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Original Article

A meta-analysis study of laparoscopic versus open splenectomy with esophagogastric devascularization in the management of liver cirrhosis and portal hypertension

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Abstract: In recent years Laparoscopic splenectomy combined with esophagogastric devascularization (LSED) for liver cirrhosis and portal hypertension has attracted important attention from surgeons worldwide due to its minimal invasion. This review is aimed to compare the results of LSED and splenectomy combined with esophagogastric devascularization (OSED). We systematically searched datasets of Pubmed, Embase, Medline and Science Direct to identify all relevant publications. The statistical analysis was carried out according to the recommendation of the Cochrane Collaboration software (Review Manager version 5.3). Dichotomous variables were calculated by odds ratio (OR) with 95% confidence interval (CI), whereas continuous variables were calculated by mean differences (MDs) with CI. In total 5 eligible studies with 345 cases were included, of which 162 cases were in the LSED group while 183 cases were in the OSED group. The LSED group was related to less blood loss (MD=-157.34 ml, 95% CI: -251.91 to -62.77, P=0.001), earlier oral intake (MD=-1.36 d , 95% CI: -2.2 to -0.52, P=0.001), shorter hospital stay after surgery (MD=-4.35 d , 95% CI: -6.59 to -2.11, P=0.0001) and decreased postoperative morbidity (OR=0.41, 95% CI: 0.20 to 0.84, P=0.01) compared with the OSED group. But the operative time was similar between the two groups (MD=31.12 min, 95% CI: -2.12 to 64.36, P=0.07). This meta-analysis indicated that LSED appeared to be safe and provide improved patient outcomes with portal hypertension compared with OSED.

Keywords: Laparoscopy, liver cirrhosis, portal hypertension, meta-analysis

Introduction

Due to the high incidence of hepatitis B and hepatitis C, liver cirrhosis is more common in Asian countries, especially in China [1, 2]. Portal hypertension is a common syndrome of liver cirrhosis [3]. The major clinical presentations of portal hypertension are hypersplenism and esophagogastric varices. OSED was first performed by Sugiura procedure more than fifty years ago and it is an effective surgical treatment because it can solve thrombocytopenia, bleeding, and leukopenia caused by portal hypertension at the same time [4]. It was once recommended as the first choice for treating portal hypertension over ten years ago, particularly for chronic viral hepatitis infective liver cirrhosis [5]. Laparosopic splenectomy has been regarded as the standard procedure for most indications since it was first introduced in 1991 [6-9]. But laparoscopy for portal hypertension is considered to be contraindicated due to the high risk of massive intraoperative hemorrhaging caused by splenomegaly, the collateral vessels around the spleen, the impaired coagulation factors and the low platelet counts [10-12]. Recently, owing to the advances in laparoscopic devices, cumulative experience and data from laparoscopic surgeries, laparoscopic techniques have been widely applied in various fields, and patients with liver cirrhosis and portal hypertension are included. LSED has been increasingly carried out recently in a lesser invasive way on patients with liver cirrhosis and portal hypertension [13, 14]. A previous meta-analysis showed that laproscopic splenectomy

(LS) and LSED had the advantage of minimal invasion compared with open splenectomy (OS) and OSED [15]. In this meta-analysis, relevant literature was reviewed and differences in operation time, blood loss, risk of major complication, time of oral intake and postoperative hospital stay were evaluated between LSED and OSED.

Methods

Literature search

A systematic search of Pubmed, Embase, Medline and Science Direct was performed for articles published between January 1990 and July 2018. Only articles written in English were accepted in this meta-analysis. And it followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [16]. The following search terms were used: Laparoscopic splenectomy, liver cirrhosis, portal hypertension, esophagogastric devascularization, and devascularization. Manual searches for reference lists of reviews and meta-analysis were supplemented to the computer search.

Inclusion and exclusion criteria

Studies comparing LSED and OSED under the circumstance of liver cirrhosis and portal hypertension were included no matter whether they were retrospective studies or randomized controlled trials. The exclusion criteria contained case reports, editorials, letters and research articles unattainable to acquire the proper information. Any discrepancies in exclusion or inclusion of clinical trials were solved by mutual discussions.

