# 90049_Auto_Edited.docx


| | | | |
|---|---|---|---|
| WORD COUNT | 4079 | TIME SUBMITTED | 19-JAN-2024 10:23PM |
| | | PAPER ID | 106280128 |

**Name of Journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 90049

**Manuscript Type:** SYSTEMATIC REVIEWS

# Quality of life after pancreatic surgery

QOL after pancreatic surgery

Shi-Zhen Li, Ting-Ting Zhen, Yi Wu, Min Wang, Ting-Ting Qin, Hang Zhang, Ren-Yi Qin

**Abstract**

BACKGROUND

Pancreatic surgery is challenging owing to the anatomical characteristics of pancreas. Increasing attention has been paid to changes in the quality of life (QOL) after pancreatic surgery.

AIM

To summarize and analyze current research results on QOL after pancreatic surgery.

METHODS

A systematic search of the literature available in PubMed and EMBASE was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The relevant studies were also searched by screening the references of the retrieved articles. Studies on the QOL of patients after pancreatic surgery published after January 1st, 2012 were included. These studies include prospective and retrospective studies of patients' QOL after several types of pancreatic surgery. The results of these primary studies were summarized in an inductive way.

RESULTS

A total of 45 articles were included in the study, of which 13 were related to pancreaticoduodenectomy (PD), 7 were related to duodenum-preserving pancreatic head resection (DPPHR), 9 were related to distal pancreatectomy (DP), 2 were related to central pancreatectomy (CP), and 14 were related to total pancreatectomy (TP). Some studies showed that QOL after PD needed 3-6 months to recover, while others showed that 6-12 months was more accurate. Although TP and PD had a similar influence on QOL, patients after TP needed a longer time to recover to preoperative or baseline level. QOL after DPPHR was better than that after PD. However, the superiority of QOL between patients after CP and PD remains controversial. The decrease in exocrine and endocrine function after surgery was the main factor affecting the QOL. Minimally

invasive surgery could indeed improve patient's QOL in early stages after PD and DP but this was in dispute in the long run.

CONCLUSION

It is controversial whether PD, DP, CP or TP have better QOL. The long-term benefits of minimally invasive *vs* open surgery are controversial. More prospective trials should be undertaken.

**Key Words:** Keywords: Quality of life; Pancreaticoduodenectomy; Duodenum-preserving pancreatic head resection; Distal pancreatectomy; Central pancreatectomy; Total pancreatectomy

Li SZ, Zhen TT, Wu Y, Wang M, Qin TT, Zhang H, Qin RY. Quality of life after pancreatic surgery. *World J Gastroenterol* 2023; In press

**Core Tip:** 1.This review summarizes and analyzes current research results on quality of life (QOL) after pancreatic surgery. 2.The article covers the discussion and analysis of the QOL of various pancreatic surgeries. Which kind of surgical procedure has better QOL is controversial. 3.The long-term benefits on QOL of minimally invasive surgery over open surgery are controversial.

## INTRODUCTION

Pancreas, located in retroperitoneum, is a glandular organ with both endocrine and exocrine functions. It can be divided into four main parts: head, neck, body and tail. Depending on the location of pancreatic tumors, pancreatic surgery can be divided into pancreaticoduodenectomy (PD), duodenum-preserving pancreatic head resection (DPPHR), distal pancreatectomy (DP), central pancreatectomy (CP) and total pancreatectomy (TP). Pancreatic surgery is challenging because of its complex anatomical structure and peripheral vascularity of pancreas and intractable post-

operative complications. Owing to the standardization of surgical steps, and improvement of relevant medical techniques as well as surgical instruments, the safety of pancreatic surgery has been significantly improved. Perioperative morbidity, mortality and other related indicators have been more acceptable. However, due to its important role in the process of digestion, absorption, and blood glucose regulation, the changes in the quality of life (QOL) of patients after surgery have been a focus of attention for surgeons.

