Surgical management of Chiari 1 Malformation in the paediatric population: A systematic review and meta-analyses of observational studies

Abstract

Background

Chiari 1 malformation(C1M) is a congenital malformation in the paediatric population is commonly encountered and often requires surgical management.. Currently there is no agreed consensus on the appropriate and specific surgical technique for management of paediatric cases ofC1M. The purpose of this systematic review and meta-analysis is to compare the clinical outcomes of posterior fossa decompression with duraplasty (PFDD) to posterior fossa decompression alone (PFD) in paediatric patients.

Methodology

Systematic review of electronic literature databases searched from January 1997 to March 2017 of paediatric patients that had posterior fossa decompression with comparative analysis of PFD and PFDD were considered for inclusion. A Meta-analyses on the retrieved data was performed.

Results

Nine reports of eligible studies involving 3404 patients met the inclusion criteria. Of the 3404 patients, 1965 were treated with PFD alone while 1439 were treated with PFDD. Mean age range of 9.6 year to 11.1 years. Patients undergoing PFDD has significantly higher rates of pseudomeningocele formation OR 1.91, 95% C1 (1.30, 2.82) and lower complication rates OR 1.30, 95% CI (1.06, 1.61) than PFD. No significant difference in clinical improvement, reoperation rates, CSF leaks, wound infection and incidence of aseptic meningitis were observed

Conclusion

PFDD is associated with fewer complications when compared to PFD alone. However the incidence of pseudomeningocoele formation is more commonly encountered following PFDD compared to PFD. PFDD is also more commonly performed following a failed improvement in symptomatology following PFD. Multicentre randomised controlled studies are needed to definitively identify the gold-standard technique for the management of answer to best surgical technique.

Introduction

The cerebellar tonsils are displaced downward into the spinal canal in a congenital abnormality known as Chiari malformation [1]. There are four forms of Chiari Malformation, the most prevalent of which is type 1. The exact mechanism of Chiari malformation remain unclear and a matter of debate but majority of scholars speculate that it may be due to a small posterior fossa. This has been observed in several morphological studies of the posterior fossa [2]. According to one study, the volume of the posterior fossa vault and cerebrospinal fluid decreased by 10% and 40%, respectively [3]. The pressure differential between two compartments, according to Williams' cranial-spinal dissociation theory [4], exacerbates tonsillar herniation, restriction of CSF flow, and displacement into the central canal, leading in syrinx development.

Surgical treatment is the only widely accepted treatment for symptomatic C1M with or without a spinal cord syrinx [5]. There exists considerable debate regarding the extent of decompression and whether a durotomy or duraplasty should performed. There is consensus however that posterior fossa decompression heralds Rclinical and concurrent radiological improvement [6,7,8]. To achieve some authors adovocate removal of bone only, whilst others claim that opening the dura [with or without duraplasty] is necessary for a favourable outcome [9, 10,]. Some authors stipulate that arachnoid should be opened and herniated cerebellar tonsils reduced by coagulation or partial tonsillectomy [5, 11]. However, there is no agreed consensus on the appropriate and specific surgical technique for management ofC1M. The goal of this systematic review and meta-analysis is to assess the clinical outcomes after posterior fossa decompression with duraplasty compared to posterior fossa decompression alone in paediatric patients with C1M.

Material and methods

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) criteria for systematic review reporting and quality evaluation of each trial with the Cochrane Collaboration Tool for Risk Bias Assessment [22]. This is a systematic review and meta-analysis of non-RCTs with no limitations on publication year or language. This review included all full text non-RCTs comparing the clinical outcomes of posterior fossa decompression with or without duraplasty in paediatric patients with C1M.

Inclusion criteria were, paediatric patients with Chiari 1 malformation for surgical intervention of posterior fossa decompression with or without duraplasty. Non-RCTs, observational studies including cohort studies, case control studies or case series of more than ten patients were evaluated.

Exclusion criteria were case-series less than ten subjects, conference articles, abstracts, protocol, guidelines and animal studies.

The primary outcome measures were clinical improvement.

