



# Intestinal autotransplantation: the next level of complexity in locally advanced pancreatic cancer

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*Comment on:* Liang T, Zhang Q, Wu G, *et al.* Radical Resection Combined with Intestinal Autotransplantation for Locally Advanced Pancreatic Cancer after Neoadjuvant Therapy: A Report of 36 Consecutive Cases. *Ann Surg* 2023. [Epub ahead of print]. doi: 10.1097/SLA.0000000000005797.

**Keywords:** Pancreatic cancer; with intestinal autotransplantation; locally advanced; arterial resection

Submitted Jun 22, 2023. Accepted for publication Jul 03, 2023. Published online Jul 06, 2023.

doi: 10.21037/hbsn-23-306

**View this article at:** <https://dx.doi.org/10.21037/hbsn-23-306>

Pancreatic ductal adenocarcinoma (PDAC) remains a devastating disease, and selecting patients who might benefit from complex arterial resection continues to be a challenge. However, in the era of modern multimodal treatments, surgery for pancreatic cancer has become increasingly safe. Neoadjuvant chemotherapy regimens such as modified-FOLFIRINOX (mFOLFIRINOX) and nab-paclitaxel/gemcitabine are effective in a significant proportion of patients. This made complex vascular resections possible and have provided meaningful prognostic benefits from an oncologic perspective for patients with borderline and locally advanced PDAC. Venous resections, which were once considered a criterion of unresectability in the past, are now routinely performed in most surgical departments treating pancreatic cancer (1). On the other hand, arterial resections still pose a challenge and are not widely carried out.

The study published by Liang *et al.* in *Annals of Surgery* in 2023 addresses the possibility and safety of performing radical resections in patients with PDAC by combining intestinal autotransplantation with mFOLFIRINOX neoadjuvant chemotherapy, with or without anti-PD-1 antibodies. The authors have to be congratulated for this innovative and challenging approach. The described technique involves the removal of the intestine followed by *en-bloc* multivisceral tumor resection. Subsequently, the

intestinal autograft is revascularized through anastomosis of the mesenteric artery and infrarenal aorta, and anastomosis of the superior mesenteric vein (SMV) and the portal vein or inferior vena cava, with or without vascular grafts. This retrospective analysis included 36 patients with superior mesenteric artery (SMA) involvement, with or without coeliac trunk involvement. From a technical standpoint, high R0 resection rates were achieved (94.4%), with confirmed histological invasion of the SMA or SMV in 89% of the patients. Additionally, mortality and severe morbidity were within acceptable limits at 5.5% and 33%, respectively. Regarding long-term outcomes, the recurrence-free survival was 13.6 months, and the median overall survival of patients after diagnosis and surgery were 21.4 and 14.5 months, respectively (2).

These results are comparable to those published in the literature for locally advanced PDAC. In a recent meta-analysis on contemporary pancreas surgery with arterial resection, overall morbidity and mortality rates were 66.8% and 5.3%, respectively. Furthermore, regarding long-term survival, the results are similar, with a weighted median survival of 18.6 months for patients undergoing arterial resections (3). *Table 1* summarizes three meta-analyses on arterial resections for PDAC (3-5).

Regarding operative techniques for resection and

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**Table 1** Outcomes from meta-analyses on arterial resection vs. standard resection

Reference	Year	Mortality	Morbidity
Rebelo <i>et al.</i> (3)	2020	OR 2.55; 95% CI, 0.69–9.42; P=0.16	OR 1.15; 95% CI, 0.58–2.28; P=0.69
Mollberg <i>et al.</i> (4)	2011	OR 5.04; 95% CI, 2.69–9.45; P<0.0001	OR 2.17; 95% CI, 1.26–3.75; P=0.006
Małczak <i>et al.</i> (5)	2020	RR 4.09; P<0.001	RR 1.4; P=0.01

OR, odds ratio; CI, confidence interval; RR, risk ratio.

reconstruction of the SMA in pancreatic surgery, the most commonly used technique is performing an end-to-end anastomosis in combination with the Cattell-Braasch maneuver after *en-bloc* tumor resection. In the case series by Liang *et al.*, the authors describe a more complex procedure involving vascular grafts (2). This highlights the increasing complexity of arterial resections for PDAC to achieve favorable outcomes. With these extended resections, the authors reported an R0 resection rate of more than 90%, which is significantly higher than those reported in the literature, even after neoadjuvant chemotherapy (3).

The implementation of mFOLFIRINOX and gemcitabine plus nab-paclitaxel has been shown to have survival benefits in patients with locally advanced pancreatic cancer. In the case series from Liang *et al.*, patients received mFOLFIRINOX every two weeks as neoadjuvant chemotherapy with or without anti-PD-1 antibodies. Stereotactic body radiation therapy (SBRT) was selectively performed. Radiological examination was performed after every four cycles of chemotherapy, and indication to surgery was discussed in a multidisciplinary team (2). In borderline resectable patients, preoperative treatment can increase the 12-month overall survival rate by more than 30% compared to upfront surgery (6). Results from the ESPAC-5 trial revealed that short-course (8-week) neoadjuvant therapy had a significant survival benefit compared to immediate surgery in patients with borderline resectable PDAC, supporting the use of neoadjuvant chemotherapy in these patients (7). Results from the PREOPANC trial, that also included patients with resectable PDAC, also showed improved overall survival for patients receiving neoadjuvant gemcitabine-based chemoradiotherapy followed by surgery and adjuvant gemcitabine compared to patients undergoing upfront surgery and adjuvant gemcitabine only (8).