An increasing number of patients with non-malignant pancreatic diseases are willing to undergo surgical treatment due to the acceptable safety. In this case, from the perspective of the postoperative patient, the significance of rehabilitation reflects not only the traditional perioperative outcome, but also QOL[1]. QOL is a new concept going beyond health. Although there is no consensus on conception of it[2], we can consider it as a multi-dimensional architecture that incorporates both objective and individual subjective views of aspects of one's own physical, psychological and social well-being[3-5]. It concludes not only the evaluation of physical health but also many subscales such as emotion, job, culture, family, sociability, economy, cognitive, happiness, sex and some symptoms[6]. Since people realized the importance of QOL, there have emerged many QOL scales, including the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30, European Quality of Life 5-dimension (EQ-5D), 36-item Short (SF-36), *etc.* However, it's not an easy task to follow up the QOL of patients once they discharge from the hospital. This has resulted in most relevant studies having small sample sizes or lacking long-term follow-up results. There is a lack of summary of these studies on QOL after pancreatic surgery.

This study will list the characteristics of QOL of PD, DPPHR, DP, CP and TP. We conducted this study to describe existing findings on quality of life in pancreatic surgery to make it easier for surgeons and patients to decide on a surgical approach. In addition, we also tried to identify controversial results to encourage more targeted research.

## MATERIALS AND METHODS

### *Search strategy*

A systematic review was conducted in PubMed and EMBASE Database, according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline[7]. The articles were screened by two authors (Li SZ and Zhen TT) independently after removing duplicates. We used a search algorithm that combine the terms: (a) "pancreatic surgery" OR “pancreatoduodenectomy” OR “duodenum-preserving pancreatic head resection” OR “distal pancreatectomy” OR “central pancreatectomy” OR “total pancreatectomy” and (b) “quality of life”. The language of articles needs to be English. References of the retrieved articles were screened for any relevant articles.

### *Inclusion and exclusion criteria*

Inclusion criteria: articles involved the QOL of PD, DPPHR, DP, CP and TP. The exclusion criteria were as follows: (a) articles not within the scope of interest of this review; (b) overlap in patient data; (c) articles were not published in English; (d) articles not published after January 1st 2012.

## RESULTS

### *Literature search*

The search results are shown in Figure 1. A total of 1515 potential literature were found: 1313 from PubMed, 190 from EMABASE and 12 additional references through a handling search. There were 1453 Left after excluding duplicates. After screening titles and abstracts, 872 pieces of literature were excluded as they were not within the scope of interest of this review. In addition to this, we excluded the inaccessible articles ($n$ = 127). 454 full-text articles were collected, and 312 articles were excluded for language ($n$ = 11), not mentioning the QOL of PD, DPPHR, DP, CP or TP ($n$ = 301), or not published after January 1st 2012 ($n$ = 97). After the selection process, 45 clinical studies were

encompassed in this study. There were 45 articles concerning 13 PD, 7 DPPHR, 9 DP, 2 CP and 14 TP included.

***Study characteristics of pancreaticoduodenectomy***

There were 13 studies, including 3 randomized controlled trial (RCT) studies, 4 prospective observational studies, and 6 retrospective ones. 6 studies were concerned about the perioperative QOL of PD. Two RCT and one retrospective study proved the QOL change post-operatively after 2 years (Table 1). Some studies demonstrated that patients' QOL significantly diminished within one month post-operatively and nearly recovered to preoperative or baseline levels at 3 months after PD no matter the kind of pathology type[8-11], others reported that 6 months even 1 year was a more accurate period[12-14]. For long-term survivors, gastrointestinal symptoms such as bloating and indigestion were factors that affected their long-term QOL, and some of these symptoms were caused by pancreatic exocrine insufficiency after PD instead of post-operative complications[15,16]. Studies reported that nearly half of the survivors needed to take pancrelipase after PD[9,17,18]. Pancrelipase could improve nutritional status but had controversy on whether it could improve QOL[9,13,19].

Most of the studies demonstrated that there were no differences between PPPD and PD on overall mortality, morbidity, survival and QOL[20-24]. Studies also reported that preoperative body weight loss, impaired preoperative pancreatic exocrine function, longer operative time, intraoperative radiotherapy, pancreatic carcinoma, and post-operative diarrhea might result in the delayed recovery of QOL[25].

