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Review

Postoperative outcomes in elderly patients undergoing pancreatic resection for pancreatic adenocarcinoma: A systematic review and meta-analysis

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ABSTRACT

Background: Pancreatic cancer is a disease of the elderly. Surgical resection is usually offered to patients in early stage disease; however, pancreatic resection in the elderly is controversial.

Methods: MEDLINE, EMBASE and Cochrane Library, were searched for studies comparing short- and long-term outcomes of elderly (above the age of 70) with non-elderly patients (below the age of 70) following pancreatic resection for pancreatic adenocarcinoma over the period from the inception of electronic database to 2017. Twelve articles documenting 4860 patients were included. A meta-analysis of data on patient characteristics, operative techniques, and perioperative outcomes were analysed. Our primary endpoint was postoperative mortality, defined as 30-day mortality or in-hospitalisation mortality.

Results: There were 919 patients in the elderly group and 3941 patients in the non-elderly group. Elderly patients had worse ASA scores ($p < 0.001$) and more cardiovascular comorbidities ($p = 0.002$). Tumour size, T-stage, N-stage and tumour grade were similar between the elderly and non-elderly group ($p > 0.05$). Fewer elderly patients received a concomitant venous resection with their pancreatectomy (RR0.80, $p = 0.003$, I2 = 0%), achieved a negative margin status (RR0.76, $p = 0.02$, I2 = 28%) and underwent adjuvant chemotherapy treatment (RR0.69, $p < 0.001$, I2 = 42%). Overall complication (RR1.15, $p < 0.001$, I2 = 47%), in particular, respiratory complications (RR2.33, $p = 0.004$, I2 = 39%), was higher in the elderly group. There was no difference in postoperative pancreatic fistula formation, postoperative haemorrhage, intraabdominal abscess and length of hospital stay between both groups ($p > 0.05$). Postoperative mortality was similar between both groups ($p = 0.17$). Subgroup analysis according to the time of enrolment (< 2000, ≥2000) showed a significant subgroup effect (Chi2 = 3.44, $p = 0.06$, I2 = 70.9%) and revealed that postoperative mortality in the elderly group improved over time (Before 2000: n = 1654, subtotal RR2.27, $p = 0.02$, I2 = 0%; From 2000 onwards: n = 3206, subtotal RR1.00, $p = 0.99$, I2 = 0%).

Conclusion: Fewer elderly patients received chemotherapy and portal vein resection to achieve a clear margin. Pancreatic resection of pancreatic adenocarcinoma can be performed safely on elderly patients with acceptable risks in experienced centres by specialist hepatobiliary surgeons. Age alone should not be the only determinant for the selection of patients for surgical treatment of pancreatic adenocarcinoma.

1. Introduction

Pancreatic cancer is a lethal malignant disease contributing to over 331,000 deaths per year [1]. Pancreatic adenocarcinoma accounts for 85% of pancreatic cancers [2,3] and more than half are diagnosed over the age of 70 [1].

Surgical resection with chemotherapy offers a potential for cure [4] but surgery in the elderly population remains controversial. As the demographics of developed countries continue to shift towards an aging population [5–7], elderly patients might be denied surgical treatment because of the perceived risks associated with chronological age alone.

Previous meta-analyses [8–10] examined postoperative outcomes of

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elderly patients following pancreaticoduodenectomy for a variety of benign and malignant disease. Elderly patients with pancreatic adenocarcinoma should be examined as a separate entity [11–23] as these tumours tend to be larger in size and histopathologically more aggressive therefore requiring more extensive radical excision compared with other periampullary tumours [24–26].

Our aim is to compare postoperative outcomes of elderly patients (≥70 years) with non-elderly patients (< 70 years) following surgical resection for pancreatic adenocarcinoma.

2. Methods

This meta-analysis was performed in accordance with the protocol from the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-P) group [27] and the Assessing the methodological quality of systematic reviews (AMSTAR) Guidelines.

2.1. Literature search strategy

Electronic databases including MEDLINE, EMBASE and Cochrane Library were systematically searched for all articles with restriction on studies published in English. Literature searches were performed from inception of these databases to November 2017. Title search strategy was performed using the following terms: 'pancreatic adenocarcinoma OR pancreatic neoplasm OR pancreatic cancer OR pancreatic carcinoma' AND 'elderly OR aged OR older OR oldest'. Two investigators independently performed the searches. References of eligible studies were manually screened to identify any relevant publications.

2.2. Inclusion and exclusion criteria

Our inclusion criteria were: (a) Studies with elderly patients defined as age ≥70, ≥75 and ≥ 80 (b) Studies with a control group (c) Studies that included only pancreatic adenocarcinoma (d) Studies that reported our predefined primary outcome. Studies that failed to fulfil the above inclusion criteria and study duplications were excluded.

2.3. Data extraction and synthesis

Two investigators (ET and JS) independently retrieved data from each article: First author, Year of publication, study design, sample size and perioperative outcomes. Discrepancies between the two reviewers were resolved by discussion and consensus. The senior investigators (CS and MC) reviewed the final results. Our primary endpoint was post-operative mortality, defined as 30-day mortality or in-hospitalisation mortality. Overall complication rate, defined as any postoperative surgical or non-surgical complications, and overall survival was our secondary endpoint. Subgroup analyses were conducted to explore the impact of cohort era (enrolment start year: Before 2000, From 2000 onwards) and age cut-off ('elderly' defined as: age ≥70, ≥75 and ≥ 80) on our primary and secondary endpoints.

