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The Optimal Primary Treatment for Pediatric Perianal Abscess and Anal Fistula: A Systemic Review and Meta-Analysis☆

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ABSTRACT

Background: Perianal abscesses and anal fistulas are common. The principle of intention-to-treat has not been considered in previous systemic reviews. Thus, the comparison between primary and post-recurrence management was confused, and the recommendation of primary treatment is obscure. The current study aims to identify the optimal initial treatment for pediatric patients.

Methods: Using PRISMA guidelines, studies were identified from MEDLINE, EMBASE, PubMed, Cochrane Library, and Google Scholar without any language or study design restriction. The inclusion criteria include original articles or articles with original data, studies of management for a perianal abscess with or without anal fistula, and patient age of <18 years. Patients with local malignancy, Crohn's disease, or other underlying predisposing conditions were excluded. Studies without analyzing recurrence, case series of <5, and irrelevant articles were excluded in the screening stage. Of the 124 screened articles, 14 articles had no full texts or detailed information. Articles written in a language other than English or Mandarin were translated by Google Translation first and confirmed with native speakers. After the eligibility process, studies that compared identified primary managements were then included in the qualitative synthesis.

Results: Thirty-one studies involving 2507 pediatric patients met the inclusion criteria. The study design consisted of two prospective case series of 47 patients and retrospective cohort studies. No randomized control trials were identified. Meta-analyses for recurrence after initial management were performed with a random-effects model. Conservative treatment and drainage revealed no difference (Odds ratio [OR], 1.222; 95% Confidential interval [CI]: 0.615–2.427, $p = 0.567$). Conservative management had a higher risk of recurrence than surgery without statistical significance (OR 0.278, 95% CI: 0.109–0.707, $p = 0.007$). Compared with incision/drainage, surgery can prevent recurrence remarkably (OR 4.360, 95% CI: 1.761–10.792, $p = 0.001$). Subgroup analysis of different approaches within conservative treatment and operation was not performed for lacking information.

Conclusion: Strong recommendations cannot be made due to the lack of prospective or randomized controlled studies. However, the current study based on real primary management supports initial surgical intervention for pediatric patients with perianal abscesses and anal fistula to prevent recurrence.

Level of evidence: Type of study: Systemic review; Evidence level: Level II.

1. Introduction

Perianal abscess (PA) and anal fistula (Fistula in ano, FIA) are frequent issues in pediatric patients. Perianal fistula occurs in individuals aged below 2 years [1–5]. Several theories explain the difference between the etiologies of adult and pediatric patients. In 1976, Takatsuki proposed that excessive or abnormal androgen level induces the oversecretion of the anal gland and abnormal hyperplasia, leading to the formation of an anal fistula [4]. Patients

Abbreviations: (PA), Perianal abscess; (FIA), Fistula-in-ano; (ROBINS-I), Risk of Bias in Non-randomised Studies of Interventions; (ORs), Odds ratios; (PRISMA), Preferred reporting items for systematic reviews and meta-analyses.

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may have deeper, shallower, or thicker anal crypts than normal individuals and thus stools block anal crypts and anal glands. The infection of the anal crypt further causes perianal abscess [1,6]. Moreover, young children and infants tend to have loose or watery stools, which easily accumulate in anal crypts. The management of PA and FIA in pediatric patients varies. Conservative treatments include sitz bath, hygiene education, antibiotic treatment, and local incision drainage. These approaches are cost effective, but recurrence rates still range from 24.6% to 52% [2,7]. Surgical management involves fistulectomy, fistulotomy, and wound debridement, which require anesthesia administration for pediatric patients. The post-operative recurrence rate, ranging from 0% to 15%, is lower than that in conservative treatment [3,8,9].

Two systemic reviews have discussed the treatments of PA and FIA in pediatric patients. Emile et al. included studies from 1990 to December 2015 enrolling patients under 2 years with PA and FIA [10]; conservative treatments were applied to 20% of the populations, showing a 70% treatment success rate. Approximately 86% of the patients who received surgical treatments had an average recurrence rate of 4.9%. Another systemic review by Stokes et al., includes nine studies enrolling 1049 patients; the study analyzed the outcomes of patients under 2 years old with FIA patients instead of similarly aged patients with PA treated with conservative treatment, reporting 23% recurrence rate after conservative treatment [11]. Both systemic reviews only discussed patients younger than 2 years. In addition, the definitions of primary treatments are controversial, and both articles did not include patients with simple PA or first-time PA. Some included articles specifically examined recurrent PA or FIA treatment. Hence, the true effects of primary management were not demonstrated well. In the present study, pediatric patients under 18 years old with PA or FIA were examined, but only the identifiable data of true primary management for simple FIA and/or PA patients were included. By comparing primary treatment protocols, differences in outcomes after different primary treatments were determined and presented by meta-analysis.

