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Is laparoscopic approach for pancreatic insulinomas safe? Results of a systematic review and meta-analysis

*An-Ping Su, MD,[1] Neng-Wen Ke, MD,[1] Yi Zhang, MD,[1] Xu-Bao Liu, MD, Wei-Ming Hu, MD, Bo-Le Tian, MD, and Zhao-Da Zhang, MD**

Department of Hepatobiliopancreatic Surgery, West China Hospital, Sichuan University, Chengdu, Sichuan Province, China

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ABSTRACT

Background: No consensus exists as to whether laparoscopic treatment for pancreatic insulinomas (PIs) is safe and feasible. The aim of this meta-analysis was to assess the feasibility, safety, and potential benefits of laparoscopic approach (LA) for PIs. The abovementioned approach is also compared with open surgery.

Methods: A systematic literature search (MEDLINE, EMBASE, Cochrane Library, Science Citation Index, and Ovid journals) was performed to identify relevant articles. Articles that compare the use of LA and open approach to treat PI published on or before April 30, 2013, were included in the meta-analysis. The evaluated end points were operative outcomes, postoperative recovery, and postoperative complications.

Results: Seven observational clinical studies that recruited a total of 452 patients were included. The rates of conversion from LA to open surgery ranged from 0%–41.3%. The meta-analysis revealed that LA for PIs is associated with reduced length of hospital stay (weighted mean difference, −5.64; 95% confidence interval [CI], −7.11 to −4.16; $P < 0.00001$). No significant difference was observed between LA and open surgery in terms of operation time (weighted mean difference, 2.57; 95% CI, −10.91 to 16.05; $P = 0.71$), postoperative mortality, overall morbidity (odds ratio [OR], 0.64; 95% CI, 0.35–1.17; $P = 0.14$], incidence of pancreatic fistula (OR, 0.86; 95% CI, 0.51–1.44; $P = 0.56$), and recurrence of hyperglycemia (OR, 1.81; 95% CI, 0.41–7.95; $P = 0.43$).

Conclusions: Laparoscopic treatment for PIs is a safe and feasible approach associated with reduction in length of hospital stay and comparable rates of postoperative complications in relation with open surgery.

1. Introduction

Pancreatic insulinoma (PI), which was first described by Whipple and Frantz [1], is the most common functional islet cell tumor, with annual incidence of one to four in every 1 million persons [2]. It occurs in all age groups but peaks during the third to fifth decade of life [3]. PI is often characterized by fasting hypoglycemia and neuroglycopenic symptoms, including sweating, tachycardia, fatigue, headache, dizziness, and coma [4,5]. Diagnosis can be confirmed by determining if the symptoms indicated in Whipple triad exist [1]. PI is usually misdiagnosed in clinical practice, especially when the tumor is <1 cm in diameter because of the rarity and aspecific clinical presentation of the disease [6]. The reported average

* *Corresponding author*. Department of Hepatobiliopancreatic Surgery, West China Hospital, Sichuan University, Chengdu 610041, Sichuan Province, China. Tel/fax: +86 28 85422475.
E-mail address: zhaodazhang@yeah.net (Z.-D. Zhang).
[1] These authors contributed equally to this study.
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duration of symptoms before correct diagnosis is 46.2 mo. The number of reported cases continued to increase in recent years even with the advances in radiographic techniques and familiarity by surgeons.

Surgical resection is the only effective cure for PIs [6–8]. Surgical approaches mainly include enucleation, partial or total pancreatic resection, and pancreaticoduodenectomy. Before the advent of laparoscopy, open approach (OA) was regarded as the most popular method for the treatment of PIs. The general features of PIs, such as small size, high benignity rate, and sporadic nature, make these tumors suitable for laparoscopic treatment [4]. Recent developments in laparoscopic techniques have allowed surgeons to treat PIs laparoscopically. A number of studies reported that this procedure can provide patients the benefits of invasive surgery [9–12]. Nevertheless, laparoscopic approach (LA) remains uncommon because of the anatomic location of the pancreas, technical difficulties in pancreatic surgery, and the need for highly experienced surgeons. LA is reported as a feasible and safe operation only in small number of patients [13–18]. In addition, multiple insidious lesions may not be determined during LA because manual palpation is not conducted. The feasibility and safety of laparoscopic treatment for PIs continue to be debated to date. Therefore, a systematic and comprehensive analysis of the existing evidence on LA and OA must be conducted to determine whether LA is safe and feasible for PIs.