Secondary outcomes measures were re-operation rate, complication including CSF leak, pseudomeningocele, wound infection and aseptic meningitis

Search methods

Electronicliterature database search was performed from January 1997 to April 2017 in the following repositories; Cochrane Central Register of Controlled trials in the Cochrane library, Medline, Embase and Science Citation Index Expanded database. Key words were mapped to Medline medical subject heading (MESH) terms and searched for as text items. Case reports and irrelevant research were filtered out of Medline and Embase using a filter. To find more prospective eligible publications for our review, we searched the references of mentioned journals by hand. For qualifying studies, researchers searched through respected neurosurgery, neurology, and neurosciences international conference journals. **Data collection**

Two reviewers independently extracted the required outcome data after reading the entire text of all included articles. Publication data, author, number of patients, interventions, study design, clinical improvement, recurrence rate, complication, CSF leak, re-operation rate and operation were documented. The data were further synthesised into a comprehensive summary of randomised trials table comparing both treatment outcomes.

Assessment of risk of bias in includes studies

The six key components of the Cochrane collaboration format [12] tool were used to assess the risk of bias in studies. Sequence generation, participant, personnel, and result assessor allocation concealment, inadequate outcome data, selective outcome reporting, and other kinds of bias were all considered. **Statistical Analysis**

The software package Review Manager 5.1 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, (Denmark) was used for data analysis. The Mantel-Hensel statistical method was used to compute the odds ratio (OR) or relative risk with 95 percent confidence interval (CI) for dichotomous outcomes in the meta-analysis. Risk difference was estimated and used for mortality results for data with zero incidents. For continuous outcomes, the mean difference with 95 % CI was employed, and the meta-analysis used the estimated result. We utilised random-effects and fixed-effects models for OR (Odd Ratio) and mean differences outcomes. The fixed-effects model was reported if there were no differences between the results of the two models. The random-effects and fixed-effects models were used to see if there were variations in the intervention effects. The random-effects model was reported if statistical heterogeneity existed. Heterogeneity was explored using χ^2 test to provide an indication for between-study, heterogeneity was considered significant when $I^2 \geq 50\%$ or when X- square test resulted in $P < 0.05$. Statistical heterogeneity for each pooled summary was estimated using I^2statistics presented as a percentage. A thorough assessment of research was carried out in order to uncover any noteworthy results of heterogeneity. To see if there was any publication bias in outcomes utilising data from the trials, researchers created a funnel plot of studies that were undergoing meta-analysis. **Validity Assessment**

Akhigbe T, Zolnourian A, and Sadek AR assessed the validity of the studies using the risk of bias guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions, with disagreements resolved by discussion. Random sequence generation, allocation concealment, insufficient outcome data, selective reporting, and other biases were all examined as potential sources of bias. As per Cochrane recommendations, no scoring or weighting procedures for validity assessments were utilised. Blinding participants and workers in surgical studies is difficult and impossible, hence it was not explored for this review. **Results**

There were 901 studies found in the literature search, with 524 in Medline, 351 in Embase, and 11 in the Cochrane Central Register of Controlled Trials. A registry search on the internet returned seven results; a journal search provided four studies, one conference proceeding, and two references. After additional screening by the investigative team, 38 out of 901 papers were selected for full text analysis, with 29 of these studies being removed due to narrative literature reviews of inappropriate intervention and studies involving adult patients. Eighteen studies were finally included for systematic review and meta-analyses. There were total 3404 patients who underwent posterior fossa decompression with or without duraplasty.

Study Characteristics

Extensive database search identified nine non-RCTs [13-21] with 3404 patients [Table 1]. A total of 3404 paediatric patients who underwent surgical treatment for Chiari 1malformation were described in nine included studies. Of these 1439 had PFDD compared to 1965 that had PFD alone. Patient age ranged 9.6 to 11.1 years. Presence of synrigomyelia was mentioned in some of the studies. Follow-up ranged from 5 months to 2 years but was largely unaddressed by majority of the studies. No blinded outcome assessment was specified in any of the studies.