2. Materials and methods

2.1. Identification of studies

A systematic review of the literature for articles evaluating the management of FIA and PA in pediatrics was conducted according to the screening guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and plotted as Fig. 1. MEDLINE/PubMed, EMBASE, Cochrane Library, and Google Scholar databases were comprehensively searched (each from database inception to May 1, 2021), and the following search terms were used (fistula OR abscess OR anal OR anal fistula OR anus disease) AND (newborn OR neonate OR infant OR child OR adolescent OR pediatric OR premature OR prepuberal OR puberty OR pre-school OR school OR teenager) AND (surgery OR operation OR fistulectomy OR fistulotomy OR resection OR seton OR ligation OR glue OR plug OR antibiotics OR conservative OR observation OR incision OR drainage OR endoscope OR laser OR management OR treatment OR procedure OR sphincter preserving OR therapy). The inclusion criteria were as follows: (1) original articles or other article types with original study data; (2) comparative studies of management for anal fistula, perianal abscess, or both; (3) age <18 years (all or subgroup). No language limitation was applied. The exclusion criteria were as follows: (1) patients with local malignancy, Crohn's disease, or other underlying predisposing conditions; (2) studies without analyzing post-treatment recurrence; (3)

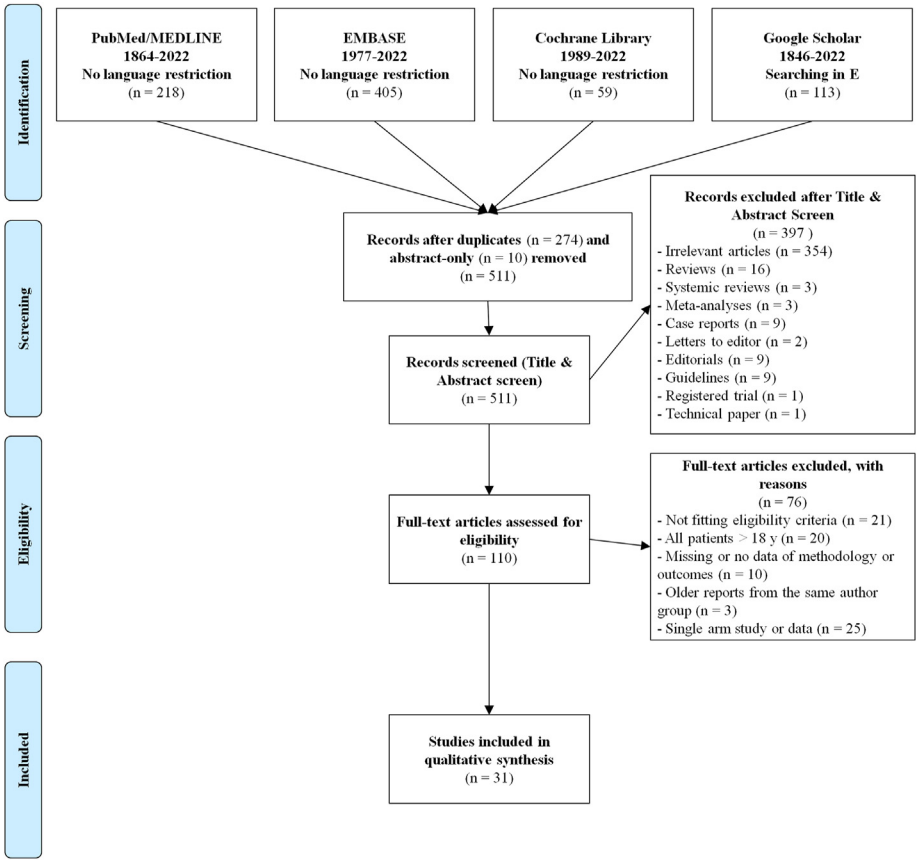

Fig. 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram illustrating the search process in this study.