2.4. Risk of bias (quality) assessment

The Newcastle-Ottawa scale (NOS) for cohort studies was used to assess the quality of included studies [28]. Studies with an NOS score of seven or more were considered "good" quality [29].

2.5. Statistical analysis

All statistical analysis was conducted with Review Manager version 5.3 and Comprehensive Meta-analysis 2.2. The estimation of mean and standard deviation (SD) from median and range, and median and interquartile range were calculated using the methodology proposed by Hozo et al. [30] and Wan et al. [31], respectively. Log (Hazard ratio) and standard error (SE) were estimated from the available survival curves using a spreadsheet developed by Tierney et al. [32]. For dichotomous data, risk ratio (RR) with a 95% confidence interval (CI) was calculated. For continuous data, mean difference (MD) with 95%CI was calculated. Hazard ratio (HR) with 95%CI was used as to compare the survival statistics between the elderly and non-elderly groups. The Higgins I^2 statistic and the Chi^2 statistic was used to estimate the total variation across studies where statistical heterogeneity is defined as $I^2 > 50\%$ and/or Chi^2 statistic $p < 0.10$ [33]. We used fixed-effects models for meta-analysis, and in the case of statistical heterogeneity, a random effects model. A p-value 0.05 was considered statistically significant. Subgroups were compared by a test of interaction [34] using the Cochrane's Q test (where Q is a Chi^2 statistic) and the Higgins I^2 statistic [35]. The I^2 statistic measures the extent of inconsistency across the subgroups' results and the proportion of total variation in subgroup estimates that is due to genuine variation across subgroups rather than sampling error [36]. $I^2 > 50\%$ and/or Chi^2 statistic $p < 0.10$ indicates interaction between subtotal estimates [37]. Publication bias was analysed visually using funnel plots and the Egger's regression test [38]. We performed a sensitivity analysis to examine the robustness of results, systematically removing one study from the analysis and recalculating the results.

3. Results

3.1. Study selection

The search of MEDLINE, EMBASE and the Cochrane Library retrieved 662 records. After adjusting for duplicates, 605 remained and were screened on the basis of title and abstracts (Fig. 1). Of these, 552 were excluded, 53 potentially relevant articles were assessed in more detail on the basis of full text and 15 additional studies were included based on references searched from relevant articles. Of these, 56 studies did not meet the inclusion criteria and 12 remaining studies were included in this review.

3.2. Study characteristics

The characteristics of the 12 retrospective studies [12–23] with 4860 patients are shown in Table 1. There were 919 patients in the elderly group and 3941 patients in the non-elderly group. The elderly group comprised of patients in studies defined as over the ages of 70 (five studies [15,16,19–21]), 75 (two studies [17,18]) and 80 (five studies [12–14,22]). There were three multicentre [14,15,21] and nine single centre studies [12,13,15–20,22,23]. Studies were conducted in the United States (Five studies [12,13,16,17,22]), Europe (four studies [15,18,21,23]) and Asia (three studies [14,19,20]). Publications reporting postoperative outcomes of elderly patients undergoing pancreatectomy increased with time with a particular growth of large studies since 2010 (Fig. 2). Eleven studies [12–18,20–23] were classified as good quality according to the NOS (Supplementary Table 1).

3.3. Clinical, pathological and operative characteristics

Details of clinical, pathological and operative characteristics are found in Supplementary Figs. 1, 2 and 3. The elderly group had higher ASA scores ($p < 0.05$). Tumour pathology (Tumour size, Tumour grade, T-stage and N-stage) was similar between both groups ($p > 0.05$). Four [14,16,20,22] of the five studies [12,14,16,20,22] reported T-stage and N-stage according to the AJCC classification. Fewer elderly patients received a concomitant venous resection with their pancreatectomy (n = 3399, RR0.80, $p = 0.003$, $I^2 = 0\%$), achieved a negative margin status (n = 4860, RR0.76, $p = 0.02$, $I^2 = 28\%$) and underwent adjuvant chemotherapy treatment (n = 3918, RR0.69, $p < 0.001$, $I^2 = 42\%$).

