Robotic versus Open Pancreatectomy: A Systematic Review and Meta-analysis

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ABSTRACT

Background. Robotic surgery is gaining momentum with advantages for minimally invasive management of pancreatic diseases. The objective of this meta-analysis is to compare the clinical and oncologic safety and efficacy of robotic versus open pancreatectomy.

Methods. A systematic review of the literature was performed to identify studies comparing robotic pancreatectomy and open pancreatectomy. Postoperative outcomes, intraoperative outcomes, and oncologic safety were evaluated. Meta-analysis was performed using a random-effect model.

Results. Seven studies matched the selection criteria, including 137 (40%) cases of robotic pancreatectomy and 203 (60%) cases of open pancreatectomy. None of the included studies were randomized. Overall complication rate was significantly lower in robotic group [risk difference (RD) = -0.12, 95% confidence interval (CI) = -0.22 to -0.01, \( P = 0.03 \)], as well as reoperation rate (RD = -0.12; CI = -0.2 to -0.03, \( P = 0.006 \)) and margin positivity (RD = -0.18; 95% CI = -0.3 to -0.06, \( P = 0.003 \)). There was no significant difference in postoperative pancreatic fistula (POPF) incidence and mortality. The median (range) conversion rate was 10% (0–12%).

Conclusions. The results of this meta-analysis suggest that robotic pancreatectomy is as safe and efficient as, if not superior to, open surgery for patients with benign or malignant pancreatic diseases. However, the evidence is limited and more randomized controlled trials are needed to further clearly define this role.

During the last decade, minimally invasive surgery played a prominent role in pancreaticobiliary surgery. The conventional laparoscopic distal pancreatectomy has been demonstrated safe and feasible for benign disease and borderline malignancy. However, there are intrinsic disadvantages to conventional laparoscopy, including lack of tactile sensation, two-dimensional only imaging, and restricted instrument movement inside the abdominal cavity that make it difficult to perform more complex surgeries. In 2003, Melvin et al. reported the first case of robotic distal pancreatectomy. The use of a surgical robotic system has been proven successful in overcoming the natural limitations of conventional laparoscopy.

Robotic-assisted pancreatic surgery is gaining momentum, and a variety of reports have demonstrated the safety and feasibility of this approach with potential advantages over open surgery in terms of estimated blood loss, overall complication rate, mortality, and hospital stay. However, these reports were all based on single-institutional experience, and evidence in the context of randomized controlled trial is not available. The aim of this study is to perform a systematic review and meta-analysis of studies comparing the safety and efficacy of robotic pancreatectomy versus open pancreatectomy.

MATERIALS AND METHODS

Review Strategy

A systematic review of the published literature examining robotic pancreatectomy for pancreatic diseases was performed referring to the previous publication. PubMed, Cochrane Library, Medline, and Embase databases were searched with the following search strategies: robot* OR “Da Vinci” OR Davinci AND pancrea* in PubMed; robot* OR “Da Vinci” OR Davinci OR robotics (Mesh) AND pancrea* in Cochrane Library; robot*: ab OR “Da Vinci”: 

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ab OR Davinci: ab OR robotics: de AND pancrea*: ab in Medline and Embase databases. No other search limits were applied. The last search was performed in April 2012. Pancreatectomy included pancreaticoduodenectomy, distal pancreatectomy, and central pancreatectomy. Abstracts of reviews, case reports, noncomparative studies, and not relevant and non-English publications were excluded. Relevant data from included studies were extracted by two independent observers and summarized. An interreviewer reliability analysis using kappa statistic was performed to determine consistency among reviewers. Disagreements on selecting studies were solved by discussion. The authors were contacted via personal correspondence as possible when additional information required was not provided in the articles.

Outcomes

The outcomes that were analyzed and compared between robotic and open approaches to pancreatectomy included postoperative outcomes of overall complication rate, POPF, mortality, reoperation, and length of hospital stay; intraoperative outcomes of operative time, estimated blood loss, and conversion rate; and oncologic safety of positive margin rate. In addition, the pathologic characteristics of the resected tumors were also analyzed.

