 8
8	Citlak 2012 (29)	Turkey	1982-1997	Non-op; FVO	Non-op: 6.0-8.0; FVO: 6.0-8.0	NR	Non-op: 16; FVO: 11	Non-op; B: 16; FVO; B: 11	NR
9	Crutcher 1992 (30)	USA	1974-1979	Combined (SIO+FVO)	7.9±1.0	9.0±1.0	12	NR	III: 9; IV: 3
10	Eamsobhana 2012 (31)	Thailand	2000-2010	Combined (SIO+FVO)	8.0±1.5	8.2±1.6	18	B: 13; C: 5	III: 8; IV: 10
11	Friedlander 2000 (32)	USA	1971-1992	FVO	6.0-10.0	NR	98	B: 30; C: 68	NR

12	Herring 2004 (8)	USA	1984-NR	Non-op; FVO; SIO	6.0-12.0	NR	Non-op: 223; FVO: 51; SIO: 66	Non-op B: 142, B/C: 36, C: 44; FVO (B: 33, B/C: 7 C: 11 SIO B: 43, B/C: 18 C: 5	NR
13	Hosny 2011 (33)	Egypt	1995-2007	AD	8.0-14.0	NR	21	NR	NR
14	Ishida 2004 (34)	Brazil	1979-1992	SIO	7.0-12.6	NR	18	NR	NR
15	Javid 2009 (35)	Canada	1988-2001	Combined (SIO+FVO)	9.9±2.2	10.5±1.2	20	B: 11, B/C: 7 C: 2	NR
16	Kamegaya 2004 (18)	Japan	Before 1985	Non-op	8.7±1.4	NA	18	NR	III: 17; IV: 1
17	Kamegaya 2016 (36)	Japan	1990-2010	FVO	8.3±NR	8.5±2.2	47	B/C: 17, C: 30	NR
18	Kaneko 2019 (19)	Japan	1989-2009	Non-op; SIO	Non-op: 6.0-7.8; SIO: 6.0-7.8	NR	Non-op: 18; SIO: 35	Non-op B: 10, B/C: 3 C: 5 SIO B: 16, B/C: 12 C: 7	Non-op III: 12; IV: 6; SIO III: 27; IV: 8
19	Kim 2006 (16)	Japan	1993-1995	Non-op; FVO; SIO	Non-op: 9.4±1.3; FVO: 9.8±1.1; SIO: 10±1.8	NR	Non-op: 47; FVO: 14; SIO: 4	Non-op B: 40, C: 7 FVO B: 12, C: 2 SIO B: 2, C: 2	Non-op III: 35; IV: 12; FVO III: 11; IV: 3; SIO III: 3; IV: 1

20	Kim 2007 (37)	Korea	1998-2001	Modified SIO	NR	7.7±1.2	16	B: 7, C: 9	III: 5; IV: 11
21	Kim 2016 (38)	Korea	1997-2007	AD	9.1±1.4	NR	7	B: 3, C: 4	III: 3; IV: 4
22	Kitakoji 2005 (39)	Japan	1972-1998	FVO; SIO	NR	FVO: 9.0-13.1; SIO 9.0-12.1	FVO: 10; SIO: 10	NR	NR
23	Kocaoglu 1999 (40)	Turkey	1993-1995	AD	7.3±1.4	7.9±1.4	9	B: 3, C: 6	III: 3; IV: 6
24	Kucukkaya 2000 (41)	Turkey	1994-1997	AD	7.8±1.1	NR	8	NR	III: 2; IV: 6
25	Laklouk 2012 (13)	Egypt	1998-2007	AD	7.8±1.7	9.3±1.5	19	B: 11, C: 8	NR
26	Li 2016 (42)	China	1994-2005	Shelf	8.5±0.9	9.2±0.9	40	B: 4, B/C: 21 C: 15	III: 15; IV: 25
27	Nakamura 2015 (43)	Japan	1986-2002	Non-op	8.1-12.6	NA	34	B/C: 21, C: 13	NR
28	Noonan 2001 (44)	USA	1974-1992	FVO	9.0-13.0	10.7±1.1	12	B: 7, C: 5	III: 10; IV: 2
29	Osman 2009 (11)	UK	1987-2003	Non-op; FVO; Shelf	Non-op: 9.7±1.5; FVO: 9.0±0.8; Shelf: 9.9±1.2	NR	Non-op: 22; FVO: 4; Shelf: 16	Non-op B: 13, C: 9 FVO B: 3, C: 1 Shelf B: 9, C: 7	NR
30	Park 2017 (45)	Korea	1998-2001	Modified SIO	NR	7.6±1.1	21	B: 9, C: 12	III: 7; IV: 14

31	Paul 2017 (46)	Bangladesh	2013-2016	FVO	8.6±1.2	9.4±1.6	22	B: 13, B/C: 4 C: 5	NR
32	Pecquery 2010 (12)	France	1992-2007	Shelf	8.9±1.9	9.8±2.0	10	B: 7, B/C: 2 C: 1	III: 4; IV: 6
33	Sarassa 2008 (47)	Colombia	NR	Combined (SIO+FVO)	9.2±1.7	NR	10	B: 3, C: 7	III: 4; IV: 6
34	Sharma 2009 (48)	UK	1990-1995	Non-op; FVO; Shelf	Non-op: 7.2±0.5; FVO: 7.3±0.6; Shelf: 7.0±0.5	NR	Non-op: 11; FVO: 7; Shelf: 5	Non-op B: 5, C: 6 FVO B: 4, C: 3 Shelf B: 1, C: 4	Non-op III: 8; IV: 3; FVO III: 4; IV: 3; Shelf III: 4; IV: 1
35	Sponseller 1988 (49)	USA	1968-1982	FVO; SIO	FVO: 8.4±1.9; SIO: 8.3±1.0	NR	FVO: 33; SIO: 33	NR	FVO III: 17; IV: 16; SIO III: 24; IV: 9
36	Terjesen 2012 (50)	Norway	1996-2000	Non-op; FVO	Non-op: 7.3-8; FVO: 7.1-7.6	NR	Non-op: 51; FVO: 70	Non-op B: 30, C: 21 FVO B: 36, C: 34	Non-op III: 27; IV: 24; FVO III: 48; IV: 22
37	Volpon 2012 (51)	Brazil	1994-2002	SIO; AD	6.0-NR	SIO: 7.9±1.4; AD: 8.3±1.4	SIO: 28; AD: 26	NR	NR

38	Wiig 2008 (15)	Norway	1996-2000	Non-op; FVO	6.0-15.2	NR	Non-op: 76; FVO: 70	Non-op NR FVO B: 36, C: 34	Non-op: NR; FVO III: 48; IV: 22
39	Wright 2013 (52)	UK	1998-2004	Shelf	8.0-12.2	9.8±NR	24	B: 18, C: 6	NR
40	Yavuz 2014 (53)	Turkey	2004-2009	SIO	9.2±1.3	NR	18	B: 7, B/C: 3 C: 8	NR
41	Yoo 2009 (54)	Korea	1999-2005	Shelf	NR	7.0-12.3	25	B: 6, B/C: 10 C: 9	III: 10; IV: 15

FVO: femoral varus osteotomy; NR: not reported; SIO: Salter innominate osteotomy; NA: not applicable; Shelf: shelf acetabuloplasty; AD: Arthrodiastasis; Non-op: non-operative