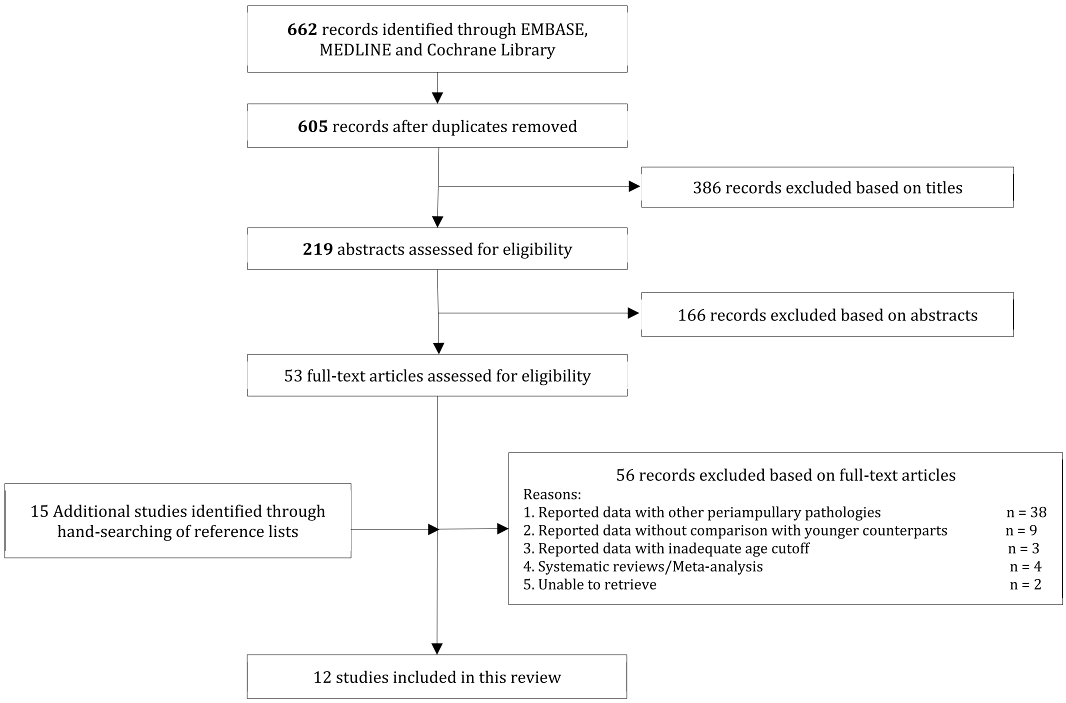

Fig. 1. Flow diagram in accordance with the Quality of Reporting of Meta-analyses (QUOROM) statement.

3.4. Postoperative mortality

12 studies [12–23] with 4860 patients reported on postoperative mortality, defined as 30-day mortality or in-hospitalisation mortality. There were 919 patients in the elderly group and 3941 patients in the non-elderly group. Postoperative mortality was similar between both groups (RR1.34, $p = 0.17$, $I^2 = 0\%$) (Fig. 3). Visually, the funnel plot appears symmetrical and Egger's test identified no significant bias (intercept = 0.660, $p = 0.401$) (Supplementary Fig. 4) Subanalysis according to the time of enrolment (Fig. 3) showed significant subgroup effect ($Chi^2 = 3.44$, $p = 0.06$, $I^2 = 70.9\%$) and revealed that postoperative mortality in the elderly group improved over time (Before 2000: n = 1654, subtotal RR2.27, $p = 0.02$, $I^2 = 0\%$; From 2000 onwards: n = 3206, subtotal RR1.00, $p = 0.99$, $I^2 = 0\%$). Subanalysis according to the definition of 'elderly' in individual studies revealed no significant subgroup effect ($Chi^2 = 1.89$, $p = 0.39$, $I^2 = 0\%$) (Supplementary Fig. 5).

3.5. Overall complication

Nine studies [12,13,15,17,18,20–23] with 2994 patients reported an overall complication rate, five studies [13,15,17,18,22] defined overall complication as any postoperative surgical or non-surgical complications. There were 643 patients in the elderly group and 2351 patients in the non-elderly group. The pooled result showed that elderly patients had a higher risk of developing complications with moderate heterogeneity (RR1.15, $p < 0.001$, $I^2 = 47\%$) (Fig. 4). Subanalysis according to the time of enrolment ($Chi^2 = 1.34$, $p = 0.25$, $I^2 = 25.5\%$) (Fig. 4) and the definition of 'elderly' in individual studies ($Chi^2 = 1.02$, $p = 0.60$, $I^2 = 0\%$) (Supplementary Fig. 6) revealed no significant subgroup effect.

Details of complications are found in Supplementary Fig. 7. Of the nine studies [14–16,18–23] that reported on procedure related complications, six studies [14,16,18,19,22,23] identified postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE) and post pancreatectomy haemorrhage (PPH) according to the International Study Group of Pancreatic Fistula (ISGPF) criteria [39] and the International Study Group of Pancreatic Surgery (ISGPS) criteria [40,41]. The pooled results for POPF, PPH and intraabdominal abscess were comparable between the elderly and non-elderly groups ($p > 0.05$, $I^2 = 0\%$). DGE were similar between the both groups with high heterogeneity (RR1.06, $p = 0.90$, $I^2 = 69\%$). Sensitivity analysis revealed Kang et al. [20] as the source and removing this study improved heterogeneity (excluded Kang et al.: RR0.76, $p = 0.39$, $I^2 = 35\%$). There was no difference in the reoperation rate between both groups (RR0.92, $p = 0.66$, $I^2 = 0\%$). Respiratory complications occurred more frequently in elderly patients (RR2.33, $p = 0.004$, $I^2 = 39\%$).

3.6. Survival

The pooled overall survival estimate was lower in elderly patients (Six studies [12–14,18,20,22], n = 2986. HR1.28, $p < 0.001$, $I^2 = 19\%$). Subanalysis according to the time of enrolment showed no significant subgroup effect ($Chi^2 = 0.68$, $p = 0.41$, $I^2 = 0\%$) (Fig. 5). Three studies [12,15,16] reported on disease free survival and individually showed no significant difference between the elderly and non-elderly group. Two studies reported on disease-specific survival (DSS), Sho et al. [14] reported significantly lower DSS in the elderly group whereas Kanda et al. [19] reported no difference.

