Deciphering the Etiology of Weight Loss Following Pancreatectomy

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Recurrence rates after resection for pancreatic cancer are high, with >70% of patients developing recurrence within 1 year following their index operation.¹ While guidelines recommend close surveillance with cross-sectional imaging every 3–6 months postoperatively for the first 2 years, population-level studies show that only 40% of patients actually undergo imaging surveillance by the 2-year mark.² Additionally, the current gold-standard serum biomarker, carbohydrate antigen (CA) 19-9, is not synthesized in 10% of patients and is normal in another one-third of patients, limiting its clinical utility.^{3,4} While patient weight is routinely recorded during physician visits, the significance of longitudinal weight tracking has not been rigorously assessed, and, as such, its prognostic significance and added value to existing surveillance programs remains largely unknown.

In this study by Hue and colleagues, the authors provided a novel assessment of the associations of weight change following pancreatectomy with outcomes using robust institutional data. In their analysis, the authors explored the impact of weight change in patients with malignant disease and compared this with patients with benign disease. In doing so, the authors were able to ‘extract’ the impact of malignancy and determine the effect of the operation itself on changes in weight. The authors subsequently evaluated the association between changes in weight and outcomes, including disease recurrence and overall survival, in patients with pancreatic ductal

adenocarcinoma (PDAC).⁵ While there were some inherent differences between the benign and malignant groups, the authors found that most patients lost more than 20 pounds following pancreatectomy. In addition, the weight loss was durable, with most failing to regain weight back to their baseline status. Patients with benign disease ended up with a total of 5.6% weight loss compared with PDAC patients, who suffered 8.5% weight loss, thus revealing that most weight loss was ‘operation mediated’, but that a significant proportion was ‘cancer-related’. However, the most important findings of this study lie in the PDAC subgroup analysis. For patients with pancreatic cancer, the authors found that those who developed early recurrence lost significantly more weight compared with patients who did not develop disease recurrence (18% vs. 11%; $p < 0.001$). Additionally, patients with early recurrences took 7.5 months to reach their nadir weight postoperatively, which was substantially and statistically significantly longer than patients without evidence of disease recurrence (2 months). This association remained significant after adjusting for confounders. In fact, patients who did not achieve their nadir weight within 12 months of their operation experienced 3.2 times higher odds of having disease recurrence.

Prehabilitation programs have gained traction as an important component of the continuum of cancer treatment, and the optimization of nutrition and aerobic conditioning preoperatively could potentially mitigate postoperative weight loss.^{6,7} While data on the impact of prehabilitation programs on postoperative weight change for patients with cancer remain lacking, a study by Nakajima and colleagues demonstrated that prehabilitation significantly reduced weight loss in patients with hepatopancreatobiliary cancers (3.3% to 1.1% with prehabilitation).⁸ The authors of that study showed that prehabilitation may play a role in augmenting postoperative cancer-related weight changes. However, whether

prehabilitation may mitigate weight loss ‘differently’ between benign versus malignant disease and, subsequently, ‘recurrence-mediated’ vs. ‘recurrence-unrelated’ weight loss among PDAC patients, provides an interesting avenue for future exploration.

This study represents one of only a few studies reporting on longitudinal weight data surrounding the time of index pancreatectomy. Naturally, the observed significance of weight loss in post-pancreatectomy patients is a retrospective association. Even in the specific setting of PDAC patients with recurrence, it remains unclear if disease recurrence resulted in weight loss (biologic mediators of cachexia) or if the weight loss predisposed patients to recurrence, both with contrasting clinical implications. If recurrence preceded weight loss, persistent postoperative weight loss might prompt ‘early’ cross-sectional imaging and serum tumor biomarker measurement. However, if weight loss and its associated physiologic milieu derangements predisposed patients to recurrence, this may instead provide a potentially actionable avenue for mitigation of disease recurrence.

Currently, the National Comprehensive Cancer Network (NCCN) guidelines recommend cross-sectional imaging and CA19-9 surveillance every 3–6 months postoperatively for the first 2 years.⁹ Adding weight tracking to surveillance programs is logistically feasible; however, it remains unknown if weight tracking would add value in detecting recurrences in the setting of an ‘NCCN-compliant’ surveillance program. It should also be noted that patients with pancreatic cancer who develop recurrence benefit from receiving additional treatment, but only 35% of patients receive treatment.¹⁰ Weight tracking could be a simple and inexpensive adjunct that provides clinicians with an additional datapoint during postoperative surveillance in an effort to detect, and subsequently treat, disease recurrence.

Finally, a critical takeaway from the authors’ findings is that weight loss following pancreatectomy seems inevitable in all patients. We routinely counsel patients on ‘distressing’ weight loss that is difficult to counteract in the first few weeks following surgery. However, what stood out in the authors’ findings was that it took patients with pancreatic cancer up to nearly 5 months to achieve nadir weight. Extended periods of weight loss beyond that might represent potential disease recurrence.

We believe these findings underscore the importance of understanding if and how prehabilitation programs help mitigate postoperative weight loss, including pancreatectomy-mediated weight loss versus cancer-related (recurrence-mediated and recurrence-unrelated) weight loss to help patients achieve the best outcomes.

DISCLOSURES Zhi Ven Fong and Motaz Qadan have no conflicts of interest to disclose.

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