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META-ANALYSIS OF OBSERV STUDIES IN EPIDEMIOLOGY

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Comparison of Laparoscopic-Assisted Operations and Laparotomy Operations for the Treatment of Hirschsprung Disease

Evidence From a Meta-Analysis

Shisong Zhang, MD, Juan Li, MD, Yurui Wu, MD, Yuanjun Hu, MD, Chunhong Duan, MD, Meiyun Wang, MD, and Zhongtao Gai, PhD

Abstract: The purpose of this meta-analysis is to compare the relative merits among laparoscopic-assisted operations and laparotomy operations for patients with Hirschsprung disease.

PubMed, Web of Science, and Wanfang databases were searched for the related articles. We analyzed dichotomous variables by estimating odds ratios (ORs) with their 95% confidence intervals (CIs) and continuous variables using the weighted mean difference (WMD) with the 95% CI. The random-effects model (REM) was used to combine the results. The outcome measures included operating time (OT), estimated blood loss (EBL), length of hospital stay (LOHS), mean first bowel movement (MFBM), and number of complications.

Sixteen articles were included in the meta-analysis. These studies involved a total of 774 patients, 396 of whom underwent laparoscopic-assisted operations and 378 of whom underwent laparotomy operations. The EBL (WMD = −1.48, 95% CI = −1.82, −1.13), LOHS (WMD = −0.67, 95% CI = −0.86, −0.49), MFBM (WMD = −0.83, 95% CI = −1.05, −0.61), and number of complications (OR = 0.60, 95% CI = 0.40, 0.89) were significantly lower in laparoscopic-assisted operations than in laparotomy operations. The OT (WMD = 0.12, 95% CI = −0.05, 0.28) showed no significant differences between laparoscopic-assisted operations and laparotomy operations.

Compared with laparotomy operations, laparoscopic-assisted operations are generally safer and more reliable for patients with Hirschsprung disease.

(*Medicine* 94(39):e1632)

Abbreviations: 95% CI = 95% confidence interval, EBL = estimated blood loss, LOHS = length of hospital stay, MFBM = mean first bowel movement, OR = odds ratios, OT = operating time, REM = random-effects model, SD = standard deviation, WMD = weighted mean difference.

Editor: Perbinder Grewal.
Received: June 21, 2015; revised: August 20, 2015; accepted: August 26, 2015.
From the Department of Pediatric Surgery, Ji'nan Children's Hospital (SZ, JL, YW,YH); and Ji'nan Children's Hospital, Ji'nan, Shandong Province, China (CD, MW, ZG).
Correspondence: Meiyun Wang, MD, Ji'nan Children's Hospital, No. 23976 Jingshi Road, Ji'nan, Shandong Province 250021, China. (e-mail: wangmeiyunjn@163.com).
The authors declare that they have no competing interest.

ISSN: 0025-7974
DOI: 10.1097/MD.0000000000001632

INTRODUCTION

Hirschsprung disease, also known as intestinal aganglionosis, is a kind of birth defects, which is mainly expressed as partial or complete intestinal ganglion cells of the intestinal tract.[1] The incidence of the disease occurs about 1 patient per 5000 live births. Furthermore, men are more likely to be affected by about 3.5 to 7.8 times than women.[2] Hirschsprung disease usually occurs in infancy, although some people will present with persistent, severe constipation in the later life.[2]

Laparotomy operations have some characteristics, such as a long operating time (OT), more blood loss, more serious trauma, and high mortality, and so on.[3] Laparoscopic-assisted operations have become the main surgical method for Hirschsprung disease and have been recognized gradually, with its advantages: small trauma, less bleeding, light intraperitoneal pollution, and less intestine adhesion.[4] The safety and efficacy of laparoscopic-assisted surgery for Hirschsprung has been the focus of attention. However, whether laparoscopic-assisted operations are superior to laparotomy operations remains lacking a synthesized and systematic analysis. Therefore, the present meta-analysis compared the relative merits among laparoscopic-assisted operations and laparotomy operations for patients with Hirschsprung disease.

