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The role of older age and obesity in minimally invasive and open pancreatic surgery: A systematic review and meta-analysis

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ABSTRACT

Background/objectives: The aim of this study was to assess the impact of older age (≥70 years) and obesity (BMI ≥30) on surgical outcomes of minimally invasive pancreatic resections (MIPR). Subsequently, open pancreatic resections or MIPR were compared for elderly and/or obese patients.
Methods: A systematic review was conducted as part of the 2019 Miami International Evidence-Based Guidelines on MIPR (IG-MIPR). Study quality assessment was according to The Scottish Intercollegiate Guidelines Network (SIGN). A meta-analysis was performed to assess the impact of MIPR or open pancreatic resections in elderly patients.
Results: After screening 682 studies, 13 observational studies with 4629 patients were included. Elderly patients undergoing laparoscopic distal pancreatectomy (LDP) had less blood loss (117 mL, $p < 0.001$) and a shorter hospital stay (3.5 days $p < 0.001$) than elderly patients undergoing open distal pancreatectomy (ODP). Postoperative pancreatic fistula (POPF) B/C, major complication and reoperation rate were not significantly different in elderly patients undergoing either laparoscopic or open pancreatoduodenectomy (OPD). One study compared robot PD with OPD in obese patients, indicating that patients with robotic surgery had less blood loss (mean 250 ml vs 500 ml, $p = 0.001$), shorter operative time (mean 381 min vs 428 min, $p = 0.003$), and lower rate of POPF B/C (13% vs 28%, $p = 0.039$).
Conclusion: The current available limited evidence does not suggest that MIPR is contraindicated in elderly or obese patients. Additionally, outcomes in MIPR are equal or more beneficial compared to the open approach when applied in these patient groups.

Introduction

Between 1980 and 2013, the global prevalence of overweight and obesity has risen by 27.5% [1]. At the same time, the proportion of elderly patients, defined as ≥ 70 years, will continue to grow [2]. Obese patients (BMI ≥30) have a higher risk for comorbidities such as diabetes mellitus, coronary artery disease and hypertension [3]

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and might therefore be prone to worse surgical outcomes. In general, advanced age, is correlated with higher co-morbidity and therefore elderly patients carry a higher surgical morbidity and mortality risk. Due to the perceived frailty, major abdominal surgery such as pancreatoduodenectomy might pose bigger challenges in old or obese patients [4,5].

Outcomes after open pancreatic resection in obese patients are inconsistent. Some studies report longer operation duration, more blood loss, higher postoperative pancreatic fistula (POPF) rate and longer length of hospital stay (LOS) than in non-obese patients [6–12]. Other studies have found no difference in perioperative outcomes between obese and non-obese patients undergoing pancreatic resection [13,14]. Perioperative outcomes in elderly patients after open pancreatic resections are equally inconclusive. Older patients have a higher incidence of postoperative mortality, cardiorespiratory morbidity, and intensive care unit admission compared to younger patients [15,16]. In contrast, other studies, usually derived from single-center specialty practices, found comparable perioperative outcomes after pancreatic resections between elderly and younger patients [10,17–19].

Several randomized controlled trials (RCT's), systematic reviews and meta-analyses have been performed comparing open to minimally invasive pancreatic resections (MIPR) [20–26]. MIPR has been shown to be associated with reduced blood loss and a shorter LOS compared to the open approach [20,23,27,28]. However, whether MIPR can be safely applied in older or obese patients remains unclear. This systematic review aimed to assess the impact of older age (≥70 years) and high BMI (≥30) on the surgical outcomes of MIPR. Subsequently, a comparison between the open and minimally invasive approach will be made specifically in elderly or obese patients.

Materials and methods

This study was performed according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [29]. The present systematic review was performed as part of the 2019 International Evidence-Based Guidelines for Minimally Invasive Pancreas Resection (IG-MIPR), which collected evidence on both laparoscopic and robotic pancreatoduodenectomy, distal pancreatectomy, central pancreatectomy, and patient selection, training, learning curve and minimal annual volume in order to obtain optimal outcomes and prevent patient safety concerns [30]. Due to the nature of this study, no IRB approval or written consent was needed.

A systematic literature search was conducted with the help of a clinical librarian in PubMed, Cochrane and Embase databases for studies published before January 2020. Search terms were based on approach (e.g. minimally invasive) and procedure (e.g. pancreatectomy) and patient groups (e.g. elderly). The search in Pubmed was as follows: ("Obesity"[Mesh] OR obes*[tiab] OR older[tiab] OR elder*[tiab]) AND ("Pancreatectomy"[Mesh] OR "Pancreatic Neoplasms/surgery"[Mesh] OR pancreat*[tiab]) AND ("Minimally Invasive Surgical Procedures"[Mesh] OR "Laparoscopy"[Mesh] OR "Robotic Surgical Procedures"[Mesh] OR laparoscop*[tiab] OR robotic[tiab] OR robot-assisted[tiab] OR minimally invasive[tiab] OR minimal invas*[tiab]).

