

## Meta-analysis

# Video endoscopic inguinal lymphadenectomy and open inguinal lymphadenectomy for penile cancer in China: a systematic review

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**Background:** To evaluate the effect between video endoscopic inguinal lymphadenectomy (VEIL) and open inguinal lymphadenectomy (OIL) for penile cancer to provide the evidence-based basis for the selection of the clinical therapy schemes.

**Methods:** The related clinical controlled trial literatures on the effective comparison of VEIL and OIL were retrieved from the databases of CNKI and Wanfang database. The screening was independently performed by reviewer according to the including and excluding criteria. The related data were extracted and the meta-analysis performed by the RevMan 5.3 software.

**Results:** A total of 9 trials were included. There were 335 cases of inguinal lymphadenectomies, in which 151 cases were VEIL and 184 cases were OIL. The meta-analysis results showed that there were no statistical differences between the two types of operations in terms of the operative time (WMD=28.74, 95% CI-4.12~61.60, P=0.09), but the difference between VEIL and OIL in term of intra-operative blood loss (WMD=-29.24, 95% CI-55.24~-22.89, P<0.01), postoperative hospital stays (WMD=-3.43, 95% CI-5.07~-1.80, P<0.01), postoperative drainage time (WMD=-3.81, 95% CI-5.38~-2.23, P<0.01), surgical complications (Number of sides OR=0.53, 95% CI 0.34~0.81, P<0.01; Number of cases OR=0.36, 95% CI 0.24~0.54, P<0.01).

**Conclusion:** VEIL has approximately the same time of operation to OIL, but has less intra-operative blood loss, hospital stay, postoperative drainage time and surgical complications.

**Keywords:** Penile cancer, laparoscopes, groin, lymph node dissection.

**Introduction**

Traditional open inguinal lymphadenectomy (OIL) is a standard surgical procedure for penile cancer with local lymph node metastasis, but the incidence of postoperative complications is high, including wound infection, subcutaneous hematoma, flap necrosis, long-term nonunion of incision, edema of the lower extremities, and so on. Complications with modified inguinal lymphadenectomy is decreased but with the risk of residual lymph node recurrence has remained<sup>1</sup>. Video endoscopic inguinal lymphadenectomy (VEIL) reduces the incidence of postoperative complications and does not increase the difficulty of the operation, which can be popularized quickly<sup>2</sup>. What needs to be specifically mentioned is that large Chinese hospitals are making VEIL more promising and opting this in

practice. However, there is a lack of objective evaluation and comparison of VEIL carried out specifically by Chinese surgeons. This paper uses the principles and methods of evidence-based medicine to make an objective assessment of the case-control study published in Chinese, to explore whether VEIL is better than OIL in China, and then provide reference for clinical promotion and application.

**Materials and Methods****Bibliography Retrieval**

The computers were used to search for China National Knowledge Infrastructure (CNKI) and Wanfang Database. The retrieval time was from January 1, 2008 to December 30, 2017. The investigator independently searched the literature on clinical comparative study

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and clinical trial data comparing the efficacy of VEIL and OIL. At the same time, by manually searching the literature references and meeting materials, relevant authors were contacted. For repeated publications, the first and most comprehensive report was included. Chinese search terms: penile cancer, video endoscopic inguinal lymphadenectomy were used.

### Methods

**Inclusion and exclusion criteria** Inclusion criteria: All the literatures comparing the clinical efficacy of VEIL and OIL, whether or not blinded, were included. However, the language is limited to Chinese. Patients with VEIL and OIL do not distinguish between age, gender and race. The operative time, intra-operative blood loss, hospital stay, postoperative drainage time, and surgical complications were compared between VEIL and OIL. Exclusion indicators: No comparison study was conducted and reported only the treatment method. Only the summaries were available and no full conference papers are available. The important information is not perfect and does not correspond with the author. When two studies from the same institution reported similar follow-up periods and the same target results, better quality or more comprehensive information was included.

### Literature quality assessment and data extraction

**Literature quality assessment:** According to the evaluation criteria of the Cochrane evaluation manual, the literature of the study was independently evaluated. The inconsistent places were involved and agreed through the discussion by other reviewers. **Literature data extraction:** Read the literature in detail, extract the relevant data independently, and convert data to the same unit.

