Review

DOI: 10.5582/bst.2019.01278

The state of minimally invasive pancreaticoduodenectomy in Chinese mainland: A systematic literature review

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Summary **The development of Minimally invasive pancreaticoduodenectomy (MIPD) in Chinese mainland has been extremely quick. However, the safety and oncologic outcomes remain controversial. This review evaluates the current status of MIPD in Chinese mainland. A systematic literature search was performed using: Pubmed, Web of Sci, CNKI, Wanfang Data and Sinomed databases to filter all studies published up to and including June 2019 using key words "pancreaticoduodenectomy," or "Whipple operation" combined with "laparoscopy," or "laparoscopic," or "robotic," or "da Vinci," or "minimally invasive," or "hand-assisted". This systematic review included 39 articles that documented 2,653 MIPDs in Chinese mainland. The weighted average operative time was 370.6 min, and the weighted average blood loss was 278.0 mL. The overall morbidity was 31.9%, which Clavien-Dindo ≥ 3 complications accounted for 13.4%. Pancreatic fistula, delayed gastric emptying, bile leak and postoperative hemorrhage were reported in 20.9%, 5.5%, 3.5% and 6.0% of patients respectively. The average lengh of hospital stay was 16.1 days. The overall surgical mortality was 1.7%. The mean number of harvested lymph nodes was 13.5, and the rate of positive margin was 5.3%. Based on Chinese national condition, the operative volume of MIPD in Chinese mainland is the leading position in the world, and compared with some large international meta-analysis, no inferior perioperative and short-term oncological outcomes were observed in MIPD of Chinese mainland. However, research on survival analysis and phased learning curve outcomes is needed urgently before the innovative techniques are widely accepted.**

Keywords: Minimally invasive surgery, pancreaticoduodenectomy, Chinese mainland, laparoscopy, robot

1. Introduction

Pancreaticoduodenectomy (PD), as the only potentially curative option in patients with periampullary malignancy, has been recognized as one of the most complicated and risky procedures in general surgery for the past 100 years (*1*). With the development of surgery technology, the first case of minimally invasive pancreaticoduodenectomy (MIPD) was described in 1994 by Gagner (*2*). However, its challenging anatomical and anastomotic techniques and inferior short-term outcomes slowed the acceptance of this operation.

After the first report of MIPD in Chinese mainland in 2003 (*3*), more challenge-pursing and innovative Chinese surgeons have contributed to explore better approaches and procedures with the introduction of advanced technologies.

Previous literature listed advantages of minimally invasive surgery in other fields of general surgery including lower blood loss, faster post operation recovery and comparable oncology outcomes (*4*). Unlike previous years, more and more small-sample studies have been documented in recent years, which marks attempts from

Released online in J-STAGE as advance publication December 24, 2019.

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non-specialized centers.

In this paper, we reviewed the literature describing MIPD in Chinese mainland to provide a comprehensive evaluation of the current status, focusing on technical details and short-term outcomes of minimally invasive approaches.

2. Materials and Methods

2.1. *Definitions and surgical techniques*

MIPD included two main methods: laparoscopic pancreaticoduodenectomy (LPD) and robotic pancreaticoduodenectomy (RPD). Moreover, it could be further classified based on techniques used in resection and reconstruction:

1) Pure LPD, where the entire operation is completed with the assistance of laparoscopic technique;

2) Hand-assisted LPD, where a mini hand port is added to facilitate the procedure;

3) Laparoscopy-assisted LPD, where resection is carried out laparoscopically and reconstruction is completed using a small mini-laparotomy incision;

4) Robotic-assisted PD, where the entire operation or some parts of dissection and reconstruction are performed with the assistance of the da Vinci surgical system.

2.2. *Literature review*

A systematic literature search was performed using: Pubmed, Web of Sci, CNKI, Wanfang Data and Sinomed databases to filter all studies published up to and including June 2019 using key words "pancreaticoduodenectomy," or "Whipple operation" combined with "laparoscopy," or "laparoscopic," or "robotic," or "da Vinci," or "minimally invasive," or "hand-assisted." Relevant articles identified by cross-referencing were also retrieved and reviewed.

2.3. *Inclusion criteria*

Articles describing MIPD in Chinese mainland containing more than 10 cases were included. If patient data was documented more than once from the same institution, the most informative or recent article was considered to prevent data overlap.

2.4. *Exclusion criteria*

Articles lacking original data or missing lots of outcomes, studies referring to animals and cadavers, technique articles, multimedia literature, Chinese articles without English abstracts and academic degree articles were excluded.

2.5. *Data extraction*

All the retrieved studies that met the inclusion and exclusion criteria were independently reviewed by two authors (Ding JY and Zhang YH). Discrepancies between the two reviewers were resolved by discussion.

The variables extracted from the included studies were as follows:

1) Basic information (first author, publication year, study period, number of cases);

2) Technical details(surgical procedures, management of pancreatic stump, management of gastroduodenal artery, specimen extraction site, anastomotic technique in gastroenterostomy, suture technique in choledochojejunostomy, vascular resection and reconstruction);

3) Intraoperative outcomes (operative time, intraoperative blood loss, conversion rate, transfusion rate);

4) Short-term outcomes (overall morbidity, pancreatic fistula, usage of International Surgical Group of Pancreatic Fistula or not, delayed gastric emptying, bile leak, postoperative hemorrhage, length of postoperative hospital stay, Clavien-Dindo ≥ 3 complications, reoperation, surgical mortality);

5) Oncologic outcomes (malignancy rate, usage of tumor-node-metastasis stage or not, number of harvested lymph nodes, rate of margin negative resection).

2.6. *Statistical analysis*

A weighted average (WA) was used to express the statistical weighted mean of different variables:

$$WA = (w_1x_1 + w_2x_2 + ... + w_nx_n)/(w_1 + w_2 + ... + w_n)$$

where w is the number of cases in a publication and x is the mean of a specific variable. The x and its corresponding w are excluded if the variables in some studies are absent or not able to calculate.

The chi-square test was used to compare categorical variables between groups. The Student's unpaired t test or Mann-Whitney U test was used to compare continuous variables, as appropriate. Although this statistical method is not entirely rigorous, the results could be presented through a more intuitive way and some authors including Gumbs (*5*) and Boggi (*6*) have already applied this statistical method. Statistical analyses were finished by SPSS statistical software package (version 25.0, SPSS Inc., Chicago, IL, USA). A p value < 0.05 was considered statistically significant.

3. Results

This systematic review included 39 articles that documented a total of 2,653 MIPDs (Table 1) (*7-45*). Seventeen articles were published between 2010 and 2017, documenting 540 cases (20.4%), whereas twenty-two were published in the next two years, reporting on 2,113 cases (79.6%) (Figure 1).

