Original Article

Laparoendoscopic single-site versus conventional multiport laparoscopic varicocelectomy: a meta-analysis

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Abstract: Recently, several studies assessed the effectiveness of laparoendoscopic single-site (LESS) varicocelectomy for varicoceles, but the efficacy and potential advantages of LESS compared with conventional multiport laparoscopic (CML) remained controversial. Therefore, the purpose of this systematic review is to evaluate the current evidence regarding the efficiency, safety, and potential advantages of LESS compared with CML in the treatment of patients with varicoceles. Relevant articles published in English were identified by searching PubMed, EMBASE, Cochrane Library, and the ISI Web of Knowledge databases up to October 2015. The Related Articles function was also used to identify relevant manuscripts and references were explored to broaden the search. Primary outcomes (operative time, hospital stay, return to normal activities time, pain score, and cosmetic satisfaction rate) and secondary outcomes (improvements of semen parameters and postoperative complications) were pooled. The odds ratio (OR) and weighted mean difference (WMD) with 95% confidence intervals (CIs) were used to compare dichotomous and continuous variables. Two randomized controlled trials (RCTs) and four non-randomized controlled trial (NRCTs) were eligible. 407 patients were treated, 169 with LESS and 224 with CML. LESS was superior to CML in postoperative pain within 24 h (VAS in 6 h, WMD: -0.56; 95% CI, -0.93, -0.20; P=0.0003; VAS in 24 h, WMD: -0.60; 95% CI, -0.80, -0.39; P<0.00001), return to normal activities time (WMD: -1.31; 95% CI, -2.21, -0.40; P=0.005), and cosmetic satisfaction rate (OR 6.76, 95% CI 2.17, 21.07, P=0.001). Other outcomes were similar. LESS offered a safe and efficient alternative to CML with a less postoperative pain, shorter return to normal activities time and better cosmetic result for patients with varicocelectomy. Due to the inherent limitations of the included studies, future well-designed and high quality RCTs are awaited to confirm and update the findings of this analysis.

Keywords: Laparoendoscopic single-site surgery, conventional multiport laparoscopic, varicocelectomy, meta-analysis

Introduction

Varicoceles are considered to be a major cause of male infertility [1]. Ligation of the internal spermatic vein can improve testicular Leydig cell function, reduces sperm DNA damage and seminal oxidative stress, leading to remarkable improvement of basic sperm parameters [2]. Several surgical procedures have been used to varicocelectomy, including retroperitoneal, inguinal, microscopic, and laparoscopic [3-5]. Laparoscopic varicocelectomy has been recommended as one method of effective and safe to correct the varicocele [6, 7]. Minimally invasive surgery has continued to evolve. To strive for further reduce the morbidity and scar-
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cal efficacy and potential advantages of LESS compared with CML in the treatment of patients with varicoceles.

Methods

Search strategy

A systematic review of the literature was performed in October 2015, without restriction to publication types, or regions, using PubMed, EMBASE, Cochrane Library, and the ISI Web of Knowledge databases. The language was restricted in English. The relevant medical subject heading (MeSH) terms and their combinations were searched in [Title/Abstract]: single site/port/incision, natural orifice transumbilical, and laparoscopic/laparoendoscopic varicocelectomy. The Related Articles function was also used to identify relevant manuscripts and references were explored to broaden the search.

Study selection

The process of study selection was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. Selected studies met all of the following criteria: (1) randomized controlled trails (RCTs) or non-randomized controlled trials (NRCTs); (2) compared LESS and CML; (3) revealed at least one of the outcomes: operative time, hospital stay, postoperative abdominal pain, cosmetic satisfaction, return to normal activities time, semen parameters, hydrocele rate, and recurrence rate. The studies were excluded if: (1) the surgery was not varicocelectomy; (2) single incision was not mentioned; (3) the studies were reported without detailed information of outcomes. When multiple articles describing the same population were published, the article with the most recent or detailed information was selected. The eligibility of all retrieved articles was evaluated by two authors independently. All the disagreements were resolved by discussion or in consultation with a third author.

Data extraction

Data were extracted from all the eligible studies by two of the authors. Primary outcomes between the two surgical approaches were compared including operative time, hospital stay, postoperative abdominal pain, cosmetic satisfaction rate, and return to normal activities time. Pain scores from using a visual analogue scale (VAS) were pooled to evaluate postoperative abdominal pain. Three postoperative time points (6 h, 24 h, and 48 h) were used to evaluate pain. Secondary outcomes evaluated included improvements of semen parameters and postoperative complications. The sperm analyses were collected to assess for improvement of semen parameters. Postoperative complications included postoperative hydrocele rate and recurrence rate.

