Systematic Review and Meta-Analysis

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Comparison of clinical efficacy of laparoscopic splenectomy versus open splenectomy for idiopathic thrombocytopenic purpura

A meta-analysis

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Abstract

Background: The purpose of this study is to compare the clinical efficacy of laparoscopic splenectomy (LS) and open splenectomy (OS) in the treatment of Idiopathic thrombocytopenic purpura.

Methods: We systematically searched PubMed, Web of science, EMBASE, Clinicaltrials.gov, and Cochrane Central Register for studies (study published from July 1992–January 2020). This study analyzed the clinical effect of LS and OS on idiopathic thrombocytopenic purpur.

Results: This study showed that compared with OS, the LS's Overall response (OR: 0.60, 95% confidence interval (CI): 0.23–1.59, $P = .30$), Complication (OR: 0.59, 95% CI: 0.18–1.94, $P = .38$), Accessory spleen(OR: 1.70, 95% CI: 0.98–2.98, $P = .06$), Wound infections (OR: 0.65, 95% CI: 0.26–1.59, $P = .34$), Pancreatic fistula (OR: 0.73, 95% CI: 0.16–3.30, $P = .68$), was no significant, the Operative time (weighted mean difference (WMD): 49.33, 95% CI: 36.29–62.37, $P < .00001$)was longer, and the Estimated blood loss (WMD: –172.59, 95% CI: –319.96 to –25.22, $P = .02$), Postoperative length of stay (WMD: –4.68, 95% CI: –7.75 to –1.62, $P = .003$)was less.

Conclusions: The therapeutic effect of LS was the same as that of OS in Overall response Complication Accessory spleen, while The operative time was longer, the Estimated blood loss was less, and the postoperative length of stay was shorter.

Abbreviations: CI_S = confidence interval, EBL = estimated blood loss, ITP = idiopathic thrombocytopenic purpura, LS = laparoscopic splenectomy, ORS = odd ratio, OS = open splenectomy, WMD = weighted mean difference.

Keywords: idiopathic thrombocytopenic purpura., laparoscopic splenectomy, open splenectomy

1. Introduction

Idiopathic thrombocytopenic purpura (ITP) is an acquired hemorrhagic disease of unknown origin, characterized by thrombocytopenia, normal or increased megaloid cells in the bone marrow, and the absence of any cause. The incidence of ITP in women of childbearing age is higher than that in men, and there is no difference in the ratio of male to female in other age groups. The course of disease is mostly chronic. It is characterized by autoantibody mediated platelet destruction and inhibition of platelet production, resulting in low platelet count and easy bleeding. Most ITP can be treated with drugs, but some patients are not sensitive to prednisone or anti-D-globulin, so they need splenectomy. Splenectomy is the standard second-line therapy for chronic ITP. It is the first choice for most ITP patients who have no effect on corticosteroid therapy. It is mainly aimed at the patients whose corticosteroid is forbidden or whose compliance with drug therapy is low. The beneficial effect of splenectomy on ITP is related to spleen function, which is believed to lead to thrombocytopenia, including the removal of platelets from circulation and the production of antiplatelet antibodies.[1] At present, splenectomy can be divided into open splenectomy (OS) and LS. Although laparoscopic surgery has considerable appeal, including shorter hospital stay, and smaller incision, it was initially considered that LS is not feasible due to the complexity of blood vessels, peritoneal appendages, and difficulty in identifying the accessory spleen.[2] With the continuous research of scholars, it is found that vascular control is the key link of surgery, and the development of vascular treatment equipment, LS has been conquered, and has been used in clinical surgery. Although for many spleen diseases, especially for patients with refractory ITP, LS has become the first choice,[3] However, there is a lack of systematic understanding of the clinical efficacy of LS and OS in the treatment of ITP. In this paper, meta-analysis is used to elaborate.

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All data generated or analyzed during this study are included in this published article.

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2. Methods

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systemic Reviews and Meta-analysis statement. We searched PubMed, Web of science, EMBASE, Clinicaltrials.gov, and Cochrane Central Register for studies (articles published in English between July 1992 and January 2020). The search term was Laparoscopic splenectomy, OS, Idiopathic thrombocytopenic purpura. We also used the combined Boolean operators "AND" or "OR". The 2 investigators reviewed the results of the differences together.