Critical Appraisal

Methodological quality was assessed by Newcastle-Ottawa scale (NOS) [22] scoring of included studies (Table 2). NOS is a tool for assessing the quality of nonrandomised studies in meta-analyses. Study quality scores ranged from 4 to 8 out of possible 9 points. Scoring for comparability was poor because insufficient details about patients selection of varied surgical techniques. Potential confounding variables were addressed by three studies [18, 19, 21]. Varied outcome due to report inconsistencies across studies

Assessment of risks of bias of RCTs

The six key components of the Cochrane method were used to assess the risk of bias in RCTs. Bias was introduced by sequence generation, allocation concealment, participant, personnel, and outcome assessor blinding, inadequate outcome data, selective result reporting, and other methods. **Outcome measure**

Clinical Improvement

Four studies [13, 16, 18, 20] recorded the clinical improvement rate between the two groups with total of 148 patients, 26 out 68 for PFD and 50 out of 86 for PFDD, there was no difference between the two group, [1.84, 95% CI (0.89, 3.82), P <0.05]. Study by Lamondi et al [21] used a novel outcome scale with scores ranging from 1 to 2 points and demonstrated greater clinical improvement in patients who had PFD as compared to PFDD although this did not reach statistical significance.

Reoperation

Four studies [14, 18, 19, and 20] recorded the incidence of re-operation. Of the 1178 patients who underwent a PFD 25 underwent a second procedure to manage there ongoing symptoms. Of the 1697 cases undergoing a PFDD 26 underwent a further procedure.. No statistical difference in the incidence of either procedure resulting in a second procedure to manage ongoing symptoms was observed 1.33, 95% CI (0.77, 2.31).

CSF Leak

Two studies [13, 14] reported CSF leak. Patients that had PFD were more like to have CSF leak in comparison to PFDD patients this however was not observed to be statistically significant0.90, 95% CI (0.65. 1.26).

Pseudomeningocele

Three studies [14, 15, 17] reported pseudomeningocele as complication, PFDD patients are significantly more likely to develop pseudomeningocele in comparison to PFD OR 1.91 95% CI (1.30, 2.82), P=0.001

Wound Infection

One study [13] reported wound infection. There was no predilection for wound infection in either of the surgical techniques.

Aseptic Meningitis

Four studies [14, 18, 19, and 21] reported aseptic meningitis with PFD less likely to develop aseptic meningitis in comparison to PFDD ?stats?.

Overall complication {whats the definition of overall complications?- needs to be defined in the text}

Four studies [14, 18, 19, 21) reported overall complication. PFD patients are significantly more likely to have more complications than PFDD. OR 1.30 95% CI(1.06, 1.62), P=0.01

Discussion

C1M is herniation of cerebellar tonsil below the level of foramen magnum into the upper cervical spine and is commonly associated with syringomyelia as a result of deranged CSF dynamics [23]. There is a consensus that asymptomatic patients with C1M do not require surgical intervention[24]. However, symptomatology is an indication for surgery, with tussive headaches, neck, arm or back pain, swallowing difficulties, drop attacks, upper extremity sensory disturbance and presence of syrinx being critical cues for surgical

intervention[25]. The results of our meta-analysis of studies comparing PFD with PFDD suggest that patients who had PFDD encounter fewer post-operative complications but are move likely to develop a pseudomeningocoele.

Post-operative symptomatic clinical improvement f

Reoperation rate was reported by various authors[13,16] to evaluate the effectiveness of PFD and PFDD in the management of CM-1 which may be as a result of persistent symptoms or possibly due to complication, but reasons as to why patients underwent a second procedure were not clearly stated in these studies. Our study has shown there to be no difference between the two groups with respect to the rate of re-operation for the management of ongoing or worsening symptoms.

Follow-up data is sparse and was absent from five studies of the studies included in the meta-analysis [14, 17, 18, 19, 20] Data from the remaining studies heralded an mean follow-up time of 1.4 years.