Laparoscopic pancreaticoduodenectomy (LPD) could provide a better QOL for patients with a better functional status within the first 6 months after the operation[26]. However, the advantage disappeared after 6 months[27].

***Study characteristics of duodenum-preserving pancreatic head resection***

The results are shown in Table 2. The sample sizes of the 7 studies were 74, 80, 25, 40, 85, 17 and 16. Only 1 Literature looked at the change in QOL within one year. One

group of researchers held that DPPHR and PD were comparatively effective in improving long-term QOL after surgery[28-30]. The other group thought that DPPHR could bring better outcomes in the form of less frequent nausea, pain, diarrhea and better physical status, working ability as well as global QOL[31].

Studies found that the Frey and the Berne had advantages in shorter operation time and duration of hospital stay than the Beger. However, all of them had no obvious difference on improving patients' postoperative QOL[32-35].

***Study characteristics of distal pancreatectomy***

There were 9 studies involving DP in total (Table 3). 2 studies showed the perioperative QOL of DP, and 7 of them mainly compared the differences between open and minimally invasive ways. Studies showed that minimally invasive distal pancreatectomy (MIDP) had a shorter length of hospital stay and shorter time in terms of functional recovery when compared to open distal pancreatectomy (ODP)[36,37]. MIDP had better short-term QOL than ODP up to 30 days postoperatively[38,39]. But which one is better for the long-term QOL of more than one year is controversial. During this period, some studies demonstrated no difference between MIDP and ODP[38,40], while others reported that MIDP could bring better QOL for patients in the aspects of their physical function, cognitive function, social function, role function, and some symptoms such as nausea, vomiting as well as insomnia.[41,42]

4

Laparoscopic spleen-preserving distal pancreatectomy (LSPDP) and laparoscopic distal pancreatectomy with splenectomy (LDPS) had similar perioperative outcome[43]. Patients who experienced LSPDP had significantly better vitality than those who experienced LDPS, and were less likely to contract the common cold and flu[44,45].

Modified Appleby not only improved the ratio of R0 resection, but also relieved pain and improved patients' overall QOL[46].

***Study characteristics of central pancreatectomy***

A total of 2 studies were included in Table 3, with sample sizes of 36 and 42 respectively. Laparoscopic central pancreatectomy (LCP) could help patients stay in better working and living conditions than open central pancreatectomy (OCP)[47]. While comparing with DP and PD, some researchers thought that CP showed a significant benefit in specific symptoms such as loss of appetite, insomnia, nausea, and vomiting [48]. Others held different opinions that CP was associated with better pancreatic function but the same even worse long-term QOL and significantly increased post-operative morbidity and risk than DP or PD [49,50].

***Study characteristics of total pancreatectomy***

As for TP, only 2 prospective observational studies (Table 4). 2 Literatures showed the result of QOL within 1 year. It has been extensively verified that the perioperative and long-term outcomes of TP were almost comparable to PD in terms of morbidity, mortality, survival rates and QOL, no matter the age of patients or the pathology of tumors [51-56]. When compared to the general people, one study demonstrated that the long-term post-operative QOL of TP was lower[57], but more studies thought that they had no significant differences[53,58]. Regarding pain relief, especially for most chronic pancreatitis patients who were narcotics dependent, TP could alleviate pain largely so that half of the chronic pancreatitis patients could relieve from narcotics and return to a normal life a year after surgery. And this is a process of continuous improvement. As time goes by, more and more patients would not need narcotics to control the abdominal pain[59-63]. More than half of patients reflected that their bowel habits changed so that they needed to take pancreatin[64-66]. A quarter to more than half of patients could achieve insulin independence after islet cell autotransplantation (IAT), especially children[67]. Although the insulin independence rate could decline over time, most of the patients could almost control glycemic stably with an acceptable dose of insulin[60,61,68-70]. The stable control of glucose provided a more enjoyable life with better QOL for patients to have a normal social, work and study life[71].