The inclusion criteria were as follows:

(1) original literature;
(2) comparison of LS and OS.

The exclusion criteria were as follows:

(1) case report, review, articles without relevant data;
(2) non comparative study. The identification process of relevant research is shown in Figure 1. This study is a meta-analysis and does not require ethical approval.

2.1. Statistical analysis

We use Review Manager Version 5.3 (The Cochrane Collaboration, Oxford, UK) to analyze the data. We used the GRADE approach to evaluate the quality of the evidence. We use I^2 to evaluate heterogeneity; when the value of $I^2 < 50\%$, the heterogeneity is low and fixed effect model was used. However, if the value of $I^2 > 50\%$, there was heterogeneity, using the random effect model. For quantitative data, we use the weighted mean difference (WMD) or standard mean difference of continuous variables. We used odd ratio (ORs) and 95% confidence interval (CIs) for binary data.

3. Results

Our meta-analysis included 10 studies. Figure 1 summarized the process of obtaining these studies. 329 studies were obtained from the selected database. 309 studies were excluded after the title and summary were screened. After detailed treatment of the remaining studies, 10 other studies were excluded. Finally, 10 studies were included in our meta-analysis.[3–12]Table 1 summarizes the baseline characteristics and assessments for 10 studies.

3.1. Quality assessment

We used the New Ottawa Scale to assess the risk of bias for inclusion in the study. The NOS scores were evaluated using a 9-point system. NOS score of 7 or more indicated high quality, and NOS score of 3 or less indicated low quality. Two reviewers assessed the quality of the included studies. Table 2 showed the bias risk for the selected study.