4. Discussion

Pancreatic cancer is common in the elderly population and is projected to be the second leading cause of cancer-related death before 2030 [42]. Surgery offers a potential for cure; however, age-related treatment disparities still exist despite advances in treatment options [43,44]. This meta-analysis brings together all the available evidence comparing surgical outcomes of elderly patients over the age of 70 with non-elderly patients following pancreatic resection for pancreatic adenocarcinoma.

The present study differs from previous meta-analyses [8–10] in several ways that increase its reliability. Firstly, this study pays particular attention to surgical outcomes of elderly patients with pancreatic adenocarcinoma, whereas all three previous meta-analyses examine elderly patients undergoing pancreaticoduodenectomy for a variety of malignant and benign diseases. The percentage of patients with known

Table 1
Characteristics of included studies comparing short- and long-term outcomes of elderly patients undergoing pancreatic resection for pancreatic adenocarcinoma.

No	Authors	Year published	Country	Study type	Source	Title	Sample size	Elderly	Non-elderly	Centre type
1	Khan et al.	2010	United States	Retrospective	Mayo Clinic Rochester	Pancreatoduodenectomy for Ductal Adenocarcinoma in the Very Elderly; Is It Safe and Justified?	617	53	564	Single
2	Brozzetti et al.	2006	Italy	Retrospective	Department of surgery, University of Rome Medical School & Department of General and Thoracic Surgery, University of Perugia Medical School	Surgical treatment of pancreatic head carcinoma in elderly patients.	166	57	109	Multi
3	Kang et al.	2007	Korea	Retrospective	Yonsei Medical Centre	Pancreaticoduodenectomy of pancreatic ductal adenocarcinoma in the elderly.	77	11	66	Single
4	Melis et al.	2012	United States	Retrospective	NYU Medical Centre	The safety of a pancreaticoduodenectomy in patients older than 80 years: Risk vs. benefits.	200	25	175	Single
5	Lee et al.	2010	United States	Retrospective	The Pancreas Centre of Columbia University Medical Centre	Pancreaticoduodenectomy can be Performed Safely in Patients Aged 80 years and Older.	391	45	346	Single
6	Barbas et al.	2012	United States	Retrospective	Duke University Medical Centre	Comparison of Outcomes and the Use of Multimodality Therapy in Young and Elderly People Undergoing Surgical Resection of Pancreatic Cancer.	203	32	171	Single
7	Frakes et al.	2015	United States	Retrospective	Moffitt Cancer Centre	Resected pancreatic cancer outcomes in the elderly.	193	87	106	Single
8	Kanda et al.	2014	Japan	Retrospective	Department of gastroenterological surgery, Nagoya University, Nagoya	Pancreatoduodenectomy with Portal vein resection is feasible and potentially beneficial for elderly patients with pancreatic cancer	272	90	182	Single
9	Sho et al.	2016	Japan	Retrospective	Multicenter Study Group of Pancreatobiliary Surgery Authors are from 7 capitals - Hiroshima, Wakayama, Sendai, Osaka, Tokyo, Nara, Kobe	Prognosis after surgical treatment for pancreatic cancer in patients aged 80 years or older: a multicenter study	1401	99	1302	Multi
10	Gangl	2014	Austria	Retrospective	Elisabethinen Hospital Linz	Surgical quality data and survival after pancreatic cancer resections: a comparison of results for octogenarians and younger patients	108	9	99	Single

(continued on next page)

Table 1 (*continued*)

No	Authors	Year published	Country	Study type	Source	Title	Sample size	Elderly	Non-elderly	Centre type
11	Renz et al.	2016	Germany	Retrospective	Pancreatic Cancer Centre Munich	Pancreaticoduodenectomy for adenocarcinoma of the pancreatic head is justified in elderly patients: A Retrospective Cohort Study.	300	59	241	Single
12	Turrini et al.	2013	Europe	Retrospective	37 institutions: France (34 institutions), Belgium (1 institution), Monaco (1 institution), Switzerland (1 institution)	Pancreatectomy for adenocarcinoma in elderly patients: Postoperative outcomes and long term results: A study of the French Surgical Association.	932	352	580	Multi
						Total	**4860**	**919**	**3941**	

