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The value of postoperative measurement of amylase in abdominal drainage fluid after pancreatic surgery

F Safi, S Bakathir, M Taha, T Lange, H El Salhat, F Branicki

ABSTRACT

Introduction: Clinical symptoms accompanied by a continuous increase of amylase concentration in abdominal drainage fluid and change in color of drainage fluid may indicate the presence of fistula or leakage. Aims: To investigate the clinical relevance and utility of post-operative (PO) monitoring of amylase and lipase estimations in the serum and abdominal drainage fluid following pancreatic surgery. Methods: Seventy patients (37 males, 33 females) who underwent duodenum-preserving pancreatic head resection [n = 12 (GI)], pylorus preserving Whipple's procedure [n = 39 (GII)], segmental resection of the body of the pancreas [n = 4 (GIII)] and pancreas tail/body resection [n = 15] were enrolled in the study prospectively. In G I, II and III (n = 55) duct mucosa anastomosis with the remnant of distal pancreas was fashioned. The serum amylase and lipase levels and levels of amylase in drainage fluid were measured pre-operatively and from PO day 1, until removal of the drain. Only 32 patients received subcutaneous octreotide, 100 µg three times daily for five days. Results: Elevation of serum amylase (≥100 IU/l) was found in 20/52 (38%) patients following pancreatic surgery. The elevated amylase levels returned to normal within four days. Abdominal drainage fluid amylase values were found increased in 19/47 (40%) of patients. All elevated levels returned to normal by the tenth post-operative day. The color of abdominal drainage fluid was sero-sanguinous in all cases. No clinical pancreatic fistula or anastomotic leakage was evident (0/55 patients), all patients were discharged home. Conclusion: Documentation of transient elevation of serum amylase and abdominal drainage fluid amylase levels did not appear to be of clinical significance.

Keywords: Pancreatic anastomosis, Leakage, Fluid amylase level.

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INTRODUCTION

The three fundamental techniques for reconstruction to enable pancreatic exocrine secretion after proximal pancreas resection are end to side pancreatico-jejunostomy, end to side pancreatico-gastrostomy and end to end invaginating anastomosis.

The mortality rate after pancreatic resection has decreased to less than 5% but reported morbidity remains high [1]. Even today, following resection, morbidity ranges from 6–57%. Fistula rate after resection is 0–20% with a morbidity of 0–13% [1]. The main cause of serious morbidity and mortality is postoperative anastomotic leakage due to intra-peritoneal release of enterokinases and activation of pancreatic enzymes that lead to sepsis and hemorrhagic complications. Failure of the remnant proximal pancreatic duct closure after left sided pancreatic resection causes milder complications as compared to anastomotic failure of an entero-entero anastomosis but it can result in fistula formation or an intra-abdominal fluid collection [1].

The failure in the integrity of an anastomosis between the remnant pancreas and the gastrointestinal tract can result in a fistula with leakage of pancreatic secretions outside the abdominal cavity. This may occur without significantly affecting the general condition of the patient or it may prolong in-hospital treatment or lead to discharge of the patient with the fistula until spontaneous closure occurs. Failure of anastomotic integrity may well give rise to intra-abdominal fluid collections, sepsis, hemorrhage, peritonitis and death. Strasberg et al. classified pancreatic anastomotic failure into five grades depending on the clinical course following this complication. Pancreatic anastomotic failure grade I requires normal post-operative therapy without any need for additional treatment; in grade II there is need for pharmacological support; grade III requires interventional therapy; grade IV requires surgical and intensive care treatment and grade V is death [2].

The International Study Group for Pancreatic Fistula Definition reviewed several previous scores/definitions of pancreas anastomotic failure on the basis of two parameters; 1) daily output in ml, 2) and amylase concentration in the drained abdominal fluid, and 3) the duration of the fistula. Suspicion of and diagnosis of fistula depends on monitoring the output of the abdominal drainage system, the concentration of amylase in drainage fluid more than three times the serum concentration after third post-operative day, color of the fluid, general condition of the patient, and radiologic documentation. The Group also proposed an A, B or C clinical grading system: a) well patient, b) often well, and c) appearing ill [1].

