

Multicenter, Prospective Trial of Selective Drain Management for Pancreatoduodenectomy Using Risk Stratification

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Objective: This multicenter study sought to prospectively evaluate a drain management protocol for pancreatoduodenectomy (PD).

Background: Recent evidence suggests value for both selective drain placement and early drain removal for PD. Both strategies have been associated with reduced rates of clinically relevant pancreatic fistula (CR-POPF)—the most common and morbid complication after PD.

Methods: The protocol was applied to 260 consecutive PDs performed at two institutions over 17 months. Risk for ISGPF CR-POPF was determined intraoperatively using the Fistula Risk Score (FRS); drains were omitted in negligible/low risk patients and drain fluid amylase (DFA) was measured on postoperative day 1 (POD 1) for moderate/high risk patients. Drains were removed early (POD 3) in patients with POD 1 DFA $\leq 5,000$ U/L, whereas patients with POD 1 DFA $> 5,000$ U/L were managed by clinical discretion. Outcomes were compared with a historical cohort (N = 557; 2011–2014).

Results: Fistula risk did not differ between cohorts (median FRS: 4 vs 4; $P = 0.933$). No CR-POPFs developed in the 70 (26.9%) negligible/low risk patients. Overall CR-POPF rates were significantly lower after protocol implementation (11.2 vs 20.6%, $P = 0.001$). The protocol cohort also demonstrated lower rates of severe complication, any complication, reoperation, and percutaneous drainage (all $P < 0.05$). These patients also experienced reduced hospital stay (median: 8 days vs 9 days, $P = 0.001$). There were no differences between cohorts in the frequency of bile or chyle leaks.

Conclusions: Drains can be safely omitted for one-quarter of PDs. Drain amylase analysis identifies which moderate/high risk patients benefit from early drain removal. This data-driven, risk-stratified approach significantly decreases the occurrence of clinically relevant pancreatic fistula.

Keywords: amylase, drain, Fistula Risk Score, pancreatic fistula, pancreatoduodenectomy

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Considerable controversy persists regarding the practice of drainage for pancreatoduodenectomy (PD).^{1–11} Proponents for routine drainage cite its ability to evacuate bile, chyle, blood, pus, or degradative pancreatic juice that may occur postoperatively. Moreover, drainage can serve as an early indication of, and management approach for, postoperative pancreatic fistula (POPF), the most common and morbid complication after PD. Conversely, others have argued that drainage can be detrimental—potentially serving as a

nidus for infection^{4,7} or for allowing prolonged high-pressure closed-suction drainage to erode the anastomotic site.³

Two recent randomized controlled trials have evaluated the impact of routine drainage after PD.^{8,11} The first study by Van Buren et al⁸ demonstrated reduced morbidity and mortality with routine drainage; conversely, the most recent randomized trial reported higher rates of reintervention and clinically relevant pancreatic fistula (CR-POPF) after drainage.¹¹ A secondary analysis of the Van Buren study⁹ focused specifically on CR-POPF using risk stratification and identified the potential for a middle-ground approach to drain management. Patients with moderate/high CR-POPF risk—calculated using the validated Fistula Risk Score (FRS)¹²—demonstrated significantly reduced CR-POPF rates when drainage was employed; alternatively, patients with negligible/low risk actually experienced higher rates of CR-POPF when drains were placed.

The optimal timing for drain removal after major pancreatic resections has also been a focus of recent attention in the literature. A prospective study by Kawai et al¹³ reported lower rates of abdominal complications and pancreatic fistula following early drain removal. These findings were confirmed in a randomized study by Bassi et al;¹⁴ patients were eligible for randomization to early [postoperative day (POD) 3] or standard (POD 5 or later) drain removal if their POD 1 drain fluid amylase (DFA) value revealed reduced CR-POPF risk (ie, $\leq 5,000$ U/L).^{15,16} Within this subgroup, early drain removal was associated with significantly a fewer postoperative complications, including CR-POPF.

In a recent study, we integrated the concepts of selective drainage and early drain removal into a drain management pathway for PD.¹⁰ It proposes the omission of prophylactic drainage for negligible/low CR-POPF risk patients but routine drain placement for moderate/high CR-POPF risk patients. Next, POD 3 drain removal is advocated for moderate/high risk patients with POD 1 DFA $\leq 5,000$ U/L. Finally, prolonged drain duration can occur at the surgeon's discretion for moderate/high risk patients with POD 1 DFA $> 5,000$ U/L, or for those patients otherwise suspected to be at risk for fistula development based upon clinical intuition.

Applying these approaches, the current study sought to validate this drain management protocol in a prospective multicenter setting. The primary aim was to determine whether implementation of the protocol improved CR-POPF outcomes when compared with a recent historical patient cohort. A secondary aim was to discover characteristics associated with those cases that are especially vulnerable to CR-POPF development—patients with POD 1 DFA $> 5,000$ U/L.

METHODS

This study was approved by the institutional review board at the University of Pennsylvania and the Ethical Committee on Clinical Investigation of Verona University Hospitals. The drain

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