Table 1. Summary of current articles on minimally invasive pancreaticoduodenectomy in more than 10 cases

First author (*Ref.*)	Publication year	Study period	Methods	Cases
Chao Lu (*32*)	2018	2012-2017	PL	320
Xueqing Liu (*30*)	2018	2013-2017	PL	300
Yunqiang Cai (*9*)	2018	2015-2018	PL	238
Hang Zhang (*43*)	2018	2014-2016	PL	202
Wei Chai (*10*)	2019	2015-2017	PL/LA	102/86
Qingchun Li (*27*)	2019	2014-2017	PL	134
Xiaohui Duan (*17*)	2017	2014-2017	PL	101
Guolin Li (*25*)	2018	2016-2017	PL	100
Tao Zhang (*45*)	2018	2012-2016	RA	100
Yong An (*7*)	2019	2017-2018	PL	90
Yun Liang (*28*)	2019	2015-2018	PL	82
Defei Hong (*19*)	2016	2013-2016	PL,RA	80
Yusheng Du (*16*)	2019	2016-2017	PL	67
Shi Chen (*14*)	2015	2010-2013	RA	60
Fangkuan Li (*24*)	2017	2012-2016	PL	50
Peng Chen (*13*)	2018	2015-2018	PL, RA	40
Ronggui Lin (*29*)	2018	2017-2017	PL, RA, HA	35
Jianjun Li (*26*)	2013	2002-2012	PL, LA	34
Menghua Dai (*15*)	2018	2016-2018	PL	34
Zhigang Wei (*37*)	2018	2015-2018	PL	33
Fan Yang (JL) (*41*)	2018	2017-2017	PL	30
Rong Tang (*34*)	2017	2010-2013	LA	29
Fan Yang (CQ) (*42*)	2019	2016-2018	PL	29
Jianhui Chen (*12*)	2016	2012-2014	LA	25
Zuguang Wu (*39*)	2017	2014-2016	PL	22
Lei Zhang (*44*)	2019	2015-2018	PL	21
Jiacheng Wu (*38*)	2018	2017-2017	PL	21
Zhao Liu (*31*)	2015	2011-2012	LA	21
Qiang Huang (*22*)	2017	2016-2016	PL	20
Qiuya Wei (*36*)	2016	2013-2015	PL	19
Wentao Gao (*18*)	2017	2016-2016	PL	18
Hai Hu (*20*)	2019	2015-2018	RA	18
Qinzheng Bai (*8*)	2016	2015-2016	LA	16
Jinmeng Hu (*21*)	2018	2015-2017	PL	16
Huanwei Chen (*11*)	2019	2015-2018	PL/LA	10/5
Mingsheng Sun (*33*)	2015	2010-2015	LA	12
Jun Xu (*40*)	2010	2005-2008	LA, HA	12
Hongbo Wei (*35*)	2014	2012-2013	PL	11
Wu Ji (*23*)	2014	2010-2012	RA	10

PL, pure laparoscopic pancreaticoduodenectomy. LA, laparoscopy-assisted pancreaticoduodenectomy. RA, robotic-assisted pancreaticoduodenectomy. HA, hand-assisted pancreaticoduodenectomy. JL, Jilin Province. CQ, Chongqing City.

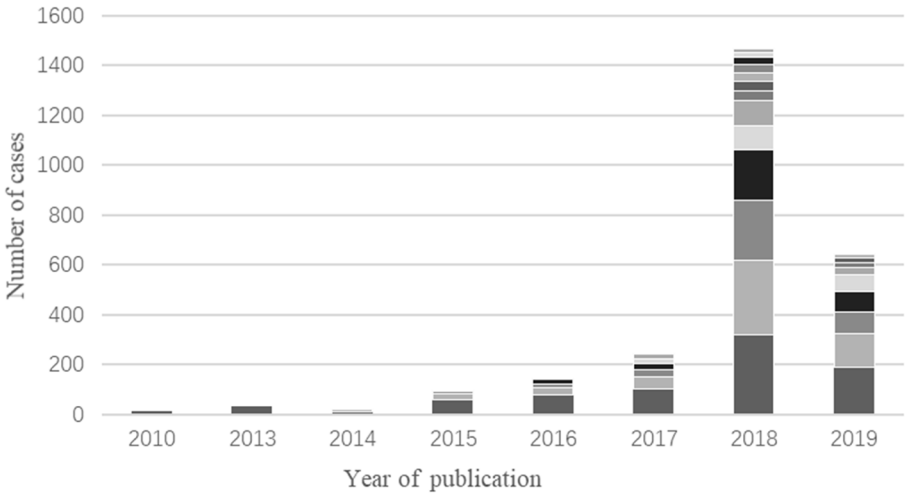

Figure 1. Number of cases documented yearly. The different depth of gray color in each bar represent different studies in that year and their heights mean the sample size of the corresponding study.

Table 2. Management of pancreatic stump in minimally invasive pancreaticoduodenectomy

First author (*Ref.*)	Management of pancreatic stump			
	PJ	PG	Technique	Stent
Chao Lu (*32*)	320	0	[E-to-S and D-to-M]	Selectively
Xueqing Liu (*30*)	295[a]	0	30[E-to-E and Invaginating], 265[E-to-S and D-to-M]	Selectively
Yunqiang Cai (*9*)	238	0	[E-to-S and D-to-M]	Yes
Hang Zhang (*43*)	202	0	[E-to-S and D-to-M]	Yes
Wei Chai (*10*)	102(PL), 86(LA)	0	102[E-to-S and D-to-M], 86[E-to-S and Invaginating]	Yes
Qingchun Li (*27*)	134	0	[E-to-S and D-to-M]	Yes
Xiaohui Duan (*17*)	101	0	[E-to-S and D-to-M]	Yes
Guolin Li (*25*)	100	0	[E-to-S and D-to-M]	Selectively
Tao Zhang (*45*)	100	0	[E-to-S and D-to-M]	Yes
Yong An (*7*)	90	0	[E-to-S and D-to-M]	NA
Yun Liang (*28*)	82	0	[E-to-S and D-to-M]	NA
Dfei Hong[b] (*19*)	70	7	70[E-to-S and D-to-M], 7[E-to-S and Invaginating]	Yes
Yusheng Du (*16*)	67	0	67[E-to-S and D-to-M]	Yes
Shi Chen (*14*)	59	1[c]	59[E-to-S and D-to-M]	Yes
Fangkuan Li (*24*)	50	0	[E-to-S and D-to-M]	NA
Peng Chen (*13*)	40	0	[E-to-S and D-to-M]	Yes
Ronggui Lin (*29*)	35	0	NA	NA
Jianjun Li (*26*)	34	0	[E-to-S and D-to-M]	Yes
Menghua Dai (*15*)	NA	NA	NA	NA
Zhigang Wei (*37*)	NA	NA	NA	NA
Fan Yang (JL) (*41*)	30	0	[E-to-S and D-to-M]	Yes
Rong Tang (*34*)	NA	NA	NA	NA
Fan Yang (CQ) (*42*)	29	0	[E-to-S and D-to-M]	Yes
Jianhui Chen (*12*)	NA	NA	NA	NA
Zuguang Wu (*39*)	22	0	[E-to-S and D-to-M]	NA
Lei Zhang (*44*)	21	0	[E-to-S and M-to-M]	Selectively
Jiacheng Wu (*38*)	21	0	[E-to-S and D-to-M]	Yes
Zhao Liu (*31*)	21	0	[E-to-S and D-to-M]	Yes
Qiang Huang (*22*)	20	0	[E-to-S and D-to-M]	Yes
Qiuya Wei (*36*)	19	0	[E-to-S and D-to-M]	Yes
Wentao Gao (*18*)	18	0	[E-to-S and D-to-M]	NA
Hai Hu (*20*)	18	0	NA	NA
Qinzheng Bai (*8*)	16	0	[E-to-S and D-to-M]	Yes
Jinmeng Hu (*21*)	16	0	[E-to-S and D-to-M]	Yes
Huanwei Chen (*11*)	5(PL), 10(LA)	0	[E-to-S and D-to-M], [E-to-S and D-to-M]	NA, Yes
Mingsheng Sun (*33*)	NA	NA	NA	NA
Jun Xu (*40*)	12	0	[E-to-E and Invaginating]	Selectively
Hongbo Wei (*35*)	11	0	[E-to-E and Invaginating] or [E-to-S and D-to-M]	NA
Wu Ji (*23*)	10	0	[E-to-S and D-to-M]	Yes