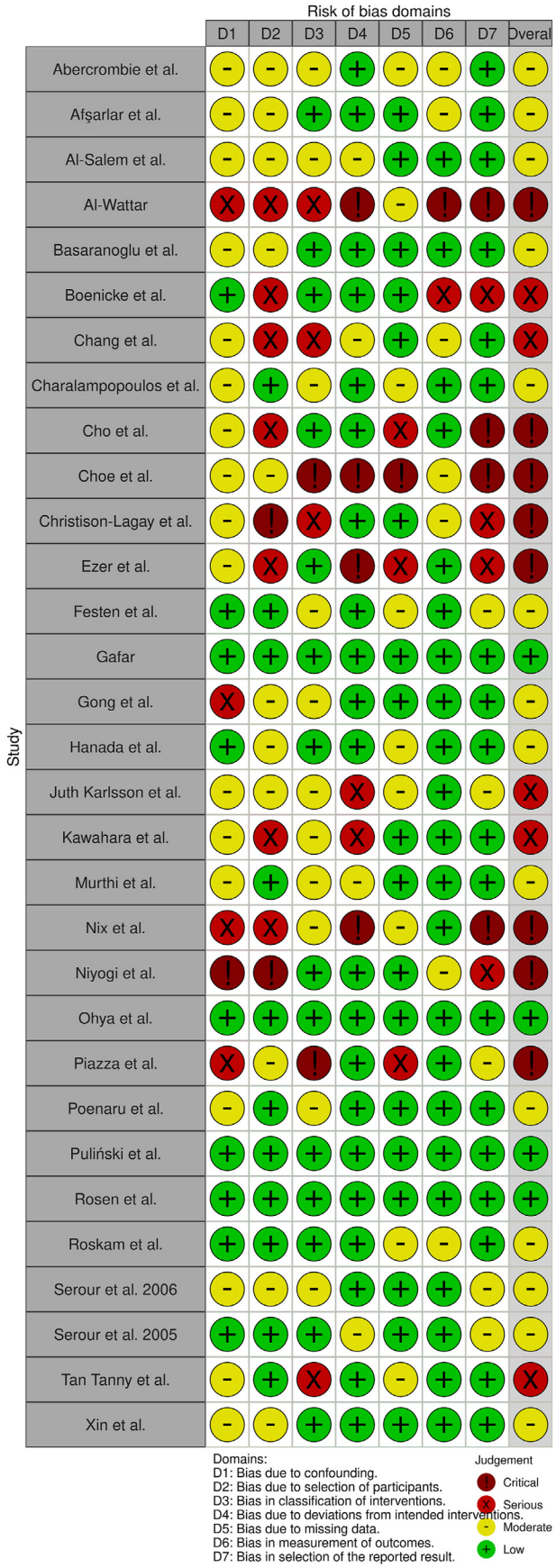

Fig. 2. Evaluation of included studies using ROBINS-I. The figure was generated by Risk-of-bias VISualization (+) [38].

case series with a patient number less than five; (4) irrelevant articles, editorials, systematic reviews, and meta-analyses. Two reviewers independently reviewed the article titles and abstracts using the inclusion and exclusion criteria (C.A.L. and S.Y.H.). Full papers were further investigated when disagreements existed, and agreement was achieved by consensus with the senior author (C.M.C.). For different reports involving the same patient group, the latest studies were included. The included papers must provide a clear definition of true primary treatment when the doctor initially contacted patients; otherwise, they would be classified as irrelevant articles. For single-arm studies, the authors believed that lacking comparative data of different approaches from a single group would increase the bias of meta-analyses. Thus, some fine articles failed to provide definite initial approaches along with true recurrence rates, were not included in the quantitative survey.

2.2. Data extraction

Data extraction was performed separately by two investigators (C.A.L. and S.Y.H.) by using a standardized data extraction form. The following data were extracted from each study: (1) first author, year of publication, location of study, and language; (2) study design; (3) sample size, mean age, and gender follow-up duration; (4) true primary treatment and recurrence. Full papers were reviewed again when disagreements occurred, and agreement was achieved by consensus with the senior author (C.M.C.). Recurrence was defined as recurrent abscess or anal fistula presentation with or without symptoms mentioned in the studies.