Quality assessment

The level of evidence was rated for the included studies according to the criteria provided by the Center for Evidence-Based Medicine in Oxford, UK. The methodological quality of RCTs was assessed by Jadad scale (score ranging between 0 and 5, with 0-2 being low, 3-5 high) [18]. The methodological quality of NRCTs was assessed by the Newcastle-Ottawa Scale, which consist of three factors: patient selection, comparability of the study groups, and assessment of outcome; and score ranging between 0 and 9, with 0-2 being low, 3-5 moderate, and 6-9 high [19].

Statistical analysis

All the meta-analyses were performed using Cochrane Review Manager software (Cochrane Collaboration, Oxford, UK, Version 5.2). The odds ratio (OR) and weighted mean difference (WMD) with 95% confidence intervals (CIs) were used to compare dichotomous and continuous variables, respectively. For studies that presented continuous data as means and range values, we calculated the standard deviations using the technique described by Hozo et al. [20]. The inconsistency (I²) statistic was used to evaluate the heterogeneity. Low, moderate and high represented I² values of 40, 70 and 100%, respectively. Where I²≤40% indicates there was no evidence of heterogeneity, the fixed-effects model was used, otherwise the random-effects model was used. The fixed-effects model was used if I²≤40%, which indicates there was no evidence of heterogeneity; otherwise, the random-effects model was used. Detailed subgroup analyses were performed based on different time points to evaluate postoperative VAS scores. The influence of single study on the overall risk estimate was investigated by sequentially removing study to test the robustness of the main results. Funnel plots were used to identify potential publication bias.
Results

Literature search

The initial search obtained 42 articles. After screening the abstracts and the full texts, there were 2 RCTs [12, 13], and 4 NRCTs [14-17] were included in this meta-analysis. A detailed PRISMA flowchart of the selection process was shown in Figure 1.

Study characteristics

Table 1 shows the major characteristics of the 6 studies. Of the 6 studies, 2 were performed in Italy [16, 17], 1 were performed in the USA [15], 1 in Germany [14] and the remaining in China [13] and Korea [12] respectively, during the period between 2012 and 2015. The sample size of included studies ranged from 24 to 99 (407 in total). 169 patients were treated with LESS and 238 patients were treated with CML. Four studies [14-17] used commercial single-port devices (ie, X-Cone Port, TriPort, and SILS Port), and two studies [12, 13] used homemade devices. According to Jadad scale for RCTs, one study scored 4 points, and another study scored 3 points (Table 2). The quality of NRCTs according to Newcastle-Ottawa Scale, one study scored 5 points and another three studies scored 6 points (Table 2).

Primary outcome: operative time

All the 6 studies reported operative time for the 407 included patients. There was no significant difference between the LESS and CML groups (WMD: -6.71; 95% CI, -14.48 to 1.06; P=0.09) (Figure 2).

Primary outcome: length of hospital stay

There were 4 studies [12-14, 17] reported length of hospital stay in 295 patients, and the pooled data showed no significant differences between the LESS and CML groups (WMD: -0.91, 95% CI -1.95 to 0.12, P=0.08) (Figure 3).

Primary outcome: VAS scores

Figure 4 lists the postoperative VAS scores at different time points and the result showed significant lower VAS scores in the LESS group than the CML group (WMD: -0.43; 95% CI, -0.66 to -0.20; P=0.0002). In the results of subgroup analyses, 2 studies reported [13, 16] postoperative VAS scores in 6 hour in 159 patients, and the pooled data showed a significant lower VAS scores in the LESS group than the CML group (WMD: -0.56; 95% CI, -0.93 to -0.20; P=0.0003), 4 studies [12-14, 16] compared postoperative VAS in 24 hour in 340 patients, and lower VAS scores was showed in LESS group (WMD: -0.60; 95% CI, -0.80 to -0.39; P<0.00001). The pooled data of 3 studies [12-14] showed that there was no significant statistic difference between the LESS and CML groups on postoperative VAS in 48 hour in 271 patients (WMD: -0.21; 95% CI, -0.71 to -0.29; P=0.41).