[a]Another 5 cases underwent total pancreatectomy. [b]Another 3 cases were not described due to conversion to laparotomy. [c]Pancreaticogastrostomy was not described in detail. PL, pure laparoscopic pancreaticoduodenectomy. LA, laparoscopy-assisted pancreaticoduodenectomy. PJ, pancreatojejunostomy. PG, pancreatogastrostomy. NA, not applicable. D-to-M, duct-to-mucosa. E-to-E, end-to-end. E-to-S, end-to-side. JL, Jilin Province. CQ, Chongqing City.

Pure laparoscopic pancreaticoduodenectomy (PL) have held a dominant position in MIPD according to the literature of recent years. 2070 PL (78.0%) were documented in our review. And 7 authors (*8,10-12,31,33,34*) describing 194 cases (7.3%) laparoscopy-assisted pancreaticoduodenectomy (LA).

Robotic-assisted pancreaticoduodenectomy (RA) was gradually put into application for pancreatic surgery in the recent few years. 188 cases (7.1%) RA were included in our analysis, while only 5 cases (0.2%) hand-assisted pancreaticoduodenectomy (HA) of two articles (*29,40*) are mentioned in our review.

In addition, seven authors applied more than one technique (*10,11,13,19,26,29,40*), and three of them (*13,19,29*) simultaneous applied LPD and RPD without data separation. Therefore, the three articles were excluded either in comparison of LPD and RPD or in classification of technique.

3.1. *Technical details*

Technical details of MIPD are listed in Table 2 and Table 3, including management of pancreatic stump, closure of gastroduodenal artery, specimen extraction site, anastomotic technique in gastroenterostomy, suture technique in choledochojejunostomy and vascular resection and reconstruction.

Details on management of pancreatic stump were provided in 34 articles (87.2%). Pancreatojejunostomy (PJ) was the major selection to manage pancreatic stump while pancreatogastrostomy(PG) was only mentioned in 8 cases of 2 articles (*14,19*) and no duct occlusion was reported. Details about anastomosis methods were described in 32 articles (82.1%), including end-to-end

Table 3. Technical details of minimally invasive pancreaticoduodenectomy

First author (*Ref.*)	Management of GDA	Extraction site	Anastomotic technique in gastroenterostomy	Suture technique in choledochojejunostomy	Vascular resection and reconstruction
Chao Lu (*32*)	Clips	NA	Stapled	Selectively	NA
Xueqing Liu (*30*)	Clips or Ligature	Subxiphoid	Stapled (68.7%), Hand-sewn (31.3%)	RS	10
Yunqiang Cai (*9*)	NA	NA	NA	NA	0
Hang Zhang (*43*)	Clips	Infra-umbilical	Stapled	Selectively	2
Wei Chai (*10*)	NA	Subxiphoid	NA	NA	NA
Qingchun Li (*27*)	NA	Umbilical	NA	NA	NA
Xiaohui Duan (*17*)	Ligature and Clips	Infra-umbilical	Stapled	Selectively	NA
Guolin Li (*25*)	Ligature	NA	Stapled	RS	NA
Tao Zhang (*45*)	NA	Umbilical	NA	NA	0
Yong An (*7*)	NA	NA	Stapled	RS	3
Yun Liang (*28*)	NA	NA	NA	NA	NA
Defei Hong (*19*)	NA	NA	NA	NA	5
Yusheng Du (*16*)	NA	NA	NA	RS	NA
Shi Chen (*14*)	Ligature	NA	NA	Selectively	3
Fangkuan Li (*24*)	Clips	NA	Stapled	RS	NA
Peng Chen (*13*)	Ligature	NA	Stapled	NA	NA
Ronggui Lin (*29*)	Clips	NA	NA	NA	NA
Jianjun Li (*26*)	Ligature	Subxiphoid	NA	NA	NA
Menghua Dai (*15*)	NA	NA	NA	NA	2
Zhigang Wei (*37*)	Clips	NA	NA	NA	NA
Fan Yang (JL) (*41*)	NA	NA	Hand-sewn	NA	1
Rong Tang (*34*)	NA	Subxiphoid	NA	NA	NA
Fan Yang (CQ) (*42*)	Clips	NA	NA	RS	NA
Jianhui Chen (*12*)	NA	Subxiphoid	NA	NA	0
Zuguang Wu (*39*)	NA	Infra-umbilical	Stapled	NA	0
Lei Zhang (*44*)	NA	Subxiphoid	NA	NA	NA
Jiacheng Wu (*38*)	NA	Infra-umbilical	Stapled	RS	0
Zhao Liu (*31*)	Clips	Subxiphoid	NA	IS	0
Qiang Huang (*22*)	NA	NA	NA	NA	0
Qiuya Wei (*36*)	NA	NA	Stapled	RS	0
Wentao Gao (*18*)	NA	NA	Hand-sewn	RS	0
Hai Hu (*20*)	Ligature	Subxiphoid	NA	NA	0
Qinzheng Bai (*8*)	Clips	Subxiphoid	NA	NA	NA
Jinmeng Hu (*21*)	NA	NA	NA	NA	0
Huanwei Chen (*11*)	Ligature and Clips	Subxiphoidv (LA), Suprapubicv (PL)	Stapled	RS	0
Mingsheng Sun (*33*)	Clips	Subxiphoid	NA	NA	0
Jun Xu (*40*)	NA	Subxiphoid	NA	NA	0
Hongbo Wei (*35*)	NA	NA	NA	NA	NA
Wu Ji (*23*)	NAhi	Subxiphoid	NA	NA	NA

GDA, gastroduodenal artery. RS, running suture. IS, interrupted suture. NA, not applicable. JL, Jilin Province. CQ, Chongqing City.

and invaginating PJ, end-to-side and invaginating PJ, end-to-side and duct-to-mucosa PJ, end-to-side and invaginating PG according to Barreto's classification (*46*). Among the above methods, the end-to-side and duct-to-mucosa PJ was the most popular one. Undoubtedly, duct-to-mucosa anastomosis is the most difficult point in PJ. Hence, some modified or innovative methods such as purse-string, Bing's anastomosis (*9*) or Hong's single-stitch method (*47*) were applied for further reinforcing the junction between pancreatic duct and intestinal wall (*9,10,16,19,21,41*). Nevertheless, various modified methods haven't been marked in the tables so as to simplify our classification. As for stent for pancreatic duct, 25 authors (64.1%) implied entirely or selectively in their studies.