METHODS

Literature Search

Two authors independently searched the databases of PubMed, Web of Science, and Wanfang databases for relevant articles published before May 2015 using the following search terms: "surgery" OR "laparoscopy" OR "laparotomy" OR "laparoscopic-assisted" AND "Hirschsprung disease" with written in English or Chinese. In addition, we reviewed references of obtained articles. The ethical approval was not necessary in our study because we did not include any patients. We only used the data from each individual study.

Inclusion Criteria

The inclusion criteria for this meta-analysis were as follows: analysis of either a retrospective or prospective study; comparison of laparoscopic-assisted operations with laparotomy operations for treatment of Hirschsprung disease; available mean and standard deviation (SD) were provided for operation time, evaluation of the following outcomes, estimated blood loss, length of hospital stay (LOHS), mean first bowel movement (MFBM), and number of complications (or data available to calculate them); written in English or Chinese.

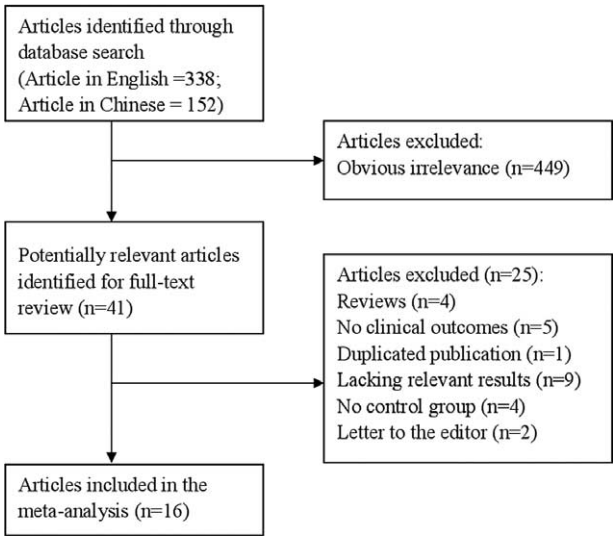

FIGURE 1. The flow diagram for exclusion/inclusion process.

Exclusion Criteria

The exclusion criteria for this meta-analysis were as follows: reviews; the above-mentioned outcomes of interest were not reported; it was impossible to extract the appropriate data from the published results.

When the same institution reported more than once, the most recent publication was included. Two investigators carefully reviewed all identified studies independently to determine whether an individual study was eligible for inclusion criteria in this meta-analysis. Any disagreements were resolved by discussion between the reviewers.

Data Extraction

The following data were collected from all studies independently by 2 investigators: name of the first author, publication year, study type, country where the study was performed, the number of cases, mean age, the mean and SD for continuous variables, the number of patients from each individual study, and the outcome of interest for dichotomous variables. We will estimate the mean and SD if the individual study only reported the median and range or interquartile range.[5]

Statistical Analysis

Pooled measure was performed on the standardized mean difference (SMD) with 95% confidence interval (95% CI) for continuous variables and odds ratios (ORs) with their 95% CIs for dichotomous variables. Random-effects model (REM) was used to combine the pooled effect. I^2 of Higgins and Thompson was used to assess heterogeneity among studies, and I^2 values of 0%, 25%, 50%, and 75% represent no, low, moderate, and high heterogeneity.[6] Sensitivity analyses were performed by sequential removal of each study to assess the stability of the results.[7] Meta-regression with restricted maximum likelihood estimation was performed to assess the potentially important covariates that might exert substantial impact on between-study heterogeneity.[8] Possible publication bias was assessed by Begg test.[9] Subgroup analyses by different surgery technique used in each article were conducted among laparoscopic-assisted operations and laparotomy operations for patients with Hirschsprung disease. STATA version 10.0 (Stata Corporation, College Station, TX) was used to perform statistical analyses. All reported probabilities (P) were 2-sided, with P value <0.05 considered representative of statistically significant.