Data extraction

Two reviewers independently assessed the available studies. Any discrepancies were solved by mutual discussion. The extracted data consisted of the following items: name of first author, publication year, total number of cases and controls, age, sex, operation time, blood loss, oral intake time and hospital stay after surgery and complications. We contacted the authors for any missing or unclear data.

Quality assessment

The quality assessment of observational studies was performed following the modified criteria suggested by the New-Ottawa quality assessment tool. Three major aspects were evaluated: selection of the study groups, comparability and assessment of the outcome. The maximum score was 9 stars that could be achieved. Two authors assessed the scale components of each study independently. And any differences between authors were solved by mutual discussion until an agreement was reached.

Statistical analysis

All analysis was performed with Review Manager software version 5.3 from cochrane collaboration. Meta-analysis was carried out by OR for dichotomous outcomes and MDs for continuous outcomes. To standardize the continuous variables data, including the standard deviation for each variable reported by each study was very important. The range values for each variable were converted to standard deviations and analyzed. Polled estimates were presented with 95% CIs. The fixed effects model was applied in our study. $P<0.05$ was considered statistically significant. Funnel plots were generated to screen publication bias.

Results

Study characteristics

Figure 1 illustrates the study screening and selection process. A total of 197 potential studies were identified. After duplicates were removed, a total of 181 articles remained. After the abstract and full-text were reviewed, 53 studies were included for meta-analysis. Finally, 48 of the 53 papers were excluded because they lacked suitable data, were not proper types of articles or were not written in English. Five studies were regarded as meeting the inclusion criteria and all studies were single centre Non-randomized control trails [17-21]. There were no significant differences in patient demographics between groups except for Ando et al, in which some basic characteristic data could not be obtained (**Table 1**).

Quality of included studies

Study quality assessment was performed with the New-castle-Ottawa Scale part for cohort or Case-control studies. The characteristics of the