2.3. Quality assessment

Study quality was assessed using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) for cohort, case–control, and cross-sectional studies. The ROBINS-I tool consists of seven domains and one overall evaluation. The results of bias revaluation for the included studies are illustrated in Fig. 2. The low risk assessed by authors of a domain was scored as 1. The final score ranged from 0 to 8 for the quality of study: 7 to 8 was considered “good,” 4 to 6 as “fair” and 0 to 3 as “poor.”

2.4. Statistical analysis

The raw numerical data were extracted, and the odds ratios (OR) were calculated instead of direct quotation. Studies for recurrence after primary treatment were compared using forest plots. The random-effects model was used in calculating pooled OR. The I^2 statistic was used in testing heterogeneity among studies. Values less than 25% indicated low heterogeneity, whereas values greater than 50% indicated notable (moderate to severe) heterogeneity. Statistical analyses were performed using MedCalc version 20.110 (Medcalc software, Mariakerke, Belgium).

3. Results

3.1. Included studies and patient characteristics

Thirty-one studies satisfied the eligibility criteria and were published from 1992 to 2020, and 2507 patients were involved [1,3,7–9,12–37]. The median age of the patients ranged from 3.8 months to 7.2 years. The proportions of males ranged from 80% to 100%. Two studies were prospective (Gafar 2013 and Rosen et al. 2000) [23,32], and twenty-nine were retrospective. The summaries of the included studies are provided in Table 1. For articles not written in English or Mandarin, a native speaker was consulted for reading. According to the treatments mentioned in the articles, the

primary treatments were divided as follows: (1) conservative treatments, including hygiene education, sitz bath, antibiotics treatments, and observation; (2) operation, including fistulectomy, fistulotomy, debridement, and seton tie; (3) drainage, including incision and drainage with or without general anesthesia, and needle aspiration; (4) Other treatments, such as traditional medicine (i.e., Hainosankyuto, Juzentaihoto, Ginseng, and Tang-kuei Ten Combination, were described separately and regarded as conservative treatments.

3.2. Conservative treatment versus drainage

In the twenty studies comparing primary conservative treatment and primary drainage, 712 patients received conservative treatments, and 1077 patients received drainage [7,12–17,21–26,28,29,31–35]. The recurrence rates were 28.2% (201/712) and 34.2% (369/1077), respectively. The OR was 1.222 (95% CI: 0.615–2.427, $p = 0.567$), which was not significantly different between two primary treatments. The heterogeneity of the tests was high (I^2: 77.84%, $p < 0.0001$). The forest plot is shown in Fig. 3.

3.3. Operation versus conservative treatment

The meta-analysis comparing primary operation and primary conservative treatment using the random-effects model is illustrated in Fig. 4. Ten studies and 326 patients were included [8,12,14,17,22,23,25,28,30,31,35]. The recurrence rates for primary operation and primary conservative were 10.6% (22/208) and 28.0% (33/118), respectively. The OR was 0.278 (95% CI: 0.109 to 0.707, $p = 0.007$), indicating significant difference. Across the studies, the primary operation was either fistulectomy (n = 61, 29.3%) or fistulotomy (n = 147, 70.7%). The heterogeneity of the included articles was low (I^2: 8.19%, $p = 0.366$). Meta-analysis was performed again using the fixed-effect model, and the tendency was the same (OR 0.251, 95% CI: 0.114–0.551, $p = 0.001$).

3.4. Drainage versus operation

In eighteen studies comparing primary drainage and primary operation, 508 patients received drainage, and 437 patients received operation initially [1,3,9,12,14,17–20,22,23,25,27,28,31,35–37]. The recurrence rates were 30.7% (156/508) and 12.1% (53/437), respectively. The OR was 4.360 (95% CI: 1.761–10.792, $p = 0.001$), indicating significant difference. However, the heterogeneity of the studies was high (I^2: 71.11%, $p < 0.0001$). The forest plot is plotted in Fig. 5.

4. Discussion

The current concept of FIA/PA is the cryptoglandular theory, which was first described by Park et al. according to the histopathology of the anal fistula specimen; they found cystic dilation at the end of the anal gland and the anal–gland epithelium lining of the fistula tract; the infected anal gland contributing to the anal fistula was suggested [39]. Thus, FIA commonly coexists with PA in the fistula cavity. In this study, the two diseases were not discussed separately for the etiology and clinical practice. In the included patient group, males outweighed females in terms of number. This result may be concordant to congenital or hormone theory of the infant anal fistula. Two systemic reviews were found in the literature. The review of Emile et al. involved 490 infants, and surgery was the most used management strategy (86.3%); the post-

Table 1
Summary of the included studies.