RESULTS

Search Results and Study Characteristics

In total, the electronic database searches identified 338 articles from PubMed and Web of Knowledge, 152 articles from Wanfang databases. After screening the title or abstract, 449 studies were excluded and 41 were retrieved and evaluated in detail. Finally, 16 articles[10–25] involving a total of 774 patients were included in this meta-analysis. Figure 1 presented the flow chart for exclusion/inclusion process. Seven studies come from China, 3 from Italy, 2 from British, and there was 1 study each from America, Japan, Netherlands, and New Zealand. All included studies were retrospective or prospective studies. Among included articles, 4 articles used Duhamed, 9 used Soave, and 3 used other surgery technique. The study characteristics and participant features are given in Table 1.[10–25]

Operative Outcomes of Laparoscopic-Assisted Operations and Laparotomy Operations

OT

Fourteen studies[10–22,25] reported operation time, and pooled results suggested that no statistically significant differences in OT for laparoscopic-assisted operations compared with laparotomy (WMD = 0.12, 95% CI = −0.05, 0.28) (Fig. 2). Laparoscopic-assisted operations had lower OT compared with laparotomy (WMD = −0.49, 95% CI = −0.80, −0.18) in Duhamed surgery technique. However, the OT was longer in laparoscopic-assisted operations than in laparotomy (WMD = 0.58, 95% CI = 0.33, 0.84) for soave surgery technique. No statistically significant differences found in other technique (WMD = 0.04, 95% CI = −0.29, 0.36). The detailed results are shown in Table 2.[10–25]

Estimated Blood Loss (EBL)

Six studies[12,13,17,20,22,25] showed significantly lower EBL in laparoscopic-assisted operations than in laparotomy (WMD = −1.48, 95% CI = −1.82,−1.13) (Fig. 3). When conducted subgroup analysis by different surgery techniques, significantly lower EBL in laparoscopic-assisted operations than in laparotomy were found both in Soave (WMD = −1.65, 95% CI = −2.09, −1.21) and other surgery technique (WMD = −1.19, 95% CI = −1.75, −0.62) (Table 2).

LOHS

Eleven studies[10–12,14–18,21,22,25] reported the LOHS, and pooled data demonstrated a significantly reduction in the laparoscopic-assisted operations group compared with laparotomy operations group (WMD = −0.67, 95% CI = −0.86, −0.49) (Fig. 4). About different surgery techniques, significantly lower LOHS in laparoscopic-assisted operations than in laparotomy were found in Duhamed (WMD = −0.44, 95% CI = −0.75, −0.13), Soave (WMD = −0.73, 95% CI = −0.99, 0.99, −0.48), and other surgery techniques (WMD = −1.18, 95% CI = −1.76, −0.59) (Table 2).

MFBM

Seven studies[10,11,14,17–20] were conducted to assess the MFBM, and the association was significant between

TABLE 1. Characteristics and Methodological Quality of Included Studies

First Author, (Year)	Study Type	Country	Number of Patients		Surgery Technique	Outcome Measures	Ref.
			laparoscopic-assisted	Laparotomy			
Langer et al[12] (2000)	Retrospective	America	15	13	Soave	OT, EBL, LOHS, EBL, Complication	12
Shi et al[22] (2002)	Prospective	China	6	16	Soave	OT, EBL, LOHS,	22
Kubota et al[13]. (2004)	Retrospective	Japan	21	20	Soave	OT, EBL,EBL, Complication	13
Tang et al[19] (2005)	Retrospective	China	54	48	Other (LHSC)	OT, MFBM, Complication	19
Ghirardo et al[15] (2007)	Retrospective cohort	Italy	21	21	Duhamel	OT, LOHS, Complication	15
Craigie et al[16] (2007)	Prospective	British	20	22	Soave	OT, LOHS, Complication	16
Travassos et al[23] (2007)	Retrospective	Netherlands	30	25	Duhamel	Complication	23
Fujiwara et al[24] (2007)	Retrospective	New Zealand	22	13	Soave	Complication	24
Huang et al[21] (2007)	Prospective	China	29	35	Soave	OT, LOHS, Complication	21
Mattioli et al[11] (2008)	Prospective	Italy	25	21	Soave	OT, LOHS, MFBM, Complication	11
Hao et al[17] (2009)	Retrospective	China	15	8	Other (Soave Ikeda)	OT, EBL, LOHS, MFBM,	17
Liu et al[20] (2009)	Retrospective	China	23	23	Soave	OT, EBL, MFBM, Complication	20
Lin[25] (2009)	Retrospective	China	18	18	Other (not reported)	OT, EBL, LOHS,	25
Giuliani et al[14] (2011)	Retrospective	Italy	32	24	Duhamel	OT, LOHS, MFBM, Complication	14
Nah et al[10] (2012)	Prospective	British	35	41	Duhamel	OT, LOHS, MFBM, Complication	10
Li et al[18] (2012)	Retrospective	China	30	30	Soave	OT, LOHS, MFBM, Complication	18

EBL = estimated blood loss, LOHS = length of hospital stay, MFBM = mean first bowel movement, OT = operating time.