Conclusion

PFDD can be considered as a preferable technique for CM-1 and also tend to be considered in case of failed PFD however PFDD is associated with higher rate of pseudomenigocele.

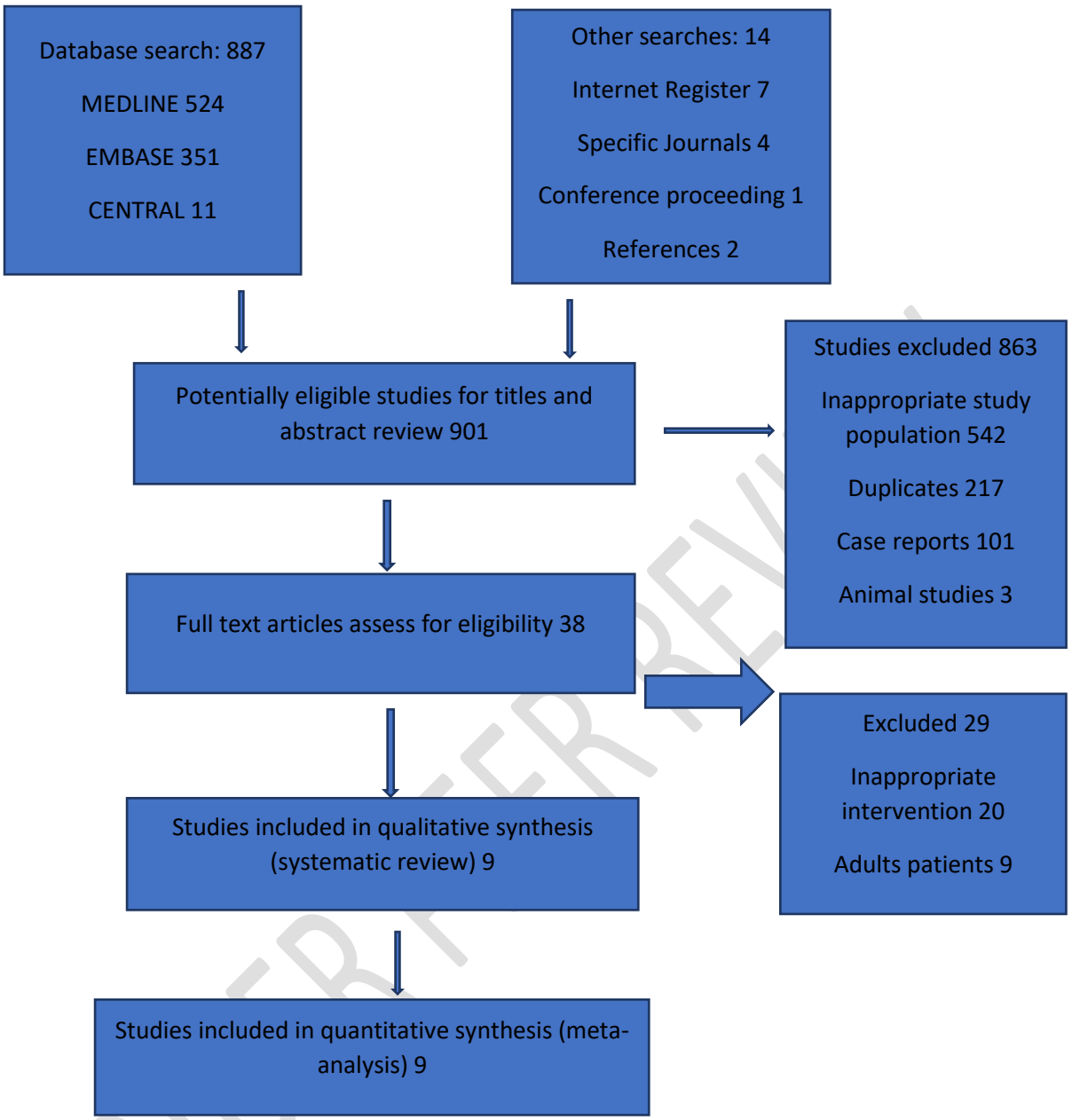

Fig 1: Flow diagram of study search

Table 1 Study Characteristics

Study/ year	Operation PFD/PFDD	Total	Mean Age YRS	Study Design	Follow up (years)
Les 2014	29/36	65	9.6	Retrospective cohort	2
Shweikeh 2014	1593/ 1056	2649	10.3	Retrospective cohort	NA
MutchnInk 2010	56/64	120	11.1	Retrospective cohort	0.5