Primary outcome: return to normal activities time

There were 3 studies [12, 13, 17] reported return to normal activities time in 196 patients, and the pooled data showed a significant shorter reported return to normal activities time in the LESS group than the CML group (WMD: -11.63; 95% CI, -18.93 to -4.34; P=0.0013).
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Table 1. Characteristics of the studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Study/year</th>
<th>Country</th>
<th>Surgical approach</th>
<th>Patients</th>
<th>Port</th>
<th>Instruments</th>
<th>Ligation approach</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seung 2012</td>
<td>Korea</td>
<td>LESS</td>
<td>39</td>
<td>CML</td>
<td>A homemade single-port</td>
<td>Flexible laparoscopic instruments</td>
<td>Hem-o-lok clips</td>
</tr>
<tr>
<td>Frank 2013</td>
<td>Germany</td>
<td>LESS</td>
<td>43</td>
<td>CML</td>
<td>Conventional multiple port</td>
<td>Prebent laparoscopic instrument</td>
<td>10-mm Dexon clips or Hem-o-lok clips</td>
</tr>
<tr>
<td>Wang 2014</td>
<td>China</td>
<td>LESS</td>
<td>79</td>
<td>CML</td>
<td>Conventional multiport</td>
<td>10-mm trocar and 6-mm working channel</td>
<td>5-mm rigid instrument, a 2-0 silk suture and needle</td>
</tr>
<tr>
<td>Danesh 2014</td>
<td>USA</td>
<td>LESS</td>
<td>11</td>
<td>CML</td>
<td>Conventional multiport</td>
<td>Olympus TriPort</td>
<td>5-mm flexible laparoscope EndoEye camera system</td>
</tr>
<tr>
<td>Antonio 2014</td>
<td>Italy</td>
<td>LESS</td>
<td>32</td>
<td>CML</td>
<td>Conventional multiport</td>
<td>SILS port</td>
<td>Two curved Rochester-Pean clamps</td>
</tr>
<tr>
<td>Salvatore</td>
<td>Italy</td>
<td>LESS</td>
<td>10</td>
<td>CML</td>
<td>Conventional multiport</td>
<td>SILS port</td>
<td>5-mm flexible laparoscope EndoEye camera system</td>
</tr>
</tbody>
</table>

LESS, laparoendoscopic single site; CML, conventional multiport laparoscopic; NA, not available; Outcome: 1 operative time, 2 hospital stay, 3 visual analogue scale score, 4 cosmetic satisfaction, 5 return to normal activities time, 6 semen parameters, 7 hydrocele, 8 recurrence.

Table 2. Quality assessment of the studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Study/year</th>
<th>Study type</th>
<th>Quality assessment scale</th>
<th>Quality score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seung 2012</td>
<td>RCT</td>
<td>Jadad scale</td>
<td>3 out of 5 points</td>
</tr>
<tr>
<td>Frank 2013</td>
<td>NRCT</td>
<td>Newcastle-Ottawa Scale</td>
<td>6 out of 9★★</td>
</tr>
<tr>
<td>Wang 2014</td>
<td>RCT</td>
<td>Jadad scale</td>
<td>4 out of 5 points</td>
</tr>
<tr>
<td>Danesh 2014</td>
<td>NRCT</td>
<td>Newcastle-Ottawa Scale</td>
<td>5 out of 9★★</td>
</tr>
<tr>
<td>Antonio 2014</td>
<td>NRCT</td>
<td>Newcastle-Ottawa Scale</td>
<td>6 out of 9★★</td>
</tr>
<tr>
<td>Salvatore</td>
<td>NRCT</td>
<td>Newcastle-Ottawa Scale</td>
<td>6 out of 9★★</td>
</tr>
</tbody>
</table>

RCT, randomized controlled trial; NRCT, non-randomized controlled trial.

-1.31; 95% CI, -2.21 to -0.40; P=0.005) (Figure 5).

Primary outcome: cosmetic satisfaction

Three studies [12, 14, 17] compared cosmetic satisfaction rate in 188 patients, and a higher cosmetic satisfaction rate was associated with LESS group (95.6% and 74.2%; OR 6.76, 95% CI 2.17 to 21.07, P=0.001) (Figure 6).

Secondary outcome: semen parameters improvements

The semen parameters, which include sperm count, motility, and normal morphology, were analyzed in 2 studies [12, 13]. The pooled data showed that there was no significant statistic difference on count improvement (WMD: 0.25; 95% CI, -1.40 to 1.91; p=0.76), motility improvement (WMD: -0.15; 95% CI, -2.35 to 2.05; p=0.89), and normal morphology improvement (WMD: 0.05; 95% CI, -1.41 to 1.51; P=0.95) (Figure 7).