Theoretically, the drainage fluid should be rich in amylase when pancreatic fluid leaks from the pancreatic stump and anastomotic failure. Therefore, 'amylase rich' drainage has been one of the most popular definitions of pancreatic duct leakage used in the literature [3]. The purpose of are study was: 1) to investigate the value of measurement of amylase concentration in serum and abdominal drainage fluid in diagnosing anastomotic or stump failure after pancreatic surgery and to determine if a correlation exists between the dynamics of post-operative changes in amylase concentration in drainage fluid with clinical outcome, 2) identify whether high concentrations of amylase in the serum or in abdominal drainage fluid postoperatively or during deteriorating clinical status of the patient are essential for the diagnosis of anastomotic failure, 3) to follow up the patients with high abdominal drainage/serum amylase levels in order to document whether the patient developed surgical complications in the form of anastomotic or stump failure and, 4) to evaluate the value of octerotide in reducing failures.

MATERIALS AND METHODS

A prospective study was conducted which included all patients undergoing pylorus preserving proximal pancreaticoduodenectomy (PD), duodenum preserving pancreas head resection (DPPHR), segmental resection of the pancreas with anastomosis (SR) and distal pancreatectomy (DP) by the same surgeon between January 2000 - July 2011. Data collected included patient demographics, type of operation carried out, hospital mortality, morbidity, and the need for reoperation and readmission.

Instructions were given to nurses and residents regarding the need to measure the serum and abdominal drainage fluid amylase and lipase concentrations daily starting from the first postoperative day and to inject octereotide subcutaneously in a dosage of 3x100 µg; 3x200 µg or 3x300 µg for variable periods. All patients who underwent pancreatic resection and anastomosis had two drains (without suction), one placed in a sub-hepatic location, the second adjacent to the pancreatic anastomosis. A single abdominal drain was used for patients undergoing DP and was placed adjacent to the pancreatic stump. The decision to remove the drains was dependent on the levels of amylase recorded postoperatively, the color of the abdominal fluid and the general clinical condition of the patient. The upper limit of the reference range of amylase in our laboratory was 100 IU/L.

Surgical technique: Pancreaticojejunostomosis was performed by the same surgeon (FS) in all patients as follows. A retro-colic jejunal limb was brought through a window in the transverse colon, an end to side pancreatico-jejunal anastomosis was fashioned in two layers; a duct to mucosa anastomosis was made using PDS® 5/0 or 6/0 interrupted sutures; all knots were placed outside the lumen. The second layer involved a pancreas parenchyma-seromuscular interrupted sutures using 4/0 PDS®. This technique was performed regardless of the diameter of the pancreatic duct. Following distal pancreatectomy, the pancreatic duct was closed separately using prolene® 4/0 U shaped sutures, followed by parenchyma-parenchyma suturing using interrupted prolene® 4/0 sutures.

RESULTS

Results are summarized in table 1–4. The tables show the number of patients with serum amylase values of more than 100 IU/L. There was missing data for

amylase drainage fluid later in the post-operative course when drains had been removed or no samples were sent for testing to the laboratory. The study included 70 patients. There male to female ratio was 1.12:3. Means age of all patients was 57.4 years.

There were no post-operative deaths. Morbidity not related to pancreatic surgery was observed in 18 patients (26%). Four patients (5.7%) required re-operation for control of hemorrhage. None of the patients developed any clinical signs of fistula and or anastomotic/stump leakage. No abdominal collection was documented based on clinical signs and symptoms.

Pancreatic surgery caused post-operative amylasaemia in about 40% patients without any clinical signs of pancreatitis. The elevated serum amylase values return to normal, less than 100 IU/L, within one week of operation. High serum values were as high as 10 fold the normal levels (Table 2). No patient exhibited clinical signs of acute pancreatitis.

More than 50% operated patients showed elevated amylase values in the abdominal drainage fluid collections. The concentration of the amylase was as high as 200 fold the normal value. All increased levels returned to normal within 7–10 days. The color of collected body fluid was initially serosanginous then serous. The observed amylase levels did not play any role in the decision as to when the drain can be removed. The decision to remove the drain was made considering the color of the fluid, normalizing or decreasing amylase concentrations and the general condition of the patient. Neither abdominal sepsis nor intra-abdominal collections of fluid were documented in any patients (Tables 3, 4).