No	Study period	Mean procedure per year	Pathology	Intervention	Age groups	Postoperative Outcomes	Postoperative mortality, n (%)			Follow-up, mth
1	1981–2007	24	PA	PD	< 80, ≥80	1, 1+, 2, 2+, 3, 3+, 4	b	7	(1%)	18.3[d]
2	1990–2000	–	PA	PD	< 70, ≥70	1, 1+, 2, 2+, 3, 3+	a,b	10	(6%)	–
3	1990–2005	5	PA	PD	< 70, ≥70	1, 1+, 2, 2+, 3, 3+, 4	a,b	1	(1%)	24.5[c]
4	1990–2009	11	PA	PD	< 80, ≥80	1, 1+, 2, 2+, 3, 4	a	2	(1%)	35[d]
5	1992–2009	23	PA	PD	< 80, ≥80	1, 1+, 2, 2+, 3, 3+, 4	a,b	17	(4%)	–
6	1996–2008	17	PA	PD	< 75, ≥75	1,1+, 2,2+, 3, 3+, 4	a,b	7	(3%)	–
7	2000–2012	16	PA	PPPD/PD	< 70, ≥70	1,1+, 2, 4	a	6	(3%)	–
8	2000–2012	23	PA	PD	< 70, ≥70	1, 1+, 2, 3, 4	-	0	(0%)	–
9	2001–2012	–	PA	Pancreatic resection	< 80, ≥80	1, 1+, 2, 4	a,b	28	(2%)	–
10	2001–2010	12	PA	PPPD/PD/TP/DP	< 80, ≥80	1, 1+, 2, 2+,3	a,b	5	(5%)	–
11	2002–2012	30	PA	PPPD/PD/TP	< 75, ≥75	1, 1+, 2, 2+, 3, 4	a	10	(3%)	16[d]
12	2004–2009	–	PA	PD/DP/TP	< 70, ≥70	1, 1+, 2, 2+, 3, 3+, 4	a,b	30	(3%)	19[d]

1: Any postoperative mortality data, 1+: 30-day mortality after surgery or in-hospital death, 2: Any postoperative complications data, 2+: Overall complications, 3: Length of stay (any units of measurement), 3 + Length of stay (mean + sd or median + IQR), 4: Overall survival curves, median survival.

PA: Pancreatic Adenocarcinoma, PD: Pancreaticoduodenectomy, PPPD: Pylorus preserving pancreaticoduodenectomy, TP: total pancreatectomy, DP: Left pancreatectomy/Distal pancreatectomy.

[a] 30-day mortality.

[b] In-hospital mortality.

[c] Mean.

[d] Median.

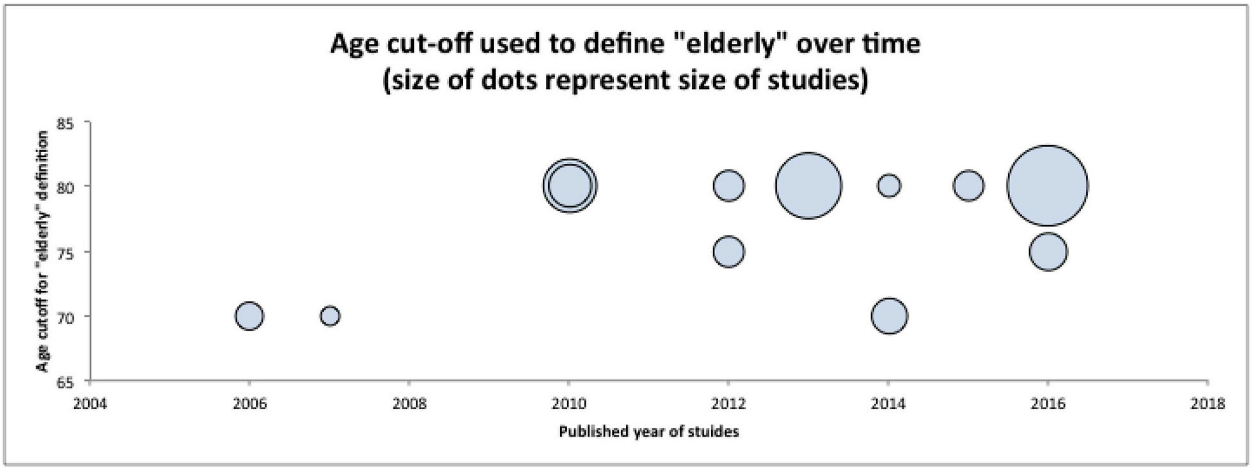

Fig. 2. Age cut-off used to define 'elderly' over time (year of publication). Sizes of dots represent size of studies.

malignant pancreatic tumours in these previous reviews were 55.2% [8], 32.5% [9] and 8% [10] of their sample population. This variation introduces high levels of between-study clinical heterogeneity [45]. Secondly, the elderly group in our study comprised of 19% of our sample population (919 of 4860 patients) compared with previous meta-analyses [8–10] where elderly patients were less than 10% of the study population (Sukharamwala et al. [8], 494 of 5186 patients; Casadei et al. [9], 1090 of 12,930 patients; Kim et al. [10], 3993 of 49,449 patients). Although, this is most likely due to a higher age-off used to define "elderly", bias can be introduced when there is a substantial imbalance between comparative groups [46].