Secondary outcome: postoperative complications

Pooling the data from 5 studies [12-16] that assessed postoperative hydrocele rate in 380 patients showed no significant difference between the LESS and CML groups (2.53% and 3.6%; OR: 0.83; 95% CI 0.26 to 2.71; p=0.76) (Figure 8A). 3 studies [12, 13, 16] reported postoperative recurrence rate in 238 patients, and the pooled data showed no significant statistic difference (2.36% and 2.70%; OR: 0.85, 95% CI 0.17 to 4.30, p=0.84) (Figure 8B).

Sensitivity analysis and publication bias

Sensitivity analysis was performed by sequentially removing each study, the result showed that when the study (Antonio 2014) was removed, the result of recurrence rate demonstrated no significant statistic difference between the two groups (OR 1.04, 95% CI 0.14-7.55, p=0.97). In addition, no other significance of pooled ORs and 95% CIs were influenced by
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<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>LESS Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seung 2012</td>
<td>48.1</td>
<td>11.7</td>
<td>39</td>
<td>48.3</td>
<td>14.6</td>
<td>43</td>
<td>16.3%</td>
<td>-0.30 [-0.00, 5.40] 2012</td>
<td></td>
</tr>
<tr>
<td>Frank 2013</td>
<td>59.1</td>
<td>15.6</td>
<td>20</td>
<td>51.2</td>
<td>14.4</td>
<td>79</td>
<td>15.3%</td>
<td>7.90 [0.40, 15.40] 2013</td>
<td></td>
</tr>
<tr>
<td>Salvatore 2014</td>
<td>45.4</td>
<td>8.5</td>
<td>10</td>
<td>88.3</td>
<td>9.2</td>
<td>14</td>
<td>15.5%</td>
<td>-42.90 [-50.04, -35.76] 2014</td>
<td></td>
</tr>
<tr>
<td>Antonio 2014</td>
<td>22.6</td>
<td>2.68</td>
<td>44</td>
<td>21</td>
<td>2.29</td>
<td>25</td>
<td>17.8%</td>
<td>1.00 [-0.20, 2.20] 2014</td>
<td></td>
</tr>
<tr>
<td>Danesh 2014</td>
<td>46.1</td>
<td>4.1</td>
<td>11</td>
<td>55</td>
<td>4.5</td>
<td>32</td>
<td>17.5%</td>
<td>-9.00 [-11.88, -6.12] 2014</td>
<td></td>
</tr>
<tr>
<td>Wang 2014</td>
<td>36.7</td>
<td>7.7</td>
<td>45</td>
<td>37.6</td>
<td>4.8</td>
<td>45</td>
<td>17.5%</td>
<td>1.10 [-1.55, 3.75] 2014</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 169 238 100.0% -6.71 [-14.48, 1.06]

Heterogeneity: Tau^2 = 87.85; Chi^2 = 180.48, df = 5 (P < 0.00001); I^2 = 97%
Test for overall effect: Z = 1.69 (P = 0.09)

**Figure 2.** Forest plot and meta-analysis of operative time. LESS, laparoendoscopic single site; CML, conventional multiport laparoscopic.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>LESS Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Length of Hospital Stay</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seung 2012</td>
<td>4.5</td>
<td>1.1</td>
<td>39</td>
<td>3.9</td>
<td>1.5</td>
<td>43</td>
<td>28.4%</td>
<td>0.45 [0.01, 0.89] 2012</td>
<td></td>
</tr>
<tr>
<td>Frank 2013</td>
<td>1.6</td>
<td>0.7</td>
<td>20</td>
<td>1.8</td>
<td>0.5</td>
<td>79</td>
<td>28.0%</td>
<td>-0.36 [-0.88, 0.13] 2013</td>
<td></td>
</tr>
<tr>
<td>Wang 2014</td>
<td>1.9</td>
<td>0.5</td>
<td>45</td>
<td>2.1</td>
<td>0.5</td>
<td>45</td>
<td>28.5%</td>
<td>-0.40 [-0.81, 0.02] 2014</td>
<td></td>
</tr>
<tr>
<td>Salvatore 2014</td>
<td>0.7</td>
<td>0.3</td>
<td>10</td>
<td>2.1</td>
<td>0.2</td>
<td>14</td>
<td>15.0%</td>
<td>-5.50 [-7.38, -3.61] 2014</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 114 181 100.0% -0.91 [-1.95, 0.12]