Study	Year of publishing	Country	Language	Study duration	Patient number	Age (month)	Male	Quality of the study
Abercrombie et al. [12]	1992	England	English	4 years	16	60	14	2 (poor)
Afşarlar et al. [13]	2011	Turkey	English	Jan. 2005–Dec. 2010	136	7.2		4 (fair)
Al–Salem et al. [1]	1994	Saudi Arabia	English	1988–1991	36	17	29	3 (poor)
Al-Wattar [14]	2002	Iraq	English	Jan. 1988–Dec. 2001	81	2 weeks-2 years	80	0 (poor)
Basaranoglu et al. [15]	2019	Turkey	English	Jan. 2005–Jul. 2015	47	7.7	44	5 (fair)
Boenicke et al. [16]	2020	Germany	English	Jan. 2001–Dec. 2016	113	55.7	99	4 (fair)
Chang et al. [17]	2010	South Korea	English	Jan. 2006–Dec. 2008	112	6	112	2 (poor)
Charalampopoulos et al. [18]	2012	Greece	English	Jan. 2001–Dec. 2011	98	84	80	4 (fair)
Cho et al. [19]	1997	South Korea	Korean	Jan. 1993–Dec. 1994	50		50	3 (poor)
Choe et al. [20]	2004	South Korea	Korean	Mar. 1997–Jan. 2004	15			0 (poor)
Christison-Lagay et al. [21]	2007	US[a]/Canada	English	1995–2005	140	3	131	2 (poor)
Ezer et al. [22]	2010	Australia	English	Jan. 2000–Dec. 2005	39	29	36	2 (poor)
Festen et al. [3]	1998	Netherlands	English	Jan. 1974–Dec. 1994	73	4.7		4 (fair)
Gafar [23]	2013	Egypt	English	Jan. 2010–Dec. 2011	36	9.7	34	8 (good)
Gong et al. [7]	2018	China	English	Jun. 2014–May 2016	697	4.3	697	4 (fair)
Hanada et al. [24]	2015	Japan	English	Apr. 2011–Mar. 2014	48	4.2	48	5 (fair)
Juth Karlsson et al. [25]	2016	Sweden	English	Jan. 2008–Apr. 2014	112	5	106	1 (poor)
Kawahara et al. [26]	2011	Japan	English	Feb. 2007–Jun. 2009	15	33 days	15	3 (poor)
Murthi et al. [9]	2002	UK[b]	English	Jan. 1992–Jan. 1997	33	Boy: 10.5 Girl: 7.5	29	4 (fair)
Nix et al. [27]	1997	UK	English	Jan. 1992–Apr. 1996	20		20	1 (poor)
Niyogi et al. [28]	2010	UK	English	Jan. 2002–Apr. 2006	78		63	3 (poor)
Ohya et al. [29]	2004	Japan	English		22	3.8	22	8 (good)
Piazza et al. [8]	1990	Canada	English	Jul. 1978–May 1989	40		33	2 (poor)
Poenaru et al. [30]	1993	Canada	English	1980–1991	36	9.5	36	5 (fair)
Puliński et al. [31]	2020	Poland	English	2014–2019	44	3.58		8 (good)
Rosen et al. [32]	2000	US	English	1990–1999	18	4.2		8 (good)
Roskam et al. [33]	2020	Netherlands	English	Jan. 2000–Dec. 2014	62	5	60	5 (fair)
Serour et al. [34]	2006	Israel	English	Jan. 1990–Dec. 2003	40	86.4	37	3 (poor)
Serour et al. [35]	2005	Israel	English	Jan. 1990–Jun. 2002	77	7.9	75	5 (fair)
Tan Tanny et al. [36]	2020	Australia	English	2007–2017	108		107	4 (fair)
Xin et al. [37]	2017	China	Mandarin	Jul. 2010–Dec. 2016	17		17	5 (fair)

[a] US: United States.
[b] UK: United Kingdom.