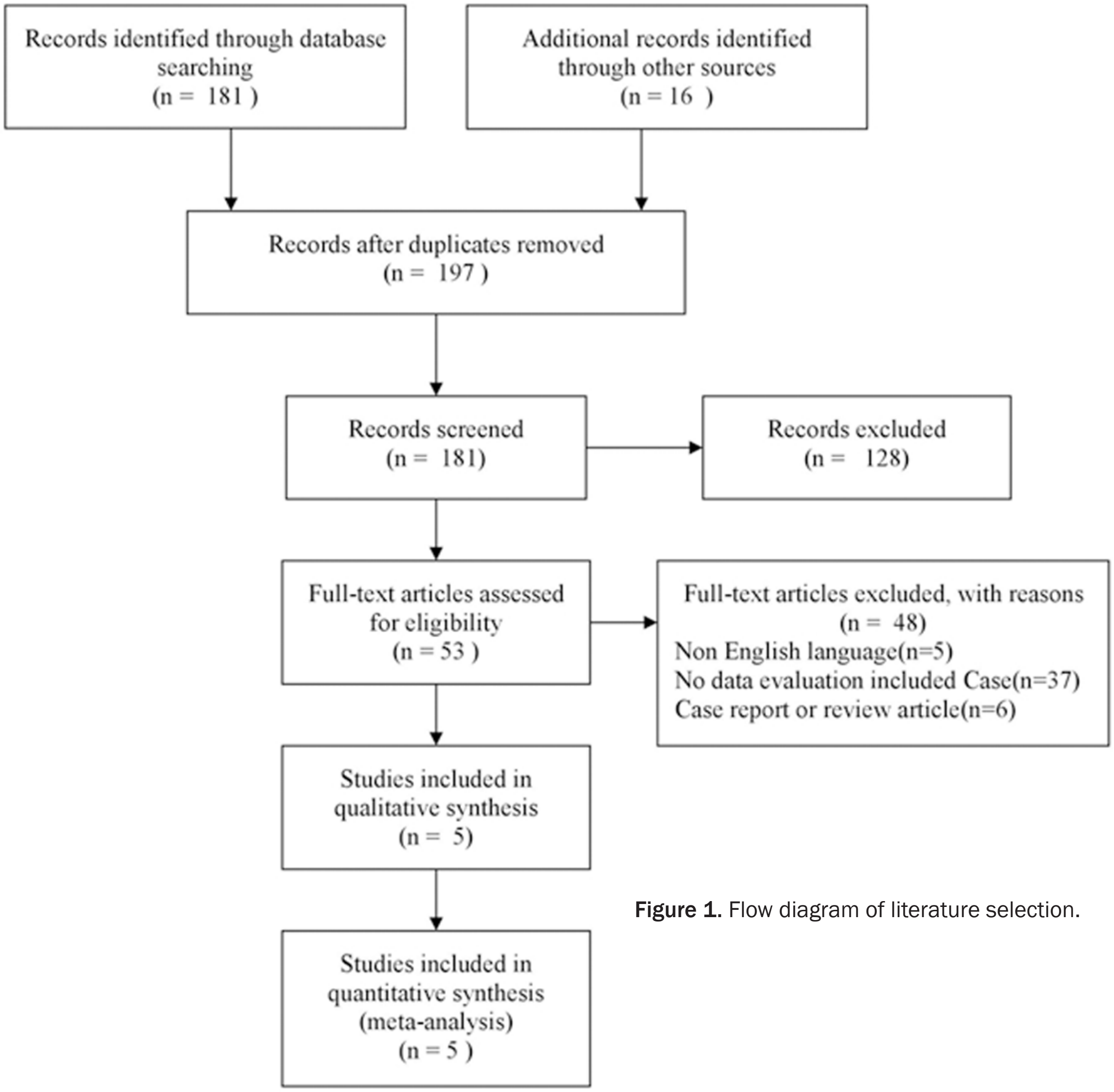

Figure 1. Flow diagram of literature selection.

Table 1. Baseline characteristics of included studies

References	Year	Study design	Country	Sample Size (LSED/OSED)	Age (LSED/OSED)	Sex (Male) (LSED/OSED)	Child-Pugh Class A/B/C (LSED/OSED)
Ando et al [20]	2012	cohort study	Japan	6/33	62.5±13.1/NA	(6/0)/NA	(6/0/0)/NA
Jiang et al [18]	2009	cohort study	China	26/26	41.5±21.8/44.6±16.9	(19/7)/(21/5)	(17/8/1)/(20/5/1)
Liu et al [17]	2016	case control study	China	26/21	44.3±8.35/48.6±10.72	(15/11)/(13/8)	(8/18/0)/(6/15/0)
Zhe et al [19]	2013	case control study	China	80/73	48.5±12.2/43.6±12.4	(63/17)/(51/22)	(34/46/0)/(25/48/0)
Zheng et al [21]	2013	cohort study	China	24/30	43±18.75/47±16	(7/17)/(13/17)	(15/9/0)/(16/14/0)

selected studies are presented in **Table 2**. Results of the quality assessment showed that two out of five studies got 8 stars [17, 21], two got 7 stars [18, 19] and one got 6 stars [20].

Operative time

All five studies described the data of operation time and they were all included for meta-analysis, with a total of 162 patients. There was a significant difference in the heterogeneity analysis of the intraoperative time (P<0.00-001; I^2=86%), then a random-effect model was performed. The patients who underwent LSED had a similar time with those who unde-rwent OSED (MD=31. 12 min, 95% CI: -2.12 to 64.36, P=0.07) (**Figure 2**).

Table 2. Assessment of quality of studies

Study	Quality of selection	Quality of comparability	Quality of outcome/exposure	Total stars (*)
Ando et al	2	3	1	6
Jiang et al	3	3	1	7
Liu et al	3	4	1	8
Zhe et al	3	3	1	7
Zheng et al	3	4	1	8

Blood loss

Blood loss was also described in all five studies. The heterogeneity in these studies was significant (P<0.00001; I^2=90%), so with the random-effect model, we observed that the blood loss was significantly lower in the laparoscopic group than that in the open group (MD=-157.34 ml, 95% CI: -251.91 to -62.77, P=0.001) (**Figure 3**).