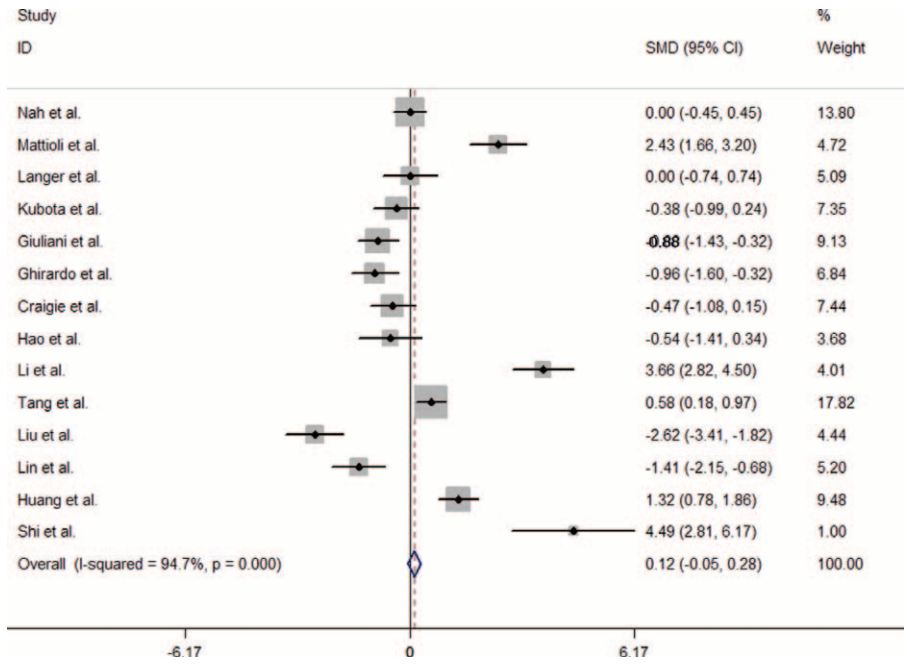

FIGURE 2. Comparison of laparoscopic-assisted operations and laparotomy operations with respect to operating time.

laparoscopic-assisted operations and laparotomy operations (WMD = −0.83, 95% CI = −1.05, −0.61) (Fig. 5). Statistically significant differences were found in Soave (WMD = −1.44, 95% CI = −1.84, −1.03) and other (WMD = −1.21, 95% CI = −1.59, −0.82) surgery techniques when comparing laparoscopic-assisted operations and laparotomy. No statistically significant differences were found in Duhamed technique (WMD = −0.03, 95% CI = −0.39, 0.32) (Table 2).

Number of Complications

Thirteen studies[1,10–16,18–21,24] reported the number of complications. Analysis of the pooled results also showed that the number of complications was significantly lower in

TABLE 2. Pooled ORs With Their 95% CIs or Pooled WMD with the 95% CI of Hirschsprung Disease for the Comparison of 2 Different Treatments (Laparoscopic-Assisted Operations and Laparotomy Operations). The subgroup analyses by surgery technique were also conducted