## DISCUSSION

### *Pancreaticoduodenectomy*

PD, developed by Kausch[72] and Whipple[73], is a major surgical operation used to treat middle and lower-segment cancer of the common bile duct, periampullary tumors and so on. The safety of PD has been significantly improved these years. The mortality rate of PD has decreased from more than 50% to less than 5%, and the incidence of surgical complications has also decreased significantly[74]. Under the circumstances, people gradually shifted their focus from discharging from the hospital safely to the recovery of QOL. Therefore, more and more studies have been carried out on the changes in QOL of patients after PD. However, studies came from different countries with different demographic characteristics, and were almost always small sample data, especially prospective studies. As can be seen from Table 1, 7 of studies had a sample size of less than 100, and only 1 of them had a sample size of more than 300.

In 1943, pylorus-preserving pancreaticoduodenectomy (PPPD) was first performed by Watson[75] and then popularized by Traverso and Longmire[76]. While the merits of PPPD *vs* classic PD are still under debate, especially in terms of perioperative risk, PPPD does provide surgeons with another option[77]. Most studies demonstrated that PPPD and PD had the same influence on the QOL of patients. Factors that lead to the delayed recovery of QOL, such as preoperative body weight loss and impaired preoperative pancreatic exocrine function, are being explored.

PD was traditionally performed openly. Since LPD was first described by Gagner in 1994, many surgeons have conducted research to explore the advantages between LPD and open pancreatoduodenectomy (OPD). Our previous multi-center, open-label, randomized controlled trial proved that LPD was associated with a shorter length of stay, similar short-term morbidity, and mortality rates than OPD. Because of the better safety of LPD and maturity of surgical techniques, more and more surgeons focus on comparing differences in QOL between LPD and OPD. LPD does have a better quality of life advantage than OPD in the first 6 months, but our new study shows that this advantage disappears three years after surgery[27]. However, owing to the difficulty of

collecting data, the data of most of the related research were unrepresentative. Given the problem, more high-quality RCTs should be performed in the future.

***Duodenum-preserving pancreatic head resection***

PD had long been the first choice of surgeons in the face of benign or low-grade malignant lesions of the pancreatic head until the appearance of DPPHR. For these patients, since DPPHR was developed by Beger and his colleagues in the early 1970s, one more choice has emerged because of more organs preserved which might mean they could possess better endocrine and exocrine function after surgery. Therefore, there have broken out a lot of studies about the priority of PD and DPPHR. Except for perioperative parameters, whether DPPHR is superior to PD in terms of QOL is still controversial[78]. Most researchers thought that both DPPHR and PD relieved the obstruction of the pancreatic head, which was the cause of symptoms. So, they had no different influence on long-term QOL after surgery[28,29]. A study has also suggested that more digestive tract reconstruction during PD surgery led to lower exocrine function and worse QOL postoperatively[31]. But this study has poorer representativeness because of a smaller sample size and earlier publication time.

As people realized the superiority of the Beger, modifications of the original Beger procedure appeared, such as the Frey and the Berne[79,80]. Compared with the Beger, the Frey and the Berne were technically more straightforward. They all maintained the same volume of the pancreas and the exocrine and endocrine function of the pancreas. Therefore, they had advantages on operation time and duration of hospital stay but had no noticeable difference in improving QOL after surgery[32-35,79,80]. In conclusion, surgeons can choose any one of them according to the individual surgeons' expertise and intraoperative findings. Owing to the shorter operation time and length of hospital stay, modifications of the original Beger should be preferred.

***Distal pancreatectomy***

DP is the standard surgical method for treating tumors in the body or tail of the pancreas. Traditionally it was performed with an open approach. However, due to the technological developments in laparoscopic and robotic instruments these years, MIDP has been performed routinely by surgeons worldwide. Nearly all studies demonstrated that MIDP could bring better QOL for patients than ODP perioperatively. But which one was better in the long term was controversial. Larger sample sizes and more convincing studies have reported no differences between MIDP and ODP over the long term[38,40].