Seventeen authors (43.6%) described the closure of gastroduodenal artery (GDA). The methods contain clips (9 articles) or ligature (5 articles). In addition, Duan *et al*. (*17*) and Chen *et al*. (*11*) applied clips plus ligature while Liu *et al*. (*30*) used clips or ligature. Specimen extraction site was described in 19 articles (48.7%). Chen *et al*. (*11*) applied two different incisions to extract specimens in different surgical procedures. 13 authors (68.4%) used a subxiphoid incision to extract specimens. In 4 articles (21.1%), the specimen was delivered through an infra-umbilical incision or enlarged port, in 2 articles (10.5%) through an umbilical incision or enlarged port. Besides, suprapubic incision was used by Chen *et al*. as the second method. Seven authors described the jejunal loop used for duodenal or gastric anastomosis (17.9%), and all patients in their studies followed an antecolic route. The retromesenteric and retrocolic routes were hardly employed according to the data we pooled. Anastomotic technique in gastroenterostomy and suture technique

Table 4. Intraoperative outcomes of minimally invasive pancreaticoduodenectomy

First author (*Ref.*)	Operative time (min)	Blood loss (mL)	Conversion *n* (%)	Transfusion *n* (%)
Chao Lu (*32*)	352.3 ± 53.2	198.8 ± 127.6	NA	59 (18.4%)
Xueqing Liu (*30*)	6.7 (2.5-12.0)[c] h	500 (100-3000)[c]	NA	NA
Yunqiang Cai (*9*)	358 (220-495)[a]	112 (50-800)[a]	1 (0.4%)	11 (4.6%)
Hang Zhang (*43*)	301 ± 175	194 ± 107	3 (1.5%)	19 (9.4%)
Wei Chai (*10*)	419.7[b]	288.1[b]	NA	NA
Qingchun Li (*27*)	275.7[b]	114.5[b]	0 (0%)	9 (6.7%)
Xiaohui Duan (*17*)	325.7 (220-575)[c]	175.9 (100-550)[c]	NA	2 (2.0%)
Guolin Li (*25*)	277.5[b]	151.7[b]	NA	NA
Tao Zhang (*45*)	357.87 ± 93.28	171.13 ± 144.46	5 (5.0%)	NA
Yong An (*7*)	377[b]	296[b]	NA	18(20.0%)
Yun Liang (*28*)	364.6[b]	NA	7 (8.5%)	NA
Defei Hong (*19*)	351.2 ± 84.1	204.7 ± 165.9	3 (3.8%)	NA
Yusheng Du (*16*)	343.5[b]	213.2[b]	0 (0%)	5 (7.5%)
Shi Chen (*14*)	410[b]	NA	NA	8 (13.3%)
Fangkuan Li (*24*)	396.4 ± 81.9	282.0 ± 192.4	4 (7.4%)	NA
Peng Chen (*13*)	487.73 ± 113.13	360.00 ± 407.49	NA	NA
Ronggui Lin (*29*)	NA	150.0 ± 34.6	0 (0%)	NA
Jianjun Li (*26*)	440.0 (382-510)[c]	NA	0 (0%)	NA
Menghua Dai (*15*)	427.16 ± 78.05	597.06 ± 327.74	4 (11.8%)	NA
Zhigang Wei (*37*)	414.5 (340-498)[c]	420 (150-800)[c]	0 (0%)	NA
Fan Yang (JL) (*41*)	4.3 ± 1.5 h	300 ± 75	0 (0%)	NA
Rong Tang (*34*)	7.5 ± 0.8 h	326.4 ± 86.5	0 (0%)	NA
Fan Yang (CQ) (*42*)	482 ± 86	400.0 (300-800)[a]	NA	10 (34.5%)
Jianhui Chen (*12*)	474.6 ± 54.2	265.5 ± 72.6	NA	2 (8.0%)
Zuguang Wu (*39*)	414.0 ± 31.0	176.0 ± 50.4	NA	NA
Lei Zhang (*44*)	317.14 ± 44.06	523.91 ± 261.54	0(0%)	NA
Jiacheng Wu (*38*)	352 ± 25	168 ± 34	0(0%)	0 (0%)
Zhao Liu (*31*)	316 (260-410)[c]	240 (30-1000)[c]	1 (4.8%)	NA
Qiang Huang (*22*)	645.0 ± 139.9	750.0 ± 417.6	0 (0%)	NA
Qiuya Wei (*36*)	407.8 ± 146.5	309.7 ± 151.2	NA	NA
Wentao Gao (*18*)	476 ± 50	439 ± 228	NA	NA
Hai Hu (*20*)	450 ± 30	525 ± 125	1 (5.6%)	0 (0%)
Qinzheng Bai (*8*)	470.31 ± 61.09	568.75 ± 298.26	0 (0%)	NA
Jinmeng Hu (*21*)	459.8 ± 121.6	178.1 ± 118.3	NA	NA
Huanwei Chen (*11*)	528.7[b]	NA	0 (0%)	0 (0%)
Mingsheng Sun (*33*)	280 (240-340)c	300 (150-1200)[c]	2 (16.7%)	NA
Jun Xu (*40*)	6.5 (5-10)[c] h	435 (200-800)[c]	3 (25.0%)	NA
Hongbo Wei (*35*)	410.2 ± 85.0	168.2 ± 87.4	0 (0%)	NA
Wu Ji (*23*)	7.3 ± 3.6 h	320.0 ± 123.5	1 (10.0%)	0 (0%)
Total/mean	370.6	278.0	35 (2.6%)	143 (10.8%)

[a]Data are expressed as median and interquartile range. [b]Date are integration from multi-group data. [c]Data are expressed as mean and range. JL, Jilin Province. CQ, Chongqing City. NA, not applicable.

in choledochojejunostomy were mentioned in 14 and 15 articles respectively. The staple technique occupied the majority in gastroenterostomy (85.7%) and running suture was most common in choledochojejunostomy (66.7%). Besides, 4 authors (*14,17,32,43*) applied running or interrupted suture selectively depending on diameter of bile duct (26.7%). The information of vascular resection and reconstruction was mentioned by 7 authors while 14 studies regarded cases with vascular invasion as contraindications. Overall, 26 cases of vascular involvement were performed with vascular resection and reconstruction.

3.2. *Intraoperative outcomes*

Intraoperative outcomes of MIPD are documented in Table 4, containing operation time, blood loss, conversion rate to laparotomy and intraoperative transfusion rate.

The mean operation time was provided in 37 articles (94.9%) and ranged from 258 to 645 min, with a WA of 370.6 min. The median operative time was only mentioned in Cai's study (*9*) with a result of 358 min. The mean blood loss was provided in 33 articles (84.6%) ranged from 114.5 to 750 mL, with a WA of 278.0 mL. The median blood loss was mentioned in 2 articles (*9,42*) with a result of 112 mL and 400 mL.

The information of conversion rate to laparotomy was available in 25 studies (64.1%). A total of 35 MIPDs were converted to laparotomy (2.6%). The reasons were as follows: uncontrolled vascular bleeding (n = 9, 25.7%), severe adhesions (n = 5, 14.3%), limited working space (n = 1, 2.9%), and unspecified reasons (n = 20, 57.1%). The data of intraoperative transfusion rate was available in 14 articles (35.9%). A total of 143 MIPDs performed intraoperative transfusion (10.8%).