Data		N*	Pooled OR (WMD) (95% CI)	I^2 (%)	Articles Included (Refs.)
Operating time	Overall	14	0.12 (−0.05, 0.28)	94.7	10–22,25
	Duhamed	3	−0.49((−0.80,-0.18)	76.4	10,14,15
	Soave	8	0.58 (0.33,0.84)	96.3	11–13,16.18,20-22
	Other	3	0.04 (−0.29,0.36)	91.6	17,19,25
Estimated blood loss	Overall	6	−1.48 ((−1.82,−1.13)	90.5	12,13,17,20,22,25
	Soave	4	−1.65 ((−2.09,−1.21)	94.0	12,13,20,22
	Other	2	−1.19 ((−1.75,−0.62)	0	17,25
Length of hospital stay	Overall	11	−0.67 ((−0.86,−0.49)	78.4	10–12,14–18,21,22,25
	Duhamed	3	−0.44 ((−0.75, −0.13)	90.2	10,14,15
	Soave	6	−0.73 ((−0.99,−0.48)	63.0	11,12,16,18,21,22
	Other	2	−1.18 ((−1.76,−0.59)	86.0	17,25
Mean first bowel movement	Overall	7	−0.83 (−1.05,−0.61)	94.7	10,11,14,17-20
	Duhamed	2	−0.03 ((−0.39,0.32)	94.6	10,14
	Soave	3	−1.44 ((−1.84,−1.03)	96.7	11,18,20
	Other	2	−1.21 ((−1.59,−0.82)	60.2	17,19
Number of complications†	Overall	13	0.60 (0.40, 0.89)	0	1,10–16,18–21,24
	Duhamed	4	0.89 (0.44,1.80)	0	10,14,15,23
	Soave	8	0.44 (0.23,0.83)	10.1	11–13,16,18,20,21,24

CI = confidence interval, OR = odds ratio, WMD = weighted mean difference.
* The number of studies included.
† There is only study conducted by other surgery technique, so we do not list it separately.

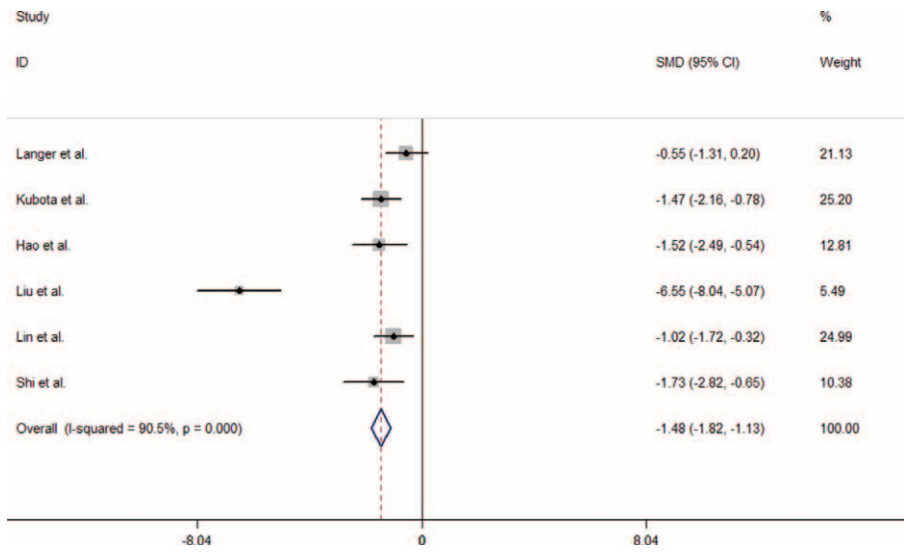

FIGURE 3. Comparison of laparoscopic-assisted operations and laparotomy operations with respect to estimated blood loss.

laparoscopic-assisted operations group than in laparotomy operations group (OR = 0.60, 95% CI = 0.40, 0.89) (Fig. 6). There is only study conducted in other surgery technique, so the analysis was separated into Soave and Duhamed subgroup. Soave surgery technique showed significantly smaller complications in laparoscopic-assisted operations than in laparotomy (OR = 0.44, 95% CI = 0.23, 0.83). However, no statistically significant difference was found in Duhamed technique (OR = 0.89, 95% CI = 0.44, 1.80) (Table 2).

Meta-Regression and Sensitivity Analyses

Significant heterogeneity existed, mainly in OT, estimated blood loss, LOHS, and MFBM. Univariate meta-regression with the covariates of publication year, location where the study conducted, and number of participants was performed. However, no significant findings were found in the above-mentioned analysis. A sensitivity analysis was conducted to assess the influence of each study, by sequential omission of each eligible study. The results showed that the results were not affected by any single study.

Publication Bias

Begg test showed no evidence of significant publication bias between laparoscopic-assisted operations group and open operations group for the treatment of Hirschsprung disease, when compared with the OT, estimated blood loss, LOHS, MFBM, and number of complications.