Hospital stay after surgery

A total of four studies including 138 patients with liver cirrhosis and portal hypertension described the hospital stay after surgery. Heterogeneity was also detected (P<0.0001; I^2=88%). The pooled outcome using random-effect model indicated that the hospital stay was shorter in the LSED group by 4.35 days than that in the OSED group (MD=-4.35 d, 95% CI: -6.59 to -2.11, P=0.0001) (**Figure 4**).

Time of oral intake

The time of oral intake was evaluated in four studies. Heterogeneity analysis showed significance of the oral intake time (P<0.0001; I^2=88%) and the random-effect model was performed. It was shown that the oral intake time in the LSED group was shorter compared with the OSED group (MD=-1.36 d, 95% CI: -2.2 to -0.52, P=0.001) (**Figure 5**).

Complication rate

Four studies focused on the complication rate after surgery. Homogeneity was detected among studies (P=0.96; I^2=0%) and fixed-effect model meta-analysis showed that, the complication rate in the LSED group was significantly lower than that in OSED group (OR=0.41, 95% CI: 0.20 to 0.84, P=0.01) (**Figure 6**).

Publication bias

The funnel plot of postoperative complications was used to assess the publication bias (**Figure 7**). The funnel plot was basically inverted and funnel-shaped with no obvious asymmetry.

Discussion

Surgery is the main treatment for portal hypertension in patients with liver cirrhosis [22]. Liver transplantation appears to be the most effective treatment for portal hypertension. However, organ shortages and high medical costs limit its broad clinical application. Other treatments of portal hypertension mainly consist of shunt and devascularization. Due to the different etiology of liver cirrhosis, shunt is mainly performed in western countries while devascularization is carried out mainly in Asian countries, especially in China. In this review, all the studies were from Asian countries and most of them were Chinese studies. Splenectomy combined with pericardial devascularization can address the problems of bleeding, leukocyte reduction and thrombocytopenia at the same time and therefore has become the most effective surgical treatment for portal hypertension [23]. OSED has been generally accepted for a long time [24, 25]. However, it is extremely invasive in the aspects of wound pain and blood loss, which may aggravate ascites and hepatic disfunction. Recent researches have shown that LSED has the obvious advantage of being minimally invasive in the treatment of portal hypertension. In this review, clinical comparative studies of LSED versus OSED for portal hypertension and liver cirrhosis were searched in four databases. No randomized controlled trials were included, and ultimately five retrospective studies were included according to the inclusion criterion in the meta-analysis.

A previous meta-analysis showed that LS and LSED had the advantage of minimal invasion compared with OS and OSED [15]. In this meta-analysis, it was shown that the LSED group had similar operative time with the OSED group. However, a previous meta-analysis indicated that the operative time of LSED was longer than that of OSED [26]. This meta-analysis sele-cted

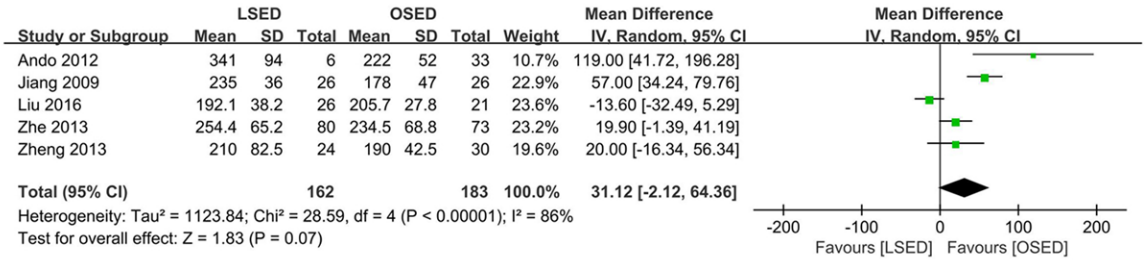

Figure 2. Meta-analysis of assessing the Operative time (min).