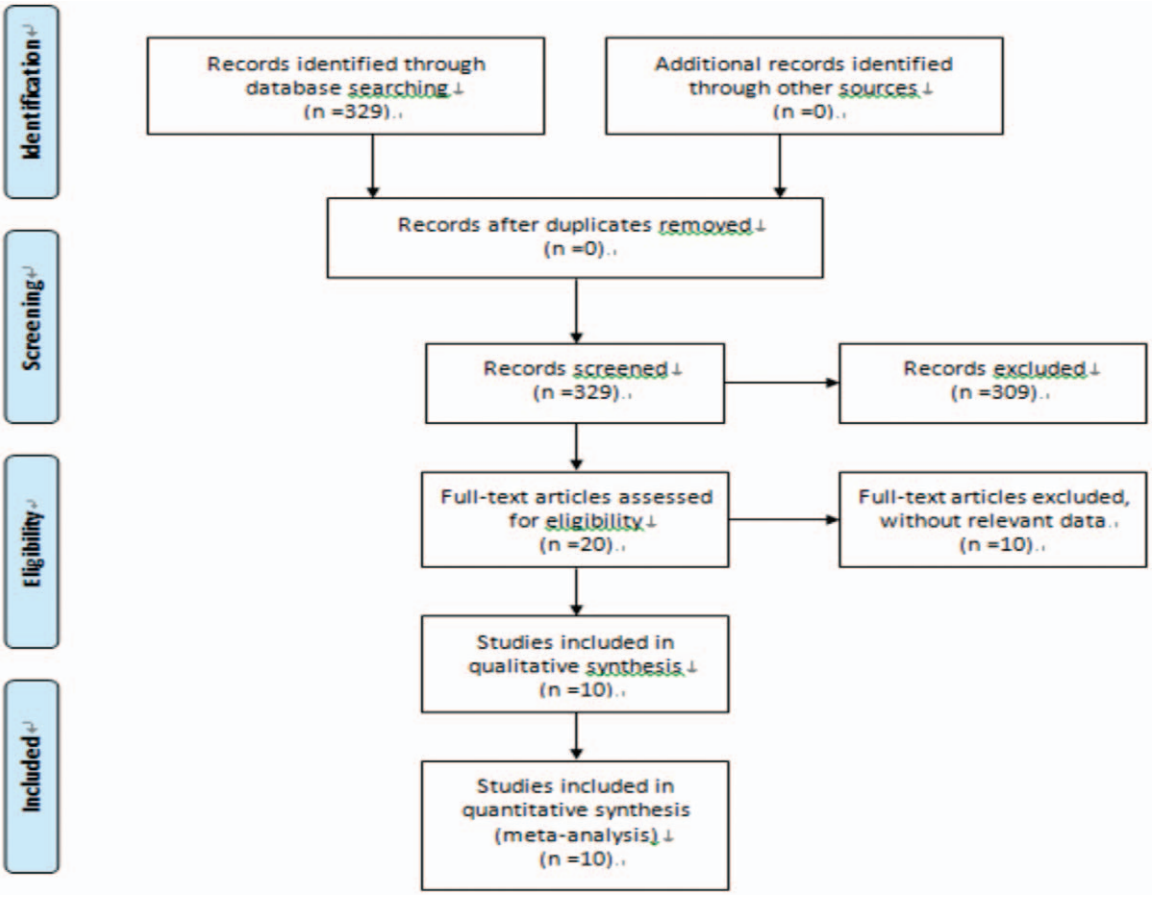

Figure 1. Flow chart of literature selection.

Table 1

Basic characteristics of the included studies.

Study	Design	Yr	Case		Age (yr)		Preoperative platelets (10^9/L)	
			LS	OS	LS	OS	LS	OS
Berends	R	2004	50	31	42.4[a]	36.0[a]	NA	NA
Cordera	R	2003	42	44	52.5[b]	49.9[b]	58.4[a]	65.4[a]
Friedman	R	1996	29	18	50[a]	41[a]	98[a]	97[a]
Qu	R	2014	32	41	37.9[a]	35.6[a]	35[a]	42[a]
Ruiz-tovar	R	2007	20	38	41[a]	39.7[a]	78[a]	69[a]
Sampath	R	2007	51	54	43[a]	46[a]	56[a]	60[a]
Schlinkert	R	1995	7	14	53[a]	60[a]	NA	NA
Shimomatsuya	R	1999	14	20	47.9[a]	44.4[a]	NA	NA
Tada	R	2017	22	10	33[a]	37[a]	90[a]	59[a]
Vecchio	R	2013	20	20	29.8[a]	30.1[a]	NA	NA

R = retrospective study.

[a] = Mean.

[b] = Median, NA = not available.

3.2. Evidence grading

We used the GRADE approach to evaluate the evidence. This method included evaluating the basic quality of evidence, evaluating the main statistical results, and classifying the evidence of each result. The evidence is divided into high, medium, low or very low quality. Criteria for assessing evidence included an assessment of the deviation risk identified by the Cochran deviation risk tool.[13]

3.3. Meta-analysis results

3.3.1. Overall response. There were 3 studies that reported the data of overall response. According to the results of meta-analysis, the overall response of LS and OS was not statistically significant (n = 153, 92 cases in LS group, 61 cases in OS group). Fixed effect model was used ($I^2 = 0\%$, OR: 0.60, 95% CI: 0.23–1.59, $P = .30$, Fig. 2).

3.3.2. Complication. There were 7 studies that reported the data of complication. According to the results of meta-analysis, there was no statistical significance in the complication of LS and OS (n = 427, 211 cases in LS group, 216 cases in OS group). The random effect model was used ($I^2 = 76\%$, OR: 0.59, 95% CI: 0.18–1.94, $P = .38$, Fig. 3).

3.3.3. Operative time (minutes). There were 5 studies that reported the data of operative time. According to the results of meta-analysis, the operative time of LS was longer than that of OS, which was statistically significant (n = 272, 139 cases in LS group and 133 cases in OS group). Fixed effect model was used ($I^2 = 54\%$, WMD: 49.33, 95% CI: 36.29–62.37, $P < .00001$, Fig. 4).

3.3.4. Estimated blood loss (mL). There were 4 studies that reported the data of Estimated blood loss(EBL). According to the results of meta-analysis, the EBL of LS was less than that of OS, which was statistically significant (n = 186, 97 cases in LS group, 89 cases in OS group). The random effect model was used ($I^2 = 84\%$, WMD: –172.59, 95% CI: –319.96 to –25.22, $P = .02$, Fig. 5).