Table 5. Morbidity of minimally invasive pancreaticoduodenectomy

First author (*Ref.*)	Morbidity *n* (%)	Pancreatic fistula *n* (%)	Usage of ISGPF	Delayed gastric emptying *n* (%)	Bile leak *n* (%)	Postoperative hemorrhage *n* (%)
Chao Lu (*32*)	103 (32.2%)	56 (17.5%)	+	3 (0.9%)	12 (3.8%)	29 (9.1%)
Xueqing Liu (*30*)	95 (31.7%)	NA	+	12 (4.0%)	12 (4.0%)	28 (9.3%)
Yunqiang Cai (*9*)	NA	51 (21.4%)	+	17 (7.1%)	6 (2.5%)	3 (1.3%)
Hang Zhang (*43*)	61 (30.2%)	29 (14.4%)	+	2 3(11.4%)	3 (1.5%)	5 (2.5%)
Wei Chai (*10*)	67 (35.6%)	40 (21.3%)	+	12 (6.4%)	2 (1.1%)	3 (1.6%)
Qingchun Li (*27*)	18 (13.4%)	16 (11.9%)	+	2 (1.5%)	4 (3.0%)	3 (2.2%)
Xiaohui Duan (*17*)	NA	23 (22.8%)	+	4 (4.0%)	2 (2.0%)	7 (6.9%)
Guolin Li (*25*)	NA	63 (63.0%)	+	5 (5.0%)	4 (4.0%)	4 (4.0%)
Tao Zhang (*45*)	58 (58.0%)	24 (24.0%)	+	15 (15.0%)	11 (11.0%)	22 (22.0%)
Yong An (*7*)	19 (21.1%)	NA	+	5 (5.6%)	1 (1.1%)	1 (1.1%)
Yun Liang (*28*)	22 (26.8%)	NA	+	1 (1.2%)	NA	7 (8.5%)
Defei Hong (*19*)	NA	11 (13.8%)	+	5 (6.3%)	6 (7.5%)	6 (7.5%)
Yusheng Du (*16*)	20 (29.9%)	14 (20.9%)	+	2 (3.0%)	4 (6.0%)	1 (1.5%)
Shi Chen (*14*)	21 (35.0%)	8 (13.3%)	+	5 (8.3%)	5 (8.3%)	4 (6.7%)
Fangkuan Li (*24*)	12 (24.0%)	8 (16.0%)	+	2 (4.0%)	2 (4.0%)	0 (0%)
Peng Chen (*13*)	NA	10 (25.0%)	−	5 (12.5%)	NA	8 (20.0%)
Ronggui Lin (*29*)	NA	5 (14.3%)	+	1(2.9%)	1 (2.9%)	1 (2.9%)
Jianjun Li (*26*)	10 (29.4%)	2 (5.9%)	+	0 (0%)	0 (0%)	5 (14.7%)
Menghua Dai (*15*)	15 (44.1%)	NA	+	0 (0%)	NA	1 (2.9%)
Zhigang Wei (*37*)	NA	3 (9.1%)	+	6 (18.2%)	1 (3.0%)	NA
Fan Yang (JL) (*41*)	NA	10 (33.3%)	+	NA	NA	0 (0%)
Rong Tang (*34*)	14 (48.3%)	6 (20.7%)	−	2 (6.9%)	3 (10.3%)	1 (3.4%)
Fan Yang (CQ) (*42*)	16 (55.2%)	8 (27.6%)	−	1 (3.4%)	1 (3.4%)	5 (17.2%)
Jianhui Chen (*12*)	7 (28.0%)	2 (8.0%)	−	0 (0%)	1 (4.0%)	2 (8.0%)
Zuguang Wu (*39*)	8 (36.4%)	4 (18.2%)	−	0 (0%)	0 (0%)	1 (4.5%)
Lei Zhang (*44*)	4 (19.0%)	1 (4.8%)	−	2 (9.5%)	0 (0%)	1 (4.8%)
Jiacheng Wu (*38*)	NA	15 (71.4%)	+	0 (0%)	0 (0%)	0 (0%)
Zhao Liu (*31*)	5 (23.8%)	1 (4.8%)	+	2 (9.5%)	0 (0%)	0 (0%)
Qiang Huang (*22*)	6 (30.0%)	6 (30.0%)	+	5 (25.0%)	1 (5.0%)	2 (10.0%)
Qiuya Wei (*36*)	NA	1 (5.3%)	−	0 (0%)	1 (5.3%)	2 (10.5%)
Wentao Gao (*18*)	10 (55.6%)	7 (38.9%)	+	4 (22.2%)	0 (0%)	1 (5.6%)
Hai Hu (*20*)	7 (38.9%)	4 (22.2%)	+	0 (0%)	1 (5.6%)	3 (16.7%)
Qinzheng Bai (*8*)	NA	6 (37.5%)	+	NA	NA	NA
Jinmeng Hu (*21*)	8 (50.0%)	5 (31.3%)	+	2 (12.5%)	0 (0%)	0 (0%)
Huanwei Chen (*11*)	NA	4 (26.7%)	+	1 (6.7%)	0 (0%)	0 (0%)
Mingsheng Sun (*33*)	3 (25.0%)	2 (16.7%)	+	0 (0%)	1 (8.3%)	0 (0%)
Jun Xu (*40*)	1 (8.3%)	0 (0%)	−	0 (0%)	1 (8.3%)	0 (0%)
Hongbo Wei (*35*)	4 (36.4%)	NA	−	NA	NA	NA
Wu Ji (*23*)	1 (10.0%)	1 (10.0%)	−	0 (0%)	0 (0%)	0 (0%)
Total/mean	615 (31.9%)	446 (20.9%)		144 (5.5%)	86 (3.5%)	156 (6.0%)

IGSPF, international surgical group definition of pancreatic fistula. JL, Jilin Province. CQ, Chongqing City. NA, not applicable.

3.3. *Short-term outcomes*

Short-term outcomes of MIPD are reported in Table 5 and Table 6, including morbidity, pancreatic fistula (PF) rate, delayed gastric emptying (DGE) rate, bile leak rate, postoperative hemorrhage rate, length of postoperative hospital stay (LOS), Clavien-Dindo ≥ 3 complication rate, reoperation rate and rate of mortality.

The data of morbidity was included in 27 articles (69.2%). The morbidity ranged from 8.3 to 58.0%. Overall, 615 cases of postoperative complications occurred (31.9%). Particularly, the incidence of pancreatic fistutla was mentioned in 38 articles (97.4%). The usage of International Surgical Group of Pancreatic Fistula (ISGPF) was employed in 29 articles (76.3%). In this analysis, we excluded the articles which only presented the data of clinical relevant PF (grade B/C). Incidence of overall PF ranged from 0 to 71.4%. Overall, 446 cases developed PF, giving a total PF rate of 20.9%. The data of DGE was available in 36 articles (92.3%), and ranged from 0 to 25.0%. In a total of 144 cases DGE occurred (5.5%). 33 studies(84.6%) mentioned bile leak, and ranged from 0 to 11.0%. Overall, 86 cases suffered from bile leak (3.5%). 36 articles (92.3%) recorded postoperative hemorrhage rate, and ranged from 0 to 22.0%, which included intraperitoneal and gastrointestinal hemorrhage. In a total of 156 cases postoperative hemorrhage occurred (6.0%).