While performing DP, the traditional approach is to remove the spleen because the spleen is closely attached to the distal pancreas anatomically. As people realized the function of the spleen, more and more surgeons chose to perform LSPDP for the benign and low malignant tumors of the distal pancreas. Owing to the preservation of the spleen in LSPDP, it was comprehensible that LSPDP was significantly superior QOL than LDPS[44,45].

Appleby surgery was adopted for progressive carcinoma of pancreatic body and tail by Nimura for the first time in 1976. Due to the difficulty of Appleby technology and the advent of neoadjuvant therapy, the number of Appleby surgeries is decreasing, so there is a lack of relevant studies concerning QOL after Appleby.

***Central pancreatectomy***

Guillemin successfully performed CP with an anastomosis to both pancreatic remnants with an omega-shaped jejunal loop in 1957[81]. Letton and Wilson completed it in two pancreatic injury patients with a Roux-en-Y jejunal loop anastomosis to the tail and closure to the head remnant[82]. More and more surgeons prefer to perform it in cases while the lesion is limited to the pancreatic neck or body. Because normal pancreas has significantly less parenchymal loss, which means the more pancreatic function can be retained. According to the existing studies, the functional recovery and the mean QOL were comparable to a standard control population[48]. It was generally

believed that patients with CP had better QOL but higher perioperative risk[47-50]. But there is still a deficiency of study about the QOL after CP.

***Total Pancreatectomy***

Since Rockey performed the first TP on a patient with pancreatic cancer in 1942, some surgeons have tried to do the same. However, owing to the poor perioperative outcomes and QOL in the beginning, the feasibility of TP has been questioned. To find the answer, many relative studies have been carried out successively. In fact, the safety of TP has been improved dramatically due to the mature surgery technique and other reasons. The impaired exocrine function was also one of the several reasons why the feasibility of TP had been questioned. However, the optimization of pancreatin had indeed improved patients' exocrine function than before. Another reason was the high risk of brittle diabetes. Many factors were found to be associated with insulin independence, such as nonhereditary chronic pancreatitis, younger age, lower body surface area, and higher total islet equivalents. The pancreas is the only organ that can produce insulin. Because of removing the entire pancreas, TP has great damage to the ability of patients to keep blood sugar stable. To solve this problem, a new technology named IAT was first described in 1977. IAT is to isolate patients' islet cells and transplant them into the portal vein. With the advent of pancreatin and IAT, the endocrine and exocrine functions of patients after TP were significantly improved[60,61,64-66,68-70]. It seemed unlikely that TP could maintain or even improve the patient's QOL. However, this was possible only if the patient preoperatively suffered from endocrine and exocrine pancreatic dysfunction or chronic pain. TP could indeed improve the QOL of these patients to some extent. In conclusion, TP can be considered in selected patients with neoplasms involving the entire pancreas or refractory chronic pancreatitis ignoring the age of patients and pathology of the neoplasms.

## CONCLUSION

Because of the importance of endocrine and exocrine functions of pancreas, surgeons have tried their best to preserve normal pancreatic tissue and surrounding organs. Therefore, different surgical procedures have been developed depending on the location of neoplasms. However, no matter which kind of procedure it is, their perioperative outcomes were generally acceptable. PD and TP had similar influences on the patients' QOL. The time that patients needed to basically recover to preoperative or baseline level was 3 to 6 months after PD but longer in TP. At this stage, more than half of them still need to take pancreatin to relieve gastrointestinal symptoms. Compared to PD, most studies demonstrated that PPPD had a similar influence on perioperative and long-term outcomes. DPPHR could provide a better QOL with less pain, nausea, diarrhea symptoms, better physical and working status. In addition to this, because of the influence of the higher incidence of perioperative complications in CP than PD, whether CP could provide a better QOL is still debatable. As far as minimally invasive surgery was concerned, it seemed that they could indeed bring better QOL in the early stage after PD and DP, but the long-term outcomes still need to be confirmed by more studies. For DP, the preservation of the spleen could preserve patients' immunology function to defeat usual virus.

This is a shortcoming that we didn't finish a systematic analysis of the data from previous studies but just analyze their conclusion. And the scope of our study is not comprehensive enough, there are still some surgical procedures not included in the study. Anyway, our goal is to provide some directions for future researches.

