

# Comment on “Total Pancreatectomy With Islet Autotransplantation as an Alternative to High-Risk Pancreatojejunostomy After Pancreaticoduodenectomy: A Prospective Randomized Trial”

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Following the publication of the article by Dr Balzano et al,<sup>1</sup> several members of the International Study Group of Pancreatic Surgery have been informed that this method has now been proposed to patients with pancreatic adenocarcinoma as a possible alternative to Whipple surgery in European centers. This novel approach proposes to perform a total pancreatectomy to avoid the high-risk pancreatojejunostomy and to isolate the islets of Langerhans from the body and tail of the pancreas to perform an autotransplantation into the liver to prevent the consequences of severe diabetes.

During the recent congress of the International Pancreas and Islet Transplantation Association in San Diego (October 25th to October 29th, 2023), the indications and contraindications for total pancreatectomy with islet autotransplantation were discussed by Dr Ty Dunn who mentioned that pancreatic cancer remained a contraindication for islet autotransplantation in the United States (personal communication). Indeed, does the risk of postoperative pancreatic fistula and diabetes mellitus override that of cancer?

We therefore propose to limit this new approach for patients with pancreatic malignant tumoral diseases to specialized centers using regulated prospective protocols with Institutional Review Board approval as no clear conclusions have been reported regarding the safety and efficacy of this approach.

Two of the cosignatories (LB and AF) have previously commented on some limitations of this published study, such as the low sample size and its lack of statistical power.<sup>2</sup>

We would like to add several comments regarding any further widespread application of this method:

The quoted number of clinically relevant postoperative pancreatic fistula in the Whipple surgery group was close to 60%,<sup>1</sup> twice as high than the 30% rate reported by the international study group on pancreatic surgery.<sup>3</sup> Furthermore, the overall complication rate reached 90%,<sup>1</sup> whereas other multicenter data have evaluated this to be around 60%.<sup>3</sup>

For patients with an extremely high-risk of a postoperative pancreatic fistula, most cases are of Grade B and can be treated with conservative care and time. Grade C postoperative fistula represent only 6% of all patients undergoing Whipple surgery.<sup>3</sup>

Finally, many patients who undergo total pancreatectomy are not able to receive adjuvant therapy such as chemo or radiotherapy, even in the absence of diabetes.<sup>4</sup> This will also influence the outcome of this method and should be tested in strictly monitored clinical trials.

In conclusion, we recommend that total pancreatectomy combined with islet autotransplantation be proposed as treatment for patients with pancreatic adenocarcinoma only within controlled trials with Institutional Review Board approval and informed consent in specialized centers. Extreme precaution must be taken to rule out any possible malignant cells in the islet transplant lot, that the frozen section histology is negative.

Of note, 2 prospective multicenter trials have been initiated, one in France in 2022, and the other in Germany in 2023, with the aim to test the safety and efficacy of this approach and are currently ongoing.<sup>5,6</sup>

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