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REVIEW ARTICLE

The outcomes of the pancreaticoduodenectomy in patients aged 80 or older. A systematic review and meta-analysis

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Abstract

Background: There is an increasing needed to consider pancreaticoduodenectomy (PD) for the treatment of pancreatic and periampullary malignancy in patients aged 80 and over, given the increasing aging population.

Methods: A systematic literature search was undertaken to identify selected studies that compared the outcomes of patients aged 80 years or over to those younger undergoing PD.

Results: In total 18 studies were included for evaluation. Octogenarian or older populations had significantly higher 30-day post-operative mortality rate (OR: 2.22, 95% CI = 1.48–3.31, $p < 0.001$) and length of hospital stay (OR: 2.23, 95% CI = 1.36–3.10, $p < 0.001$). The overall post-operative complication rate was higher in the older group compared to the younger population (OR: 1.51, 95% CI = 1.25–1.83, $p < 0.001$). Elderly patients were more likely to develop pneumonia (OR: 1.72, 95% CI = 1.39–2.13, $p < 0.001$) and experience delayed gastric emptying (DGE) (OR: 1.77, 95% CI = 1.35–2.31, $p < 0.001$). The incidence of post-operative pancreatic fistula and bile leak were not significantly different between the groups. Rehabilitation and home nursing care services was also more frequently required by the older patient group at the time of hospital discharge.

Conclusion: Patients aged 80 years and older have approximately double the risk of 30-day post-operative mortality and 50% increased rate of complications following PD. Careful patient selection is required when offering surgery in this age group.

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Introduction

Pancreaticoduodenectomy (PD) offers a chance of cure in patients with pancreatic cancer involving the head of the pancreas and other peri-ampullary malignancies and can improve quality of life.[1,2] It is also a valid treatment option in selected patients with benign tumours and non-cancerous conditions such as chronic pancreatitis.[3] The overall morbidity and mortality associated with PD ranges between 45 and 52%[4–6] and 0–5%[7–10] respectively.

There are concerns about the potential increased risk of morbidity and mortality associated with PD in older patient subgroups, with age itself having been used to determine the suitability for operative intervention by some centres.[11] The population of people over 80 years of age is increasing worldwide, constituting approximately 1% of total population and is predicted to increase by four-fold in the next 40 years.[12] There will be an increasing need to consider patients over the age of 80 for PD, particularly for the treatment of pancreatic cancer, where the incidence increases with age.[12,13]

In the last 20 years, the outcomes of PD have improved with better surgical techniques and optimal post-operative care of patients.[12] However, offering this surgery to elderly patients is still a controversial issue, particularly for the treatment of pancreatic cancer which itself has a very poor prognosis.[12] The 5-year actuarial survival rate of pancreatic cancer following surgical resection ranges from 12 to 24% even in large volume centres.[14,15] Although

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there are studies from several countries comparing the outcomes of elderly patients treated by PD with younger groups,[10,12,16] definitive conclusions regarding the relative risk of age in relation to mortality and specific complications, incorporating data from more recent studies are lacking.[17]

This study aims to provide a comprehensive update on the outcomes patients aged over 80 years undergoing PD compared to younger age group and quantitate possible differences in overall mortality and morbidity, including comparison of specific complications.

Methods

Search strategy

This systematic review and meta-analysis was prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[18] A computerised search of Discovery, PubMed, OVID and Science Direct was carried out using medical subject headings (MeSH) terms on articles published between June 1990 and January 2016, limited to the English language. An advanced search was conducted using the following search headings: 'age 80 and over', 'Octogenarians', 'pancreaticoduodenectomy', 'Whipple's procedure', and 'adverse outcomes'. Reference lists were compiled and relevant articles were screened manually and cross-referenced to identify any additional studies.

Inclusion and exclusion criteria

Abstracts of all retrieved articles were reviewed. Studies that compared post-operative outcomes in patients aged 80 and over with younger patients, who underwent pancreaticoduodenectomy were included in this review. These studies reported on post-operative mortality and morbidity outcomes. In the case of duplicate studies, only the most recently published article was included. Where two studies were reported from the same institution, they were included if the study period and the number of patients recruited differed. Studies that were not in English language were excluded. This review also excluded letters to the editors, case reports, non-comparative patient series and studies that did not specifically focus on patients aged 80 and over undergoing PD.

Outcomes of interest

Post-operative mortality and overall complications were the primary end points examined between the two age groups. The secondary endpoints examined included pancreatic-specific complications such as post-operative pancreatic fistula (POPF), delayed gastric emptying (DGE), bile leak and haemorrhage. Complications such as pneumonia, cardiac events, and wound infections were also examined. Data relating to length of hospital stay and post-operative survival were recorded where available.

Statistical analysis

Statistical analysis was undertaken using Review Manager (RevMan) version 5.3. Data of interest was extracted from each study and analysed. For data that was dichotomous, the Mantel-Hansel method was utilised using a fixed-effect model with a 95% confidence interval (CI). p-Values <0.05 was considered to be statistically significant in this review. For continuous data, inverse variance was used as a statistical method, with a CI of 95%. The median survival and 5-year survival data from each study comparing between the two age groups were presented in this review.

Results

Study selection

The study flow diagram of the research papers selected is shown in Fig. 1.

Study results

Overall there were 49,449 patients in the studies examined. This included 3993 (8.1%) elderly patients aged 80 and 45,456 (91.9%) patients aged under 80 years. The characteristics of the studies are shown in Supplementary Table 1. The summary of the results of the meta-analysis are shown in Table 1.

Pre-operative health status

Pre-operative health status based on American Society of Anaesthesiologists' (ASA) scoring were reported in six studies[6,9,14,19–21] enabling comparison of ASA scores equal to 3 or 4 in each age group. Elderly population was more two fold more likely to have ASA score of $\geq$3 when compared to the younger population (983/1191 (82.5%) vs 7751/11,442 (67.7%) -Odds Ratio (OR) 2.33, 95% CI: 1.98–2.74, $p < 0.001$) (Supplementary Fig. 1).

Post-operative mortality

In total 12[4,5,8,9,12,14,16,20–24] of the 18 studies reported the incidence of 30-day post-operative mortality among elderly patients versus the younger patients (Fig. 2). The difference in mortality rate was statistically significant, showing that the post-operative mortality in the older group was 2 times higher than younger group (OR: 2.22, 95% CI = 1.48–3.31, $p < 0.001$). There 90-day mortality rates could not be determined as this was not reported by the series examined.

The causes of mortality in the elderly patients aged 80 or over (n = 76) was reported by one series.[12] In this study 9 patients in the elderly age group died post-operatively (11.8%), of which 7 were the result of cardiorespiratory complications, specifically myocardial infarction (AMI) and pneumonia. Other causes included sepsis from colitis and haemorrhagic shock. All of the 9 patients who died had chronic obstructive pulmonary disease (COPD). The mortality in patients younger than 80 years (n = 1629) was 2.5%.

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