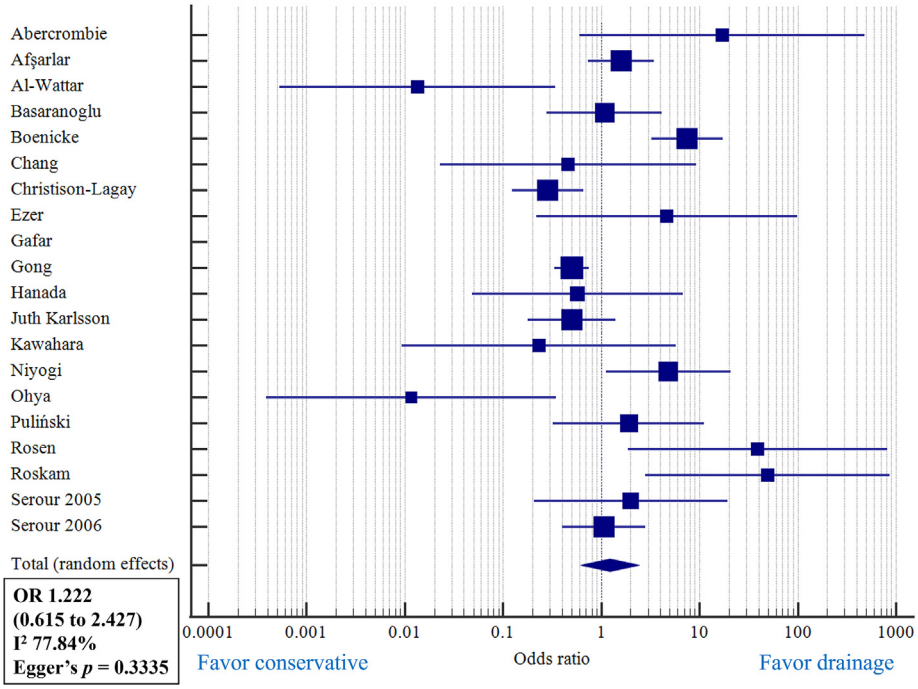

Fig. 3. Primary conservative versus primary drainage for recurrence.

operative recurrence rates ranged from 2.7% to 13% and were higher in fistulotomy groups than in fistulectomy groups, and conservative treatment was initially applied only to 91 patients, and 73.6% were resolved spontaneously; however, the study involved patients with recurrent PA or FIA, which prevented the clear definition of primary treatment; moreover, few patients had high trans-sphincteric and complex fistulas [10]. In Stokes et al., the main purpose was to compare the outcome of PA patients treated with or without general anesthesia; they concluded that for patients receiving treatment without general anesthesia, only 5.6% required further treatment under general anesthesia [11]. However, these two systemic reviews included patient with primary and recurrent PA or FIA. The pooled results showed that 73.6% of patient with FIA/PA may be cured by conservative treatment. The average recurrence rate was 4.9% for patients receiving surgical treatment [10,11]. The recurrent rate of surgical treatment of the current review was 10.8% (55/505), 27.9% (201/720) for conservative, and 32.3% (414/1282) for drainage. The recurrence rates of all approaches were higher than those in the literature. Two reasons might explain the results. First, the existing systemic reviews did not reveal the recurrence

