Drain Management after Pancreatoduodenectomy: Reappraisal of a Prospective Randomized Trial Using Risk Stratification

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BACKGROUND: A recent randomized trial used the Fistula Risk Score (FRS) to develop guidelines for selective drainage based on clinically relevant fistula (CR-POPF) risk. Additionally, postoperative day (POD) 1 drain and serum amylase have been identified as accurate postoperative predictors of CR-POPF. This study sought to identify patients who may benefit from selective drainage, as well as the optimal timing for drain removal after pancreatoduodenectomy.

STUDY DESIGN: One hundred six pancreatoduodenectomies from a previously reported RCT were assessed using risk-adjustment. The incidence of CR-POPF was compared between FRS risk cohorts. Drain and serum amylase values from POD 1 were evaluated using receiver operating characteristic (ROC) analysis to establish cut-offs predictive of CR-POPF occurrence. A regression analysis compared drain removal randomizations (POD 3 vs POD 5).

RESULTS: Three-quarters of patients had moderate/high CR-POPF risk. This group had a CR-POPF rate of 36.3% vs 7.7% among negligible/low risk patients ($p = 0.005$). The areas under the ROC curve for CR-POPF prediction using POD 1 drain and serum amylase values were 0.800 ($p = 0.000001$; 95% CI 0.70−0.90) and 0.655 ($p = 0.012$; 95% CI 0.55−0.77), respectively. No significant serum amylase cut-offs were identified. Moderate/high risk patients with POD 1 drain amylase $\leq$5,000 U/L had significantly lower rates of CR-POPF when randomized to POD 3 drain removal (4.2% vs 38.5%; $p = 0.003$); moreover, these patients experienced fewer complications and shorter hospital stays.

CONCLUSIONS: A clinical care protocol is proposed whereby drains are recommended for moderate/high FRS risk patients, but may be omitted in patients with negligible/low risk. Drain amylase values in moderate/high risk patients should then be evaluated on POD 1 to determine the optimal timing for drain removal. Moderate/high risk patients with POD 1 drain amylase $\leq$5,000 U/L have lower rates of CR-POPF with POD 3 (vs POD $\geq$ 5) drain removal; early drain removal is recommended for these patients. (J Am Coll Surg 2015;221:798−809. © 2015 by the American College of Surgeons)

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The risks and benefits of routine drainage after pancreatoduodenectomy (PD) have been a source of controversy in the contemporary surgical literature.[1-9] Advocates of this practice cite its ability to evacuate bile, chyle, blood, or pancreatic juice that may accumulate during the postoperative period. Additionally, it can act as an early warning system for, and potentially mitigate,[9] postoperative pancreatic fistula, one of the most common and deadly complications after PD.[10] A recent prospective randomized trial suggested that routine drainage after PD was associated with a decreased incidence of major morbidity

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Abbreviations and Acronyms

CR-POPF = clinically relevant postoperative pancreatic fistula
DFA = drain fluid amylase
FRS = Fistula Risk Score
IQR = interquartile range
ISGPF = International Study Group on Pancreatic Fistula
PD = pancreatoduodenectomy
POD = postoperative day
ROC = receiver operating characteristic

and mortality.[8] Notably, results of a secondary aim of that study revealed a benefit to selective drainage based on the degree of risk for the development of clinically relevant postoperative pancreatic fistulas (CR-POPF).[9]

In contrast, routine drain placement has been associated with higher complication rates after other major abdominal operations,[11-14] possibly because drains can act as a nidus for infection.[4,7] A randomized trial reported by Conlon and colleagues[3] investigating routine drainage with PD, as well as other studies, have correlated drainage with a higher incidence of fistula and abdominal complications. However, these reports did not use the International Study Group on Pancreatic Fistula (ISGPF) definition for fistula and failed to distinguish between the incidence of innocuous biochemical fistulas and CR-POPFs.[3,7]

Further controversy persists regarding optimal timing for drain removal after major pancreatic resections. Contrary to traditional practice, recent studies have demonstrated a potential benefit to early drain removal[15,16]; a prospective study by Kawai and associates[15] reported lower rates of abdominal complications—including pancreatic fistula. Furthermore, a randomized study by Bassi and colleagues[16] correlated prolonged drainage with a greater incidence of postoperative complications. This association reflected a marked difference in POPF incidence, with an absolute reduction in POPF rates by nearly 25% (1.8% vs 26%, p = 0.0001) when drains were removed on postoperative day (POD) 3 rather than POD 5.

Although the merits of routine drainage and early drain removal have been evaluated in isolation, these concepts have not yet been integrated into a risk-adjusted clinical care pathway. The Fistula Risk Score (FRS) has been established as a reliable predictor of CR-POPF (Table 1), and it can identify specific patients who may benefit from routine drainage.[9,17,18] Additionally, other works have suggested POD 1 drain fluid amylase (DFA)[19-26] and serum amylase[27-30] values accurately predict POPF development after major pancreatic resections. Applying these CR-POPF risk assessment approaches, this investigation reappraised data from a previously reported prospective randomized trial, while focusing exclusively on PD.[16] The aims were to develop a risk-stratified protocol for identification of patients who may benefit from drainage and to establish the optimal timing for drain removal.

Table 1. Fistula Risk Score for the Prediction of Clinically Relevant Fistula After Pancreatoduodenectomy

Risk factor, parameter	Points*
Gland texture	
Firm	0
Soft	2
Pathology	
Pancreatic adenocarcinoma or pancreatitis	0
Ampullary, duodenal, cystic, islet cell, etc	1
Pancreatic duct diameter, mm	
≥5	0
4	1
3	2
2	3
≤1	4
Intraoperative blood loss, mL	
≤400	0
401–700	1
701–1,000	2
>1,000	3

*Total 0 to 10 points.
(Reprinted from Callery and colleagues[18] with permission from Elsevier.)

METHODS

This study was approved by the Ethical Committee on Clinical Investigation of Verona University Hospitals and the IRB at the University of Pennsylvania. At the Department of Surgery at the University of Verona, 106 consecutive patients underwent PD between March 2008 and April 2009 as part of a previously reported randomized controlled trial. Details of the original methodologic approach are described in the work by Bassi and colleagues.[16] Briefly, a passive drainage system was used, with 2 flat Penrose drains placed in each patient. A 0.1-mg dose of prophylactic octreotide was administered subcutaneously 1 hour before surgery and continued postoperatively (every 8 hours) until tolerance of a solid diet. Pancreatoduodenectomy patients with POD 1 DFA values >5,000 U/L (n = 31) were excluded from the original randomization process and not reported. In this investigation, these patients were combined with the remaining 75 patients (70.8%), who were randomized to either early drain removal on POD 3 (n = 38) or standard drain removal on or after POD 5 (n = 37). The original study