DISCUSSION

The mortality rate following duodeno-pancreatectomy has been reported between 3%–5% in some large series [3, 4]. A mortality rate of zero has been reported in some series of more than a hundred patients [5–7]. The major cause of mortality is sepsis and/or hemorrhage resulting from failure of pancreatico-jejuno or gastrostomosis [8]. To prevent this life threatening complication after surgery, various modifications for pancreatico-enteric reconstruction have been proposed like pancreatico-jejunostomy or pancreatico-gastrostomy, invagination or duct to mucosa anastomosis, stented or nonstented anastomosis, end to end or end to side anastomosis and the use of fibrin glue. However, no universal consensus has been reached as to which particular variation of pancreatico-enteric reconstruction is safer and less prone to anastomotic failure. Randomized controlled trials and metaanalysis showed no difference in leak rates between pancreatico-gastro or jejunostomosis [9,

Table 1: Patient demographic data (n = 70).

Data	Number of patients
Sex:	
Male	37
Female	33
Age:	
Mean	57.4
Median	58.5
Range	(15–87)
Histological diagnosis:	
Adenocarcinoma	43
Others tumors	4
Chronic pancreatitis	19
Cystadenoma	4
Operation:	
Duodenum preserving pancreas head resection	12 ⎤
Pylorus preserving pancreaticoduodenectomy	39 ⎥ 55
Pancreas segmental resection with anastomosis	4 ⎦
Distal pancreatectomy	15

Table 2: Serum amylase levels pre- and post-pancreatic resection (n = 70).

	Serum Amylase Pre-op	**Post-operative day**									
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Number of patients											
Amylase levels present*	17	52	56	55	51	43	29	27	22	10	7
Amylase levels missing**	53	18	14	15	19	27	41	43	18	60	63
Amylase Concentration levels											
Mean	152	134	119	66	38	29	26	24	25	17	13
Median	102	73	55	30	24	21	18	14	22	13	13
Minimum	21	13	0	0	2	4	4	3	1	8	5
Maximum	596	588	1089	895	240	100	103	110	66	33	21
Percentiles 25th	46	34	30	17	14	12	10	9	12	8	11
Percentiles 75th	210	205	117	46	33	37	30	38	32	27	17
Number of patients with levels ≥100 IU/L (%)	9 (53)	20 (38)	18 (32)	9 (16)	4 (8)	1 (2)	1 (3)	1 (3)	0 (0)	0 (0)	0 (0)

Amylase reference range (upper limit) – 100IU/L
* estimation of amylase level done
** estimation of amylase level not done

Table 3: Postoperative abdominal drainage amylase levels (subhepatic drain).

	Day 1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Number of patients										
Amylase levels present*	47	55	51	49	39	28	14	05	05	03
Amylase levels missing**	23	15	19	21	31	42	56	65	65	67
Amylase Concentration levels										
Mean	400	824	576	159	194	142	13	11	37	18
Median	77	110	55	20	13	12	06	03	10	17
Minimum	3	2	1	1	1	2	1	3	2	5
Maximum	4878	22069	9479	3282	2982	1451	53	33	100	32
Percentiles 25th	19	27	25	11	6	6	4	2	2	5
Percentiles 75th	304	344	221	66	26	83	15	23	85	-
Number of patients with levels ≥100 IU/L (%)	19 (40)	28 (51)	23 (45)	7 (14)	7 (18)	6 (21)	0 (0)	0 (0)	0 (0)	0 (0)

Table 4: Postoperative abdominal drainage amylase Levels (drain adjacent to pancreatic anastomosis).

	Day 1	2	3	4	5	6	7	8	9
Number of patients									
Amylase levels present*	43	47	48	50	35	23	12	09	01
Amylase levels missing**	27	23	22	20	35	47	58	61	69
Amylase levels Concentration									
Mean	406	1149	622	617	299	222	33	26	15
Median	93	169	61	33	21	17	15	4	15
Minimum	3	4	1	6	4	3	1	3	15
Maximum	3040	15500	8296	11400	4757	3939	174	161	15
Percentiles 25th	22	28	16	14	9	7	7	3	15
Percentiles 75th	531	1150	448	150	122	87	30	27	15
Number of patients with levels ≥100 IU/L (%)	20 (46)	27 (57)	20 (42)	16 (32)	10 (28)	5 (22)	1 (8)	1 (11)	0 (0)

10]. Observational clinical studies demonstrate that the surgeon's experience and preferences play to influence operative outcome. Having become familiar with principles relating to pancreatic surgery the same technique has been used to connect the remnant pancreas with the jejunum and employs an end to side duct mucosa double layer with interrupted 4/0 PDS® sutures. No evident leakage in our study with our surgical technique provides evidence for the selection of this safe anastomotic procedure [11].