Eligibility criteria

Studies comparing all technical approaches of minimally invasive pancreatic resections (either laparoscopic, robot-assisted or hybrid) with open pancreatic resections (OPR) or within the patient group of interest; either high BMI or elderly age were included. Studies in other languages than English, review articles, articles not available in full text, duplicates and editorials were excluded.

Study selection

Titles, abstracts and full-text articles were all assessed independently by two authors (NH and AB) to establish eligibility. All references of included articles were manually screened for possible additional studies. In case of conflicting assessments, consensus on which articles to include was reached through discussion.

Assessment of methodological quality

Quality assessment of the selected studies was performed using checklists provided by the Scottish Intercollegiate Guidelines Network (SIGN) [31]. SIGN was established for the development of evidence based clinical guidelines. Each study type was assessed with a corresponding checklist, resulting in a quality level of high (++), acceptable (+), low (−) or unacceptable (reject).

Risk of bias was assessed using the Newcastle Ottawa scale (NOS) by both authors independently for all studies. A maximum of 9 point could be granted, divided over 3 categories "selection of patients," "comparability," and "outcome of study participants." Studies with a NOS score of ≤5 were considered as high risk for bias.

Data extraction

In case of insufficient data, the corresponding author was contacted to provide the additional information (in 1 study). The extracted data included study design, study period, sample size and type of surgical procedure, patient characteristics (such as sex, age, BMI, tumor size, diagnosis), operative outcomes [conversion, blood loss, operative time, resection margin involved (R-status)] and postoperative outcomes (including Clavien Dindo ≥3 complication [32], clinically relevant POPF Grade B/C according to the International Study Group on Pancreatic Fistula [33] and LOS).

Statistical analysis

Data analyses were performed using Review Manager, (RevMan, version 5.3, Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2014). Categorical data were presented as frequencies and percentages. Continuous data were presented as stated in original articles. If a minimum of 3 studies in the same patient group had comparable reported outcome data we used DerSimonian and Laird random effects models to pool the data [34]. The numbers of POPF B/C and sample size per group were used to calculate odds ratios and entered means, SD and sample size per group to calculate mean differences (MD) for LOS and blood loss. Cochran's Q and the I^2-statistics were used to assess between-study heterogeneity [35]. Publication bias was assessed using Egger's test if applicable. Statistical significance was set at $p < 0.05$.

Results

Search results

After removal of duplicates, a total of 682 studies were identified, which were screened on title and abstract after which 643 studies were excluded for not meeting inclusion criteria. Of the 39 studies that remained, 26 studies were excluded after full text assessment. Of these 13 remaining studies, a total of 10 studies with 3997 patients was included in the elderly subgroup; four studies on distal pancreatectomy and six on pancreatoduodenectomy. Overall, three studies with 632 patients were included in the obesity subgroup. No additional studies were included after manually screening the references. The PRISMA study selection flow-chart is shown in Fig. 1 and the characteristics of all included studies are shown in Table 1. The main perioperative outcomes per study are summarized in Table 2 for distal pancreatectomy and Table 3 for pancreatoduodenectomy.

Methodological quality

Using the SIGN methodology, three out of 13 studies (23%) were of low quality with the remaining studies being of acceptable quality. One of all 13 studies had a high risk of bias (≤5 NOS score) [36]. All studies had a retrospective design and one study used matching [37]. In the meta-analyses there was moderate to considerable heterogeneity.

Elderly patients, distal pancreatectomy

Three studies including a total of 249 patients compared laparoscopic (LDP) with open distal pancreatectomy (ODP) in elderly patients [38–40]. Meta-analyses showed that elderly patients undergoing LDP had less blood loss (MD -117; 95% CI -159 to −74; $p < 0.001$) (Fig. 2a) and a shorter LOS (MD -3.6 95% CI -5.1 to -2.1; $p < 0.001$) (Fig. 2b) than elderly patients undergoing ODP. The rate of POPF B/C was comparable (Fig. 2c) (OR 0.97; 95% CI 0.4 to 2.4). There was low heterogeneity between the studies ($I^2 = 0\%$). Since only few studies were included it was difficult to test for publication bias, although Egger's intercept suggested there was no publication bias in terms of blood loss (β = 2.68, SE = 1.99, p = 0.20), LOS (β = 2.68, SE = 2.57 and p = 0.24) and POPF B/C (β = 0.96, SE = 0.71 p = 0.20).

In a cohort of 402 LDPs, Sahakyan et al. found that elderly patients undergoing LDP less often developed POPF (p = 0.009) and had lower readmission rates (p = 0.025) compared to the younger group. The rate of Clavien-Dindo ≥3 complications did not differ significantly. The groups were comparable in terms of sex, BMI, history of upper abdominal surgery and indication for surgery [41].