Statistical Analysis

The outcomes that were analyzed and compared between robotic and open approaches to pancreatectomy included postoperative outcomes of overall complication rate, POPF, mortality, reoperation, and length of hospital stay; intraoperative outcomes of operative time, estimated blood loss, and conversion rate; and oncologic safety of positive margin rate. In addition, the pathologic characteristics of the resected tumors were also analyzed.

Q test (also known as Chi-square test) was used to assess the heterogeneity among studies. The $I^2$ index evaluates the extent of true heterogeneity, that is, dividing the difference between the result of $Q$ test and its degrees of freedom $(k-1)$ by the $Q$ value itself, multiplied by 100 %. The $I^2$ index can be interpreted as the percentage of the total variability due to between-studies variability in a set of effect sizes. Statistical heterogeneity was considered high when $I^2$ was greater than 50 %, and no pooling was performed when $I^2$ was close to 50 % or greater. In meta-analysis, a random-effects method was used. For dichotomous variables, meta-analysis of risk difference or risk ratio was performed. For continuous variables, meta-analysis of mean difference was performed by inverse variance method. Review Manager 5.1 software was used for meta-analyses and graphical representation. Confidence intervals were set at 95 %. $P$ value $\leq 0.05$ was considered to be statistically significant.

RESULTS

The search in PubMed, Embase, Medline, and Cochrane Library databases identified 336 abstracts. After excluding duplicates, 221 abstracts were reviewed to yield 8 full articles and 2 conference abstracts that were retrieved. The study by Kang et al. was excluded because of its combination of laparoscopic and robotic surgery as one group from which we could not extract data about outcomes of robotic versus open surgery independently. The studies by Zeh et al. and Chan et al. were excluded because they only reported the outcomes of robotic surgery and were not comparative studies. Finally, five full articles and two conference abstracts were included for comprehensive review. The interreviewer reliability for reviewers was found to be kappa $= 0.971 \ (P < 0.001)$. A flowchart of the search history is shown in Fig. 1. The quality of the seven included studies was evaluated. There were no randomized controlled trials. All studies were case-matched studies with prospectively collected data except the study by Kang et al. Overall, the quality of the included studies was satisfactory.

This review included 137 robotic and 203 open surgeries. Specific details of operative management were provided in all studies except the conference abstracts by Hammill et al. and Walsh et al. The characteristics of the studies and patients are presented in Table 1. In summary, most studies were undertaken in the USA with the intervention of pancreaticoduodenectomy. There were no significant differences in sex and age between the two groups. In addition, except the study by Hammill et al., the total number of patients with benign pancreatic diseases was 125 (60 for robotic surgery versus 65 for open surgery) and with malignant diseases was 138 (66 for robotic surgery versus 72 for open surgery).

FIG. 1 Flowchart of study selection for meta-analysis
approach versus 72 for open approach). There was no significant difference in the selection of indications between the two techniques.

Outcomes

Overall Complication Rate The range of overall complication rate in the seven studies was 1–36.4% for robotic surgery and 18–75% for open surgery. There was a significant difference in the risk difference for all studies with low heterogeneity ($I^2 = 0\%$). Only one study found a significant difference in overall complication rate favoring robotic surgery. The result of meta-analysis shows a statistically significant risk difference of 12% [95% confidence interval (CI) 1–22%, $P = 0.03$] favoring robotic surgery. The overall complication rate is lower for robotic surgery compared with open surgery (Fig. 2).

Postoperative Pancreatic Fistula All the studies except the two conference abstracts by Hammill et al. and Walsh et al. reported the incidence of postoperative pancreatic fistula. The result of meta-analysis indicates that there was no significant difference in risk ratio between the two methods (risk ratio $= 0.61$; 95% CI 0.33–1.14; $P = 0.12$). The heterogeneity was low ($I^2 = 0\%$).