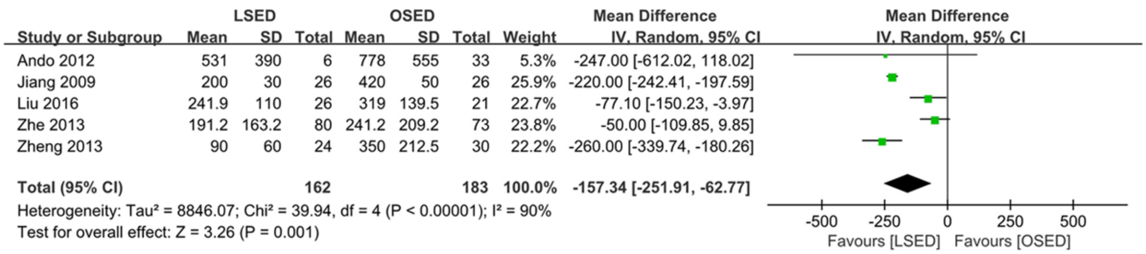

Figure 3. Meta-analysis of assessing the Blood loss (ml).

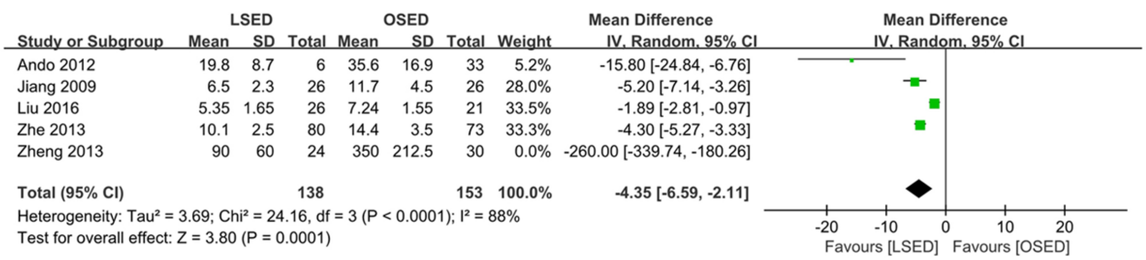

Figure 4. Meta-analysis of assessing Hospital stay after surgery (days).

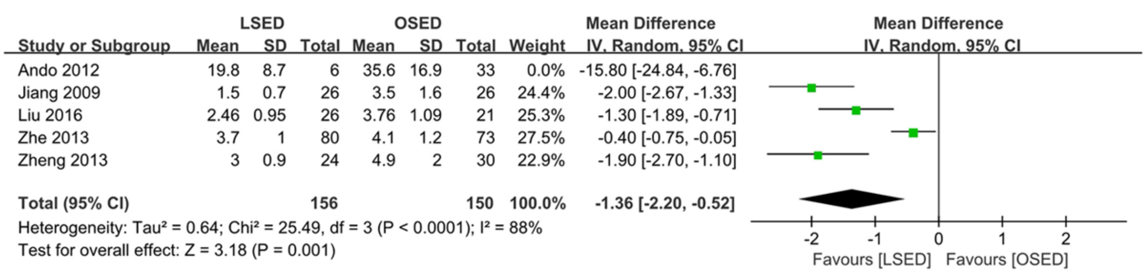

Figure 5. Meta-analysis of assessing Time of oral intake (days).

plenty of studies written in Chinese from different sized institutions and operators were with different laparoscopic proficiency levels which might influence the results. Furthermore, recent improvements in both laparoscopic experience and technology have significantly shortened the laparoscopic operative time. The results of this study showed that the blood loss of LSED was lower than that of the OSED group. There may be two reasons: [1] to prevent bleeding which seriously interfere with the operation sight, more attention is paid; and [2] application of laparoscopic operation instruments, such as ligasure and ultrasonic knife, can reduce the hemorrhage significantly [27]. This meta-analysis revealed that the incidence of