The mean LOS was reported in 30 articles (76.9%), and ranged from 8.8 to 27.41 days, with a WA of 16.1 days. As for Clavien-Dindo ≥ 3 complications, only 12 studies listed the results (30.8%), which ranged from 0 to 32.5% and in 116 cases patients developed Clavien-Dindo ≥ 3 complications, with an overall rate of 13.4%. The information of reoperation was described in 20 articles (51.3%), and ranged from 0 to 17.2%. A total of

Table 6. Short-term outcomes of minimally invasive pancreaticoduodenectomy

First author (*Ref.*)	LOS (days)	Clavien-Dindo ≥ 3 complications *n* (%)	Reoperation *n* (%)	Mortality *n* (%)
Chao Lu (*32*)	18.3 ± 11.7	35 (10.9%)	17 (5.3%)	2 (0.6%)
Xueqing Liu (*30*)	17 (6-89)	NA	NA	13 (4.3%)
Yunqiang Cai (*9*)	10.2 (5-19)[a]	NA	2 (0.8%)	1 (0.4%)
Hang Zhang (*43*)	12.97 ± 7.21	NA	2 (1.0%)	1 (0.5%)
Wei Chai (*10*)	12.3[b]	NA	3 (1.6%)	3 (1.6%)
Qingchun Li (*27*)	18.9[b]	NA	NA	2 (1.5%)
Xiaohui Duan (*17*)	14.8 (8-29)[c]	9 (8.9%)	3 (3.0%)	1 (1.0%)
Guolin Li (*25*)	12.9[b]	NA	NA	NA
Tao Zhang (*45*)	18 ± 13.46	22 (22.0%)	6 (6.0%)	3 (3.0%)
Yong An (*7*)	13.3[b]	NA	1 (1.1%)	NA
Yun Liang (*28*)	NA	22 (26.8%)	5 (6.1%)	3 (3.7%)
Defei Hong (*19*)	16.6 ± 10.1	NA	8 (10.0%)	NA
Yusheng Du (*16*)	15.4[b]	2 (3.0%)	1 (1.5%)	0 (0%)
Shi Chen (*14*)	20.0 ± 7.4	7 (11.7%)	2 (3.3%)	1 (1.7%)
Fangkuan Li (*24*)	17.17 ± 6.628	NA	NA	NA
Peng Chen (*13*)	25.86 ± 12.22	13 (32.5%)	NA	3 (7.5%)
Ronggui Lin (*29*)	12.9 ± 3.2	NA	NA	NA
Jianjun Li (*26*)	NA	3 (8.8%)	3 (8.8%)	1 (2.9%)
Menghua Dai (*15*)	NA	NA	1 (2.9%)	NA
Zhigang Wei (*37*)	NA	NA	NA	NA
Fan Yang (JL) (*41*)	16.3 ± 7.2	NA	NA	0 (0%)
Rong Tang (*34*)	9.0 ± 2.1	NA	NA	NA
Fan Yang (CQ) (*42*)	17 (15-20)[a]	NA	5 (17.2%)	2 (6.9%)
Jianhui Chen (*12*)	15.5 ± 4.2	NA	1 (4.0%)	0 (0%)
Zuguang Wu (*39*)	17.3 ± 2.0	NA	NA	NA
Lei Zhang (*44*)	27.41 ± 5.82	1 (4.8%)	1 (4.8%)	NA
Jiacheng Wu (*38*)	11.3 ± 2.0	NA	NA	0 (0%)
Zhao Liu (*31*)	NA	NA	NA	NA
Qiang Huang (*22*)	25.0 ± 9.3	0 (0%)	0 (0%)	0 (0%)
Qiuya Wei (*36*)	8.8 ± 2.1	NA	NA	0 (0%)
Wentao Gao (*18*)	15.5 ± 6.8	NA	NA	0 (0%)
Hai Hu (*20*)	16 ± 4	NA	0 (0%)	1 (5.6%)
Qinzheng Bai (*8*)	NA	NA	NA	0 (0%)
Jinmeng Hu (*21*)	19.1 ± 6.0	NA	NA	NA
Huanwei Chen (*11*)	14b	NA	NA	0 (0%)
Mingsheng Sun (*33*)	NA	2 (16.7%)	2 (16.7%)	0 (0%)
Jun Xu (*40*)	15.0	NA	NA	0 (0%)
Hongbo Wei (*35*)	17.0 ± 2.2	NA	NA	0 (0%)
Wu Ji (*23*)	9.6 ± 4.3	0 (0%)	0 (0%)	0 (0%)
Total/mean	16.1	116 (13.4%)	63 (3.6%)	37 (1.7%)

[a]Data are expressed as median and interquartile range. [b]Date are integration from multi-group data. LOS, length of hospital stay. JL, Jilin Province. CQ, Chongqing City. NA, not applicable.

63 cases demanded reoperation (3.6%). Unfortunately, only 27 studies (69.2%) recorded the rate of mortality, which ranged from 0 to 7.5%, and in 37 cases patients died, with an overall postoperative mortality rate of 1.7%.

3.4. *Oncologic outcomes*

The pathology results are shown in Table 7, comprising the rate of malignancy, the number of harvested lymph nodes and the rate of negative tumor margin (R0).

The etiology was described in 35 articles (89.7%). We regarded ampullary adenocarcinoma, pancreatic ductal adenocarcinoma, distal cholangiocarcinoma, duodenal adenocarcinoma and other malignant tumors clearly identified by the authors as malignancy in our review because of the different attitudes to borderline tumors from diffierent authors. Overall, 2084 cases (80.7%) were diagnosed with maligancy. Furthermore, only 7 authors (17.9%) described the etiology using tumor-node-metastasis (TNM) stage. The mean number of harvested lymph nodes was provided in 20 articles (51.3%), and ranged from 7.02 to 23.1, with a WA of 13.5 lymph nodes. Margin status was documented in 25 articles (64.1%). In 9 articles, the R0 rate was 100%, whereas it ranged from 10 to 99.2% in the other 16 studies. A total of 79 cases were diagnosed with positive margins out of 1,492 malignancy cases (5.3%)

3.5. *Comparison of the results of different surgical techniques*

Comparisons of the outcomes between LPD, RPD and open pancreaticoduodenectomy (OPD) are summarized in Table 8. Excluding cumulative data of multiple techniques from three studies, a total of 2,310 LPD, 188 RPD and 779 OPD were accepted for comparison.