Pancreatic fistula remains a significant cause of post-operative morbidity and mortality in patients undergoing pancreatic head resection [12]. Traditionally, the diagnosis of a fistula has been made on the basis of amylase rich drainage fluid or radiological evidence of disruption of the pancreatic anastomosis. The reported incidence of post-operative pancreatic fistula is between 0–30% [1]. The true incidence is, however, unknown because of the varying definition as to what constitutes a post-operative pancreatic fistula [1]. Anastomotic or stump failure after pancreatic surgery is a serious surgical complication. It occurs in immediate or easy postoperative period causing deviation from the normal post-operative course requiring careful management [2]. Whether the diagnosis of this complication can be made on clinical grounds or by measurement of amylase levels merits consideration.

We analyzed data relating to amylase levels in serum and abdominal drainage fluid to determine how useful these are to identify anastomotic or stump failure. Hyperamylasaemia has been reported after many surgical procedures. Occasionally, the origin is salivary amylase and this does not reflect injury of the pancreas. In such cases amylase levels return to normal within one week post-operatively [13]. Measurement of serum amylase after pancreatic surgery is not mandatory and should be done only if there is clinical suspicion of pancreatitis. In all our patients with hyperamylasaemia no clinical features of pancreatitis were documented.

The volume of drainage fluid per day has been selected as one indicator of pancreatic fistula. In the review reported by Shinchi et al. [14], some authors chose 50 ml/day as a 'cut-off' value, others selected 30 ml/day and in some publications the volume is not defined, as in our analysis. We decided to remove drains after three to four days according to the color of the drainage fluid and the general condition of the patient. A drain producing serous fluid with a normal amylase concentration can be removed independent of the volume of drainage fluid.

High concentrations of amylase in body fluids do not always indicate anastomotic or stump failure. The measurement of amylase concentration only once postoperatively in the third, fifth, seventh or tenth post-operative day in body fluid is also of no value for the diagnosis and definition of anastomotic fistula or anastomotic failure. Some authors have chosen two fold, two and half fold, three fold, five fold or absolute values of ≥1000, 2000, or 5000 for amylase concentration as cut off values for the recognition of this complication [15, 16]. Our study is consistent with the reports from Hiroyuki et al. [14] and Yi-Ming Shyr et al. [17] that there are patients without any clinical signs of leakage or symptoms who have high amylase value in body fluids even seven to 10 days post-operatively. Perhaps, in some patients, pancreatic juice leaks from needle hole sites or

from the anastomosis itself, which has not fully healed. It may be that amylase levels are high and do actually indicate leakage of pancreatic fluid but this is subclinical in nature without overt manifestation of leakage like large intra-abdominal collections or features of systemic sepsis.

The dynamic and course of amylase concentration in each patient during the complete post-operative period is of more diagnostic value than the estimation of amylase on a particular post-operative day. In all our patients without leakage the high amylase concentration returned to normal levels. Yi-Ming Shyr et al. [17], reported that all patients without leakage showed a continuous decrease in amylase levels. In addition, patients without leakage reported by Hiroyuki et al had a reduction in amylase concentration and near normalization by the 13th post-operative day. Decreasing concentrations of amylase re-increasing were found only in patients with clinical leakage [14] with very high values beyond the 10th post-operative day.

Neither the isolated estimation of amylase in serum, nor the volume or amylase concentration of abdominal drainage fluid, on a single post-operative day appears to be indicative of the complications of fistula, anastomotic failure or leakage. More important is the dynamic of daily evaluation of the amylase concentration, which after 10 days, is more likely to be of diagnostic value. Suspicion of these complications may be raised clinically on daily patient rounds. The diagnosis can be confirmed, better delineated and followed by additional laboratory tests, imaging studies and monitoring of the course of measuring amylase concentrations in body fluids [18, 19].

CONCLUSION

Increase in serum amylase concentration and abdominal drainage fluid without clinical symptoms after pancreatic surgery on a single post-operative day did not appear to be indicative of the complications of fistula, anastomotic failure or leakage. Only the continuous increase beyond tenth post-operative days in drain fluid amylase concentration with change in colour of drainage fluid and appearance of clinical symptoms indicate the above mentioned complications.