Postoperative Mortality There was a similar incidence of postoperative mortality among all studies, with low heterogeneity ($I^2 = 0\%$). No study showed a significant difference in risk difference in mortality between the two techniques. The result of meta-analysis indicates no evidence of a difference between robotic and open surgery for postoperative mortality: risk difference $= 0.02$ (95% CI $-0.03$ to $0.06$; $P = 0.45$; Fig. 3).

Reoperation Rate The study by Waters et al. and the conference abstract by Hammill et al. did not report data about reoperation rate and were excluded from meta-analysis. All the remaining five studies showed no significant difference in risk difference for reoperation rate between robotic and open surgery. The result of meta-analysis indicates a significant difference between the two methods: risk difference $= -0.12$ (95% CI $-0.20$ to $-0.03$; $P = 0.006$), favoring robotic approach with low heterogeneity ($I^2 = 0\%$).

Positive Margin We extracted the data about positive margin for malignant cases in four studies. All studies showed no difference in the rate of positive margin except the study by Chalikonda et al. reporting a significant difference favoring the robotic technique. The result of meta-analysis indicates that robotic surgery has a significantly lower rate of positive margin compared with open surgery with low heterogeneity ($I^2 = 0\%$): risk difference $= -0.18$ (95% CI $-0.30$ to $-0.06$; $P = 0.003$; Fig. 4).

Hospital Stay Due to incomplete data, only three studies were included for heterogeneity test, with $I^2$ of 47%, close to 50%. We performed systematic review of hospital stay instead of meta-analysis. All seven included studies reported shorter mean length of hospital stay in robotic surgery group than in open surgery group (Table 2). Two studies by Zhou et al. and Walsh et al. reported significant difference in hospital stay between the two approaches ($P < 0.05$).

Conversion Rates Conversion was defined as converting robotic approach to open approach or laparoscopic
approach during the surgery due to a series of reasons. Based on an intent-to-treat principle, all conversions were considered as being in the robotic group. The median (range) conversion rate was 10% (0–12%) for all the studies in this review (Table 2). The commonest reasons for conversion were bleeding, failure to progress, and adhesion.

Operation Time

Three studies were included for heterogeneity test, with $I^2$ of 96%, higher than 50%. Systematic review of operation time was performed instead of pooling the data. The operation time for robotic and open pancreatectomy was not routinely defined by authors, except Zhou et al., who defined that the operating time for robotic surgery included setup, draping, docking of the robot, and robotic surgery, and for open surgery from opening the abdomen to closing the abdomen completely. All studies except the study by Buchs et al. reported longer mean operation time for robotic surgery than open surgery (Table 2).

**Estimated Blood Loss**

Due to incomplete data, only three studies were included for heterogeneity test, with $I^2$ of 92%, higher than 50%. We performed systematic review of estimated blood loss instead of pooling the data. All studies reported less mean estimated blood loss in robotic surgery group than in open surgery group (Table 2). The difference between the two techniques was reported significant in three studies; it was reported as not significant in two studies.

**DISCUSSION**

With the development of computer science and technology, a robotic surgical system was introduced in the field of general surgery including pancreatic surgery. The robot (Da Vinci) surgical system has emerged as one of the most promising surgical advances since its launch at the turn of the millennium and become an attractive technique to surgeons. However, the feasibility, safety, and efficacy of this novel approach to previously accepted
procedures have not been fully determined. This review evaluated the current best available evidence for the role of robotic versus open surgery in pancreatic diseases.

The results of this meta-analysis suggest some advantages of robotic pancreatectomy over open approach in several aspects. First and utmost, the result of this meta-analysis shows that robotic pancreatectomy is associated with significantly lower overall complication rate with an absolute risk reduction of 12%. Along with the decreased overall complication rate, the reoperation rate of robotic surgery is also significantly lower than that of open approach, with an absolute risk reduction of 12%. Finally, the margin positivity, one of the oncologic outcomes, is significantly lower in robotic approach.