Table 7. Oncologic outcomes of minimally invasive pancreaticoduodenectomy

First author (*Ref.*)	Malignancy[a] *n* (%)	TNM stage	Harvested lymph node	R0 (%)
Chao Lu (*32*)	221 (69.1%)	−	NA	NA
Xueqing Liu (*30*)	258 (86.0%)	−	12 (2-60)	99.3%
Yunqiang Cai (*9*)	161 (67.6%)	−	NA	NA
Hang Zhang (*43*)	147 (72.8%)	+	9.81 ± 5.19	99.0%
Wei Chai (*10*)	188 (100.0%)	−	14.9[b]	93.6%
Qingchun Li (*27*)	134 (100.0%)	+	23.1[b]	92.5%
Xiaohui Duan (*17*)	101 (100.0%)	−	16.7 ± 4.2	95.0%
Guolin Li (*25*)	45 (45.0%)	−	NA	NA
Tao Zhang (*45*)	78 (78.0%)	−	7.02 ± 4.30	100.0%
Yong An (*7*)	71 (78.9%)	−	17.2[b]	100.0%
Yun Liang (*28*)	60 (73.2%)	−	12.5[b]	95.0%
Defei Hong (*19*)	71 (88.8%)	−	NA	100.0%
Yusheng Du (*16*)	60 (90.0%)	−	NA	NA
Shi Chen (*14*)	38 (63.3%)	+	13.6 ± 6.0	97.4%
Fangkuan Li (*24*)	46 (92.0%)	−	11.56 ± 6.174	97.8%
Peng Chen (*13*)	3 (75.0%)	−	NA	10.0%
Ronggui Lin (*29*)	24 (68.6%)	−	10.6 ± 4.0	100.0%
Jianjun Li (*26*)	34 (100.0%)	−	NA	NA
Menghua Dai (*15*)	31 (91.2%)	−	NA	93.5%
Zhigang Wei (*37*)	33 (100.0%)	−	NA	100.0%
Fan Yang (JL) (*41*)	26 (86.7%)	−	NA	92.3%
Rong Tang (*34*)	29 (100.0%)	+	NA	NA
Fan Yang (CQ) (*42*)	20 (69.0%)	+	NA	90.0%
Jianhui Chen (*12*)	25 (100.0%)	−	12.6 ± 3.3	100.0%
Zuguang Wu (*39*)	NA	−	9.3 ± 3.0	NA
Lei Zhang (*44*)	NA	−	7.24 ± 4.81	100.0%
Jiacheng Wu (*38*)	21 (100.0%)	−	NA	100.0%
Zhao Liu (*31*)	18 (85.7%)	−	14 (8-26)	94.4%
Qiang Huang (*22*)	18 (90.0%)	−	NA	NA
Qiuya Wei (*36*)	17 (89.5%)	−	17.7 ± 6.5	76.5%
Wentao Gao (*18*)	13 (72.2%)	−	NA	69.2%
Hai Hu (*20*)	9 (50.0%)	+	16 ± 4	88.9%
Qinzheng Bai (*8*)	12 (75.0%)	−	NA	NA
Jinmeng Hu (*21*)	NA	−	17.1 ± 9.7	100.0%
Huanwei Chen (*11*)	13 (86.7%)	−	NA	NA
Mingsheng Sun (*33*)	12 (100.0%)	+	10	100.0%
Jun Xu (*40*)	11 (91.7%)	−	NA	NA
Hongbo Wei (*35*)	NA	−	9.2 ± 4.0	100.0%
Wu Ji (*23*)	9 (90.0%)	−	NA	NA
Total/mean	2,084 (80.7%)		13.5	1,413 (94.7%)

[a]Malignancies include Ampullary adenocarcinoma, Pancreatic ductal adenocarcinoma, Distal cholangiocarcinoma, Duodenal adenocarcinoma and other malignant tumors clearly identified by the authors. [b]Date are integration from multi-group data. TNM, tumor-node-metastasis. JL, Jilin Province. CQ, Chongqing City. NA, not applicable

The operative time was significantly longer in LPD and RPD groups than in OPD groups. Compared with OPD, LPD shortened LOS significantly. As for morbidity, LPD, RPD and OPD had a result of 30.4%, 46.3% and 37.9% respectively. Interestingly, every two of them had a significant difference, and the three techniques had similar results in blood loss, pancreatic fistulas and mortality rates.

3.6. *Comparison of the results of large and small series*

Twenty-one articles documented on 30 or more MIPD (*n* = 2,318), whereas eighteen studies on 29 or fewer MIPD (*n* = 335). (Table 9)

In aspects of operative time and morbidity, the large series had more significant advantages than the small one. No significance, however, was mentioned in blood loss, LOS, PF and mortality rate.

4. Discussion

Early in 1994, Gagner described the first case of laparoscopic pylorus-preserving pancreatoduodenectomy for chronic pancreatitis, which marked the beginning of a new era. However, the multiple technical complications covered the benefit of a laparoscopic approach (*2*). Furthermore, inherent technical limitations of laparoscopy and a long learning curve made this advanced technique develop slowly. Nine years later, Lu reported the first LPD for duodenal papillary cancer in Chinese mainland and achieved comparable outcomes to OPD in perioperative blood loss and short-term recovery (*3*). Afterwards, an increasing number of reports describing the attempt at MIPD were published.

Table 8. Comparison of surgical techniques

Items	LPD (*n* = 2,310)	RPD (*n* = 188)	OPD (*n* = 779)	*p*		
				LPD vs RPD	LPD *vs* OPD	RPD *vs* OPD
WA of operative time (min.)	367.5 (*n* = 2,072)	387.6 (*n* = 188)	327.7 (*n* = 779)	NS*	0.014*	0.007*
WA of blood loss (mL)	284.7 (*n* = 1912)	232.5 (*n* = 128)	374.6 (*n* = 613)	NS^	NS^	NS*
WA of LOS (days)	15.7 (*n* = 1811)	18.0 (*n* = 188)	20.9 (*n* = 733)	NS*	0.006*	NS*
Morbidity (%)	528 (30.4%) (*n* = 1737)	87 (46.3%) (*n* = 188)	267 (37.9%) (*n* = 704)	< 0.001°	< 0.001°	0.038°
Pancreatic fistula (%)	383 (21.4%) (*n* = 1793)	37 (19.7%) (*n* = 188)	150 (20.5%) (*n* = 731)	NS°	NS°	NS°
Mortality (%)	29 (1.5%) (*n* = 1894)	5 (2.7%) (*n* = 188)	14 (2.6%) (*n* = 537)	NS°	NS°	NS°

**t* test unpaired. ^Mann-Whitney *U* test. °Chi squared. LPD, laparoscopic pancreaticoduodenectomy. RPD, robotic pancreaticoduodenectomy. OPD, open pancreaticoduodenectomy. WA, weighted average. NS, no significant difference. LOS, length of hospital stay.

Table 9. Comparison of large vs smaller series

Items	Large series (*n* = 2,318)	Smaller series (*n* = 335)	*p*
WA of operative time (min.)	360.0 (*n* = 2045)	435.1 (*n* = 335)	0.013*
WA of blood loss (mL)	266.1 (*n* = 1904)	356.0 (*n* = 291)	NS^
WA of LOS (days)	16.1 (*n* = 1897)	15.8 (*n* = 257)	NS*
Morbidity (%)	466 (28.1%) (*n* = 1661)	94 (35.6%) (*n* = 264)	0.012°
Pancreatic fistula (%)	373 (20.6%) (*n* = 1812)	73 (22.5%) (*n* = 324)	NS°
Mortality (%)	34 (1.8%) (*n* = 1896)	3 (1.3%) (*n* = 226)	NS°

**t* test unpaired. ^Mann-Whitney *U* test. °Chi squared. WA, weighted average. NS, no significant difference. LOS, length of hospital stay.