Galarza 2007	20/21	41	10.4	Retrospective cohort	1.8
McGirt 2007	151/128	256	10	Retrospective cohort	NA
Yet 2006	40/90	130	9.2	Prospective cohort	
Limonadi 2004	12/12	24	9.6	Prospective cohort	1.3
Navarro 2004	56/24	80	9.5	Retrospective cohort	NA
Ventureyra 2003	8/8	16	10.5	Retrospective cohort	NA

NA: Not available

Table 2: Newcastle-Ottawa Scale Scoring of Included Studies

Author & year	***Selection (4 point max)***	***Comparability (2 points max)***	***Outcome (3 points max)***	***Total Score***
Lee 2014	3	1	2	6
Shweikeh 2014	4	2	1	7
Mutchnik 2010	3	1	1	5
Galarza 2007	3	0	1	4
McGirt 2007	3	1	1	5
Yeh 2006	3	1	2	6
Limonadi 2004	4	1	3	8
Navarro 2004	3	1	2	6
Ventureyra 2003	3	0	1	4

Selection*- one point for each of the following: representativeness of exposed cohort, selection of non-exposed cohort, attainment of exposure and no outcome of interest at the start.*

Comparability*- One point awarded if study controls for 1 important factor and 1 additional point if study controls >1 important factor*

Outcome*- One point awarded for each of the following: assessment of outcome, adequate length of follow up and adequacy of follow up*

Outcomes	***Number of studies***	***Number of patients***	***PFD***	***PFDD***	***Model***	***OR (95% CI)***	***I^2 (%)***	***Ph***
Reoperation	*4*	*2875*	*25/1178*	*26/1697*	*FE*	*1.33[0.77, 2.31]*	*76*	*0.31*
Clinical	*4*	*148*	*26/62*	*50/86*	*FE*	*1.84 [0.89,*	*0*	*0.10*

Improvement						*3.82]*		
CSF Related complication	*2*	*2694*	*98/1602*	*62/1092*	*FE*	*0.90 [0.65, 1.26]*	*0*	*0.54*
Pseudomeningocoele	*3*	*3025*	*47/1765*	*60/1260*	*FE*	*1.91 [1.30, 2.82]*	*0*	*0.001*
Wound infection	*1*	*65*	*1/29*	*0/36*	*FE*	*0.26 [0.01, 6.63]*	*0*	*0.42*
Aseptic Meningitis	*2*	*89*	*0/41*	*4/48*	*FE*	*4.80 [0.53, 43.50]*	*0*	*0.16*
Overall complication	*4*	*2883*	*221/1701*	*188/1182*	*FE*	*1.30[1.06, 1.62]*	*0*	*0.01*