Elderly patients, pancreatoduodenectomy

Data of three studies comparing laparoscopic pancreatoduodenectomy (LPD) and open pancreatoduodenectomy (OPD) in elderly patients were pooled in a meta-analysis [37,42,43]. Meta-analyses of postoperative outcomes are shown in Fig. 3. POPF B/C rate (OR 0.57; 95% CI 0.3 to 1.3) (Fig. 3a), major complication rate (OR 0.6; 95% CI 0.4 to 1.1)(Fig. 3b) and reoperation rate (OR 0.6; 95% CI 0.2 to 1.6) (Fig. 3c) were not statistically different between LPD and OPD. There was low to moderate heterogeneity between the studies ($I^2 = 0–53\%$). Egger's intercept suggested no publication bias in terms of POPF B/C (β = 1.85, SE = 2.18, p = 0.55), major complication (β = 0.05, SE = 2.24, p = 0.99) and reoperation rate (β = 1.22, SE = 1.79, p = 0.62).

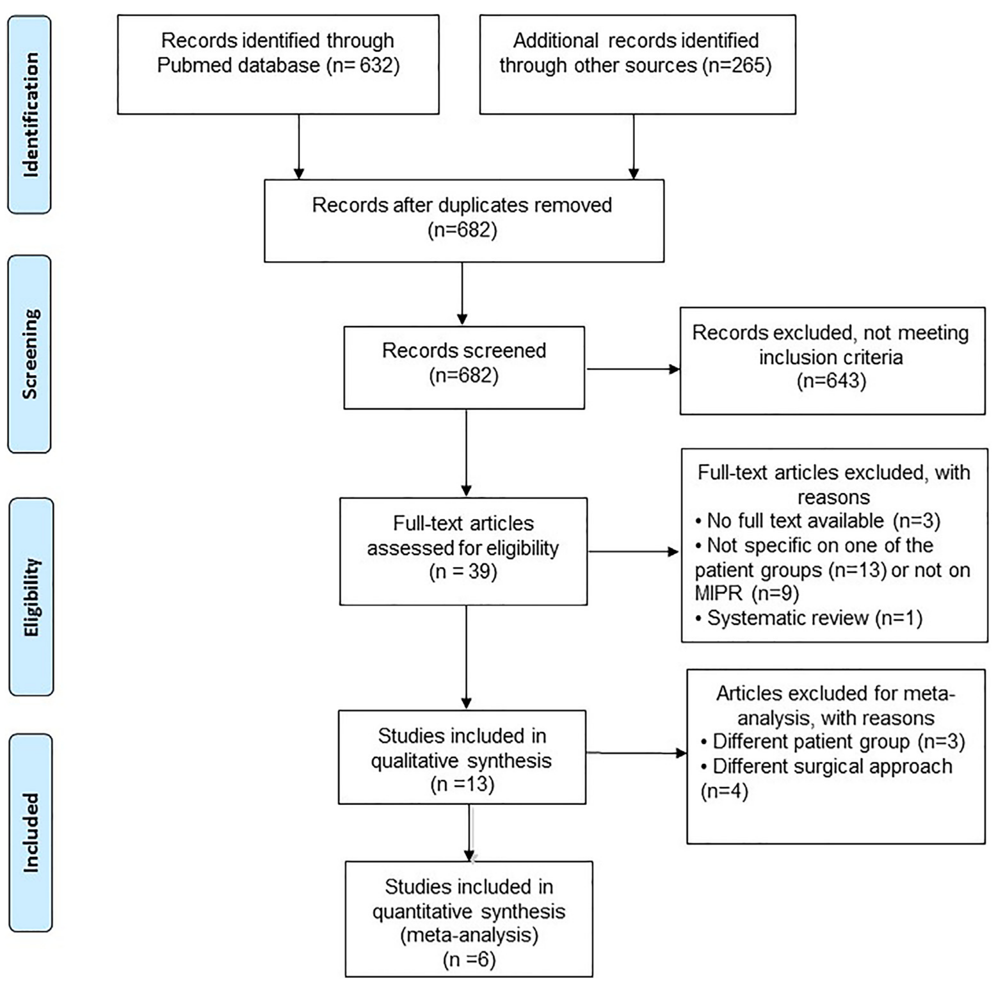

Fig. 1. PRISMA flow chart of observational studies of elderly and obese patients undergoing either minimally invasive or open distal pancreatectomy.

Table 1
Overview of included studies.