### Statistical processing

Meta-analysis was carried out with RevMan5.3 software provided by Cochrane international collaboration network. When the results were described, the continuous variables used a weighted mean difference (WMD), and the binary variables used an odds ratio (OR) and a 95% confidence interval (CI). Test the heterogeneity of the included studies, If  $P \geq 0.1$ ,  $I^2 \leq 50\%$ , indicating no statistical heterogeneity between studies, using a fixed-effects model. If  $P < 0.1$ ,  $I^2 > 50\%$ , it means that each study has heterogeneity, analyzes the source of its heterogeneity, and if it cannot solve or cannot determine the source of heterogeneity, the random effect model is used. If necessary, sensitivity analysis is used to

determine the stability of the results. Descriptive analysis is used for indicators that cannot be combined. When  $P < 0.05$ , the difference was statistically significant.

## Results

### Literature retrieval results

A total of 158 literatures were initially searched. After further reading of the full text and quality assessment, 9 articles were eventually included in the literature according to the inclusion and exclusion criteria<sup>3-11</sup>. One of them was randomized controlled trials and 8 were retrospective clinical controlled trials. A total of 335 cases, group VEIL and group OIL were 151 cases and 184 cases respectively. Summarized in Table 1.

### Results of the meta-analysis

#### Intraoperative blood loss

A total of 8 studies<sup>3-10</sup> reported intraoperative blood loss, 132 in the VEIL group and 165 in the OIL group. The effect index is expressed in WMD,  $P < 0.01$ ,  $I^2 = 92\%$ , using random effect model. The results showed that the difference of blood loss between VEIL and OIL was statistically significant (WMD = -29.24, 95% CI -55.24 ~ -22.89,  $P < 0.01$ ) (Figure 1).

**Hospital stay** A total of 8 studies<sup>3-10</sup> reported hospital stays, 132 in the VEIL group and 165 in the OIL group. The effect index is expressed in WMD,  $P < 0.01$ ,  $I^2 = 94\%$ , using random effect model. The results showed that the difference of hospital stays between VEIL and OIL was statistically significant (WMD = -3.43, 95% CI -5.07 ~ -1.80,  $P < 0.01$ ) (Figure 2).

**Operative time** A total of 8 studies<sup>3-6,8-10</sup> reported operative time, 124 in the VEIL group and 161 in the OIL group. The effect index is expressed in WMD,  $P < 0.01$ ,  $I^2 = 98\%$ , using random effect model. The results showed that the difference of operative time between VEIL and OIL was no statistically significant (WMD = 28.74, 95% CI -4.12 ~ 61.60,  $P = 0.09$ ) (Figure 3).

**Postoperative drainage time** A total of 8 studies<sup>3-4,6-11</sup> reported postoperative drainage time, 139 in the VEIL group and 170 in the OIL group. The effect index is expressed in WMD,  $P < 0.01$ ,  $I^2 = 94\%$ , using random effect model. The results showed that the difference of postoperative drainage time between VEIL and OIL was statistically significant (WMD = -3.81, 95% CI -5.38 ~ -2.23,  $P < 0.01$ ) (Figure 4).

**Surgical complications (number of sides)** A total of 3 studies<sup>3-4,6</sup> reported surgical complications (number of

sides), 104 in the VEIL group and 104 in the OIL group. The effect index is expressed in OR,  $P < 0.96$ ,  $I^2 = 0\%$ , using fixed effect model. The results showed that the difference of surgical complications (number of sides) between VEIL and OIL was statistically significant (OR=0.53, 95%CI 0.34~0.81,  $P < 0.01$ ) ( Figure 5).

**Surgical complications (number of cases)**

A total of 6 studies<sup>5,7-11</sup> reported surgical complications (number of cases), 99 in the VEIL group and 132 in the OIL group. The effect index is expressed in OR,  $P < 0.92$ ,  $I^2 = 0\%$ , using fixed effect model. The results showed that the difference of surgical complications(number of cases) between VEIL and OIL was statistically significant(OR=0.36, 95% CI 0.24~0.54,  $P < 0.01$ ) ( Figure 6).