3.3.5. Postoperative length of stay (days). There were 3 studies that reported the data of postoperative length of stay. According to the results of meta-analysis, the postoperative length of stay of LS is less than that of OS, which was statistically significant (n = 165, 93 cases in LS group, 72 cases in OS group). The random effect model was adopted ($I^2 = 89\%$, WMD: –4.68, 95% CI: –7.75 to –1.62, $P = .003$, Fig. 6).

Table 2

Newcastle-Ottawa Scale for risk of bias assessment of the included studies.

Study	Design	Selection				Comparability	Outcome			Total
		Representativeness of exposed cohort	Representativeness of non-exposed group	Ascertainment of exposure	Outcome not present at start		Assessment of outcome	Adequate follow-up length	Adequacy of follow-up	
Berends 2004	R	*	*	*	*	*	*			6
Cordera 2003	R	*	*	*	*	*	*	*		7
Friedman 1996	R	*	*	*	*	*	*	*		7
Qu 2014	R	*	*	*	*	*	*			6
Ruiz-tovar 2007	R	*	*	*	*	*	*			6
Sampath 2007	R	*	*	*	*	*	*			6
Schlinkert 1995	R	*	*	*	*	*				5
Shimomatsuya 1999	R	*	*	*	*	*				5
Tada 2017	R	*	*	*	*	*	*			6
vecchio 2013	R	*	*	*	*	*	*			6

R = retrospective study.

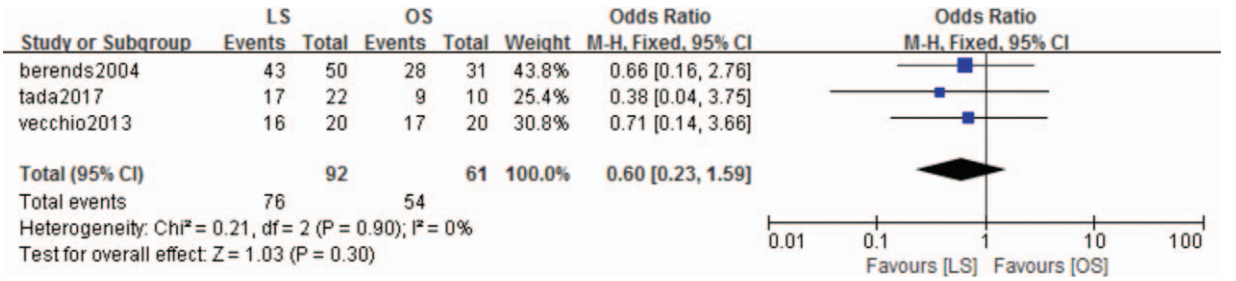

Figure 2. Overall response forest plot.

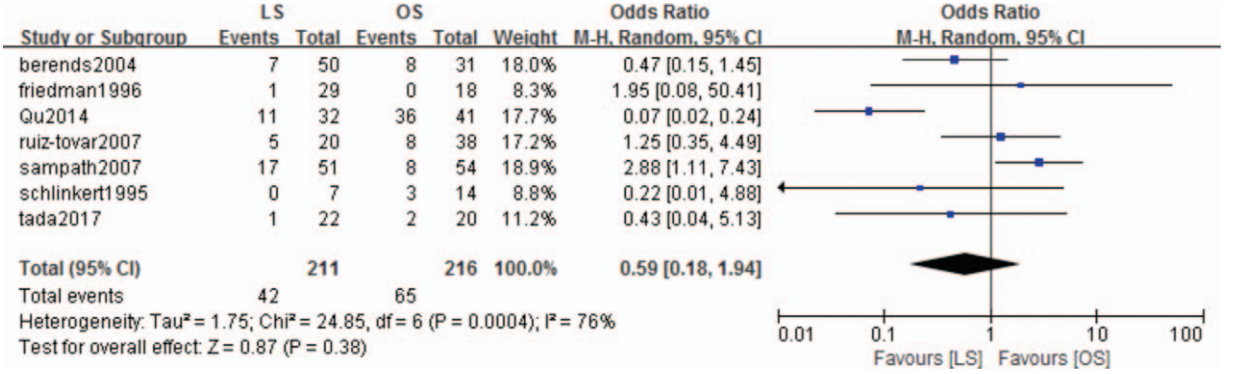

Figure 3. Complication forest plot.