Heterogeneity: Tau^2 = 0.94; Chi^2 = 40.00, df = 3 (P < 0.00001); I^2 = 93%
Test for overall effect: Z = 1.73 (P = 0.08)

**Figure 3.** Forest plot and meta-analysis of length of hospital stay. LESS, laparoendoscopic single site; CML, conventional multiport laparoscopic.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>LESS Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>VAS Scores</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seung 2012</td>
<td>6.2</td>
<td>0.8</td>
<td>42</td>
<td>6.0</td>
<td>0.7</td>
<td>40</td>
<td>7.9%</td>
<td>-0.10 [-0.75, 0.55] 2012</td>
<td></td>
</tr>
<tr>
<td>Frank 2013</td>
<td>6.2</td>
<td>0.9</td>
<td>45</td>
<td>6.0</td>
<td>0.7</td>
<td>45</td>
<td>12.7%</td>
<td>-0.40 [-0.82, 0.02] 2014</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>125</td>
<td>70</td>
<td>23.4%</td>
<td>6.08 [-0.93, -0.20] 2014</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau^2 = 0.02; Chi^2 = 1.32, df = 1 (P = 0.25); I^2 = 24%
Test for overall effect: Z = 3.00 (P = 0.003)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>LESS Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>VAS Scores</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seung 2012</td>
<td>6.2</td>
<td>0.9</td>
<td>42</td>
<td>6.0</td>
<td>0.7</td>
<td>40</td>
<td>7.9%</td>
<td>-0.10 [-0.75, 0.55] 2012</td>
<td></td>
</tr>
<tr>
<td>Frank 2013</td>
<td>6.2</td>
<td>0.9</td>
<td>45</td>
<td>6.0</td>
<td>0.7</td>
<td>45</td>
<td>12.7%</td>
<td>-0.40 [-0.82, 0.02] 2014</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>125</td>
<td>70</td>
<td>23.4%</td>
<td>6.08 [-0.93, -0.20] 2014</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau^2 = 0.02; Chi^2 = 1.32, df = 1 (P = 0.25); I^2 = 24%
Test for overall effect: Z = 3.00 (P = 0.003)

**Figure 4.** Forest plot and meta-analysis of VAS scores. VAS, visual analogue scale; LESS, laparoendoscopic single site; CML, conventional multiport laparoscopic.

**Figure 9** shows a funnel plot of the studies included in this meta-analysis that reported the omission of any single study, this suggested that the results of this meta-analysis were stable.
**Discussion**

LESS is a minimally invasive technique that brings a revolution of technique to surgical postoperative hydrocele and recurrence rate. All studies lie inside the 95% CIs, with an even distribution around the vertical, indicating no obvious publication bias.

### Figure 5

Forest plot and meta-analysis of return to normal activities time. LESS, laparoendoscopic single site; CML, conventional multiport laparoscopic.

### Figure 6

Forest plot and meta-analysis of cosmetic satisfaction rate. LESS, laparoendoscopic single site; CML, conventional multiport laparoscopic.

### Figure 7

Forest plot and meta-analysis of semen parameters improvements, including sperm count improvements (A), motility improvements (B), and normal morphology improvements (C). LESS, laparoendoscopic single site; CML, conventional multiport laparoscopic.
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This meta-analysis of 2 RCTs and 4 NRCTs including 407 patients comparing the efficacy of LESS and CML for varicoceles demonstrated that LESS was safe, with significantly reduced postoperative pain, shorter return to normal activities time and better cosmetic results. There were no significant differences in operative time, length of hospital stay, improvements of semen parameters, and postoperative complications.

In some previous studies, the operative time seems to be longer in LESS than CML, because of the much narrower space for operation, and the interference of different instruments [9-11]. Recently, some current studies reported that there were no significant differences in opera-
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In conclusion, this meta-analysis indicates that LESS for varicoceles may be with reduced post-operative pain, shorter return to normal activities time and better cosmetic satisfaction without compromising surgical safety. The two surgical approaches appear to be equivalent in terms of operative time, length of hospital stay, improvements of semen parameters, and post-operative complications. Nevertheless, despite our rigorous methodology, the inherent limitations of included studies prevent us from reaching definitive conclusions, and the role of LESS for varicoceles remains to be defined. Future well-designed, large, prospective, randomized, multi-center RCTs are awaited to confirm and update the findings of our current meta-analysis.

Acknowledgements

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Disclosure of conflict of interest

None.

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