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# Total parenteral nutrition in patients following pancreaticoduodenectomy: lessons from 1184 patients



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## ABSTRACT

**Background:** Total parenteral nutrition (TPN) has historically been used conservatively in the management of patients after pancreaticoduodenectomy (PD). Herein, we evaluate the indications for and outcomes associated with TPN use in a high-volume pancreatic surgery center. **Materials and methods:** We retrospectively queried our institution's pancreatic surgery database for patients who received TPN after PD from 2006 through 2015.

**Results:** Of 1184 patients who underwent PD, 232 (19.6%) received TPN perioperatively. The most common indications for TPN were delayed gastric emptying (DGE,  $n = 171$ , 73.7%), pancreatic fistula ( $n = 102$ , 44%), and generalized malnutrition ( $n = 25$ , 10.8%). The median day of TPN initiation was postoperative day 4 (range:  $-31$  to 22), with a median usage of 9 days (range: 1-115). Forty-four (19%) patients received short-course TPN ( $\leq 3$  days), primarily those diagnosed with isolated grade A DGE without associated complications ( $P = 0.0003$ ). Multivariate analysis suggests the presence of deep surgical site infection (odds ratio: 3.09, [1.16-5.06],  $P = 0.018$ ) or pancreatic fistula (odds ratio: 2.57, [1.03-6.41],  $P = 0.043$ ) at the time of DGE presentation as predictive of long-term TPN requirement. Hyperglycemia (34.5%) was the most common complication resulting from TPN use, whereas central line-associated bloodstream infections (2.6%) were rare. Readmissions (35.3% TPN cohort; 15% historical institutional rate) were most commonly due to poor oral intake (26.8%). The 30-day mortality rate in the overall TPN cohort was 3.4% (0.8% historical institutional rate).

**Conclusions:** TPN is a critical and safe adjunct for patients who develop PD-associated complications; however, it may be of limited utility for patients with isolated DGE.

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## Introduction

Pancreaticoduodenectomy (PD) is the standard intervention of choice for treating patients with benign and malignant disease of the pancreatic head, neck, and uncinate process.<sup>1</sup> Although 30-day mortality rates for PD have fallen to as low as 1%-3% at many high-volume centers, morbidity rates remain high.<sup>1,2</sup> High morbidity rates have a significant effect on patient recovery and quality of life, with pancreatic fistula (PF) and delayed gastric emptying (DGE) being the most common significant postoperative complications.<sup>3,4</sup> PF is defined as a parenchymal leak of amylase-rich fluid, whereas DGE is characterized by excessive postoperative nausea, vomiting, and failure to progress with oral dietary intake due to gastroparesis.<sup>3,4</sup> Prolonged DGE can severely impact nutritional support during recovery and can lead to malnutrition. Malnutrition is a known independent predictor of poor outcomes after surgery, contributing to increased morbidity, mortality, length of stay, and financial burden on the health care system.<sup>5,6</sup> To combat the physiologic catabolism that is the hallmark of the postsurgical state and to promote wound healing, the initiation of high caloric intake in the immediate postsurgical period is essential. This is routinely done with the oral intake of food, but in patients in whom this is problematic, alternative sources of nutritional supplementation are essential such as enteral tube feeds and intravenous total parenteral nutrition (TPN).<sup>7</sup>

Nutritional supplementation in some form has been the standard of care for treating patients with acute pancreatitis, perioperative malnutrition, and severe gastroparesis.<sup>8,9</sup> TPN use is an effective form of nutritional supplementation; however, it carries the risk of complications such as central line-associated bloodstream infection (CLABSI), hyperglycemia, liver function abnormalities, and other electrolyte imbalances.<sup>8</sup> Similarly, intravenous lipids have been suggested by some to adversely affect the immune system and clinical outcomes.<sup>6</sup> The cost of TPN is also an important consideration in weighing its appropriate usage, given the cost at our institution is from \$650 to \$950 per day. Despite those significant negative factors, TPN continues to play a role in the rescue of patients with severe postsurgical complications and those at high risk for perioperative malnutrition. Patients who lack proper nutrition for greater than 14 days have vastly increased complication and mortality rates<sup>6</sup>; therefore, identifying the appropriate indications for early nutritional supplementation to avoid these poor outcomes is essential.

In this study, we set out to understand the indications for TPN use, its effectiveness in improving outcomes, as well as the negative consequences of its use in post-PD patients. We also chose to study a group of patients in whom it was perhaps overprescribed (short-term TPN administration of  $\leq 3$  days) to better understand when TPN should not be initiated.

## Methods

This study was approved by the Institutional Review Board of the Sidney Kimmel Medical College at Thomas Jefferson

University. The IRB granted a waiver of informed consent. All cases of PD at the Thomas Jefferson University Hospital from December 2006 to December 2015 were retrospectively reviewed, querying our prospectively maintained pancreatic surgery database. Patients were excluded if they underwent distal or total pancreatectomy or if they did not receive TPN in the perioperative period. Patients were then separated into two cohorts ( $\leq 3$  days versus  $> 3$  days) based on the length of TPN use, with the hypothesis that those patients who were started on TPN but received it for 3 days or less due to an improvement in their clinical condition most likely were overprescribed TPN. Studying this group could give us further insight into the appropriate and inappropriate indications for TPN use.

Patient data were prospectively entered into a pancreatic surgery database and included patient demographics, intraoperative data, pathologic features, postoperative complications, radiographic results, preoperative and postoperative laboratory results, postoperative length of hospital stay, readmission data, and 30-day mortality. The use of TPN was prospectively recorded, but details regarding indications, timing, and duration of use were gathered retrospectively.

Postoperative complications were reviewed. Complications that were considered included DGE, hyperglycemia, anastomotic leak, infection (abscess, CLABSI, pneumonia, urinary tract, and surgical site), PF, sepsis, and small bowel obstruction. DGE was identified and assessed according to the International Study Group of Pancreatic Surgery (ISGPS) criteria,<sup>10</sup> and PF was also graded according to the ISGPS fistula grading system.<sup>11</sup> Hyperglycemia was defined as blood glucose  $> 200$  mg/dL. Infectious complications including abscess, urinary tract, and surgical site infection were defined as a positive culture or empiric initiation of antibiotic therapy based on clinical suspicion (physical examination, urinalysis, and so forth). CLABSI were defined by a positive blood culture in a patient with a central line or a peripherally inserted central catheter. The factors of preoperative weight loss, tolerance of oral intake, and nutrition labs were subjectively used by the attending surgeon to determine the presence of generalized malnutrition.

All operations during the study period were performed by six surgeons as previously described.<sup>12</sup> The pylorus was preserved unless a classic resection was required to achieve an R0 resection or if there was concern regarding the viability of the duodenal stump. All duodenojejunal and gastrojejunal anastomoses were hand-sewn in two layers as previously described.<sup>13</sup> At our institution, post-PD patients requiring TPN often receive a standardized 1-L formulation, maximizing protein and caloric intake while minimizing volume. This standard formula administers 70-g protein, 150-g dextrose, and 35-g fat for a total caloric intake of 1140 kcal/L.

Statistical analysis of the groups was performed. Categorical variables were compared by a Fisher's exact and chi-square tests. Continuous variables were compared by a *t*-test. A *P* value  $< 0.05$  was considered to be statistically significant. Multivariate logistic regression was used to determine odds ratios (ORs) for significant predictors of long-term TPN use. STATA v12.1 (College Station, TX) was used to perform and analyze multivariate logistic regression.

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