



Review

Postoperative drain amylase predicts pancreatic fistula in pancreatic surgery: A systematic review and meta-analysis



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ABSTRACT

Background and objectives: This study to evaluate the utility of drain fluid amylase as a predictor of PF in patients undergoing pancreatic surgery based on the International Study Group of Pancreatic Fistula definitions of pancreatic fistula.

Methods: A comprehensive search was carried out using Pubmed (Medline), Embase, Web of science and Cochrane database for clinical trials, which studied DFA as a diagnostic marker for pancreatic fistula after pancreatic surgery. Sensitivity, specificity and the diagnostic odds ratios with 95% confidence interval were calculated for each study. Summary receiver-operating curves were conducted and the area under the curve was evaluated.

Results: A total of 10 studies were included. The pooled sensitivity and specificity of drain fluid amylase Day 1 for the diagnosis of postoperative pancreatic fistula were 81% and 87%, respectively (area under the curve was 0.897, diagnostic odds ratios was 16.83 and 95%CI was 12.66–22.36), the pooled sensitivity and specificity of drain fluid amylase Day 3 for the diagnosis of postoperative pancreatic fistula were 56% and 79%, respectively (area under the curve was 0.668, diagnostic odds ratios was 3.26 and 95%CI was 1.83–5.82)

Conclusions: The drain fluid amylase Day 1, instead of drain fluid amylase Day 3, may be a useful criterion for the early identification of postoperative pancreatic fistula, and a value of drain fluid amylase Day 1 over than 1300 U/L was a risk factor of pancreatic fistula. And the diagnostic accuracy and the proposed cut-off levels of drain fluid amylase Day 1 in predicting the postoperative pancreatic fistula will have to be validated by multicenter prospective studies.

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1. Introduction

Pancreaticoduodenectomy (PD), distal pancreatic resection (DP) and pancreatectomy are now standardized interventions for benign and malignant pancreatic lesions [1–7]; however, pancreatic surgeries are associated with significant postoperative morbidity despite technical improvements in recent years [8,9]. A frequent, serious and costly contributor to postoperative morbidity or complication in pancreatic surgery is postoperative pancreatic fistula (PF) [9,10], but there is a remarkable variability in the incidence of pancreatic anastomotic leakage after PD, ranging from 5 to 30% [11,12]. PF can lead to more troublesome complications including intra-abdominal abscess, delayed gastric emptying, hemorrhage, sepsis, and even death [13]. Additionally, PF may delay or even preclude adjuvant chemotherapy or chemoradiation [14,15].

Despite its importance, PF has still not been uniformly defined until 2005, when International Study Group of Pancreatic Fistula (ISGPF) [3] established the commonly accept PF definition based on the clinical impact of PF-related complications. According to the definition, PF is diagnosed when there is measurable drain output on or after postoperative day 3, with drain fluid amylase (DFA) concentration equals or higher than 3 times the upper limit of normal serum value. Additionally, PF was classified as grade A, B, or C. Grade B and C POPF are severe, clinically significant fistulas that require major deviations in clinical management. Currently, in most centers, the surgical drain is left in situ until PF is excluded by a normal DFA value on postoperative day 5, which is thought to be unnecessary by many investigators.

The earlier diagnosis (and exclusion) of PF has a number of potential advantages. For example, in patients with PF, early diagnosis would allow timely intervention (e.g. antibiotics and parenteral nutrition) before the clinical deterioration, while in patients without PF, surgical drains may be removed promptly and oral intake may be introduced earlier, which would potentially facilitate wound healing and physical recovery. Up to now, several studies [16–26] have explored the concept of analyzing drain fluid or DFA in the early postoperative period in predicting the PF (grade A, B and C) after pancreatic surgery. But the results still remain controversial. In addition, the optimal DFA (day 1 or 3) cutoff value varies among different study centers and the diagnostic accuracy of DFA has not been systematically assessed.

Current meta-analysis aims to provide a comprehensive summary of randomized controlled or clinical cohort trials. Specifically, we conducted the meta-analysis to evaluate the utility of DFA as a predictor of PF in patients undergoing pancreatic surgery (PD, DP or pancreatectomy) based on the ISGPF definitions. Also the diagnostic accuracy of DFA had been assessed in the present meta-analysis. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria [27] were used as guidelines in the construction of this analysis.

2. Methods

2.1. Literature search

A comprehensive search of the literatures was performed. Specifically, we systematically searched the Pubmed (Medline), Embase, Web of science and Cochrane database for studies published until October 31st 2014 by using the search terms “pancreaticoduodenectomy or PD”, “Whipple” or “pancreatectomy”, “pancreatic resection”, “distal pancreatectomy”, “drain amylase”, “amylase” and “intraperitoneal drainage amylase”. We searched for additional references by crosschecking bibliographies of retrieved full-text articles. Two reviewers (J.Y., C.W.) independently screened the titles and abstracts of all the articles according to predefined inclusion and exclusion criteria. Any differences were resolved by mutual agreement and in consultation with the third reviewer (Q.H.).

2.2. Inclusion and exclusion criteria

The inclusion criteria were: (1) English language articles published in peer-reviewed journals, including the case controlled or cohort studies or randomized controlled trials; (2) Diagnosis was clear and definite (benign and malignant pancreatic lesions) and had indication of surgical treatment; (3) human trials testing the value of postoperative DFA in predicting the PF after the pancreatic surgery, the PF conclude of grade A, B and C according to the ISGPF definition; (4) Only studies with data available for the construction of a 2 × 2 contingency table with true-positive, false-negative, false-positive, and true-negative values were included.

The exclusion criteria were: (1) studies that did not evaluate the accuracy of DFA in predicting the PF; (2) studies and/or abstracts with insufficient data; (3) reviews, editorials, expert opinions, reviews, case reports or correspondence letters that did not report their own data; and (4) case reports and studies with less than 10 patients.

2.3. Data extraction

Data were extracted by three independent observers using standardized forms. The recorded data included population characteristics, residence, date of patient admission and urinary sampling, and etiology. Diagnostic parameters including true positivity (TP), false positivity (FP), false negativity (FN) and true negativity (TN) were extracted directly or by calculating the sensitivity and specificity of DFA (DFA1, 3 and 5) for diagnosis the PF after the pancreatic surgery. TP, FP, FN and TN were also extracted for DFA (1 and 3) if these were reported.

2.4. Quality assessment of the included studies

Currently, there is no consensus or criteria to evaluate the

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