OXFORD

BJS Open, 2023, zrac156
https://doi.org/10.1093/bjsopen/zrac156
Invited Commentary

Postoperative pancreatic fistula: focus should be shifted from early drain removal to early management

Hjalmar C. van Santvoort*

Department of Hepato-Pancreato-Biliary Surgery, Regional Academic Cancer Center, St. Antonius Hospital Nieuwegein & University Medical Center, Utrecht, The Netherlands

*Correspondence to: Hjalmar C. van Santvoort, Professor of Pancreatic Surgery, Regional Academic Cancer Center, St. Antonius Hospital Nieuwegein & University Medical Center Utrecht, The Netherlands (e-mail: h.vansantvoort@umcutrecht.nl)

Postoperative pancreatic fistula (POPF) rightfully remains a priority topic in clinical research to improve outcomes after pancreatoduodenectomy[1]. Many attempts have been made to establish clinical and biochemical predictors for POPF, of which none have been truly implemented in daily practice[2]. Garnier *et al.* have made significant advances in this field, with their recent observational study on the serum-based inflammatory marker neutrophil-to-lymphocyte ratio (NLR)[3]. Using a solid statistical approach in a prospective database of 451 patients undergoing pancreatoduodenectomy between 2012 and 2020, the authors investigated the predictive value of the NLR in excluding POPF. The NLR performed well: a cut-off of less than 8.5 on postoperative day 3 was associated with the absence of POPF, with an OR of 5.13 (95 per cent confidence intervals 1.67 to 15.76) in an external validation cohort. As the authors acknowledge, their study has some limitations. These include the absence of routine drain amylase measurements before 2017 and postoperative drain management being left to the discretion of the treating surgeon. Both may have affected the incidence of POPF and influenced both internal and external validity of the study. The authors are commended for currently performing a prospective follow-up study in which these issues are addressed.

Theoretically, the clinical application of predicting POPF mainly lies in aiding early postoperative drain removal, thereby shortening duration of hospital stay. Many markers, including NLR in the present study, are evaluated on postoperative day 3[2]. As POPF is per definition diagnosed on day 3 and onward[1], these markers may rather be considered (surrogate) diagnostic tools, instead of predictors. Their added clinical value over the widely used drain amylase is therefore questionable. Moreover, as long as a new predictive marker does not yield a specificity of (near) 100 per cent, it seems unwise to use it as decision tool to routinely remove drains on day 3. Whereas this may be safe in most patients, a small subset of patients will develop a POPF and, as a consequence of early drain removal, may develop severe complications such as bleeding, organ failure, and death. As these events are fortunately uncommon after pancreatoduodenectomy, the association with early drain removal may hardly be noticed in clinical practice. Notably, also in randomized trials on drain management after pancreatoduodenectomy, these severe outcomes are difficult to study given the lack of statistical power[4]. In reality, there is plausibly a large 'number needed to treat' for (prolonged) postoperative drainage, this means that the majority of patients receive an unnecessary drain to prevent a severe complication in a single patient. In light of possible adverse events associated with drains, as pancreatic surgeons we should ask ourselves, what is the number needed to treat that we find acceptable?

The recent Dutch stepped-wedge randomized PORSCH trial studied the implementation of an algorithm combining common clinical and biochemical markers for early recognition and treatment of POPF[5]. This led to a nationwide reduction of severe complications (bleeding, organ failure, and death) from 14 to 8 per cent, including a decrease in 90-day mortality rate from 5 to 2.7 per cent. In patients treated using the algorithm, CT, antibiotic treatment, and radiological drainage were performed more often and earlier in the postoperative course. This also increased the rate of grade B/C POPF from 21 to 28 per cent, of which many are therefore not clinically very relevant[5]. These results emphasize that focus in pancreatic surgery research should be shifted from prediction of POPF and early drain removal to early diagnosis and management of POPF. The valuable data on the NLR from the study by Garnier *et al.*[2] can be used to further improve strategies combining clinical and biochemical markers to timely treat POPF.

Funding

The authors have no funding to declare.

Disclosure

The authors declare no conflict of interest.

References

1. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M *et al.* The 2016 update of the international study group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. *Surgery* 2017;**161**:584–591

Received: October 18, 2022. **Accepted:** October 25, 2022

2. Smits FJ, Molenaar IQ, Besselink MG, Borel Rinkes IHM, van Eijck CHJ, Busch OR *et al.* Early recognition of clinically relevant postoperative pancreatic fistula: a systematic review. *HPB (Oxford)* 2020;**22**:1–11
3. Garnier J, Alfano M, Robin F, Ewald J, Al Farai A, Palen A *et al.* The neutrophil-to-lymphocyte ratio: a useful tool for the exclusion of post-operative pancreatic fistula after pancreatoduodenectomy. *BJS Open* 2022
4. Zhang W, He S, Cheng Y, Xia J, Lai M, Cheng N *et al.* Prophylactic abdominal drainage for pancreatic surgery. *Cochrane Database Syst Rev* 2018;**6**:CD010583
5. Smits FJ, Henry AC, Besselink MG, Busch OR, van Eijck CH, Arntz M *et al.* Algorithm-based care versus usual care for the early recognition and management of complications after pancreatic resection in The Netherlands: an open-label, nationwide, stepped-wedge cluster-randomised trial. *Lancet* 2022;**399**:1867–1875