Over the last decade, death associated with pancreatic resection has declined with mortality rates below 5% [12–21,47,48] [49,50]. Winter et al. [50] reported one of the largest single institutional series on pancreaticoduodenectomy with three surgeons performing 80% of the resections. In their study of 1423 patients, postoperative mortality rate decreased from 30% in the 1980s to 1% in the 2000s. Pancreatic surgery has become a safer procedure. The question is: 'Do elderly patients derive similar benefits from this pattern of improvement?' Advocates for elderly patients undergoing surgical resection for pancreatic adenocarcinoma believe mortality rates have improved. This meta-analysis demonstrates a reduction in postoperative mortality in elderly patients undergoing pancreatic surgery over time. Postoperative mortality rate in elderly patients, when compared with non-elderly patients, shift from being significantly higher (before 2000) to being similar (from 2000 onwards) (Fig. 3). Furthermore, our study reveals that increasing age cut-offs used to define 'elderly' (Age ≥70, ≥75 and ≥ 80 years) did not modify the mortality rate of the elderly group (Supplementary Fig. 5) [51]. This pattern of improvement suggests that postoperative mortality in elderly patients was more likely related to surgical and anaesthetic techniques coupled with better patient selection and/or postoperative care management rather than chronological age alone. With statistical

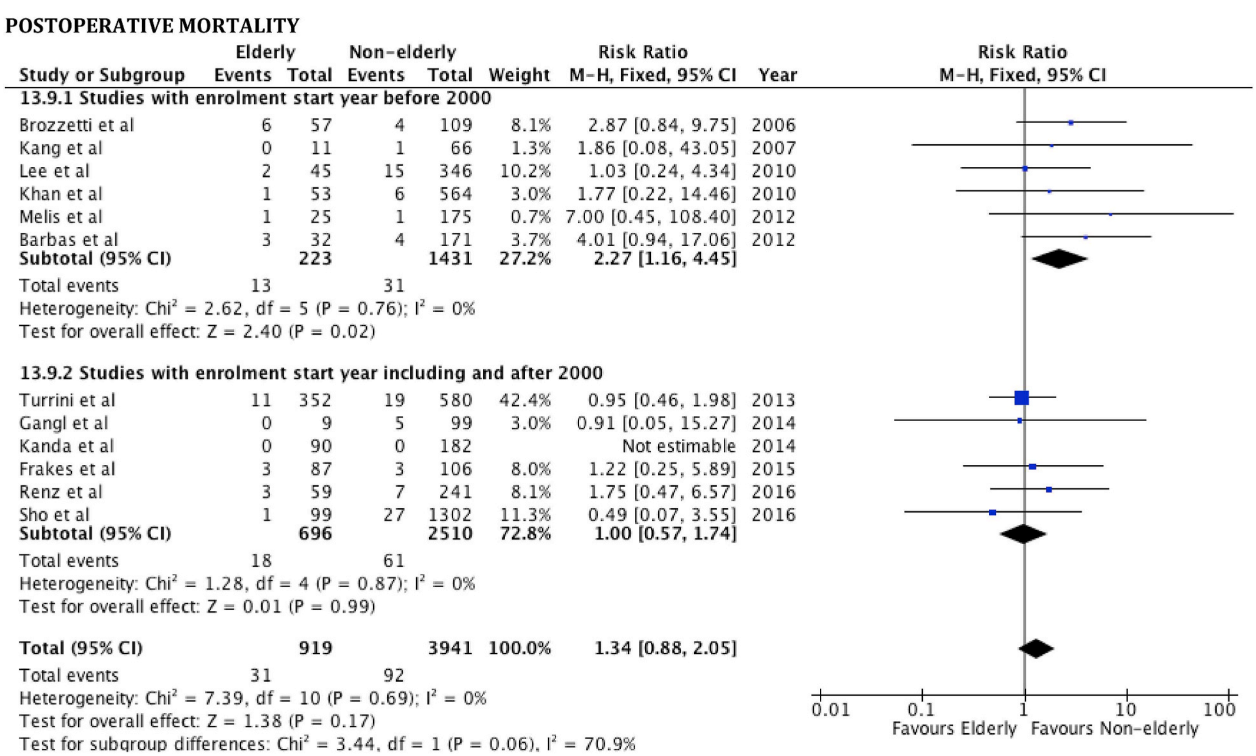

Fig. 3. Forest plot of the comparison of postoperative mortality between elderly and younger patients following pancreatic surgery - Subgroup analysis stratified according to the different start dates of the enrolment period in individual studies (before the year 2000; including and after the year 2000).