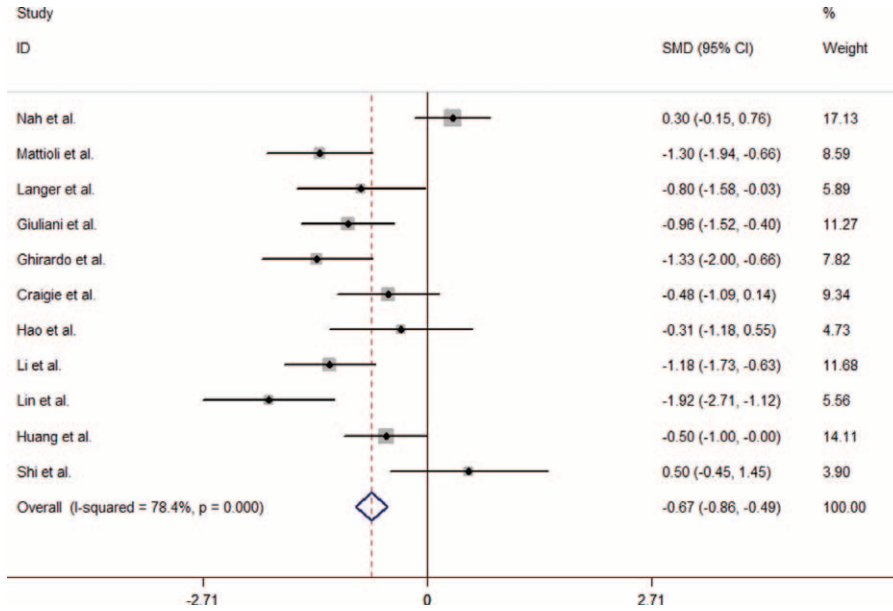

FIGURE 4. Comparison of laparoscopic laparoscopic-assisted operations and laparotomy operations with respect to length of hospital stay.

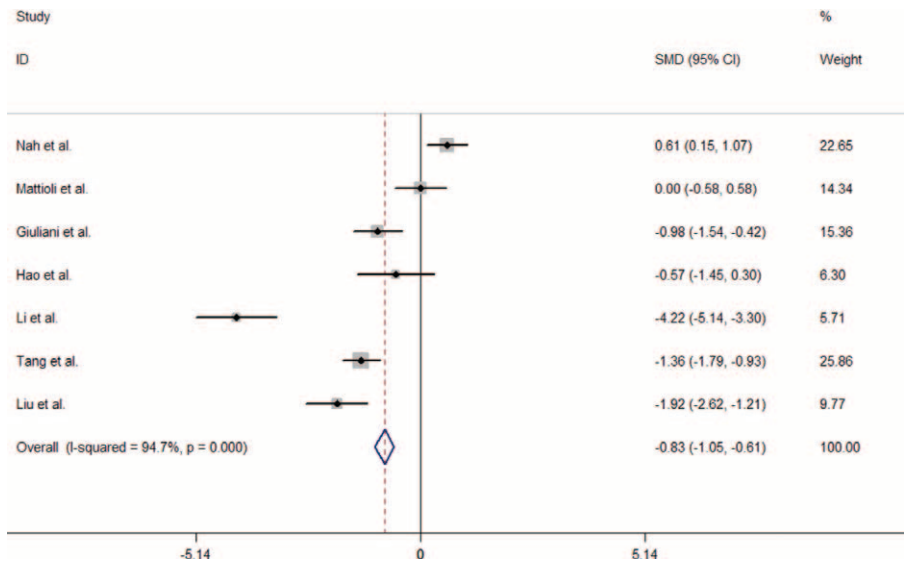

FIGURE 5. Comparison of laparoscopic laparoscopic-assisted operations and laparotomy operations with respect to mean first bowel movement.