Table 3: Outcome of meta-analysis

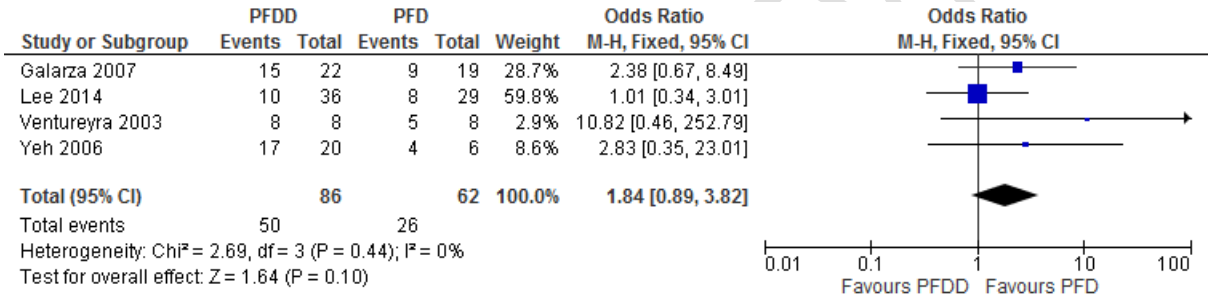

Figure 2: Clinical Improvement

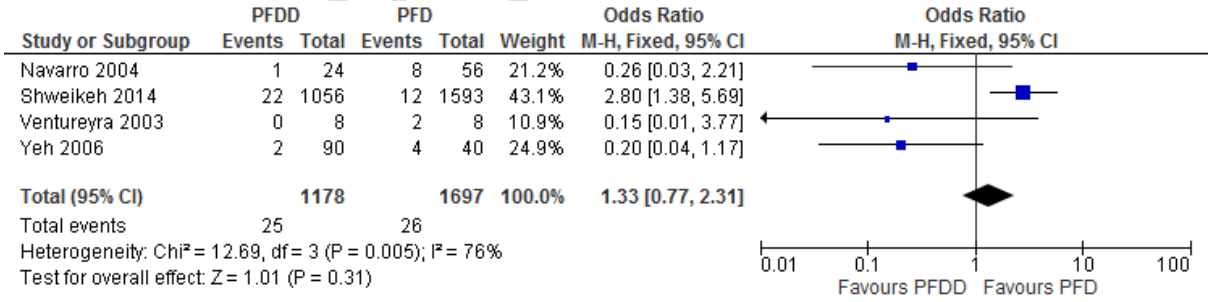

Figure 3: Reoperation

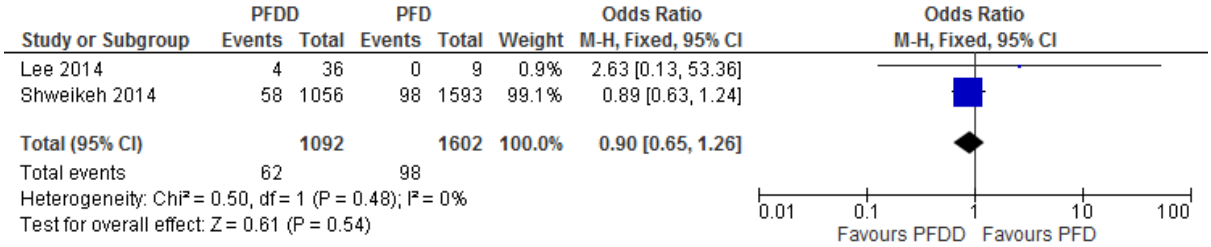

Figure 4: CSF leak