First author	Subject	Study period	Sample size MIPR	Sample size OPR	Type of MIPR	Comparison (n)	Study design	Case matched
Elderly patients, distal pancreatectomy								
Aprea et al.	Elderly	2012–2015	7	15	Laparoscopic	Elderly LDP (7) vs. elderly ODP (15)	Retrospective	No
Chen et al.	Elderly	2005–2018	334	48	Laparoscopic	Elderly LDP (70) vs. ODP (48) vs non- elderly LDP (264)	Retrospective	No
Sahakyan et al.	Elderly	1997–2015	402	–	Laparoscopic	Elderly LDP (118) vs. non-elderly LDP (284)	Retrospective	No
Souche et al.	Elderly	1995–2017	53	56	Laparoscopic	Elderly LDP (53) vs. ODP (56)	Retrospective	No
Elderly patients, pancreatoduodenectomy								
Buchs et al.	Elderly	2007–2010	41	–	Robotic	Elderly (15) vs. non elderly (26)	Retrospective	No
Chapman et al.	Elderly	2010–2013	248	1520	Laparoscopic	Elderly LPD (248) vs. OPD (1520)	Retrospective	No
Liang et al.	Elderly	2015–2018	27	19	Laparoscopic	Non-elderly LPD (55) vs. Elderly LPD (27) vs. Elderly OPD (19)	Retrospective	No
Meng et al.	Elderly	2010–2017	41	–	Laparoscopic	Non-elderly LPD (158) vs. Elderly LPD (41)	Retrospective	No
Shin et al.	Elderly	2014–2017	56	270	Laparoscopic	Elderly LPD (56) vs. Elderly OPD (270)	Retrospective	Yes
Tee et al.	Elderly	2007–2014	281	579	Laparoscopic	Elderly LPD (113) vs. OPD (225) vs. non-elderly LPD (168) vs. OPD (354)	Retrospective	No
Total	Elderly	1995–2018	1490	2507				
Obesity patients, distal pancreatectomy								
Sahakyan et al.	Obesity	1997–2015	402	–	Laparoscopic	Normal weight (191) vs. overweight (155) vs. obese (56)	Retrospective	No
Wang et al.	Obesity	2004–2013	85	–	Robotic	Obese (28) vs. non-obese (57)	Retrospective	No
Obese patients, pancreatoduodenectomy								
Girgis et al.	Obesity	2011–2015	70	75	Robotic	Obese RPD (70) vs. obese OPD (75)	Retrospective	No
Total	Obesity	1997–2015	557	75				

Abbreviations: LDP: laparoscopic distal pancreatectomy, LPD: Laparoscopic pancreatoduodenectomy, MIPR: minimally invasive pancreatic resection, OPR: open pancreatic resection, ODP: open distal pancreatectomy, OPD: open pancreatoduodenectomy RDP: Robot distal pancreatectomy, RPD: Robot pancreatoduodenectomy.

Table 2
Summary of perioperative outcomes of comparative studies of elderly and obese patients undergoing distal pancreatectomy.

First author	Approach	Groups being compared	Operative time (min), mean, SD	Blood loss (mL), mean, SD	Conversion, n (%)	LOS, days Mean, SD	POPF B/C, n (%)	Reoperation rate, n (%)	Clavien-Dindo ≥ 3, n (%)	Mortality 90 days, n (%)
Elderly patients										
Aprea et al.	Laparoscopic	>70 years	186 ± 11	342 ± 104	na	11 ± 4	1 (14.3)	na	na	0 (0)
	Open	>70 years	180 ± 7	212 ± 62	–	7 ± 1	1 (6.7)	na	na	0 (0)
Chen et al.	Laparoscopic	≥70 years	186 ± 54	191 ± 113	2 (2.9)	11 ± 6	7 (10.0)	na	7 (10.0)	na
	Open	≥70 years	208 ± 41	292 ± 172	–	15 ± 7	5 (10.4)	na	7 (14.6)	na
	Laparoscopic	<70 years	175 ± 53	193 ± 108	4 (1.5)	10 ± 6	17 (6.4)	na	21 (8.0)	na
Sahakyan et al.	Laparoscopic	≥70 years	162 (29–374)[a]	264 ± 44	0 (0)	7 ± 6	11 (9.3)	5 (4.2)	18 (15.3)[b]	1 (0.8)
	Laparoscopic	<70 years	156 (45–520)[a]	302 ± 62	8 (2.8)	7 ± 6	57 (20.1)	17 (6.0)	59 (20.8)[b]	1 (0.4)
Souche et al.	Laparoscopic	>70 years	204 ± 57	238 ± 312	na	14 ± 10	3 (6.8)	3 (6.8)	8 (18.2)	0 (0)
	Open	>70 years	220 ± 76	425 ± 582	–	16 ± 11	4 (7.1)	3 (5.3)	7 (12.5)	3 (5.3)
Obese patients										
Sahakyan et al.	Laparoscopic	Obese BMI ≥30	190 (61–480)[a]	200 (0–2800)[a]	1 (1.8)	na	14 (25)	na	12 (21.4)[b]	1 (1.8)
	Laparoscopic	Overweight[c]	158 (56–520)[a]	50 (0–6250)[a]	5 (3.2)	na	27 (17.4)	na	35 (22.6)[b]	0 (0)
	Laparoscopic	Normal weight	153 (29–374)[a]	90 (0–2000)[a]	1 (0.5)	na	29 (15.2)	na	32 (16.8)[b]	3 (1.6)
Wang et al.	Robotic	Obese BMI ≥30	252	252	1 (3.6)	8	8 (28.5)	na	6 (21.4)	0
	Robotic	Non obese BMI <30	253	194	3 (5.4)	10	4 (7)	na	5 (8.7)	0

Abbreviations: LOS: length of stay, POPF B/C: Postoperative pancreatic fistula grade B/C, na: not available.
[a] = Median (IQR).
[b] = Accordion grade ≥3.
[c] BMI 25–29.9.