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Author Contributions
F Safi – Major Contribution in conception and design, Acquisition of data, Analysis and interpretation of data, Substantial contribution in drafting the article, critical revision of the article and submission, Corresponding author and final approval of the version to be published
S Bakathir – Minor contribution in Conception, and Acquisition of data, Minor contribution in drafting the article, Minor contribution in final approval of the version to be published
M Taha – Minor contribution in Conception, and Acquisition of data, Minor contribution in drafting the article, Minor contribution in final approval of the version to be published
T Lange – Major Contribution in conception and design, Acquisition of data, Analysis and interpretation of data, Minor contribution in drafting the article, Minor contribution in final approval of the version to be published
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Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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REFERENCES

1. Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005;138(1):8–13.
2. Strasberg SM, Linehan DC, Clavien PA, Barkun JS. Proposal for definition and severity grading of pancreatic anastomosis failure and pancreatic occlusion failure. Surgery 2007;141(4):420–6.
3. Yeo CJ, Cameron JL, Sohn TA, et al. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. Ann Surg 1997;226(3):248–57.
4. Sutton CD, Garcea G, White SA, et al. Isolated Roux-loop pancreaticojejunostomy: a series of 61 patients with zero postoperative pancreaticoenteric leaks. J Gastrointest Surg 2004;8(6):701–5.
5. Trede M, Schwall G, Saeger HD. Survival after pancreatoduodenectomy. 118 consecutive resections without an operative mortality. Ann Surg 1990;211(4):447–58.
6. Aranha GV, Hodul PJ, Creech S, Jacobs W. Zero mortality after 152 consecutive pancreaticoduodenectomies with

pancreaticogastrostomy. J Am Coll Surg 2003;197(2):223–1.

7. Cameron JL, Pitt HA, Yeo CJ, Lillemoe KD, Kaufman HS, Coleman J. One hundred and forty-five consecutive pancreaticoduodenectomies without mortality. Ann Surg 1993;217(5):430–5.
8. Duffas JP, Suc B, Msika S, et al. A controlled randomized multicenter trial of pancreatogastrostomy or pancreato-jejunostomy after pancreatoduodenectomy. Am J Surg 2005;189 (6):720–9.
9. Bassi C, Falconi M, Molinari E, et al. Reconstruction by pancreaticojejunostomy versus pancreatico-gastrostomy following pancreatectomy: results of a comparative study. Ann Surg 2005;242(6):767–1.
10. Wente MN, Shrikhande SV, Müller MW, et al. Pancreaticojejunostomy versus pancreaticogastrostomy: systematic review and meta-analysis. Am J Surg 2007;193(2):171–83.
11. You D, Jung K, Lee H, Heo J, Choi S, Choi D. Comparison of different pancreatic anastomosis techniques using the definitions of the International Study Group of Pancreatic Surgery: a single surgeon's experience. Pancreas 2009;38(8):896–902.
12. Büchler MW, Friess H, Wagner M, Kulli C, Wagener V, Z'Graggen K. Pancreatic fistula after pancreatic head resection. Br J Surg 2000;87(7):883–9.
13. Murakami Y, Uemura K, Hayasidani Y, et al. A soft pancreatic remnant is associated with increased drain fluid pancreatic amylase and serum CRP levels following pancreatoduodenectomy. J Gastrointest Surg 2008;12(1):51–6.
14. Shinchi H, Wada K, Traverso LW. The usefulness of drain data to identify a clinically relevant pancreatic anastomotic leak after pancreaticoduodenectomy? J Gastrointest Surg 2006;10(4):490–8.
15. Okano K, Kakinoki K, Suto H, et al. Persisting ratio of total amylase output in drain fluid can predict postoperative clinical pancreatic fistula. J Hepatobiliary Pancreat Sci 2011 May 19.
16. Molinari E, Bassi C, Salvia R, et al. Amylase value in drains after pancreatic resection as predictive factor of postoperative pancreatic fistula: results of a prospective study in 137 patients. Ann Surg 2007;246(2):281–7.
17. Shyr YM, Su CH, Wu CW, Lui WY. Does drainage fluid amylase reflect pancreatic leakage after pancreaticoduodenectomy? World J Surg 2003;27(5):606–10.
18. Strasberg SM, Drebin JA, Mokadam NA, et al. Prospective trial of a blood supply-based technique of pancreaticojejunostomy: effect on anastomotic failure in the Whipple procedure. J Am Coll Surg 2002;194(6):746–58.
19. Grobmyer SR, Rivadeneira DE, Goodman CA, Mackrell P, Lieberman MD, Daly JM. Pancreatic anastomotic failure after pancreaticoduodenectomy. Am J Surg 2000;180(2):117–20.