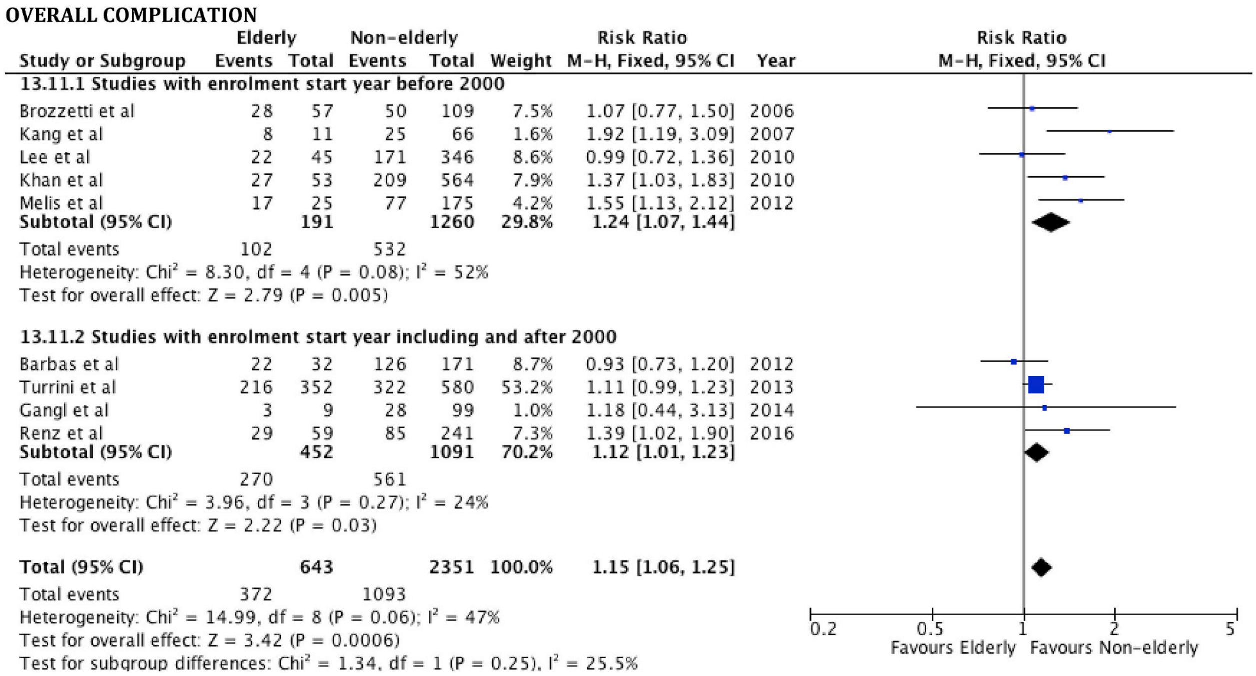

Fig. 4. Forest plot of the comparison of overall complications between elderly and younger patients following pancreatic surgery - Subgroup analysis stratified according to the different start dates of the enrolment period in individual studies (before the year 2000; including and after the year 2000).

evidence of improvement in postoperative mortality over time, this builds confidence in surgeons to optimise surgical treatment in meeting the needs of elderly pancreatic cancer patients. Further studies are required to identify preoperative medical or social risks in elderly patients that are associated with adverse outcomes following pancreatectomy.

The overall complication rate following pancreatic resection remains high at 40–70% [12–22]. Our present study reveals that patients in the elderly group had an increased risk of developing complications as suggested by previous studies [9,50]. An included retrospective study by Kang et al. [20] reported significantly higher complication rates in the elderly group (73% v 38%, p = 0.049). Their result was based on a series of 77 non-cardiovascular patients over a 15-year period, which may be a reflection of the impact of hospital volume on postoperative morbidity [50,52–55]. In contrast, Barbas et al. [17] demonstrated no difference in complication rates between the elderly and non-elderly patients (69% v 74%, p = 0.25, respectively). Most patients in their retrospective series [17] received neoadjuvant chemotherapy treatment (Elderly v Non-elderly: 56% v 53.2%, p = 0.87) despite a higher proportion of elderly patients with cardiovascular comorbidities (Coronary artery disease, p = 0.007; Hypertension, p = 0.03). The authors suggested that elderly individuals who can successfully complete the course of neoadjuvant therapy and tolerate its associated morbidity probably had adequate physiological reserve despite comorbid conditions. These findings emphasise the volume effect of pancreatic surgery, and the importance of patient selection and preoperative optimisation in higher-risk surgical candidates.

The development of major procedure related postoperative complications including POPF, DGE, PPH and intraabdominal abscess following pancreatic surgery were comparable between the elderly and non-elderly group; although these findings are consistent with two previous meta-analyses [8,9], definite conclusions cannot be made as only six studies [14,16,18,19,22,23] identified complications according to the ISGPF [39] and ISGPS criteria [40,41]. The present meta-analysis shows that medical respiratory complications occurred more frequently in the elderly population [8,18,51,56,57]. Respiratory complications due to respiratory muscle dysfunction, which can persist from days to

