Editorial

Predicting post-operative pancreatic fistula: one size may not fit all

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Comment on: Kang JS, Park T, Han Y, *et al.* Clinical validation of scoring systems of postoperative pancreatic fistula after pancreatoduodenectomy: applicability to Eastern cohorts? Hepatobiliary Surg Nutr 2019;8:211-8.

Submitted May 19, 2020. Accepted for publication Jun 02, 2020.
doi: 10.21037/hbsn-20-497
View this article at: http://dx.doi.org/10.21037/hbsn-20-497

Post-operative pancreatic fistula (POPF) is a common and dangerous complication of pancreatic resection, occurring in 5–30% of patients. It is a significant source of morbidity and mortality, leading to prolonged hospital stays and increased healthcare costs (1). The most widely accepted definition of POPF comes from the International Study Group on Pancreatic Fistula (ISGPF). Initially created in 2005, this classification system for POPF was revised in 2016 such that POPF should be associated with a clinically relevant change in status, deeming what was originally defined as a Grade A fistula as a biochemical leak and grade B and C fistulas as clinically relevant (CR) fistulae (*Table 1*) (2).

Over the past several decades, numerous fistula prediction scores have been developed that attempt to stratify patients according to their risk of developing this potentially morbid complication. Prediction scores can be used to counsel patients pre-operatively, change surgeon behavior in the operating room, direct post-operative evaluation and treatment such as early removal of drains, and potentially minimize adverse events in high-risk patients. The variety of fistula risk scores include pre-operative, intra-operative, and post-operative variables. Examples of some of the most commonly used POPF prediction scores are presented in *Table 2*. Importantly, many of the risk factors for POPF are non-modifiable, including pancreatic gland texture, diameter of pancreatic duct, diagnosis, age and gender.

The current study by Kang *et al.* (9) aimed to externally validate three Western POPF prediction models, the Callery model (also known as the Fistula Risk Score) (3), the Roberts model (7), and the Mungroop model (also known as the alternative Fistula Risk Score) (4), in a Korean cohort where patient characteristics, surgical techniques and post-operative practices may differ. Their population consisted of 1,898 patients from nine tertiary hospitals in Korea. Compared to the three western modeling populations, the Korean population had fewer rates of pancreatic ductal adenocarcinoma, lower mean body mass index (BMI), and higher estimated blood loss, though rates of CR-POPF were similar. On multivariate analysis, non-pancreatic disease, higher BMI, and soft pancreatic texture were independent predictors of CR-POPF in the Korean model. The Western scoring systems, which had exhibited reasonable discriminatory ability on previously published internal and external validation studies, performed less well in the Korean cohort, with AUC values ranging between 0.61 and 0.64.

The findings from Kang *et al.* are relevant because they suggest that POPF prediction is not necessarily a one size fits all approach. Factors unique to an institution's or geographic region's patient population, disease characteristics, or perioperative practices may influence the incidence of and unique risk factors for POPF development. These findings suggest that, despite the global burden and impact of POPF, unique risk prediction models may need to be developed to accurately capture an individual's risk for CR-POPF following pancreatectomy.

At the same time, predicting POPF is most useful if effective mitigation strategies can be implemented based on risk stratified models. Currently, there are few effective strategies to reduce the occurrence and/or

Table 1 Definition of POPF as per International Study Group for Pancreatic Surgery (ISGPS), 2016

Grade	Definition
Biochemical Leak	Increased amylase >3 times upper limit of normal
Grade B POPF	Requires change in post-operative management; drains either left in place or repositioned endoscopically or percutaneously
Grade C POPF	Requires re-operation or leads to organ failure and or death

Table 2 Examples of POPF risk prediction scores

Authors	Year	Modeling cohort (n)	Outcome of interest	Elements	AUC on internal validation
Callery *et al.* (3)	2013	233	Grades B, C	Gland texture, pathology, pancreatic duct diameter, intra-operative blood loss	0.94
Mungroop *et al.* (Dutch Pancreatic Cancer Group) (4)	2019	1,924	Grade B, C	Gland texture, pancreatic duct diameter, BMI	0.75
Li *et al.* (5)	2019	189	Grade B, C	Pre-operative serum albumin, gland texture, pancreatic duct diameter, intra-operative blood loss	0.82
Yamamoto *et al.* (6)	2011	279	Grades B, C	Sex, pancreatic duct index, relationship of tumor to portal vein, intra-abdominal fat thickness, pathology	0.81
Roberts *et al.* (7)	2014	217	Grades A–C	BMI, pancreatic duct diameter	0.75
Kantor *et al.* (8)	2017	1,212	Grades B, C	Sex, BMI, bilirubin, pancreatic duct diameter, gland texture	0.70

severity of POPF. For example, the use of perioperative somatostatin analogues remains controversial without convincing evidence of their routine efficacy (10). Pre-operative optimization of nutrition is recommended and there is some evidence that neoadjuvant chemotherapy is associated with lower rates of POPF, but these factors will not apply to all patients (11). One multinational retrospective study in patients undergoing distal pancreatectomy found that method of transection, suture ligation of the pancreatic duct, staple size, staple line reinforcement, tissue patches, biologic sealants and prophylactic octreotide were not independently associated with decreased occurrence of CR-POPF (12). Although data on technical strategies to minimize CR-POPF have largely been unsuccessful, some have suggested that the use of externalized stents may reduce the incidence of CR-POPF (13). While the use of routine drain placement after pancreatectomy remains controversial (14), one of the most promising methods of minimizing CR-POPF is early drain removal (15). Clearly, additional research in novel mitigation strategies is needed.

In summary, the study by Kang *et al.* highlights the global scope of POPF and the need for better prediction models for Eastern populations which may differ from their Western counterparts. Future studies may choose to utilize larger international cohorts and apply innovative machine-learning based techniques to optimize and generalize risk prediction strategies. In the meantime, however, more effective mitigation strategies for POPF are needed to maximize the utility of these scoring systems in clinical practice.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Hepatobiliary Surgery and Nutrition*. The article did not undergo external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-20-497/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Eskander MF, Cloyd JM. Predicting post-operative pancreatic fistula: one size may not fit all. HepatoBiliary Surg Nutr 2021;10(1):113-115. doi: 10.21037/hbsn-20-497