A variety of characteristics of robot surgical systems may contribute to these benefits. Firstly, robotic surgery is a minimally invasive technique, which could avoid the disproportionately long abdominal incision of open surgery and reduce tissue injury. Secondly, technically, the Da Vinci system possesses characteristics of a magnifiable, steady, high-definition, three-dimensional, operator-controlled image; articulated instruments with seven degrees of freedom; motion scaling and tremor filtration; stable retraction; and reduced postural strain and fatigue, which could show the operative field more clearly with magnified views and increase the ease and dexterity, all conducive to the decrease of complication rate and a more achievable minimally invasive pancreatectomy for surgeons.

No significant differences were observed in POPF and mortality between robotic surgery and open surgery, both offering low mortality (<5%). POPF is a major problem after pancreatectomy. POPF is defined as drainage of any measurable volume of fluid on or after postoperative day 3 with amylase content greater than three times the serum amylase activity by the International Study Group on Pancreatic Fistula (ISGPF). Based on clinical symptoms and interventions, the severity of fistula is further stratified in grades A, B, and C. Three of five studies used this standard definition of pancreatic fistula. However, the study by Zhou et al. used a similar definition, and the study by Waters et al. did not clarify this definition. We compared overall pancreatic fistula rate between the two approaches.

The result of meta-analysis shows that robotic surgery is associated with lower positive margin rate, one of the oncologic outcomes. However, long survival rate and lymph node retrieval were not evaluated due to incomplete data. Therefore, based on this result, it is difficult to make a reliable conclusion about oncologic safety.

With regard to the outcomes of length of hospital stay, operation time, and estimated blood loss, the results were not pooled due to incomplete data and high heterogeneity. Several factors may account for the high heterogeneity.

<table>
<thead>
<tr>
<th>Study</th>
<th>Operative time (min)</th>
<th>Estimated blood loss (ml)</th>
<th>Length of hospital stay (days)</th>
<th>Conversion no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robot</td>
<td>444 ± 93.5</td>
<td>59 ± 13.5</td>
<td>5.59 ± 13.5</td>
<td>2 (4.5 %)</td>
</tr>
<tr>
<td>Open</td>
<td>476 (363–727)</td>
<td>387 ± 33.4</td>
<td>827 ± 43.9</td>
<td>0.001</td>
</tr>
<tr>
<td>P value</td>
<td>0.0001</td>
<td>0.0005</td>
<td>0.013</td>
<td>0.0001</td>
</tr>
<tr>
<td>Robot</td>
<td>428 ± 65.7</td>
<td>420 ± 121.7</td>
<td>681 (59–3,500)</td>
<td>0.038</td>
</tr>
<tr>
<td>Open</td>
<td>458 (213–602)</td>
<td>275 (100–5,000)</td>
<td>NA</td>
<td>0.4</td>
</tr>
<tr>
<td>P value</td>
<td>0.013</td>
<td>0.005</td>
<td>0.013</td>
<td>0.04</td>
</tr>
<tr>
<td>Robot</td>
<td>298 (191–418)</td>
<td>78.75 ± 186.66</td>
<td>153.75 ± 43.4</td>
<td>0.009</td>
</tr>
<tr>
<td>Open</td>
<td>364</td>
<td>49.8 ± 16.5</td>
<td>210 ± 53.18</td>
<td>0.16</td>
</tr>
<tr>
<td>P value</td>
<td>0.0009</td>
<td>0.011</td>
<td>0.011</td>
<td>0.16</td>
</tr>
</tbody>
</table>
First, it is impossible to match the patient characteristics across all of these studies, which could have caused the heterogeneity between the groups. Second, the definitions of these outcomes were not routinely defined in the studies. Different studies may have slightly different defining criteria for these outcomes. Besides, different techniques such as a hybrid technique versus a total robotic technique may significantly affect operative time, resulting in variations in robotic approach. Third, the learning curve in adopting a new approach is very important. Surgeons at different stages of the learning curve have different operative times, just as publications have shown that surgeons with less experience have longer operative time compared with surgeons with more experience for open pancreateicoduodenectomy (PD)\textsuperscript{21}; as experience increases, this can be shortened over time.\textsuperscript{22}

