Minimally-Invasive vs Open Pancreaticoduodenectomy: Systematic Review and Meta-Analysis

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Laparoscopic approaches are routinely used for a variety of procedures in general surgery and various surgical specialties including surgical oncology. Since publication of the first series of laparoscopic cholecystectomy in the late 1980s, the field of minimally invasive surgery (MIS) has expanded dramatically and is now regarded as an established specialty. Many oncologic procedures have proved not only feasible and safe, but oncologically equivalent to traditional open procedures regarding both immediate operative variables of interest (margins, lymph node retrieval, and morbidity) and long-term outcomes.[1-10]

Pancreaticoduodenectomy (PD) poses a particular challenge. During this procedure, there is extensive retroperitoneal dissection around anatomically complex and hazardous structures, and a prolonged reconstruction that includes 3 technically demanding anastomoses. Given this complex gastrointestinal reconstruction, it has been generally thought that the minimally invasive approach would not significantly decrease recovery time (hospital stay), yet it would significantly increase operative time. Even though minimally invasive PD was reported as early as 1994,[11] laparoscopic surgeons have been reluctant to routinely perform it. Since this first description now almost 20 years ago, a large number of single-institution series of minimally invasive (including laparoscopic-assisted, totally laparoscopic, and more recently robotic) PD performed for a variety of indications have been reported.[12-27]

Based on safety data derived from those retrospective reports, these procedures are now offered to selected patients at a limited number of institutions. However, there is currently no level 1 evidence that compares outcomes between MIS and the traditional open approach. We present a systematic review of the literature and a comparative effectiveness analysis of minimally invasive vs open PD. Using meta-analytic techniques, we set out to evaluate the surgical and oncologic outcomes of patients undergoing either procedure as reported in the published literature.

METHODS

This study adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[28] We queried medical databases in search for manuscripts comparing operative, postoperative, and oncologic outcomes of minimally invasive and open PD. An experienced information scientist (IS) designed the search strategy, which was refined and revised by a surgeon (CC).

Literature search

Comprehensive literature searches were performed of the PubMed, EMBASE, and Cochrane Library databases for the years 1994 through January 2013. No language restriction was imposed. Three categories of terms were "ANDED" together: pancreaticoduodenectomy terms, laparoscopy/robot-assisted/minimally invasive terms, and outcomes terms. For PubMed, a search using Medical Subject Headings (MeSH) terms was run, as well as a textword search. For EMBASE, a search using Emtree (EMBASE vocabulary) terms was run, as was a textword search. For Cochrane, a search using MeSH terms was run, as well as a textword search. All retrieved records were added to an EndNote (Version X6 — Thomson Reuters) library. The last search was performed on January 15, 2013. A total of 703 references were retrieved, and after removal of duplicates, 527 references remained.

CME questions for this article available at http://jacscme.facs.org

Disclosure Information: Authors have nothing to disclose. Timothy J Eberlein, Editor-in-Chief, has nothing to disclose.

Received July 17, 2013; Revised August 27, 2013; Accepted September 16, 2013.

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ISSN 1072-7515/13/$36.00
http://dx.doi.org/10.1016/j.jamcollsurg.2013.09.005

Abbreviations and Acronyms
MIS = minimally invasive surgery
PD = pancreaticoduodenectomy
WMD = weighted mean difference

Study selection

Minimally invasive PD was defined as completely laparoscopic or robotic resection of the head of the pancreas and duodenum, followed by completely intracorporeal reconstruction of the pancreatic, biliary, and intestinal continuity. Hybrid procedures, in which part of the dissection or reconstruction was extracorporeal or through a "mini-laparotomy" were not considered for this study.

Studies were included only if they were original series comparing minimally invasive and open PD that reported at least 1 of the outcomes variables of interest. We included only published studies dating back to 1994 (first report of minimally invasive PD) regardless of language.

Studies were excluded from our analysis if they did not report at least 1 of the outcomes of interest, included minimally invasive or open PDs but not both, or did not perform a comparison between the 2 techniques; reported hybrid procedures; reported on fewer than 8 cases; if they were technical "how-to" reports, or if they were animal or unpublished studies for which complete data for pooling were not available.

Two authors (CC and HD) evaluated all titles to identify relevant articles. Abstracts of these were re-evaluated to identify those meeting inclusion criteria, and full texts of these articles were obtained for data extraction. Disagreement was solved by a third author (SF).

Data extraction

Two authors independently extracted the data of interest from the manuscripts. Results were compared and consensus was reached. The outcomes of interest for our study were: operative/pathology variables (operative time, estimated blood loss, R0 resection, lymph node harvest, and tumor size), postoperative outcomes (overall complications, pancreatic fistula rate [and grade $\geq$3], delayed gastric emptying, postpancreatectomy hemorrhage, wound infection, length of hospital stay, and reoperation rate). Operative outcomes largely determine the ultimate oncologic outcomes of these patients (in the setting of malignancy); the postoperative outcomes evaluated represent the major drivers of morbidity after pancreaticoduodenectomy. Because our search was not limited to a specific indication for this operation, long-term oncologic outcomes were not included in our analysis. The reference sections of the selected studies were searched for additional relevant papers. Corresponding authors were not contacted.

Statistical analysis

The meta-analysis was conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Statement.[28] Whenever missing from a study, mean and standard deviation were estimated from the data available, if possible, as previously described.[29] Studies were combined using a random-effects model and estimates were expressed as weighted mean differences (WMD) for continuous data and odds ratios (OR) for event-related outcomes. In addition, 95% confidence intervals (CI) were calculated. I^2 values were preferred for quantification of statistical inconsistency, defined as the percentage of variation between studies due to heterogeneity.[30] Analyses were performed with Comprehensive MetaAnalysis Version 2.0 (Biostat Solutions Inc).

Assessment of methodologic quality of our meta-analytic techniques

The previously validated Overview Quality Assessment Questionnaire (OQAQ)[31] was used to assess the methodologic rigor of our study. This questionnaire includes a self-reported subset of questions regarding items that should be fulfilled to ensure quality: 1. Was the search comprehensive? 2. Was selection bias avoided? 3. Was validity assessed appropriately? and 4. Were the methods used to combine results from studies appropriate?

RESULTS

The predefined inclusion criteria were met by 6 studies that included 542 patients (169 MIS and 373 open) and these were pooled in the meta-analysis.[32-37] A PRISMA flow diagram depicting the selection process is shown in Figure 1. General study characteristics are detailed in Table 1. There were no randomized controlled trials identified. All the studies found were retrospective reviews of variable quality that compared consecutive cases of minimally invasive PD with either consecutive or matched open procedures performed during the same time period. All indications were included; however, the majority of cases were performed for malignancy. All studies focused on operative and perioperative outcomes, there were no reports of long-term oncologic results, and there were no multicenter studies.

Meta-analysis

Results of the meta-analysis are summarized in Table 2. Forest plots of those comparisons that showed a significant