Of the remaining four studies, the study with the largest sample size used the National Cancer Database (NCDB) and included patients ≥75 years with pancreatic adenocarcinoma undergoing either laparoscopic n = 248 (14.0%) or open pancreatoduodenectomy, n = 1520 (86.0%). There was no difference between the groups in terms of age, sex, receipt of neoadjuvant chemotherapy, radiotherapy or tumor size (all $p > 0.05$). In perioperative outcomes there was no statistically significant difference in terms of readmission rates or 30-day mortality ($p = 0.19$ and $p = 0.26$ respectively). Ninety-day mortality was lower in the LPD group compared to OPD (7.2% versus 12.2% respectively, $p = 0.049$). Data on POPF, major morbidity and reoperation were not recorded and therefore this study could not be included in the meta-analyses [36].

One study assessed the impact of elderly age on laparoscopic pancreatoduodenectomy [44] and one on robotic pancreatoduodenectomy (RPD) [45]. The first study was a single center study including 199 patients, 158 patients <70 years and 41

Table 3
Summary of perioperative outcomes of comparative studies of elderly and obese patients undergoing pancreatoduodenectomy.

First author	Approach	Groups being compared	Operative time (min), mean, SD	Blood loss (mL), mean, SD	Conversion (%)	LOS, days Mean, SD	POPF B/C, n (%)	Reoperation rate, n (%)	Clavien-Dindo ≥ 3, n (%)	Mortality 90 days, n (%)
Elderly										
Buchs et al.	Robotic	≥70 years	420 ± 62	388 ± 282	0 (0)	14 ± 8	na	0 (0)	na	na
	Robotic	<70 years	444 ± 91	390 ± 379	2 (7.7)	11 ± 5	na	2 (7.7)	na	na
Chapman et al.	Laparoscopic	≥75 years	na	na	na	10 (7–15)[a]	na	na	na	13 (7.2)
	Open	≥75 years	na	na	–	10 (7–16)[a]	na	na	na	136 (12.2)
Liang et al.	Laparoscopic	≥70 years	368 ± 75	200 (100–400)	2 (7.4)	12 (10–21)	4 (15)	3 (11)	11 (41)	2 (7)
	Open	≥70 years	369 ± 73	400 (200–700)	–	18 (14–43)	4 (21)	1 (5)	8 (42)	2 (10)
	Laparoscopic	<70 years	363 ± 82	100 (100–200)	5 (9)	12 (10–16)	5 (9)	2 (4)	11 (20)	1 (2)
Meng et al.	Laparoscopic	≥70 years	424 ± 109	150 (100–270)	4 (9.8)	15 (12–20)	5 (12.2)	2 (4.9)	8 (19.5)	na
	Laparoscopic	<70 years	432 ± 101	150 (100–300)	11 (9.7)	14 (11–17)	17 (10.8)	10 (6.3)	25 (15.8)	na
Shin et al.	Laparoscopic	≥70 years	322 ± 56	na	na	14 ± 11	4 (7.2)	na	3 (5.4)	na
	Open	≥70 years	289 ± 69	na	–	16 ± 13	12 (21.4)	na	6 (10.7)	na
Tee et al.	Laparoscopic	≥70 years	365 ± 111	345 ± 347	5 (4.4)	8[a]	26 (23.0)	3 (2.7)	11 (9.7)	na
	Open	≥70 years	360 ± 90	869 ± 1118	–	9[a]	57 (25.3)	15 (6.7)	34 (15.1)	na
	Lap & open	<70 years	379 ± 96	729 ± 711	15 (8.9)	8[a]	119 (22.8)	24 (4.6)	46 (8.8)	na
Obese										
Girgis et al.	Robotic	Obese BMI ≥30	381	250	0 (0)	9 (7–14)	9 (13.0)	na	25 (36)	na
	Open	Obese BMI ≥ 30	428	500	–	11 (8–14)	21 (28)	na	27 (36)	na
	Robotic & open	Non obese BMI <30	392	300	–	9 (7–14)	47 (14)	na	92 (28)	na

Abbreviations: LOS: length of stay, na: not available, POPF B/C: Postoperative pancreatic fistula grade B/C.
[a] = Median (inter quartile range).

patients ≥70 years. Estimated blood loss (150, (100–300 mL) vs. 150 (100–270 mL), LOS (14, 11–17 vs. 15, 12–20 days) and Clavien-Dindo ≥3 complication (n = 25, 15.8% vs. n = 8, 19.5% p = 0.57) did not statistically significantly differ between young and older patients respectively [44]. The second study divided patients in two groups: patients <70 years (n = 26, 63.4%) and ≥70 years (n = 15, 36.6%) respectively. Other demographic characteristics (sex, BMI, ASA and comorbidities) were similar between the two groups. There was no significant difference in conversion (n = 2, 7.7% vs. n = 0, 0%, p = 0.52) or blood loss (median 390, range 50–1500 mL vs. 388, 80–1000 mL p = 0.989) between the groups [45].

