

Contents lists available at ScienceDirect

## The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com



### **Invited Commentary**

# Optimal fluid management for patients undergoing pancreatoduodenectomy



The issue of optimal fluid management for patients undergoing pancreatoduodenectomy (PD) has drawn a great deal of interest and investigation in recent years. <sup>1–7</sup> In fact, four randomized controlled trials with a focus on PD have been performed. <sup>1,3–5</sup> Pancreatoduodenectomy draws attention because the operation is long and, in the past, has required significant fluid administration. As a result, major fluid shifts between the interstitial and intravascular spaces occur in the operating room and postoperatively. In addition, while operative mortality has improved dramatically over the past half century, PD continues to be associated with a frustratingly high postoperative morbidity rate.

Current literature suggests that postoperative outcomes related to perioperative fluid administration for PD patients follow a U-shaped curve. Patients who receive ultra-restrictive intra- and postoperative fluid regimens are at increased risk for clinically-relevant postoperative pancreatic fistulas and Clavien-Dindo Grade 3 or greater complications. Patients in the highest quartile of fluid administration also have poor outcomes. Several theories have been proposed to explain this phenomenon, but one very plausible explanation relates to tissue oxygen delivery. Patients managed with ultra-restrictive fluid regimens are prone to hypotension, acidosis and reduced interstitial volume. Conversely, patients receiving high volumes of fluids develop interstitial tissue edema and hemoglobin dilution. The optimal fluid administration rate to maintain end-organ tissue perfusion and to improve outcomes is in the 6–8 ml/kg/hr range.

To achieve the optimal amount of fluid for an individual patient undergoing PD, anesthesiologists and surgeons should embrace the concept of goal directed therapy. This approach has been studied in patients undergoing major operations as well as in those with severe sepsis and septic shock. Goal-directed fluid management may be especially appropriate for PD patients given the physiologic impact of this operation which includes development of a systemic inflammatory response syndrome (SIRS). Patients having PD also are particularly predisposed to an aggressive inflammatory response especially if they develop postoperative acute pancreatitis (POAP). POAP may be related to dissection around and transection of the pancreas, and these patients are at an increased risk for development of a clinically relevant pancreatic fistula.

Thus, fluid management in patients undergoing PD needs to be carefully monitored both during the operation and in the early postoperative period. Indicators of malperfusion at the cellular level, such as serum lactate, blood urea nitrogen and creatinine, can be helpful in identifying patients who are under resuscitated. Estimates of cardiac output and, therefore, oxygen delivery including blood pressure, heart rate, central venous pressure

(CVP), pulse pressure variation and central venous oxygen saturation also can help guide fluid management. In addition, measurement of serum amylase on postoperative days 0 and 1 will indicate whether the patient has developed POAP and further help to direct fluid therapy.

Colorectal surgeons were among the first to support the concept of enhanced recovery after surgery (ERAS). In these patients conservative fluid administration has been shown to improve the return of bowel function and reduce the incidence of delayed gastric emptying as well as cardiopulmonary complications. Similarly, in liver surgery, maintaining low CVP targets and hemodilution have been found to reduce blood loss and the need for transfusions. Another strategy to achieve the goal of optimal fluid administration is the judicious use of 3% hyertonic saline (HYS). This approach was employed in the HYSLAR trial<sup>3</sup> of patients undergoing PD which demonstrated as 25% reduction in the complication rate and a 31% decrease in the cumulative number of complications.

The paper by Mahmooth et. Al<sup>8</sup> in this issue of the *American Journal of Surgery* suggests that restrictive intra-operative fluids were not associated with postoperative acute kidney injury (AKI) but did correlate with reduced minor (Clavien-Dindo Grade 1 and 2) complications. In this retrospective analysis the three intraoperative fluid groups (ultra-restrictive, restrictive and nonrestrictive) differed in several important pre- and intraoperative characteristics. Also, the focus was on intraoperative fluids which were relatively low in all three groups because of the short average operative time (approximately 3 hours).<sup>9</sup>

The three groups did differ with respect to total fluids administered in 72 hours. However, the manuscript does not emphasize postoperative fluid management, a key portion of the fluid strategy in patients undergoing PD. Interestingly, compared to the ultrarestrictive group, the restrictive patients who received 7 ml/kg/hr had less AKI (OR 0.80), ileus (OR 0.68) and pancreatic fistulas (OR 0.49). However, none of these differences reached statistical significance perhaps because the analysis was not sufficiently powered to adequately study these outcomes. Thus, while this report leaves many questions unanswered, outcomes were optimal when fluids were restricted.

#### **Declaration of competing interest**

No Conflict of Interest.

### References

1. Fisher M, Matsuo K, Gonen M, et al. Relationship between intraoperative fluid

- administration and perioperative outcomes after pancreatoduodenectomy: results of a prospective randomized trial of acute normovolemic hemodilution compared with standard intraoperative management. *Ann Surg.* 2010;252: 952–958.
- Melis M, Macon F, Masi A, et al. Effect of intra-operative fluid volume on perioperative outcomes after pancreaticoduodenectomy for pancreatic adenocarcinoma. J Surg Oncol. 2012;105:81–84.
- Lavu H, Sell NM, Carter TI, et al. A prospective randomized controlled trial of the use of a restrictive fluid regimen with 3% hypertonic saline versus lactatad Ringers in patients undergoing pancreaticoduodenectomy. *Ann Surg.* 2014;260: 445–455.
- Van Samkar G, Eshuis WJ, Bennink RJ, et al. Intraoperative fluid restriction in pancreatic surgery: a double blinded randomized controlled trial. PloS One. 2015:10:1–15.
- Weinberg L, Chao I, Nikfarjam M, et al. Restrictive intraoperative fluid optimization algorithm improves outcomes in patients undergoing pancreaticoduodenectomy: a prospective multicentre randomized controlled trial. *PloS One*. 2017:12.
- Andrianello S, Marchegiani G, Bannone E, et al. Clinical implications of intraoperative fluid therapy in pancreatic surgery. J Gastrointest Surg. 2018;22:2072–2079.
- Carter TI, Yeo CJ, Lavu H. Fluid restriction during pancreaticoduodenectomy: is it
  effective in reducing postoperative complications? Adv Surg. 2015;49:205–220.
- 8. Mahmooth Z, Jajja MR, Maxwell D, et al. Ultrarestrictive intraoperative intravenous fluids during pancreatoduodenectomy is not associated with an increase in

- post-operative acute kidney injury. *Am J Surg.* 2020;220(2):264–269.
- Simpson RE, Fennerty ML, Flick KF, et al. Two open whipples a day: excessive or efficient. Am J Surg. 2020;219(3):394–395.

Harish Lavu

Department of Surgery, Thomas Jefferson University, 1025 Walnut Street, Suite 605, Philadelphia, PA, 19107, USA E-mail address: Harish.Lavu@jefferson.edu.

Henry A. Pitt\*

Department of Surgery, Lewis Katz School of Medicine at Temple University, 3509 N. Broad Street, Boyer Pavilion, E938, Philadelphia, PA, 19140, USA

\* Corresponding author.

E-mail address: Henry.Pitt@tuhs.temple.edu (H.A. Pitt).

19 April 2020