



A critical review of pancreatotomy with concomitant superior mesenteric artery resection and intestinal autotransplantation

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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;278:e1055-62.

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We have read with great interest the study by Liang *et al.* addressing the role of radical resection combined with intestinal autotransplantation for locally advanced pancreatic cancer after neoadjuvant therapy (1). The study may attract the attention of the pancreato-biliary oncological and surgical community.

It is well known that pancreatic ductal adenocarcinoma (PDAC) is associated with poor prognosis, and, even in the modern era, only approximately 20% of cases can benefit from the best potential treatment option, represented by radical surgical resection (2).

With advances in surgical techniques and neoadjuvant therapies (the introduction of FOLFIRINOX in 2011 is a milestone in PDAC treatment as well as the introduction of Gem-Nabplitaxel), the definition of operable pancreatic malignancy has evolved (3,4).

In the last decade, a new classification of resectability has been introduced, considering the potential benefit of high-risk operations. This classification includes mainly the vascular involvement by defining cases as “resectable”, “borderline resectable”, and “locally advanced” (LA) PDAC (5). The latter are those including PDAC with arterial involvement.

Historically LA PDAC involving the regional arteries

(hepatic artery, superior mesenteric artery, and coeliac axis) was considered inoperable. However, arterial involvement is no longer an absolute contraindication to surgical resection after patient and disease biology selection after the neoadjuvant treatment. Nonetheless, due to the technical complexity and increased perioperative risks, such cases are still not commonly performed, even in tertiary pancreatic centers. This is the main reason why there is a paucity of evidence in the literature in this area, especially in the context of superior mesenteric artery (SMA) resection, where only retrospective series with small cohort studies exist (6-14).

In the article commented in this editorial, Liang *et al.* reported on 36 patients diagnosed as PDAC with SMA involvement that, after neoadjuvant chemotherapy, underwent tumor resection combined with intestinal autotransplantation.

The authors previously published this technique, and in this series, they finally gave a complete picture of postoperative morbidity, mortality, and survival outcomes (15). They claimed this technique could provide an R0 resection with accepted adverse events and may improve prognosis.

Despite their reassuring conclusions, it is crucial to make

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some considerations. The first one is that in the present series, almost 20% of patients required reintervention because of immediate postoperative adverse events such as intestinal necrosis, bleeding, or artery thrombosis, which makes this technique not as safe as the authors argued, even though the series presents an acceptable 30-day mortality of 5.6%, which is comparable to pancreas tumor resections without vascular involvement (6).

The rate of 90-day mortality in the current literature after SMA resection for PDAC varies from 0% to 23.5%, with a mean of 5% in line with the percentage presented in the commented series (7,9,10).

On the other hand, instead of the 30-day mortality, it would have been preferable to present the 90-day mortality, which gives a better caption of the mortality rate after such a challenging operation.

The selection criteria for patients with LA PDAC for whom pancreatectomy is worthwhile is still an open issue. The present study allows the reader to highlight further some criteria that should be followed, such as the biological selection: after chemotherapy, only if the CA19-9 level falls into the normal range or becomes steady after a quick reduction, resection might be considered.

The adequate disease selection for potential PDAC resection is also based on imaging response to chemotherapy. It is usually difficult to define which cases have a good response as it is challenging to discriminate between tumor invasion or local desmoplastic reaction. Regarding this topic, the authors did not clarify their strategy showing only some CT scans with an apparent decrease in tumor size and vascular involvement, which is not what mostly happens in routine practice.

In our opinion, surgical exploration should be carried out even in cases where radiological tumor response is unclear if no extrapancreatic disease is present and with a decreased/stable CA19-9.

In the neoadjuvant treatment setting, the total number of chemotherapy cycles is also essential, and few data are available in the literature concerning its association with survival. The authors proposed a modified FOLFIRINOX regimen every two weeks (aiming to give this treatment for six months), with or without anti-PD-1 antibodies according to mutation, and with concomitant stereotactic body radiation therapy (SBRT) in selected patients (total of 25 Gy in five consecutive sessions).

The selection of which cases SBRT is indicated for is not specified in this study. Despite the inadequate evidence in the current literature, considering the promising results of

recent trials, we believe SBRT should be offered to all LA PDAC patients before a potential radical resection (16).

Postoperative quality of life is paramount, especially in case of such a poor prognosis disease. Despite the study reporting a high incidence of diarrhea and gastroparesis, most patients showed satisfactory control of these events. However, a specific pancreatic and oncological test on quality of life could have given a better picture of the patient's perspective after surgery.

According to this technique, the R0 resection was achieved in all except two patients, achieving an R0 resection rate of 94.4%, significative higher than the median reported in the literature for similar advanced cases (75%) (6-14).

The present study presented an overall survival of 21.4 months after diagnosing LA PDAC. It is not easy to compare this survival data with the current literature. To date, there is a lack of homogeneity concerning the neoadjuvant treatment, with or without radiotherapy or even if borderline or LA PDAS are included. Considering the author's assumption that this survival can be higher than nonsurgical treatment (13.2 months) is acceptable. However, given this series' very short median follow-up time (15 months), it is difficult to draw firm conclusions on survival data after this procedure.

In conclusion, this valuable study allows us to evaluate an alternative surgical technique for SMA resection, especially in a particular sub-population of patients with LA PDAC with a favorable prognosis.

Future efforts should concentrate on surgical technique and patient and disease biology selection. To minimize heterogeneity and bias, it might be interesting to take advantage of this series to start a multicenter prospective cohort study on SMA resection for LA PDAC, which can represent the basis for a future randomized study.

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