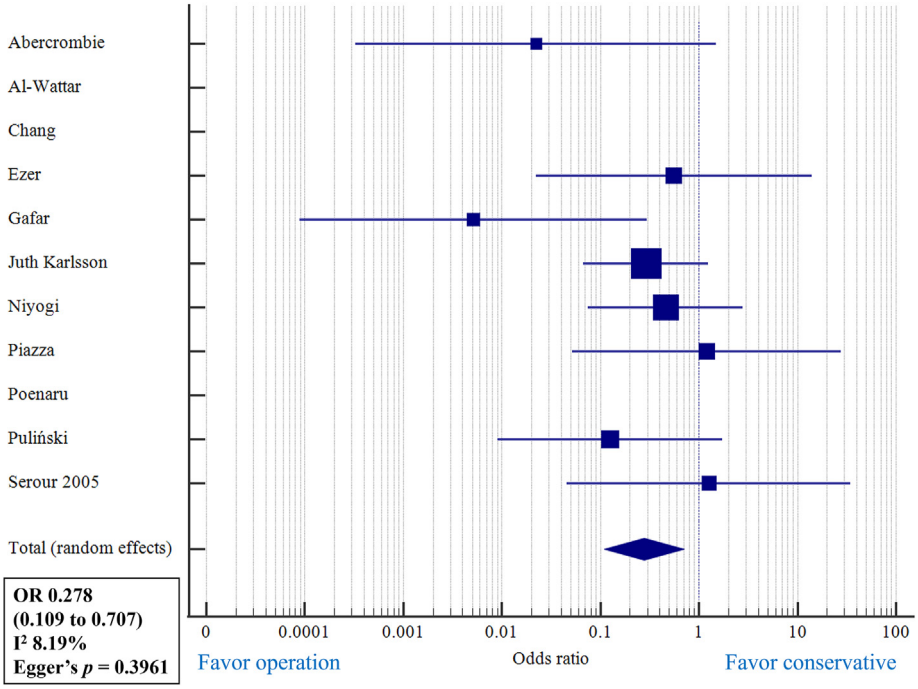

Fig. 4. Primary operation versus primary conservative treatment for recurrence.

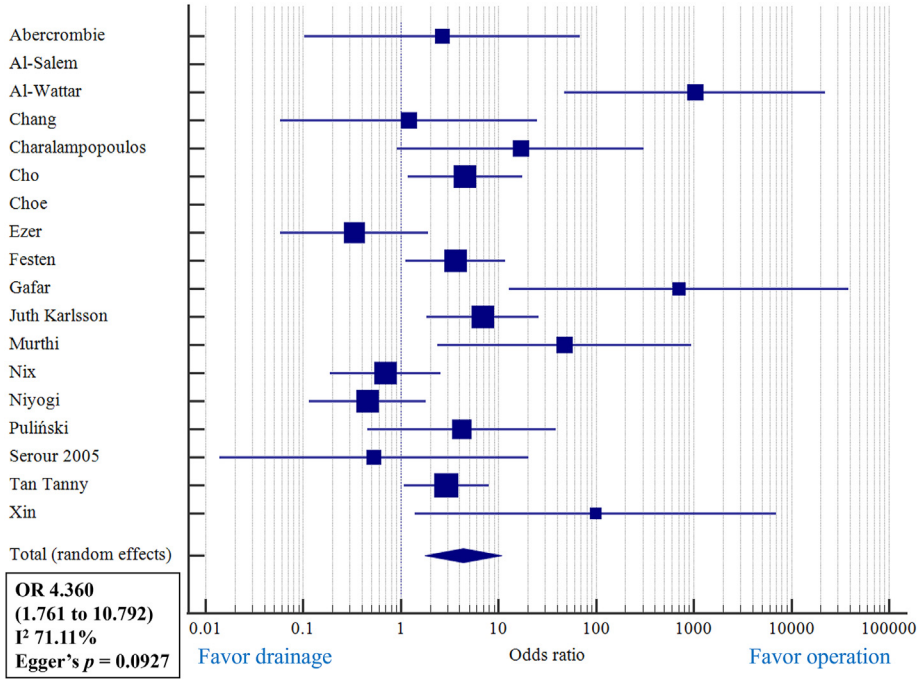

Fig. 5. Primary drainage versus primary operation for recurrence.

rate after true primary treatment, which should be defined as the first approach physicians take after initial contact with patients without previous recurrence. The multi-modality of treatment may have further decreased the recurrence rates in the literature. Second, the current review included patients older than 2 years, who were at higher risk of suffering from occult underlying diseases, such as Crohn's disease.

In the real world, when treating patients with FIA or PA, conservative treatment or simple drainage is considered more suitable than immediate surgery by surgeons and parents in most cases. In the current systemic review, more than half of the patients (51.1%, 1282/2507) received primary drainage procedures. The result was compatible with the results obtained in clinical practice. For a patient with obvious pus accumulation, drainage is often the first management performed without systemic anesthesia. However, the meta-analysis results clearly revealed that primary operation provides better outcomes than primary conservative or drainage with regard to recurrence. The low heterogeneity among articles comparing conservative and operation further strengthened this finding. As for primary conservative or drainage, no difference could be identified for recurrence. Thus, the clinical suggestion of primary operation for pediatric patients with FIA or PA can be made. The main limitation of the current review is the lack of prospective or randomized controlled studies and the poor quality of the included studies (14/31). Evidence of a high level is required in the future to provide strong suggestions.

Conflicts of interest

None.

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