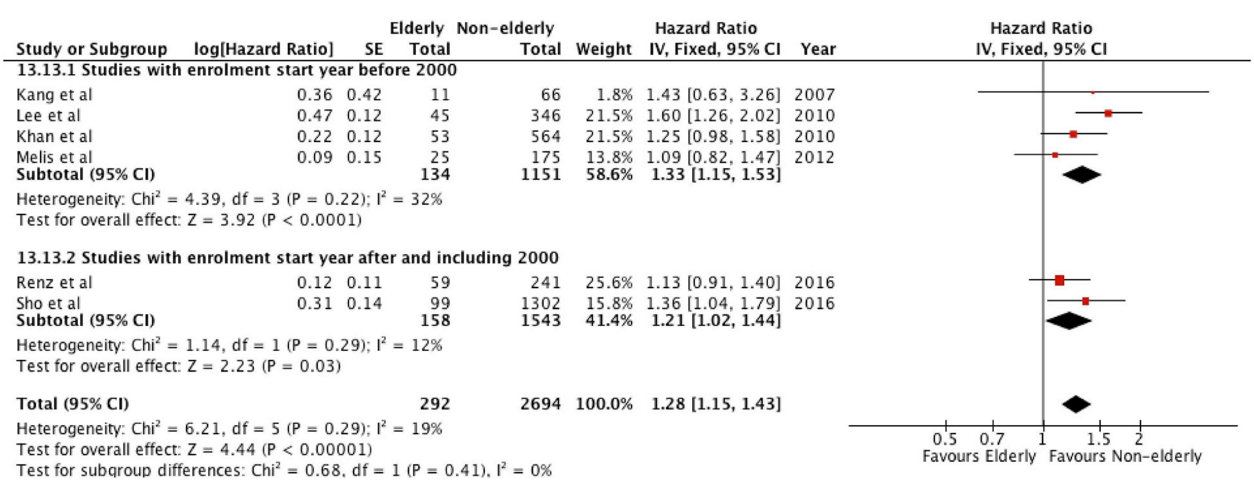

Fig. 5. Forest plot of comparison of overall survival between elderly and younger patients following pancreatic surgery stratified with subgroup analysis stratified according to the different start dates of the enrolment period in individual studies (before the year 2000; including and after the year 2000).

weeks [58], is the major cause of postoperative morbidity following upper abdominal surgery [59–61]. Procedure-related risk, in addition to poorer physical status, predisposes elderly patients to develop pulmonary complications. It is plausible that surgeons selected patients who were most likely to do best after an operation. Even so, this meta-analysis demonstrates that elderly patients had worse ASA scores and more cardiovascular comorbidities, key risk factors for developing postoperative respiratory complications [62–64]. Therefore it might be relevant to implement and intensify preoperative rehabilitation programs and postoperative pulmonary care interventions in this population [65]. Early interventions following the identification of patients with high surgical risk potentially reduce the likelihood of postoperative complications. Some scoring systems aim to assess the baseline risk of patients undergoing pancreatic surgery [66–72] but there is a scarcity of simple scoring systems that stratify preoperative risk in geriatric patients [73]. The implementation of preoperative optimisation [74], intraoperative strategies [75,76] and further research on postoperative care practices [77–79] might be beneficial when directed at high-risk surgical patients.

In this meta-analysis, the overall survival of elderly patients that underwent pancreatic resection is shorter than non-elderly patients. Adjuvant chemotherapy treatment after surgical resection of pancreatic cancer provides a survival benefit [4]. This current study shows that elderly patients did not receive standard treatment for pancreatic adenocarcinoma. Pathological tumour characteristics of patients in the elderly and non-elderly groups were similar, however, elderly patients were less likely to (i) receive pancreatectomy with concomitant venous resection (RR0.80, $p = 0.003$), (ii) achieve negative margins after surgical resection (RR0.76, $p = 0.02$) and (iii) receive adjuvant chemotherapy treatment (RR0.69, $p < 0.001$). Given a perception of poorer physical status, elderly patients might have been excluded, or might have refused standard “aggressive” therapies, which in turn may have affected their long-term survival outcomes. Moreover, patients in the eighth decade of life have a higher risk of non-cancer related mortality [80] therefore competing risk methods for survival analysis might be more appropriate to correctly estimate the probability of cancer-related deaths in the presence of competing events [81].

5. Limitations

Our analysis included studies that were retrospective in design that excluded patients with unresectable tumours or those who declined or have been declined surgical treatment leading to potential selection and information bias. Moreover, eight studies (Table 1) included only patients undergoing pancreaticoduodenectomy leading to additional selection and information bias; nonetheless it is the most common surgical procedure for pancreatic adenocarcinoma. Furthermore, the statistical power of this study is not high. The limitations of this study emphasise that conclusions regarding postoperative outcomes between the elderly and non-elderly patients cannot be made definitively.

6. Conclusion

Pancreatic resection of pancreatic adenocarcinoma can be performed safely on elderly patients with acceptable risks in tertiary centres by experienced specialist hepatobiliary surgeons. Age alone should not be the only determinant for the selection of patients for surgical treatment. A better understanding of the barriers to the provision of adjuvant chemotherapy and aggressive surgery (to achieve clear surgical margins) is needed. This conclusion needs to be confirmed in larger prospective trials with the consideration of non-operative treatment options.

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None.

Ethical Approval

This is a systematic review and meta-analysis. Ethical Approval is not required.

Research Registration Unique Identifying Number (UIN).

Research Registry.

Reviewregistry690.

https://www.researchregistry.com/browse-the-registry#registryofsystematicreviewsmeta-analyses/registryofsystematicreviewsmeta-analysesdetails/5cd5084735128d0007c109dc/

Author contribution

Dr Elinor Tan: Substantial contribution in acquisition, analysis and interpretation of data for the work. Drafting and revising the work for important intellectual content. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr Jialu Song: Substantial contribution in acquisition of data for the work. Drafting and revising the work for important intellectual content. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr Susanna Lam: Substantial contribution in acquisition, interpretation of data for the work. Revising the work for important intellectual content. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr Mario D' Souza: Substantial contribution in analysis, interpretation of data for the work. Revising the work for important intellectual content. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr Michael Crawford**:** Substantial contribution in the concept and design of the work. Revising the work critically for important intellectual content. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Associate Professor Charbel Sandroussi: Substantial contribution in the concept and design of the work. Revising the work critically for important intellectual content. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Guarantor

Associate Professor Charbel Sandroussi.

Dr Michael Crawford.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Data statement

The raw data of this systemic review and meta-analysis is available in published articles from which data is obtained.

Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2019.09.030.

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