**Discussion**

OIL is a standard surgical procedure for penile cancer with local lymph node metastasis, but the incidence of postoperative complications is very high. VEIL has been rapidly promoted and the incidence of postoperative complications has decreased significantly. Now robot assisted laparoscopic inguinal lymphadenectomy is also being applied in clinic, and it is considered a feasible technology<sup>12</sup>. Although VEIL is a new surgical method for the treatment of penile cancer, it has been proven feasible, safe and effective, but the number of cases reported worldwide is few, so it is too early to use it as a standard operation. More multicenter, large sample and long follow-up prospective control studies are needed to further evaluate its effect. The value of clinical treatment of penile cancer still requires clinicians to explore many aspects of VEIL<sup>13</sup>. The results of Meta-analysis in this study showed that VEIL has approximately the same time of operation to OIL, but has less intra-operative blood loss, hospital stays, postoperative drainage time and surgical complications. The analysis may be related to the rapid promotion of VEIL in China in recent years,

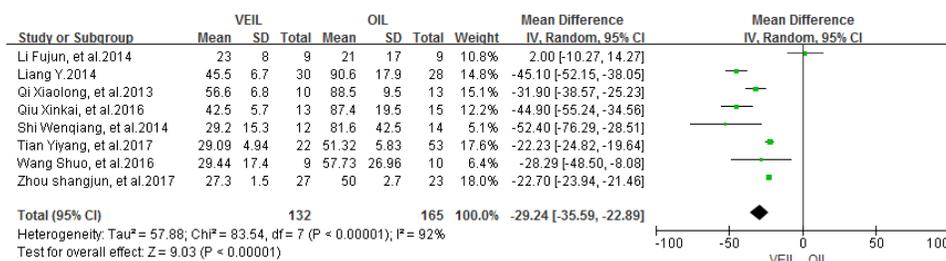
the skilled operation of surgeons, and the application of energy devices such as ultrasonic scalpel. It may also be the reason that the VEIL operation is carried out in the subcutaneous space, the skin wound in the groin area is small, the influence of the skin blood supply in the groin area is small, the bleeding in the operation is reduced, the time of hospitalization and the drainage time are reduced, and the common skin flap necrosis after the operation of OIL can also be effectively reduced. The following deficiencies in this study are as follows: Firstly, only 1 randomized controlled trials were included in the study. The other studies were retrospective controlled clinical trials. Secondly, this study is only for Chinese doctors published in Chinese studies, and it also needs to further analyze the research published by Chinese doctors in other languages. Finally, the long-term effects of these studies are not yet evaluated and need further confirmation of higher quality, larger sample and multicenter randomized controlled trials.

**Conflicts of Interest**

The Authors declares no conflict of interest.

**Table 1 Inclusion of study authors, year and patient grouping (n)**

Authors	Year	VEIL cases (n=151)	OILcases (n=184)
Liang Y.	2014	30	28
Li Fujun, et al.	2014	9	9
Shi Wenqiang, et al.	2014	12	14
Qiu Xinkai, et al.	2016	13	15
Zhou shangjun, et al.	2017	27	23
Tian Yiyang, et al.	2017	22	53
Qi Xiaolong, et al.	2013	10	13
Wang Shuo, et al.	2016	9	10
Liu Hannan.	2016	19	19