3.3.6. Detection of accessory spleen. There were 6 studies that reported the data of detection of accessory spleen. According to the results of meta-analysis, there was no statistical significance in the detection rate of accessory spleen of LS and OS (n = 349, 168 cases in LS group, 181 cases in OS group). Fixed effect model was used ($I^2 = 0\%$, OR: 1.70, 95% CI: 0.98–2.98, $P = .06$, Fig. 7).

3.3.7. Wound infections. There were 4 studies that reported the data of wound infections. According to the results of meta-analysis, there was no statistical significance in the wound infections of LS and OS (n = 345, 175 cases in LS group, 170 cases in OS group). The fixed effect model was used ($I^2 = 12\%$, OR: 0.65, 95% CI: 0.26–1.59, $P = .34$, Fig. 8).

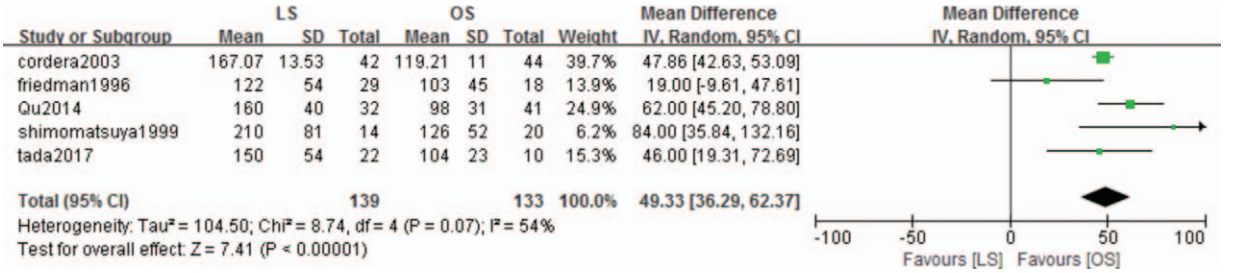

Figure 4. Operative time forest plot.

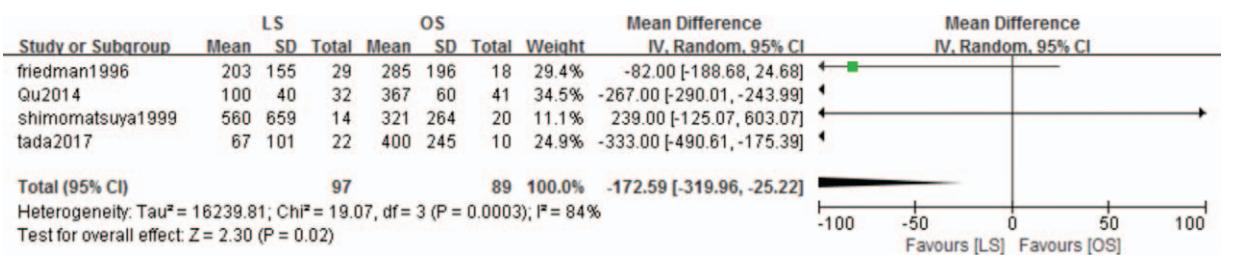

Figure 5. Estimated blood loss forest plot.

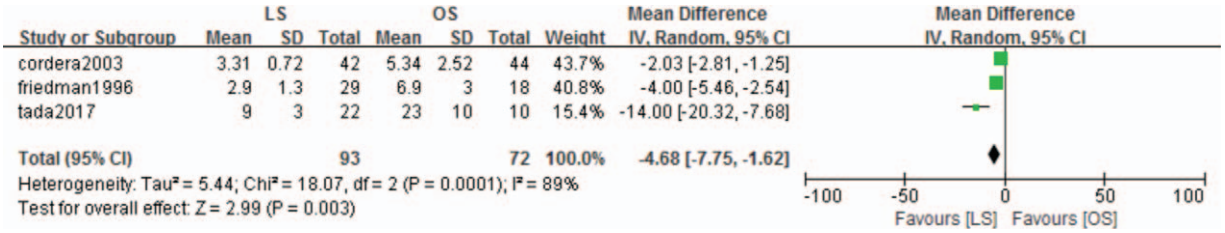

Figure 6. Postoperative length of stay forest plot.