DISCUSSION

The main therapy for Hirschsprung disease was the surgical method and many surgical approaches have been developed. As we all know, we would like to choose the more safer and reliable surgical method, with less number of complications, less estimated blood loss, shorter stay in hospital, short OT, and so on. To the best of our knowledge, there is no such comparison before; this is the first comprehensive meta-analysis to compare laparoscopic-assisted operations and laparotomy operations for the treatment of Hirschsprung disease. Finding from this meta-analysis suggested that laparoscopic-assisted surgery is safer and reliable than laparotomy with respect to complications, blood loss, hospital stay and MFBM, but is similar with laparotomy in the aspect of the OT.

Subgroup analyses by different surgery technique showed that Soave surgery technique has significantly lower EBL, LOHS, MFBM, and less number of complications in laparoscopic-assisted operations than in laparotomy. Although, when compared with laparotomy, Soave has longer OT by laparoscopic-assisted operations. Duhamed surgery technique has significantly lower OT and LOHS in laparoscopic-assisted operations than in laparotomy. When compared with

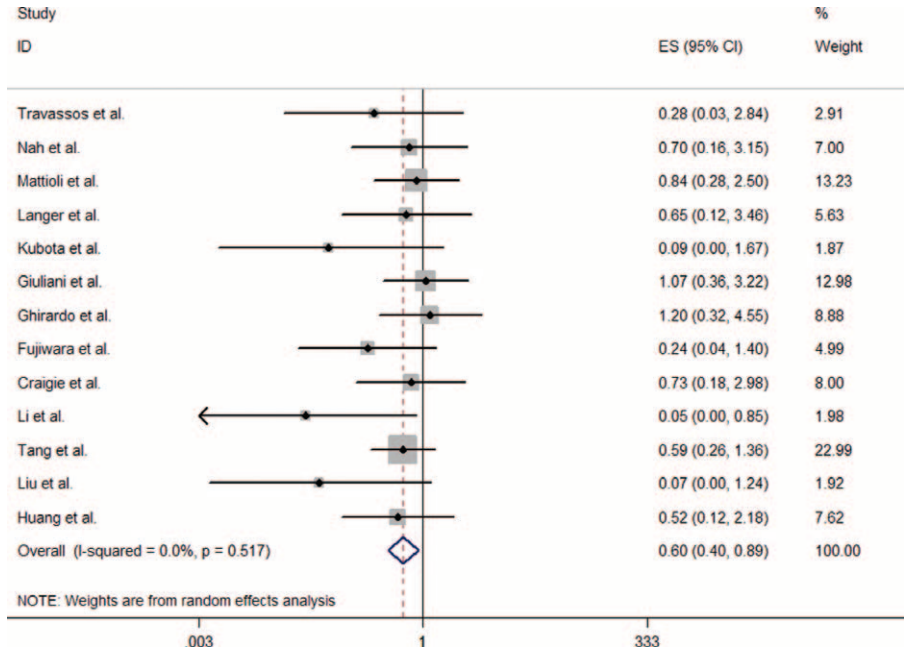

FIGURE 6. Comparison of laparoscopic laparoscopic-assisted operations and laparotomy operations with respect to number of complications.

laparotomy, Duhamed had no significant differences in MFBM and number of complication by laparoscopic-assisted operations.

After comparing laparoscopic-assisted operations and laparotomy operations, high heterogeneity was found in the pooled results. When we conducted subgroup analyses by different surgery technique, the heterogeneity still existed. The between-study heterogeneity might arise from publication year, location where the study conducted, and number of participants. Thus, we used meta-regression to explore the causes of heterogeneity. However, no covariate had a significant impact on between-study heterogeneity for the above-mentioned covariates. Sensitivity analysis showed that the results were not affected by any single study. Other genetic and environment variables, as well as their possible interaction, may be potential contributors to this high between-study heterogeneity. The results should be interpreted by taking its limitations into account. First, unpublished relevant literatures were not searched, which may lead to a potential publication bias, although no significant publication bias was found. Second, some of the data were estimated the mean and SD from median and range, which may result in inaccuracy. Finally, as laparoscopic-assisted experience increases, the expectation in OT will tend to decrease[26]; however, the original data do not support the further analysis.

In summary, this meta-analysis compare laparoscopic-assisted operations and laparotomy operations with respect to OT, EBL, LOHS, MFBM, and number of complications. Overall, the present study has shown that laparoscopic-assisted surgery is a feasible and promising method for the treatment of Hirschsprung disease, when compared with laparotomy.

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