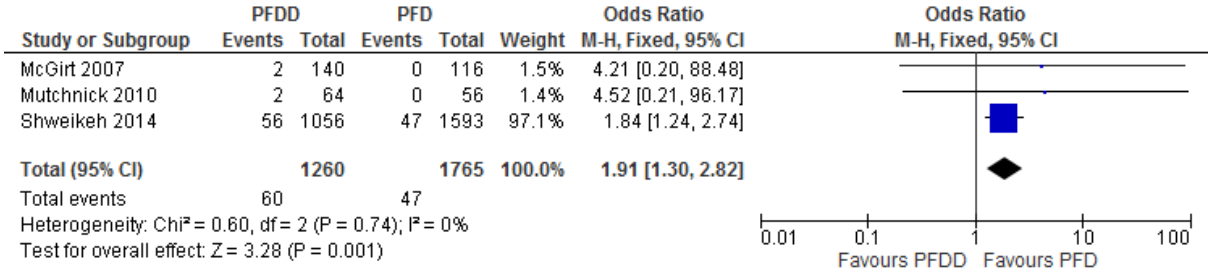

Figure 5: Pseudomeningocele

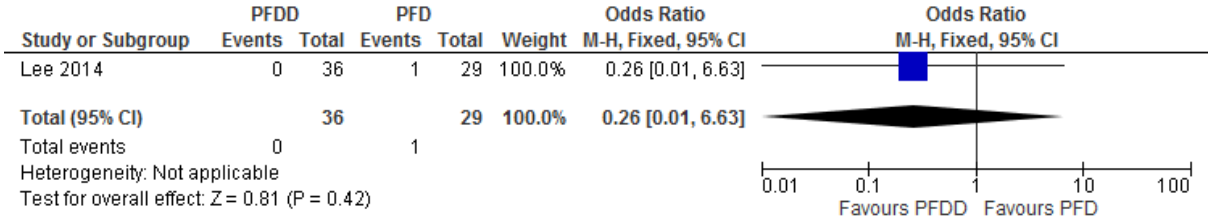

Figure 6: Wound Infection

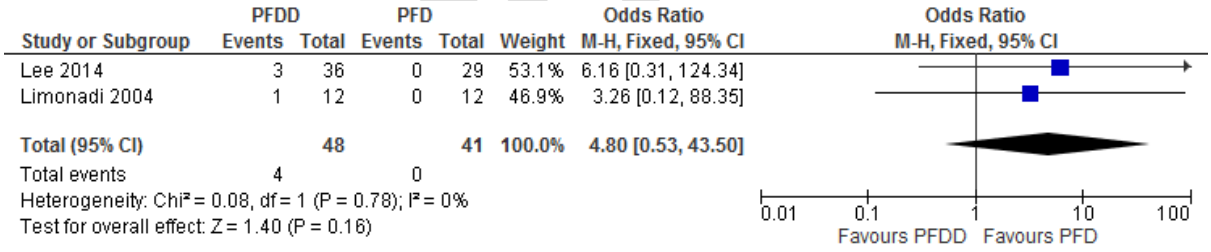

Figure 7: Aseptic Meningitis

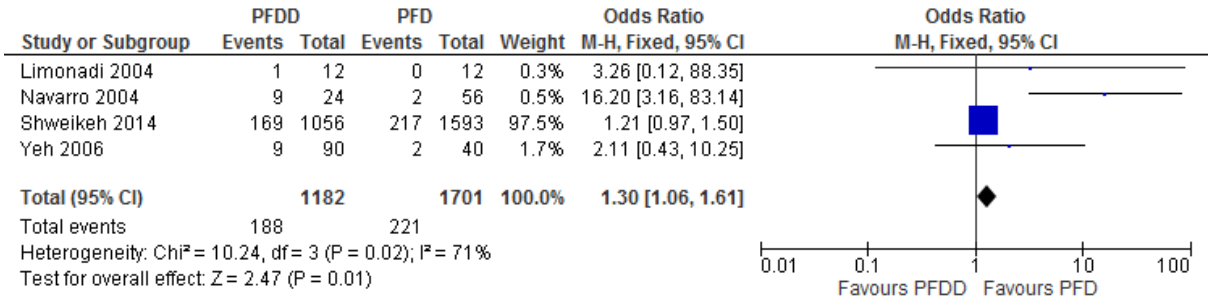