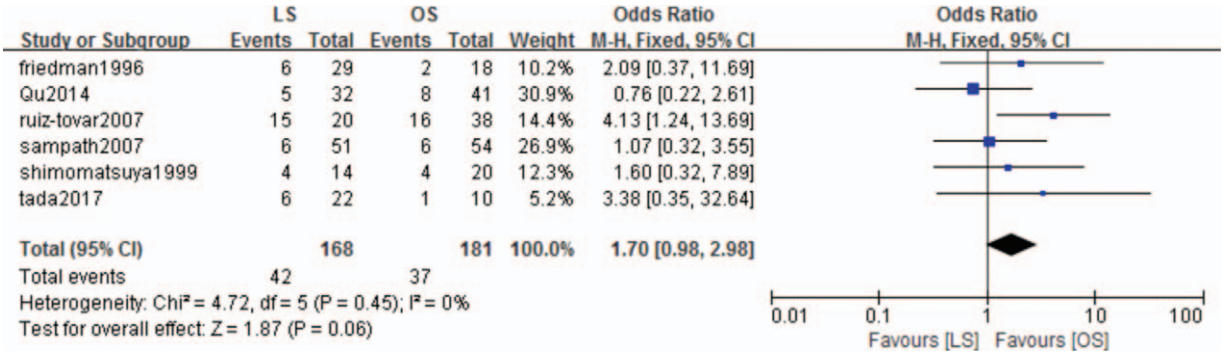

Figure 7. Detection of accessory spleen forest plot.

3.3.8. Pancreatic fistula. There were 2 studies that reported the data of pancreatic fistula. According to the results of meta-analysis, there was no statistical significance in the pancreatic fistula of LS and OS (n = 154, 82 cases in LS group, 72 cases in OS group). The fixed effect model was used ($I^2 = 34\%$, OR: 0.73, 95% CI: 0.16–3.30, $P = .68$, Fig. 9).

4. Discussion

ITP was a thrombocytopenia syndrome caused by platelet autoantibodies, which may occur alone or be related to other diseases such as leukemia, systemic lupus erythematous,. and AIDS.[14] Corticosteroid and splenectomy were the most effective methods to treat this disease. Splenectomy was an effective

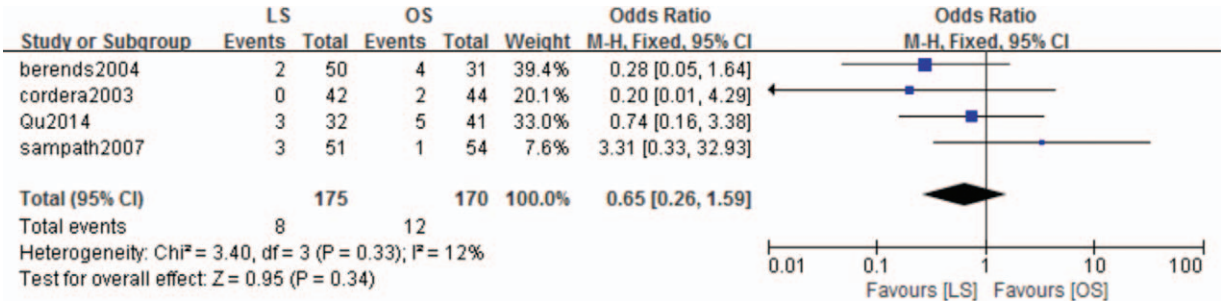

Figure 8. Wound infections forest plot.