Obese patients, minimally invasive distal pancreatectomy

Two studies assessed the impact of obesity in MIDP, one with the laparoscopic and one with the robotic approach [46,47]. The first study divided patients in three groups: normal weight (n = 191), overweight (BMI>25; n = 155), and obese (BMI>30; n = 56) patients undergoing LDP. Patients were comparable in terms of age, sex and previous abdominal operations. Obese patients had a significantly longer operative time (p = 0.009) and increased estimated blood loss (p = 0.01) compared to overweight and normal weight patients. Equally, in using stepwise multiple linear regression analyses, obesity independently predicted prolonged operative time (estimate = 30.2 [95% CI, 12.1-48.3], p = 0.001) and was found to be significantly associated with an increased intraoperative blood loss (estimate = 1.6 [95% CI, 1.1–2.3], p = 0.01). Conversion, LOS and the number of severe complications did not differ significantly between the three groups (p-values respectively 0.15, 0.13 and 0.37). Multivariate logistic regression analyses did not demonstrate an association between obesity and postoperative morbidity (p = 0.09) [46].

Wang et al. compared non-obese (n = 57) with obese (n = 28) patients undergoing robotic distal pancreatectomy who were otherwise comparable with respect to age, sex, ASA classification or preoperative diagnosis. In peri-operative parameters there were no significant differences in conversion rate (5.3% and 3.5% p = 0.71), mean operative time (252 versus 253 min p = 0.94), mean blood loss (193 versus 252 mL p = 0.47) or mean LOS (10 versus 8 days, p = 0.14) in non-obese vs. obese patients respectively. Five (8.7%) non-obese and six (21.4%) obese patients had a Clavien-Dindo ≥3 complication (p = 0.495). POPF Grade B/C was seen more often in obese patients (28.5% versus 7%) however this did not reach statistical significance (p = 0.064) [47].

MIPD in obese patients

The only study found on this subject compared RPD with OPD and divided patients in three groups: normal weight patients (n = 332), obese patients (defined as BMI ≥ 30) undergoing RPD (n = 70) and obese patients undergoing OPD (n = 75) [48]. In obese patients, intra-operative outcomes significantly differed between the robotic and open cohort: operating room (OR) time was shorter (381 min vs 428 min, p = 0.003), estimated blood loss lower (250 ml vs 500 ml, p = 0.001) and number of patients requiring red blood cell transfusions smaller (17% vs. 33%, p = 0.035) in the RPD group. The robotic cohort had a lower rate of POPF grade B/C compared to the obese OPD cohort (13% vs 28%, p = 0.039). On multivariate analysis, obese patients (BMI ≥30) were more likely to develop a Clavien-Dindo ≥3 complication (OR 1.59, CI 95% 1.0-2.5,

