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Original article

Short- and long-term outcomes after enucleation of pancreatic tumors: An evidence-based assessment

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ABSTRACT

Background and objective: Enucleation of pancreatic tumors is rarely performed. The aim of this study was to evaluate the published evidence for its short- and long-term outcomes.
Methods: PubMed (MEDLINE) and EMBASE databases were searched from 1990 to March 2016. Studies including at least ten patients who underwent enucleation of pancreatic lesions were included. Data on the outcomes were synthesized and meta-analyzed where appropriate.
Results: Twenty-seven studies involving 1316 patients were included in the systematic review. The postoperative mortality was 0.3%, and the postoperative morbidity was 50.3%, mainly represented by pancreatic fistula (38.1%). Endocrine insufficiency, exocrine insufficiency and tumor recurrence was observed in 2.4%, 1.1% and 2.3% of the patients respectively. Compared with typical resection, the operation time, blood loss, length of hospital stay, and the incidence of endocrine and exocrine insufficiency were all significantly reduced after enucleation. The occurrence of pancreatic fistula was significantly higher in enucleation group, but overall morbidity, the reoperation rate and mortality were comparable between the two groups. There was no significant difference in disease recurrence between the two groups. Compared with central pancreatectomy, enucleation had a shorter operation time, lower blood loss, less morbidity, and better pancreatic function. Compared with open enucleation, minimally invasive enucleation had a shorter operation time and a shorter length of hospital stay.
Conclusions: Enucleation is an appropriate surgical procedure in selected patients with benign or low-malignant lesions of the pancreas. The benefits of minimally invasive approach need to be validated in further investigations with larger groups of patients.

1. Introduction

The diagnosis of benign and low-grade pancreatic neoplasms has been improved in recent years due to the wide application of cross-sectional imaging and endoscopic ultrasonography. As a parenchyma sparing procedure, enucleation is thought to be a proper surgical management for these lesions because of their small size and low risk of malignancy [1]. As only a small portion of the pancreatic parenchyma is removed, patients are less likely to develop postoperative pancreatic insufficiency in the long run. But as enucleation of pancreatic lesions is mostly reported in single centers with a small number of cases, it is difficult to derive valid conclusions [2–9]. In addition, the number of studies comparing enucleation with other procedures is limited. The aim of the present study is to evaluate the short- and long-term outcomes following enucleation for pancreatic lesions based on a systematic review of the published literature available, and compare the results of enucleation *versus* resection or minimally invasive *versus* open enucleation via a meta-analysis.

2. Methods

This study was performed in accordance with the guidelines of preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2009 [10].

2.1. Literature search strategy and study identification

A systematic literature search of the PubMed (MEDLINE) and

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EMBASE databases from 1990 to March 2016 was performed to identify relevant studies. The used terms were enucleation and pancreas. Only studies on humans and in the English language reporting enucleation of pancreatic lesions were considered for inclusion. Reference lists of retrieved articles were reviewed for additional citations. Data from animal studies, abstracts, conference proceedings, case series of fewer than 10 patients, and reviews were excluded. Articles containing different patient populations from the same institution were included. Data including the first author, date, design, sample size, patient characteristics, and outcomes of interests were extracted independently by two physicians (Yanming Zhou and Min Zhao) using a standard data collection form. Discrepancy about values or analyses was resolved by consensus. The level of evidence of each study was categorized according to the Evidence-Based Medicine Levels of Evidence [11].

2.2. Outcome measures

The intraoperative outcomes included the operation time and blood loss, and the postoperative outcomes included overall morbidity, pancreatic fistula (PF), the reoperation rate, mortality, and length of hospital stay. Long-term outcomes included pancreatic endocrine insufficiency (the presence of diabetes), exocrine insufficiency (persistent postoperative diarrhea and steatorrhea requiring oral pancreatic enzyme supplementation) and tumor recurrence.

2.3. Statistical analysis

Descriptive statistics were performed and data are expressed as mean or median (range) where appropriate. In meta-analysis, pooled effect was estimated using a fixed-effect model or a random-effect model. Odds ratio (OR) or weighted mean difference (WMD) with a 95% confidence interval (95% CI) were calculated for dichotomous variables and continuous variables respectively. Heterogeneity was assessed using the χ^2 test and I^2. Statistical significance was set at $P < 0.05$. All analyses were conducted with the Review Manager (RevMan) software, version 5.1 (The Cochrane Collaboration, Software Update, Oxford).

The study was approved by the Ethics Committee of our hospital.