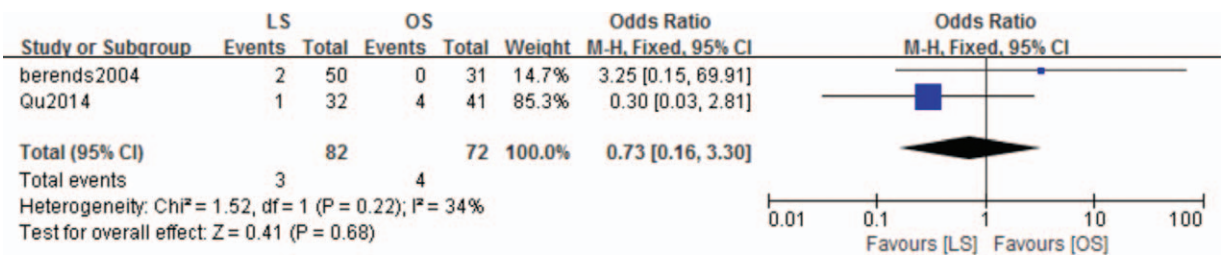

Figure 9. Pancreatic fistula forest plot.

method to treat ITP in adults. It had been proved that it was the most effective method to treat long-term remission when the effect of corticosteroid treatment was not good. In addition, splenectomy was usually performed in the early stage in patients with refractory ITP. The therapeutic effect may be related to the main parts of the production of autoimmune cells and the destruction of platelets by splenectomy, which can improve the survival time of platelets. According to the literature reported, complete remission after splenectomy was observed in 66% to 100% of cases.[12] Although splenomegaly was rare in ITP patients, splenectomy could cure about 80% of cases.[6] For many spleen diseases, especially for refractory ITP patients, LS had become the first choice. Most articles reported that the operation time of LS was longer than that of OS, but some authors had also proved that with the increase of learning curve and the accumulation of LS experience, the operation time of LS was significantly reduced, and LS was a safe process.[3]

At present, the comparative study of laparoscopic approach and open approach is mostly a retrospective study of small samples, lacking systematic understanding. This meta-analysis included 10 studies with a total of 577 cases. This meta-analysis is the largest meta-analysis of the sample size so far. The relationship between LS and OS is described in the following 6 aspects.