It is so big a project to collect data about patient's post-operative QOL levels that the majority of studies don't have enough cases. And it is not an easy thing to contact patients by e-mail or phone call once they discharge from the hospital. That means incomplete data is common, especially while collecting long-term outcomes. As can be seen from the table, the loss rate of follow-up is high and there is a lack of prospective studies, especially randomized controlled studies. We propose scientific efforts to conduct more well-designed prospective analyses to verify the results.

## ARTICLE HIGHLIGHTS

### *Research background*

Pancreatic surgery is challenging because of the anatomical characteristics of pancreas. With the progress of medical standards, the perioperative outcomes have been greatly improved these years. More and more attention has been paid to the changes of quality of life (QOL) after pancreatic surgery. There is a lack of summary of QOL after various kinds of pancreatic surgery. With the purpose of describing the results of existing researches concerning QOL of pancreatic surgery we conducted this study.

### *Research motivation*

Understanding which kind of pancreatic surgery has better quality of life can provide some basis for clinical surgical decision.

### *Research objectives*

This review aimed to summarize and analyze current research results on quality of life after pancreatic surgery including pancreaticoduodenectomy, duodenum-preserving pancreatic head resection, distal pancreatectomy, central pancreatectomy and total pancreatectomy after January 1st 2012. It provides some directions for future researches based on the results of the controversy over patients' quality of life after surgery. And it also provides some basis for clinical surgical decision-making.

### *Research methods*

A systematic review was conducted in PubMed and EMBASE Database, according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline. And references of the retrieved articles were screened for any relevant articles. We extracted the results of these articles and summarized them.

### *Research results*

1. This review summarizes and analyzes current research results on QOL after pancreatic surgery.
2. The article covers the discussion and analysis of the QOL of various pancreatic surgery. Which kind of surgical procedure has better QOL is controversial.
3. The long-term benefits on QOL of minimally invasive surgery over open surgery are controversial.

***Research conclusions***

Comparison and summary of QOL in patients with different types of pancreatic surgery. We included not only the results of the same surgical procedure, but also the results between different procedures.

***Research perspectives***

More well-designed prospective analyses of patients' QOL after pancreatic surgery are needed.

**ACKNOWLEDGEMENTS**

We appreciate the efforts of all surgeons at the centers where the included articles are located. We are also grateful to the patients who participated in these trials. We appreciate the editors and reviewers for their useful feedback that improved this paper.

# 90049_Auto_Edited.docx

ORIGINALITY REPORT

3%
SIMILARITY INDEX

PRIMARY SOURCES

| | | |
|---|---|---|
| 1 | Takao Ohtsuka, Koji Yamaguchi, Kazuo Chijiiwa, Naoko Kinukawa, Masao Tanaka. "Quality of life after pylorus-preserving pancreatoduodenectomy", The American Journal of Surgery, 2001<br>Crossref | 22 words — 1% |
| 2 | pubmed.ncbi.nlm.nih.gov<br>Internet | 19 words — < 1% |
| 3 | www.clinicaltrials.gov<br>Internet | 18 words — < 1% |
| 4 | M.-H. Dai, N. Shi, C. Xing, Q. Liao, T.-P. Zhang, G. Chen, W.-M. Wu, J.-C. Guo, Z.-W. Liu, Y.-P. Zhao. "Splenic preservation in laparoscopic distal pancreatectomy", British Journal of Surgery, 2017<br>Crossref | 13 words — < 1% |
| 5 | link.springer.com<br>Internet | 13 words — < 1% |
| 6 | bmcmusculoskeletdisord.biomedcentral.com<br>Internet | 12 words — < 1% |
| 7 | www.pubfacts.com<br>Internet | 12 words — < 1% |

| | | | |
|---|---|---|---|
| EXCLUDE QUOTES | ON | EXCLUDE SOURCES | < 12 WORDS |
| EXCLUDE BIBLIOGRAPHY | ON | EXCLUDE MATCHES | < 12 WORDS |