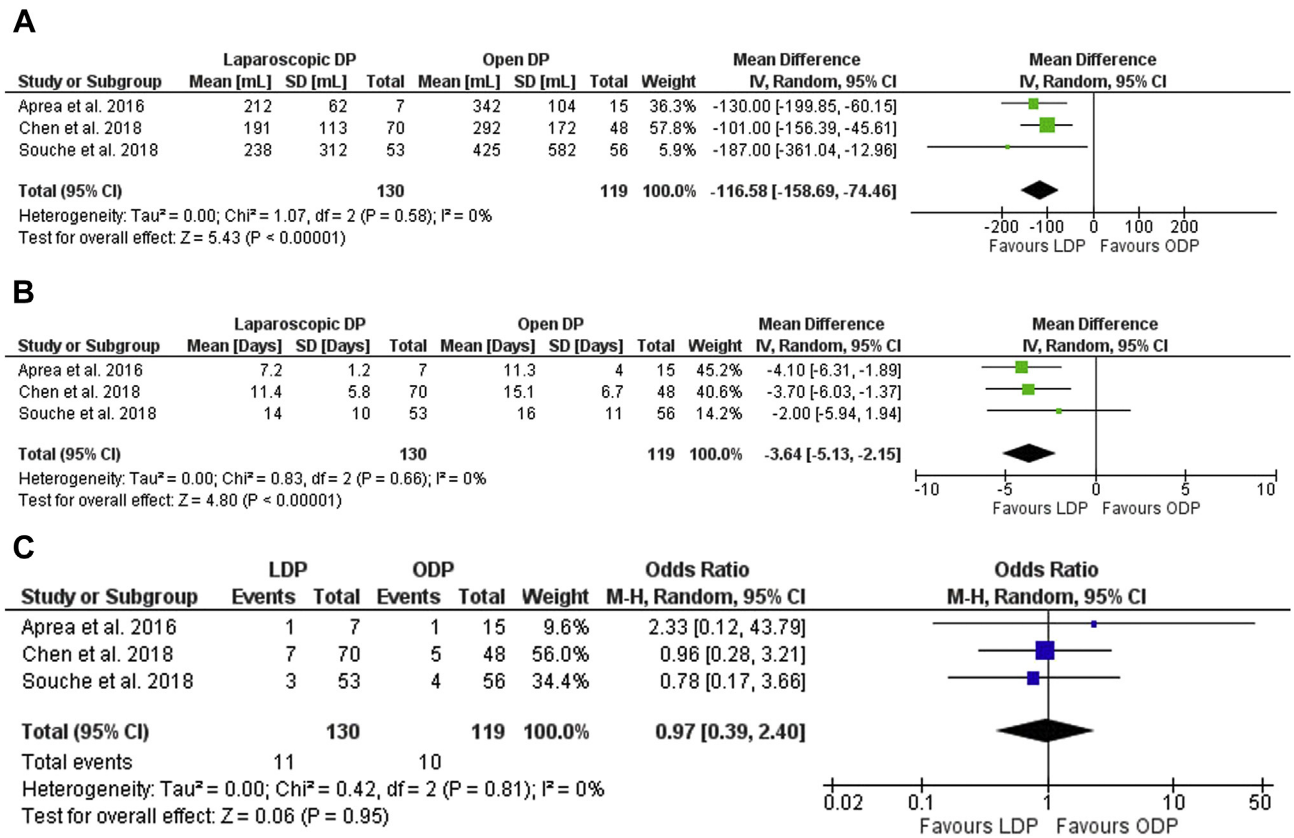

Fig. 2. Forest plot of studies examining the difference between laparoscopic and open distal pancreatectomy in terms of: A, perioperative blood loss. B, length of hospital stay. C, POPF B/C.

p = 0.036) [48].

Discussion

This systematic review and meta-analysis studied the role of older age and obesity in minimally invasive pancreatic surgery and compared outcomes between open and minimally invasive pancreatic resections specifically for these two patient categories. Regarding distal pancreatectomy, LDP appeared to be safe in elderly patients and may have some advantages over the open procedure in terms of intra-operative blood loss and length of hospital stay. In obese patients, evidence suggests that outcomes between MIDP and ODP are comparable. Regarding pancreatoduodenectomy, no evidence was found that MIPD is inferior to OPD in elderly patients. Only one study compared MIPD with OPD in obese patients and found a lower rate of POPF grade B/C in the minimally invasive group compared to open, with other peri-operative outcomes being comparable between the two groups. All in all, current evidence is relatively scarce and future research is highly recommended.

The first multicenter randomized controlled trial [27] and several meta-analyses comparing MIDP with ODP demonstrated advantages of the minimally invasive procedure in terms of blood loss, time to functional recovery and LOS [22,23,49] The only previous systematic review that focused on elderly patients undergoing either MIDP or ODP confirmed the advantages of the minimally invasive approach. In that study, however, the methodological quality of included studies was not assessed and no meta-analysis was performed [50].

Age is a well-known risk factor for increased morbidity after pancreatic surgery. A recent meta-analysis including 5186 patients found that elderly patients have an increased risk of mortality compared to younger patients after open pancreatoduodenectomy [16]. Unfortunately, recent RCTs did not report on impact of age on outcomes. A recent meta-analysis included 224 patients from three RCT's of LPD versus OPD and demonstrated no significant difference regarding 90-day mortality, Clavien-Dindo ≥3 complications, length of stay, reoperation and readmission or oncologic outcomes between both groups. No specific analysis was done for the impact of age or older age. Quality of evidence was rated as moderate to very low [51].

The two included studies on obese patients undergoing distal pancreatectomy only compared obese and non-obese patients within the MIDP group. Wang et al. looked at 85 patients undergoing robotic distal pancreatectomy and 28.5% of the obese patients had a POPF Grade B fistula compared to 7% of non-obese patients [47]. Although this did not reach statistical significance, this was most likely due to the study being underpowered. This higher pancreatic fistula rate in obese patients is in line with previous reports on the impact of body mass index on outcomes for distal pancreatectomy [52]. This could be potentially explained by the presence of a fattier and softer gland in the obese patient population. Unfortunately, due to the design of these two studies, the possible advantage of MIPR over the open approach cannot be established.

Only one previous study compared a MIPR approach (RPD) with the open approach in obese patients undergoing PD [48]. RPD was found to be associated with less overall complications without difference in POPF rate, DGE, reoperation or LOS, compared to OPD [53]. When interpreting these results it should be taken into account that this study is a single center study from a very high