2. Methods

2.1. Inclusion and exclusion criteria

All included studies fulfill the following criteria: (1) published on humans in English, (2) provide a clear documentation of the operative approach as "laparoscopic" or "open," (3) report the outcomes after surgery, and (4) when two or multiple studies are published by the same institution and/or authors, either the higher quality study or the one with the most recent evidence is included in the meta-analysis. Studies were excluded from the analysis if (1) appropriate data, such as case reports, letters, reviews, and commentaries, cannot be extracted; (2) absence of control groups; (3) laparoscopic and open surgeries were performed for pancreatic endocrine neoplasms with PIs; and (4) the number of cases is <10.

2.2. Search strategies and identification of trials

A systematic literature search (MEDLINE, EMBASE, Cochrane Library, Science Citation Index, and Ovid journals) was performed to identify relevant articles. Randomized controlled trials and observational clinical studies (OCSs) that compared LA and OA for PIs published on or before April 30, 2013, were included in the analysis. The following medical search headings were used: "laparoscopy," "minimally invasive surgery," "open approach," "insulinoma," and "comparative study." The combinations of these headings and similar other headings were also searched for, including "laparoscopic approach," "minimally invasive treatment," and "laparoscopic treatment." A personal search was also performed with reference lists of the retrieved relevant articles and reviews to identify additional trials and make sure that all the potential studies are included. Two researchers (N.-W.K. and Z.Y.) independently scanned the title and abstract of each publication to identify eligible studies. Full articles were then obtained for detailed evaluation. Any disagreement in the selection process was resolved through a discussion. If this procedure failed, a third person (Z.-D.Z.) adjudicated.

2.3. Outcome evaluation

Different outcomes were used to compare LA and OA. Operation outcomes included operation time and intraoperative blood loss. Postoperative outcomes included mortality, overall morbidity, pancreatic fistula (PF), intra-abdominal abscess/infection, postoperative hemorrhage, reoperation, length of postoperative gastrointestinal function recovery, length of mean hospital stay, hospitalization cost, and recurrence.

2.4. Data extraction and quality assessment

Two researchers (N.-W.K. and Z.Y.) independently extracted data from all eligible studies with standardized forms. Data extracted from each study included the first author, study period, study design, participant characteristics, and operative and postoperative outcomes. Disagreements were resolved in the same method as the one mentioned previously. Newcastle–Ottawa scale was modified to fit the requirements of this study. The scale was then used to assess the quality of the eligible studies [19]. The maximum scores obtained for patient selection, comparability of the study groups, and outcome categories were 3, 4, and 2, respectively. A study is considered high in quality if the quality score is ≥ 6 [20].

2.5. Statistical analysis

Meta-analysis was performed according to the recommendations of the Cochrane Collaboration and the guidelines provided by the Quality of Reporting of Meta-analyses [21,22]. Statistical analysis of dichotomous variables was performed with odds ratio (OR) as the summary statistic. Continuous variables were analyzed through weighted mean difference (WMD). Both dichotomous and continuous variables were reported with 95% confidence intervals (CIs). OR represents the odds of an adverse event occurring in the LA group in reference to the OA group; the ratio is considered statistically significant at $P < 0.05$ if 95% CI does not include the value 1. WMD summarizes the difference between the two groups in the continuous variables; it is considered statistically significant at $P < 0.05$ if 95% CI does not cross the value 0. Heterogeneity between studies was measured with $\chi 2$ and I^2. $I^2 > 50\%$ is considered statistically significant. Either fixed-effects or random-effects model was applied to calculate the pooled effect based on heterogeneity. However, random-effects model was used first to assess heterogeneity. Subgroups were used for sensitivity analysis, and a funnel plot was used to identify publication bias based on the morbidity and major complication of PF. Analysis was conducted with the statistical software Review Manager, version 5.0 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008).