The results of this meta-analysis should be interpreted with caution for several limitations. Firstly, none of the included studies are randomized or blinded, and the overall level of clinical evidence is low. However, we should take into account that it is impossible to perform an analysis in which the patients are blinded for the performed procedure. Therefore, it is difficult to conduct a prospective, randomized study because of poor patient compliance. Besides, we used comparative meta-analyses which are generally well accepted as an aid in critically comparing studies and are better accepted in the medical literature as a tool to complement qualitative reviews.\textsuperscript{23} Recently, Abrahama et al.\textsuperscript{24} reported that meta-analysis of well-designed nonrandomized comparative studies (NRCTs) of surgical procedures is probably as accurate as RCTs. In fact, all seven studies included in the current study were case-matched studies.

Secondly, there was an inevitable selection bias in the published literature, as the baseline characteristics of patients and the indications for open procedures in the two groups were not equal in all studies, tending to favor robotic technique. Besides, patient preference, surgeon referral patterns, and evaluation of resectability could each have introduced bias into the selection of approach. It is admitted that there was no significant difference between the two techniques in the selection of indications for both benign diseases and malignant diseases. Actually, the pathology was matched between open surgery and robotic surgery in all studies\textsuperscript{8,9,13,15–17} except the study by Hamill et al.\textsuperscript{14} without elaboration. The majority of malignant diseases were adenocarcinoma; nevertheless, not all studies addressed the characteristics of adenocarcinoma in detail except the studies by Zhou et al.\textsuperscript{8} and Buchs et al.\textsuperscript{9}, which could affect the outcomes.

Thirdly, potential publication bias might be present. Authors might be more likely to report positive findings. Studies with significant results are more likely to get published than those with nonsignificant results.\textsuperscript{25} Therefore, some gray literature which contained negative results was difficult to obtain. Besides, the number of pooled studies was small, which resulted in the limitation in the use of funnel plots to detect publication bias. Additionally, the small patient population included may have masked the true difference in some variables, and it was difficult to make reliable conclusions.

Fourthly, we applied a random-effect model to take between-study variation into consideration. This does not necessarily rule out the effect of heterogeneity between studies, but one may expect a very limited influence.

Furthermore, the robotic cohorts from most if not all of these institutions represented their initial experiences, which could introduce a bias against the robotic outcomes. However, even if this bias is present, the results of this meta-analysis reveal that robotic technique is associated with lower risk of overall complication rate, reoperation rate, and positive margin rate. With regard to other outcome parameters, robotic surgery shows comparable effects to open surgery, supporting the safety and efficacy of robotic pancreatectomy. Therefore, it seems plausible to reason that, with increased experience, improvements in robotic outcomes may yet be seen in the future.

Finally, cost comparison of robotic surgery versus open surgery was not assessed in all studies. We could not evaluate whether robotic technology is cost effective. It is undeniable that there would be an initial increase in cost with the robotic approach, as has been reported by other investigators.\textsuperscript{26} However, Waters et al.\textsuperscript{16} reported that the direct operative costs of robotic pancreatectomy were higher in the robotic group compared with open and laparoscopic group while the total costs demonstrated no difference between the three approaches.

In conclusion, the results of this meta-analysis favor the safety and efficacy of robotic pancreatectomy compared with open pancreatectomy for benign and malignant pancreatic diseases. However, given the aforementioned limitations, more evidence of prospective, multicenter, randomized controlled trials is needed to further address the real role of robotic technique in pancreatic surgery, not only for safety reasons but also for the real overall benefits to patients.

**Conflict of interest** The authors declare that they have no potential conflict of interest.

**REFERENCES**