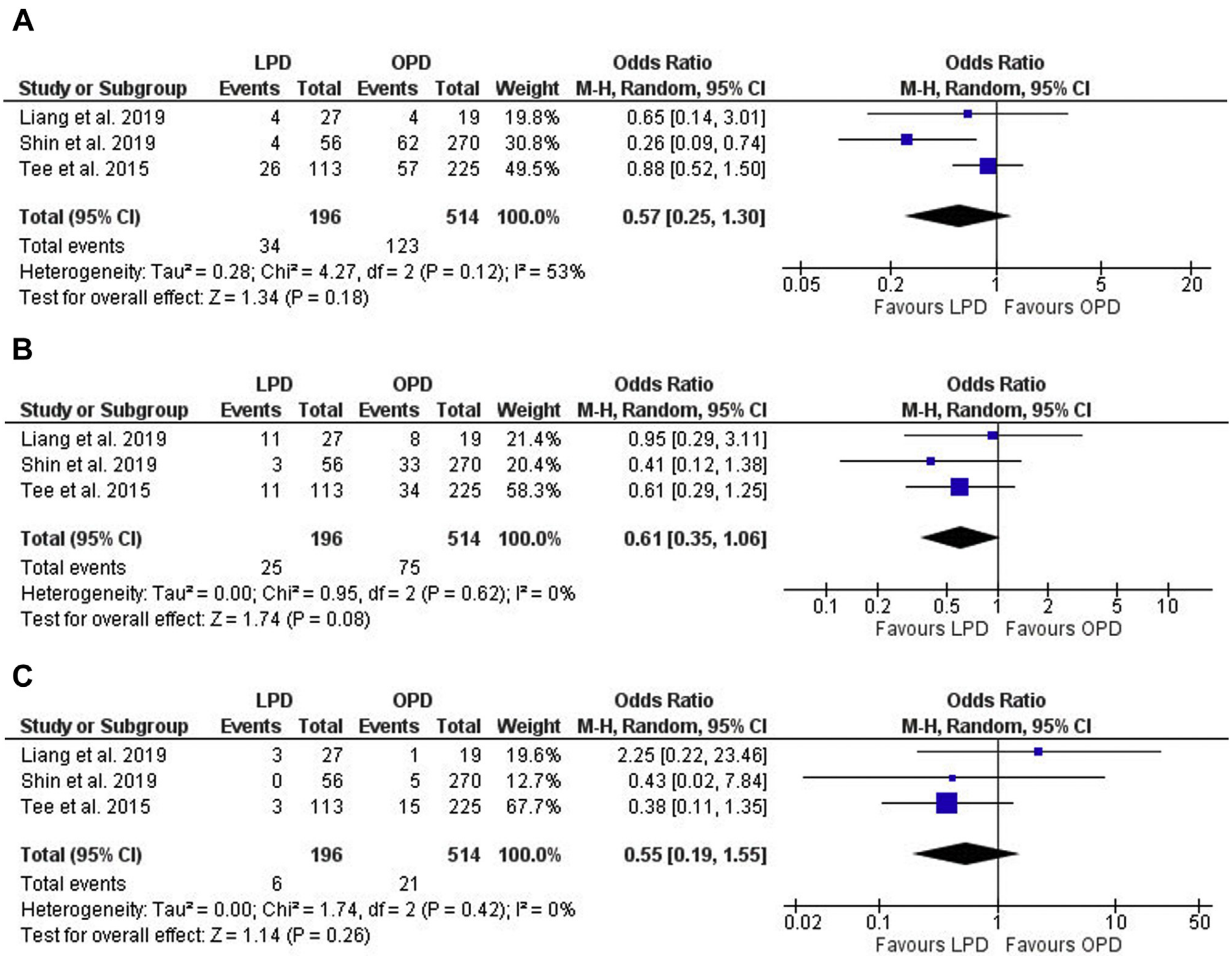

Fig. 3. Forest plot of studies examining the difference between laparoscopic and open distal pancreatecomy in terms of: A, POPF B/C, B, major morbidity, C, reoperation rate.

volume center with extensive experience in RPD.

The studies on obesity included in this systematic review all classified obese patients as patients with a BMI of ≥30, however studies suggest that patients who are prone to higher complication rates are those with severe obesity (BMI ≥35). Although BMI is commonly used to divide patient groups in different weight categories, it is debatable if this is the best way to assess adipose composition. Some previous studies have stated that visceral or abdominal fat are superior methods to define obesity [54,55].

No studies were identified comparing laparoscopic (non-robotic) and open approaches in obese patients. By comparison, in colorectal surgery the laparoscopic approach seems superior for obese patients in terms of length of stay and is comparable in perioperative and oncological outcomes [56–58].

This systematic review has some limitations. First, only few studies specifically addressed the impact of obesity and older age on outcomes of MIPR. Second, all types of MIPR were included, which subsequently led to varying outcomes making it difficult to draw conclusions for each specific approach. Third, when looking at elderly patients definitions regarding age varied. Some studies defined older patients as ≥75 years old. Heterogeneity in definitions complicated comparison of the outcomes of these studies. Besides, no studies have specifically looked at octogenarians. Fourth, none of the now four available RCTs report specifically on elderly or obese patients and all studies included in our review were retrospective which could induce statistical heterogeneity precluding firm conclusions. Fifth, heterogeneity of clinical factors could not be addressed in current meta-analyses. Meta-regression using clinical confounders was barred due to the limited amount of studies included in the meta-analysis (i.e., <10 studies) and therefore, crude pooled effect sizes were presented. The main strength of this study is that it is the first systematic review and meta-analysis focusing on perioperative outcomes in elderly and obese patients undergoing MIPR.

Conclusion

This systematic review and meta-analysis indicates that there is no evidence to suggest that elderly age and obesity are contraindications for MIPR. In older patients undergoing LDP, there may be some additional advantages over the open approach in terms of blood loss and length of hospital stay. However, all included studies were retrospective of nature and the number of studies to be included were few, so no definitive recommendations can be given and more high-quality prospective studies are needed to draw firmer conclusions. The development and validation of a comorbidity index specific to pancreatic surgery that can be used in any approach, would be beneficial for future comparisons of study outcomes and risk assessment in clinical practice.

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