3. Results

3.1. Systematic review

Twenty-seven observational studies [1–9,12–29] published between 1998 and 2016 with a total of 1316 patients meeting the inclusion criteria were included in the systematic review (Table 1). All 27 studies were classified as level-4 evidence. The median number of patients receiving enucleation in each published study was 37 (range 10–66). The mean age of the 865 patients in 19 studies ranged from 39 to 51 years (median = 52), and the proportion of male patients was 32.5% (304/936) in 20 studies. The pathology was recorded in 26 articles containing 1273 neoplasms, with neuroendocrine neoplasm (NEN) being the most common diagnosis (n = 836, 65.6%), followed by intraductal papillary mucinous neoplasm (IPMN) (n = 119, 9.3%), serous cystic neoplasm (SCN) (n = 103, 8.1%), and mucinous cystic neoplasm (MCN) (n = 95, 7.4%). Twenty-three articles reported the location of 1232 neoplasms, of which 700 (56.8%) were located in the head/uncinate process, and 532 (43.2%) in the body/tail. The mean tumor size ranged from 1.3 to 4.8 cm (median = 2.3; n = 1104, 22 studies). Table 2 summarizes the short- and long-term outcomes.

Of 1316 patients, 1062 (80.7%) underwent open procedures and 254 patients (19.3%) underwent minimally invasive procedures (laparoscopic and robotic surgery). The mean operation time ranged from 85 to 272 min (median = 154; n = 817, 21 studies), and the mean intra-operative blood loss ranged from 64 to 220 ml

Table 1
Baseline characteristics of the studies included in systematic review.

Reference	Country	Years	Study period	N	Age (years)[a]	M/F	Diagnosis	Tumor site H-U/B-T	TS (cm)[a]
Talamini et al. [1]	USA	1998	1990–1997	10	63	6/4	MCN	7/4	2.8
Kiely et al. [2]	USA	2003	1992–2003	11	53	3/8	MCN 7, SCN 2, NEN 2	5/6	1.8
Kazanjian et al. [3]	USA	2006	1990–2005	11	39.1	7/4	NEN	NA	2.1
Crippa et al. [4]	Italy Verona	2007	1990–2005	61	47	24/37	NEN 38, MCN 3, SCN 5	32/29	2.3
Liu et al. [5]	China	2007	2000–2006	26	NA	NA	NEN	12/14	1.5
Karaliotas et al. [6]	Greece	2009	1999–2008	12	55	NA	NEN	0/12	NA
Luo et al. [7]	China	2009	2000–2007	16	NA	NA	NEN	7/9	NA
Casadei et al. [8]	Italy	2010	1980–2009	15	52	7/8	NEN	7/8	1.9
Ge et al. [9]	China	2010	2001–2007	11	47.1	2/9	MCN 8, SCN 3	1/10	4.8
Dedieu et al. [12]	France	2011	1999–2007	23	49	12/11	NEN 15, MCN 1, IPMN 1	8/15	2.4
Brient et al. [13]	France	2012	1998–2008	52	52.3	14/38	NEN 35, MCN 2, SCN I2, IPMN 1	27/25	1.9
Cauley et al. [14]	USA	2012	1998–2010	45	53.3	18/27	NEN 21, MCN 10	20/25	2.3
Crippa et al. [15]	Italy Verona	2012	1990–2009	106	NA	NA	NEN	56/49	NA
Fernandez-Cruz et al. [16]	Spain	2012	1999–2007	13	56.5	NA	NEN	NA	2.8
Zhang et al. [17]	China	2012	1985–2010	129	NA	NA	NEN	91/38	1.3
Zhang et al. [18]	China	2013	2005–2011	119	44	38/81	NEN 91, MCN 2, SCN 6	94/25	2.7
Choi et al. [19]	Korea	2014	2005–2011	11	43	1/10	MCN 4, SCN 4	0/11	4.0
Heeger et al. [20]	Germany, Italy	2014	1994–2012	60	50.5	21/39	NEN 55, MCN 1, SCNI 1	41/19	1.4
Tsang et al. [21]	Hong Kong	2014	1999–2007	18	NA	NA	NEN	14/4	NA
Faitot et al. [22]	France	2015	1998–2011	126	50	44/82	NEN 46, IPMN 38, MCN 26	58/68	2.0
Song et al. [23]	Korea	2015	2005–2013	65	53	17/48	NEN 24, MCN 9, SCN 9, IPMN 7	31/34	2.5
Strobel et al. [24]	Germany	2015	2001–2014	166	58.2	43/123	NEN 60, MCN 4, SCN 21, IPMN 64	82/74	1.3
Wolk et al. [25]	Germany	2015	1996–2013	17	52.6	4/13	NEN 9	NA	1.9
Shi et al. [26]	China	2015	2010–2014	43	NA	17/26	NA	NA	2.7
Zhang et al. [27]	China	2016	2001–2014	37	48.6	11/26	NEN 17, MCN 5, SCN 4	21/16	3.4
Jilesen et al. [28]	The Netherlands	2016	1992–2013	60	NA	26/34	NEN	35/25	NA
Xiao et al. [29]	China	2016	2010–2014	53	NA	15/28	NEN 11, MCN 3, SCN 26, IPMN 8	41/12	2.6

M/F, male/female; MCN, mucinous cystic neoplasm; SCN, serous cystic neoplasm; NET, neuroendocrine neoplasm; IPMN, intraductal papillary mucinous neoplasia. H-U, head or uncinate process; B-T, body or tail; TS, tumor size; NA, not available.
[a] Median or mean.

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