Figure 8: Overall complication

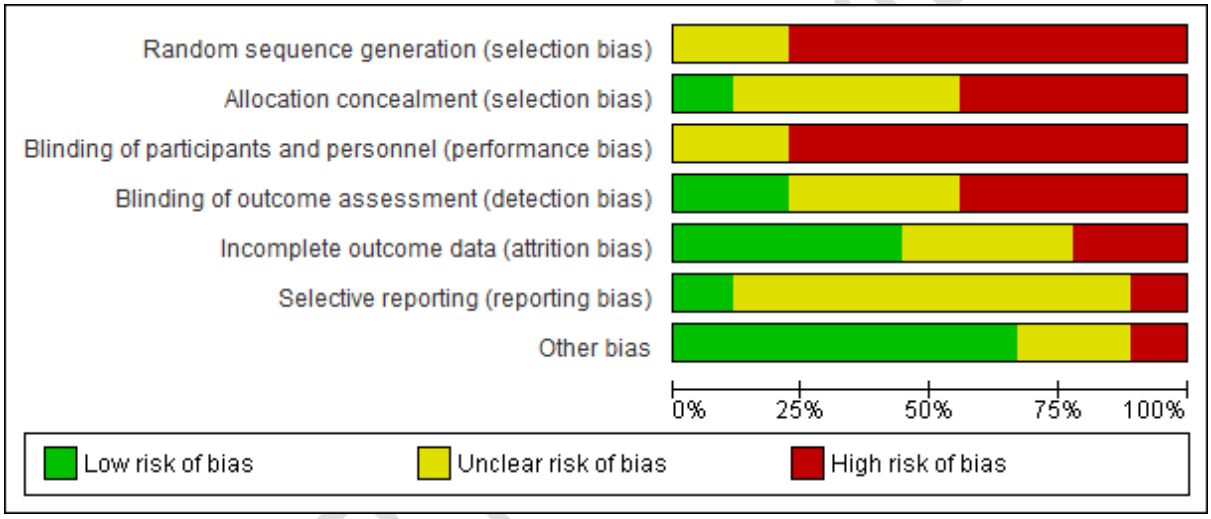

Figure 9: Risk of bias graph

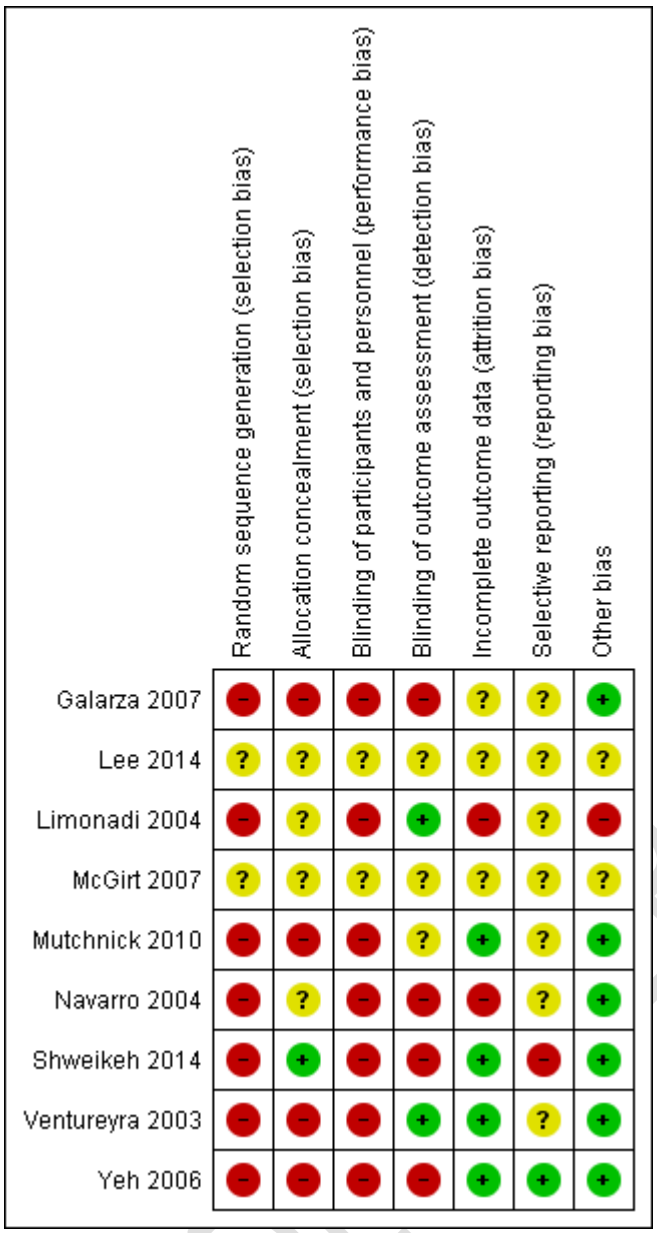

Figure 10: Risk of bias

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