Comparison of the efficacy and safety of laparoscopic-assisted operations and open operations for Hirschsprung's disease: evidence from a meta-analysis

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Abstract: Purpose: To determine the efficacy and safety of laparoscopic-assisted operations compared with open operations, used for the treatment of Hirschsprung’s disease (HD). Methods: Pertinent studies were identified by searching of PubMed and Web of Science. We analyzed dichotomous variables by estimating odds ratios (OR) with their 95% confidence interval (CI) and continuous variables using the weighted mean difference (WMD) with the 95% CI. The random effect model was used to combine the results. Results: Nine articles involving a total of 421 patients were included in this meta-analysis. For operation time of patients with HD, pooled data demonstrated a significantly shorter time in the laparoscopic operations group compared with open operations group (WMD = -0.27, 95% CI = -0.49, -0.05). The intraoperative blood loss was fewer in the laparoscopic operations group than open operations group (WMD = -1.05, 95% CI = -1.56, -0.54). The length of postoperative hospital was significantly shorter in the laparoscopic operations group. The number of complications was significantly lower in laparoscopic operations group than open operations group. Conclusions: Our results suggested that laparoscopic-assisted operation is generally safer and more reliable than open operation for patients with HD.

Keywords: Laparoscopic-assisted operations, open operations, Hirschsprung’s disease, meta-analysis

Introduction

Hirschsprung’s disease, which was defined in 1949 by Bodian [1] and by Hiatt in 1951 [2], is characterized by an absence of myenteric ganglion cells. Various methods have been developed for the surgical treatment of HD. The traditional pull-through techniques described by Swenson, Soave, and Duhamel have been modified in attempts to reduce the size of the surgical wound, minimize injury to surrounding structures during intra-abdominal dissection, and improve bowel function [3-5].

Next step was in the 1990s, when Georgeson, Duhamel, and Swenson techniques were adapted to laparoscopic-assisted approaches with all the known benefits [6]. It offers the safety and efficacy of the previous techniques plus all the advantages of a minimally invasive technique (minimizing scars, abdominal contamination, and adhesions) with excellent short-term results reported: better pain control, faster discharge from hospital, and unquestionable better aesthetic results. Up to date, a number of epidemiologic studies have been published to explore the relationship between laparoscopic operation and open operation with the risk of HD. Whether laparoscopic operation is superior to open operation remains unclear. We therefore conducted a meta-analysis compared the outcomes of these two used surgical approaches in patients with HD.

Methods

Search strategy

A comprehensive search was conducted for available articles published in English using the databases of PubMed and Web of Knowledge up to May 2015 and by hand-searching the reference lists of the computer retrieved articles. The following search terms were used: ‘lapar-
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**Inclusion criteria**

All relevant studies reporting the association between laparoscopic operations and open operations with the treatment for HD were considered for inclusion. The inclusion criteria were as follows: (1) the study type was retrospective or prospective study; (2) the exposure of interest was the treatment of laparoscopic operations or open operations; (3) the outcome of interest was HD; (4) available mean and standard deviation (SD) were provided for operation time, length of postoperative hospital and intraoperative blood loss; the number of complications were provided (or data available to calculate them); (5) written in English. Accordingly, the following exclusion criteria were also used: (1) reviews; (2) repeated or overlapped publications.

**Data extraction**

The following data were collected from all studies independently by two 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 total number of patients in each group and the number of patients with each outcome of interest for dichotomous variables. If there was disagreement between the two investigators about eligibility of the data, it was resolved by consensus with a third reviewer.

**Statistical analysis**

We analyzed dichotomous variables by estimating odds ratios (OR) with their 95% confidence interval (95% CI) and continuous variables using the weighted mean difference (WMD) with the 95% CI. Random-effects model was used to combine the pooled effect, which considers both within-study and between-study variation [7]. The I^2 was used to assess heterogeneity, and I^2 values of 0, 25, 50 and 75% represent no, low, moderate and high heterogeneity [8], respectively. Meta-regression with restricted maximum likelihood estimation was performed to assess the potentially important covariates that might exert substantial impact on between-study heterogeneity [9]. Publication bias was evaluated using Egger regression asymmetry test [10]. A study of influence analysis [11] was conducted to describe how robust the pooled estimator was to removal of individual studies. An individual study was suspected of excessive influence if the point estimate of its omitted analysis lay outside the 95% CI of the combined analysis. All statistical analyses were conducted with STATA version 10.0 (StataCorp LP, College Station, Texas, USA). Two-tailed p-value ≤ 0.05 was accepted as statistically significant.

**Results**

**Search results and study characteristics**

The electronic database searches identified 152 from PubMed and 176 articles from Web
### Table 1. Characteristics and methodological quality of included studies