In patients with initially locally advanced, unresectable non-metastatic PDAC, neoadjuvant therapy followed by surgery leads to improved overall survival compared to those patients receiving palliative treatments. A study

published by Del Chiaro *et al.*, showed that despite identical surgery-related mortality, patients undergoing palliation had significantly lower rates of 1-, 3-, and 5-year survival (9). The role of radiochemotherapy in patients with locally advanced disease has also been discussed, but the LAP07 trial showed no significant difference in overall survival with chemoradiotherapy compared to chemotherapy alone (10).

Establishing multidisciplinary teams is essential for performing these complex resections. The standard teams comprising oncologists, gastroenterologists, hepato-pancreatico-biliary (HPB) surgeons, pathologists, and anesthesiologists may need to be expanded due to the increasing complexity of the procedures. Creating surgical teams composed of transplant and vascular surgeons can provide additional expertise, including hybrid and endovascular techniques, particularly in the era of minimally invasive robotic surgery. Furthermore, the learning curves of these surgical procedures have a substantial impact on outcomes (11). Developing training and fellowship programs to learn these procedures, as those recommended and developed for robotic pancreatoduodenectomies, may help reduce the mortality and morbidity associated with the learning curve of these complex surgical resections. This will make it possible to safely take these procedures to the next level: minimally invasive pancreas resections with arterial reconstruction for locally advanced pancreatic cancer (12,13).

## Acknowledgments

**Funding:** This work was partially supported by the Advanced Clinician Scientist Program of the Medical Faculty of the Martin-Luther University Halle-Wittenberg, Halle (Saale), Germany (No. FKZ ACS23/06).

## 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-23-306/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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## References

1. Bockhorn M, Uzunoglu FG, Adham M, et al. Borderline resectable pancreatic cancer: a consensus statement by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 2014;155:977-88.
2. Liang T, Zhang Q, Wu G, et al. Radical Resection Combined with Intestinal Autotransplantation for Locally Advanced Pancreatic Cancer after Neoadjuvant Therapy: A Report of 36 Consecutive Cases. *Ann Surg* 2023. [Epub ahead of print]. doi: 10.1097/SLA.0000000000005797.
3. Rebello A, Büdeyri I, Heckler M, et al. Systematic review and meta-analysis of contemporary pancreas surgery with arterial resection. *Langenbecks Arch Surg* 2020;405:903-19.
4. Mollberg N, Rahbari NN, Koch M, et al. Arterial resection during pancreatectomy for pancreatic cancer: a systematic review and meta-analysis. *Ann Surg* 2011;254:882-93.
5. Małczak P, Sierżęga M, Stefura T, et al. Arterial resections in pancreatic cancer - Systematic review and meta-analysis. *HPB (Oxford)* 2020;22:961-8.
6. Springfield C, Ferrone CR, Katz MHG, et al. Neoadjuvant therapy for pancreatic cancer. *Nat Rev Clin Oncol* 2023;20:318-37.
7. Ghaneh P, Palmer D, Cicconi S, et al. Immediate surgery compared with short-course neoadjuvant gemcitabine plus capecitabine, FOLFIRINOX, or chemoradiotherapy in patients with borderline resectable pancreatic cancer (ESPAC5): a four-arm, multicentre, randomised, phase 2 trial. *Lancet Gastroenterol Hepatol* 2023;8:157-68.
8. Versteijne E, van Dam JL, Suker M, et al. Neoadjuvant Chemoradiotherapy Versus Upfront Surgery for Resectable and Borderline Resectable Pancreatic Cancer: Long-Term Results of the Dutch Randomized PREOPANC Trial. *J Clin Oncol* 2022;40:1220-30.
9. Del Chiaro M, Rangelova E, Halimi A, et al. Pancreatectomy with arterial resection is superior to palliation in patients with borderline resectable or locally advanced pancreatic cancer. *HPB (Oxford)* 2019;21:219-25.
10. Hammel P, Huguet F, van Laethem JL, et al. Effect of Chemoradiotherapy vs Chemotherapy on Survival in Patients With Locally Advanced Pancreatic Cancer Controlled After 4 Months of Gemcitabine With or Without Erlotinib: The LAP07 Randomized Clinical Trial. *JAMA* 2016;315:1844-53.
11. Loos M, Kester T, Klaiber U, et al. Arterial Resection in Pancreatic Cancer Surgery: Effective After a Learning Curve. *Ann Surg* 2022;275:759-68.
12. Zwart MJW, Nota CLM, de Rooij T, et al. Outcomes of a Multicenter Training Program in Robotic Pancreatoduodenectomy (LAELAPS-3). *Ann Surg* 2022;276:e886-95.
13. Asbun HJ, Moekotte AL, Vissers FL, et al. The Miami International Evidence-based Guidelines on Minimally Invasive Pancreas Resection. *Ann Surg* 2020;271:1-14.

**Cite this article as:** Rebello A, Kleeff J. Intestinal autotransplantation: the next level of complexity in locally advanced pancreatic cancer. *HepatoBiliary Surg Nutr* 2023;12(4):604-606. doi: 10.21037/hbsn-23-306