1. There were few studies on overall response (LS and OS) after ITP splenectomy. Berends et al[4] reported that there was no significant difference in the incidence of complete remission and partial remission between LS and OS. Vecchio et al[12] reported that there was no significant difference in overall response between laparoscopic group and open group. Through this meta-analysis, the overall response of LS and OS was not statistically significant. It showed that in the treatment of ITP, LS could achieve the same overall response as OS.
2. After a meta-analysis of 7 studies, there was no significant difference in postoperative complications (including wound infection, pancreatic fistula, etc) between LS and OS. Berends et al[4] suggested that the incidence of postoperative complications in OS group was significantly higher than that in LS group. Friedman et al[6] thought that LS and OS groups were not dead, and no serious complications were observed. The incidence rate and mortality statistics seemed to be more favorable for LS than OS. Qu et al[3] reported that the incidence of postoperative complications (including pneumonia, subphrenic abscess, postoperative hemorrhage, pancreatic fistula, and thromboembolism events) was higher in OS group, but there was no statistical difference compared with LS group. Sampath et al[8] reported that the incidence of complications in laparoscopic group was significantly higher, some intraoperative complications needed to be converted to open surgery, but most postoperative complications were smaller. Although the heterogeneity of each literature is high, the results of meta-analysis are basically consistent with the previous reports in the literature.
3. Five studies reported operative time, and meta-analysis showed that LS had longer operative time than OS. Previous reports such as Qu et al[3] reported that patients with LS had shorter hospital stay and shorter operation time than those with OS. Compared with open surgery, it taked more time for LS group to locate the patient, established pneumoperitoneum, putted the removed spleen into the bag, and finally taked it out through the trocar. Sampath et al[8] reported that the operation time and hospitalization time of laparoscopic group were significantly longer. Previous research reports are still controversial. This paper is based on a large sample study, which integrates previous data, and can better reflect that the operation time of LS is longer than that of OS. Because LS can't be operated by hand, but by instrument, the operation difficulty is greatly increased, so the operation time is increased.
4. There had been relevant literature reported on EBL. For example, berends et al[4] believed that there was no significant difference between LS and OS in intraoperative blood loss. Tada et al[11] reported that although the operation time of LS group was significantly prolonged ($P < .01$), there was less blood loss during operation ($P < .01$), less blood transfusion during operation ($P < .01$), and shorter postoperative hospital stay than that of OS group ($P < .01$). Friedman et al[6] found that EBL in LS group was lower. Shimomatsuya and Horiuchi[10] compared the open group and laparoscopic group, and found that the blood loss of OS was less than that of laparoscopic splenectomy. Although some studies reported that LS had more EBL than OS, there were also reported that there was no significant difference in blood loss between the 2 groups. However, most studies still showed that theEBL of LS was less than that of OS. Although there may be bias between different research units, leading to higher heterogeneity, this meta-analysis reflects that the EBL of LS is less than that of OS through large sample size after comprehensive analysis of previous data. Because laparoscopy has the function of magnifying, it can magnify the anatomy during the operation, it is easier to distinguish the blood vessels, it is more accurate during the operation, and the probability of injury will be greatly reduced.
5. Three studies reported the postoperative length of stay. The meta-analysis showed that LS had shorter postoperative hospital stay than OS, indicating that LS was more advantageous in postoperative recovery. Friedman, Cordera, Tada and other studies had reported that the average postoperative hospital stay of patients in LS group was shorter than that in OS group. Although the heterogeneity of the 3 articles is relatively high, the conclusion of the postoperative length of stay is consistent.
6. The missing accessory spleen after splenectomy is an important cause of ITP recurrence. Deliatre et al[15] attributed 70% of recurrent cases to the presence of an undetected accessory spleen during surgery. Facon et al[16] reported that one of the reasons for late recurrence was the omission of accessory spleen tissue during operation. The accessory spleen may be confined to the whole abdominal cavity, but it is mainly found in the upper left quadrant, the splenic hilum, the paracolon sulcus, near the tail of pancreas and the lesser omental sac. The current reported literature is controversial about the detection rate of LS and OS on accessory spleen. Some studies had shown that the detection of accessory spleen by laparoscopy had good sensitivity and specificity.[11] Berends et al[4] suggested that the detection rate of accessory spleen in LS and OS was the same. In this paper, after a meta-analysis of 6 studies, we find that there is no difference in the detection rate of accessory spleen during the operation. Although laparoscopy can magnify the anatomy during the operation, the total detection rate of accessory spleen is the same.

At present, there are few researches on economy, and only Cordera and Friedman reported this research. Cordera et al found that the average direct total cost per patient did not differ significantly between treatment groups. In the intention-to-treat analysis, the average billed charges (hospital and doctor costs) of the LS group were significantly higher than nearly $3000. Friedman et al found that the costs of the 2 groups were similar. In LS group, the direct cost was lower and the operating room cost was higher, but the difference was not statistically significant. At present, there are few studies on this, which need further research to elaborate.

There are still some deficiencies in this paper, most of the literature retrieved are retrospective studies, non RCT studies, some of which have high heterogeneity and have a certain impact on the results, which need to be clarified by larger sample RCT studies in the future.

5. Conclusions

Through this meta-analysis, LS has the same efficacy as OS in overall response, Complication and accessory spleen. Although the operative time is longer, the EBL is less. Moreover, laparoscopic splenectomy has more advantages than OS in rapid recovery and reducing hospital stay, which is worth clinical promotion.

Author contributions

QLZ designed the study, QLZ and WW searched the articles and analyzed the data. QLZ wrote the manuscript. All authors read and approved the final manuscript.
Conceptualization: QLZ.
Data curation: QLZ, WW.
Formal analysis: QLZ, WW.
Funding acquisition: QLZ.
Investigation: QLZ.
Methodology: QLZ.
Project administration: QLZ.
Resources: QLZ, WW.
Software: QLZ.
Supervision: QLZ.
Validation: QLZ.
Visualization: QLZ.
Writing – original draft: QLZ.
Writing – review & editing: QLZ.

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