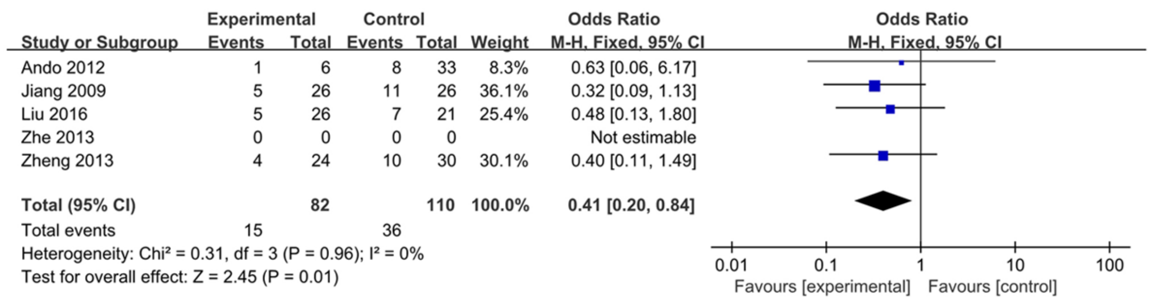

Figure 6. Meta-analysis of assessing Posoperative Complications rate (%).

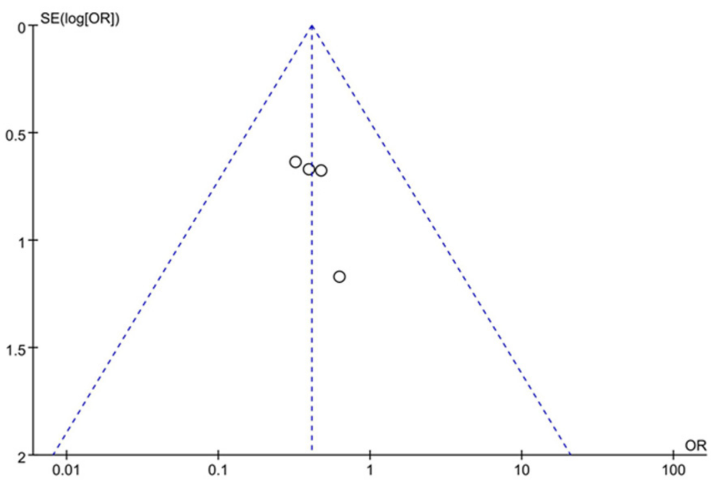

Figure 7. Funnel plot of Postoperative complications.

postoperative complications in the LSED group was lower compared with the OSED group. It was probably because laparoscopic operation has a small incision, less blood loss and little effect on the immune system of patients with minimal invasive advantage. However, portal vein system thrombosis was rarely depicted in the included studies, and a previous study reported that there was a significantly higher incidence of portal vein thrombosis after laparoscopic splenectomy than after open splenectomy [28]. Thus, further research is focusing on this issue. The laparoscopic group has a small incision and less pain, so patients are more likely to get out of bed earlier, which would accelerate recovery of gastrointestinal function. It is in accordance with the results of this meta-analysis. The oral intake time was earlier, and the postoperative stay was shorter in the LSED group than in the OSED group.

This meta-analysis showed that LSED had the advantages of; amount of blood loss, complication rate, oral intake time and hospital stay after surgery compared with OSED. However, studies included in this meta-analysis are all retrospective with a lack of randomized control trials and all from China except one from Japan which lead to limitations of sample source research in the literature and publication bias. Furthermore, the size of the samples was relatively small, reducing the quality of conclusions reached.

In conclusion, this review revealed LSED to be safe and effective in the treatment of liver cirrhosis and portal hypertension. LSED appears to be superior to OSED regarding blood loss, complication rate, oral intake time and postoperative hospital stay. However, in order to evaluate the true value of LSED in the treatment of liver cirrhosis and portal hypertension, larger randomized controlled trials are urgently recommended.

Disclosure of conflict of interest

None.

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