<table>
<thead>
<tr>
<th>Study, year</th>
<th>Country</th>
<th>Study type</th>
<th>No. of patients</th>
<th>Mean age (month)</th>
<th>Outcome results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Travassos et al. 2007</td>
<td>Netherlands</td>
<td>Retrospective study</td>
<td>30</td>
<td>8</td>
<td>Complication</td>
</tr>
<tr>
<td>Nah et al. 2012</td>
<td>United Kingdom</td>
<td>Prospective study</td>
<td>35</td>
<td>3.1</td>
<td>Operation time, length of postoperative hospital, complication</td>
</tr>
<tr>
<td>Mattioli et al. 2008</td>
<td>Italy</td>
<td>Prospective study</td>
<td>25</td>
<td>11.3</td>
<td>Operation time, length of postoperative hospital, complication</td>
</tr>
<tr>
<td>Langer et al. 2000</td>
<td>United States</td>
<td>Retrospective study</td>
<td>15</td>
<td>2.5</td>
<td>Operation time, length of postoperative hospital, intraoperative blood loss, complication</td>
</tr>
<tr>
<td>Kubota et al. 2004</td>
<td>Japan</td>
<td>Retrospective clinical data</td>
<td>21</td>
<td>5.2</td>
<td>Operation time, intraoperative blood loss, complication</td>
</tr>
<tr>
<td>Giuliani et al. 2011</td>
<td>Italy</td>
<td>Retrospective study</td>
<td>32</td>
<td>14.61</td>
<td>Operation time, length of postoperative hospital, complication</td>
</tr>
<tr>
<td>Ghirardo et al. 2007</td>
<td>Italy</td>
<td>Retrospective cohort</td>
<td>21</td>
<td>14.6</td>
<td>Operation time, length of postoperative hospital, complication</td>
</tr>
<tr>
<td>Fujiwara et al. 2007</td>
<td>Japan</td>
<td>Retrospective study</td>
<td>22</td>
<td>3.76</td>
<td>Operation time, length of postoperative hospital, complication</td>
</tr>
<tr>
<td>Craigie et al. 2007</td>
<td>United Kingdom</td>
<td>Prospective study</td>
<td>20</td>
<td>0.7</td>
<td>Operation time, length of postoperative hospital, complication</td>
</tr>
</tbody>
</table>
Comparison of the efficacy between laparoscopic operations and open operations

There are 7 studies reported the treatment of operation time, and pooled data demonstrated a significantly reduction in the laparoscopic operations group compared with open operations group (WMD = -0.27, 95% CI = -0.49, -0.05) (Figure 2). Two studies were conducted to assess the intraoperative blood loss, and the association was significant between laparoscopic operations group and open operations group (WMD = -1.05, 95% CI = -1.56, -0.54). Six of the included studies reported the association for the treatment effects of length of postoperative hospital, laparoscopic operations group had shorter time of postoperative hospital compared with open operations group (WMD = -0.61, 95% CI = -0.85, -0.36) (Figure 3).

Comparison of the safety between laparoscopic operations and open operations

There are 9 studies conducted to assess the association between treatment safety of laparoscopic operations group and open operations group for any complication. Pooled data demonstrated showed significantly fewer complications in laparoscopic operations group than in open operations group (OR = 0.61, 95% CI = 0.38-0.99, I² = 0.0%) (Figure 4).

Sources of heterogeneity and meta-regression

As seen in the pooled results of Figures 2 and 3, high heterogeneities were found in the analysis. In order to explore the high between-study heterogeneity founded in several analyses, univariate meta-regression with the covariates of publication year, location where the study was conducted, study type, outcome measures, and number of participants were performed. No significant findings were found in the above-mentioned analysis.

Influence analysis and publication bias

Influence analysis showed that no individual study had excessive influence on the association for the efficacy and safety of laparoscopic-assisted operations and open operations for HD. Egger’s test showed no evidence of signifi-
cant publication bias between laparoscopic-assisted operations group and open operations group for the treatment of HD ($P = 0.296$).

**Discussion**

Finding from this meta-analysis suggested that laparoscopic surgery is more saving time, less intraoperative blood loss and shorter stay in hospital compared with open operations. The complication in laparoscopic operations group was significantly fewer than in open operations group.

The laparoscopic-assisted approach is attractive in offering early biopsy and identification of the zone of transition. In addition, laparoscopy allows for the inspection of the orientation of the pulled-through bowel segment and an avoidance of obstruction secondary to twisting along the longitudinal axis of the colon or folded muscular cuff [20]. Laparoscopic operations offers several benefits, including (1) determination the level of the transition zone histologically before “committing oneself” by beginning the perineal dissection, (2) visualization of the pulled through bowel to ensure that there is no bleeding or twisting, and (3) mobilization of the splenic flexure when there is a more proximal transition zone [15].

Between-study heterogeneity is common in meta-analysis [21], and exploring the potential sources of between-study heterogeneity is the essential component of meta-analysis. For zinc levels with the risk of preeclampsia, evidence of heterogeneity was found in the pooled results. The between-study heterogeneity might arise from publication year, study design, geographic locations, sample type and fasting status. Thus, we used meta-regression to explore the causes of heterogeneity for covariates. However, no covariate having a significant impact on between-study heterogeneity for the above mentioned covariates. However, other genetic and environment variables, as well as their possible interaction may be potential contributors to this disease-effect un conformity.

To the best of our knowledge, this is the first comprehensive meta-analysis to compare laparoscopic operations with open operations for treatment of HD. Second, large number of cases was included, allowing a much greater possibility of reaching reasonable conclusions between laparoscopic operations and open operations with the treatment of HD. Third, no significant publication bias was found. However, there were some limitations in this meta-analysis. First, one possible further advantage of laparoscopic surgery in reducing postoperative pain and analgesic requirements could not be addressed in this study because of the limited data in the each independent study. Second, other unpublished literatures on relevant phar-
maceutical websites were not searched and only studies in English were included, which may lead to a potential publication bias, although no significant publication bias was found by Egger’s test. Third, we estimated the mean and SD from the median and range [22] if the mean and SD for continuous variables were not available, which may result in error or inaccuracy. Finally, between-study heterogeneity was found in some analysis in this meta-analysis, but the between-study heterogeneity was not successfully explained by meta-regression. However, other genetic and environment variables, as well as their possible interaction may be potential contributors to this disease-effect unconformity.

In summary, results from this meta-analysis suggest that laparoscopic-assisted operation is generally safer and more reliable than open operation for patients with HD.

Disclosure of conflict of interest

None.

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