**Figure 1 Meta-analysis of intraoperative blood loss in VEIL and OIL**

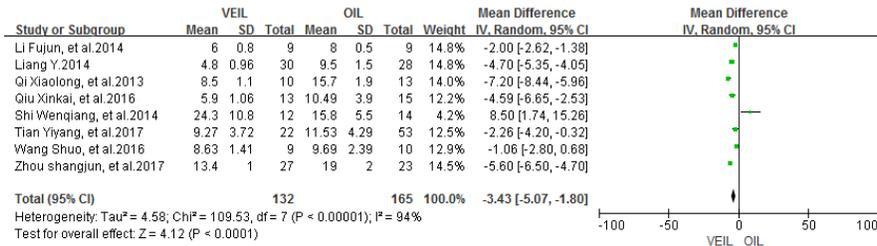


Figure 2 Meta-analysis of hospital stays in VEIL and OIL

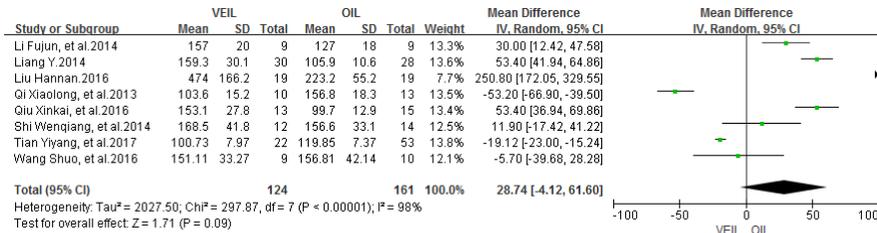


Figure 3 Meta-analysis of operative time in VEIL and OIL

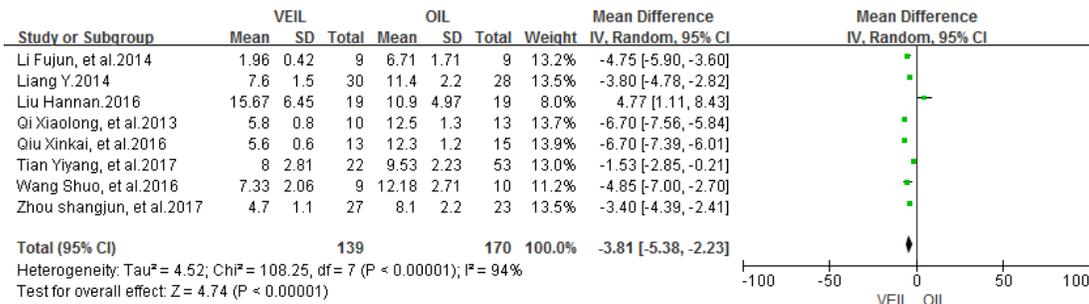


Figure 4 Meta-analysis of postoperative drainage time in VEIL and OIL

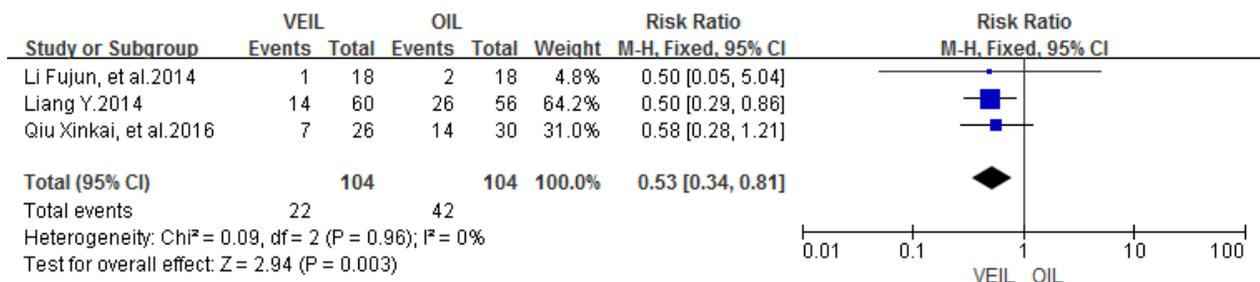


Figure 5 Meta-analysis of surgical complications(number of sides) in VEIL and OIL

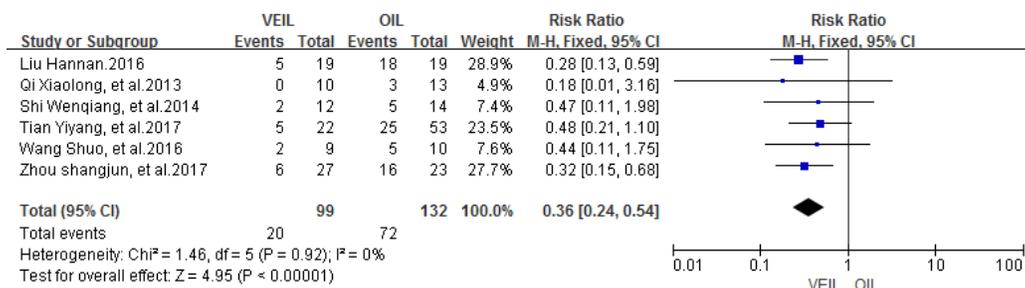


Figure 6 Meta-analysis of surgical complications(number of cases) in VEIL and OIL

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