As listed in this systematic review, the maturation of MIPD in Chinese mainland has been extremely quick. The present review is the largest study to evaluate current status of MIPD in both high-volume and low-volume hospitals of Chinese mainland. A total of 2,653 cases were reported in the recent ten years excluding articles of less than 10 cases and initial experience from some high-volume centers. The number of cases reported in the recent two years(from January 2018 to June 2019) was four times than that in the previous years. Although it can't represent the annual cases of MIPD, it demonstrated that MIPD is a research highlight in the Chinese mainland in recent years. In order to highlight distinctive characteristics of MIPD in China mainland and further analyze the difference between Chinese mainland and the world, we present several recent systematic reviews describing the development of MIPD in the world (Table 10).

As shown in this table, we have a more favorable outcome in operation time than Nickel (mean:370.6 min *vs* 417.0min). Probably, this is largely associated with the learning curve and operation mastery. Wang *et al* were of the view that the minimum number of cases needed to reach technical competency for LPD was 40 cases (*48*), while Boone *et al* were first able to reach proficiency after 80 cases in robotic-assisted PD (*49*). Based on Chinese national conditions, a large number of patients have had a tremendous advantage accumulating surgeon's experience and accelerating surgeon's learning curve, especially in high-volumn centers. While similar results of estimated blood loss were obtained by Nickel's study and this review, Jiang's research offered a worse outcome due to an initial study, which accounted for a large proportion of results.

In terms of morbidity, we found some complications related to MIPD in our review, such as PF, bile leak and postoperative hemorrhage, which were equivalent to those of MIPD as reported in the international reviews. Strangely, more cases suffering DGE were reported in Nickel's study (21.9% *vs* 5.5%). The reason that contributed to the significant difference maybe was a large number of authors in our review only selectively reported clinically related DGE(grade B/C) (*50*). Meanwhile, Nickel only selectively analyzed the clinically related PF because not all trials reported biochemical leaks. Therefore, it's not hard to conclude that we have a slightly better result in overall PF than Nickel, which largely benefited from modified or innovative methods to further reinforce the junction such as purse-string, Bing's anastomosis (*9*) or Hong's single-stitch method (*47*). Nonetheless, PF was still the most common postoperative complication no matter in Chinese or international studies. Also, the corrosiveness of pancreatic juice may increase the risk of late postoperative hemorrhage (*51*). Whatever, more effective and safer anastomosis methods are urgently needed to

Table 10. Comparison of perioperative and oncological outcomes in previous systematic reviews and this review

Variables	Nickel (*52*)	Jiang (*54*)	Wang (*55*)	This review
Intraoperative outcomes				
Operation time (min)	417.0			370.6
Blood loss (mL)	280.5	378.1		278.0
Conversion to laparotomy			61 (5.9%)	35 (2.6%)
Transfusion				143 (10.8%)
Short-term outcomes				
Morbidity			511 (49.7%)	615 (31.9%)
Pancreatic fistula	20 (17.5%)	43 (15.1%)	338 (32.9%)	446 (20.9%)
Delayed gastric emptying	25 (21.9%)		172 (16.7%)	144 (5.5%)
Bile leak	10 (8.8%)		50 (4.9%)	86 (3.5%)
Postoperative hemorrhage	10 (8.8%)	24 (9.3%)	128 (12.4%)	156 (6.0%)
length of hospital stay(days)	10.6	10.0	13.5	16.1
Clavien-Dindo ≥ 3 complications	33 (28.9%)		218 (21.2%)	116 (13.4%)
Reoperation	8 (7.0%)		88 (8.6%)	63 (3.6%)
Mortality	8 (7.0%)		25 (2.4%)	37 (1.7%)
Oncologic outcomes				
Harvested lymph node	14.3	19.4	10.5	13.5
R0 rate	91 (82.0%)	695 (79.9%)	1,004 (97.6%)	1,413 (94.7%)

decrease this formidable complication.

Regarding length of postoperative hospital stay, no significant difference existed between Nickel's and Jiang's studies. Surprisingly, the outcome we pooled was considerably longer than the former two. This difference could, in part, be caused by the different regulations and culture in different countries (*6,52*). Statistical analysis had been submitted at this point by Boggi with the result of 21.9 days in Europe, 13.0 days in Asia and 9.4 days in North America (*6*).

The first and the only patient-blinded, randomized clinical trial (LEOPARD-2) was stopped due to a higher mortality rate (14% *vs* 2%) in the LPD group when compared to the OPD group. However, the four centers included in this trial with a median of 11 LPD (range 6-15) annually. What's more, we couldn't get any information from the original article about how many LPD cases were performed by the surgeons before they participated in the trial and whether they had already finished the learning curve or not.

As for oncologic outcomes, we had a similar result as Nickel in harvested lymph nodes (13.5 *vs* 14.3), but both were less than Jiang's outcome of 19.4. However, in R0 resection, we had a significantly better result than the other two. Actually, certainty of evidence in margin status was low. Pathology information has not always been collected according to standardized methodology. Especially for borderline tumors, few authors described their classification criteria.

Wang's study is the Chinese largest multicenter study to date which pooled the data from 1,029 consecutive MIPD patients in 16 high-volume pancreatic centers in China. As shown in the table, we had slight advantages in many factors including conversion to laparotomy, overall and differing morbidity, Clavien-Dindo ≥ 3 complications, reoperation and mortality. The reasons are not unique. On the one hand, Wang *et al* pooled the data from January 2010 to August 2016. With more advanced and innovative technologies introduced and the number of surgeons completing the learning curve increasing gradually, it is reasonable to assume that we can acquire better results in either intraoperation or short-term outcomes. On the other hand, reporting bias in low-volume hospitals cannot be ignored.

Major venous resection and reconstruction in MIPD has been regarded as a surgical forbidden zone for a long time. In this study, a total of 26 cases of MIPD combined with major venous resection and reconstruction were performed in 7 high-volume pancreatic centers. Besides, in 2018, Cai *et al* (53) reported an innovative approach to perform the above-mentioned challenging surgical procedures in 18 patients. No 30-day mortality was documented while only one case was converted to laparotomy due to uncontrolled bleeding from the splenic vein. Therefore, it is reasonable to believe that MIPD with major venous resection and reconstruction is technically feasible in selected patients, and with continuous accumulation of surgeons' experience and technological innovations, patients with vascular involvement will no longer be an absolute contraindication for MIPD.

This review is also subject to limitations. First, some technique details including pylorus preservation PD, section of pancreatic neck and long-term oncological outcomes such as overall survival and recurrence-free survival were not described in this study due to a lack of enough original data. Second, the study has not further compared and analyzed the outcomes of MIPD in different periods. Therefore, we can hardly observe the improvement and progress of results from recent years. Third, the quality of evidence is generally limited to cohort studies and case series.

In conclusion, although the developmental stage of MIPD in Chinese mainland was nearly a decade late,

its development was extremely quick, especially in the recent two years. The operative volume of MIPD in Chinese mainland is in the leading position in the world. Compared with some large international meta-analysis, non-inferior perioperative and short-term oncological outcomes were observed in MIPD of Chinese mainland. What's more, nearly 50 cases were documented in the condition of major vascular resection and reconstruction in Chinese mainland, which represented the operative quality to a certain degree. However, research on survival analysis and phased learning curve outcomes is urgently needed before the innovative surgical techniques are widely accepted.

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(Received October 11, 2019; Revised December 12, 2019; Accepted December 20, 2019)