



Decision-making in high-risk leakage duodenopancreatectomy: pancreatic anastomosis or total pancreatectomy?

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The Italian team from Verona, questions the place of total pancreatectomy (TP) as an alternative to pancreaticoduodenectomy (PD) in patients at high risk of pancreatic fistula in a monocentric retrospective study running from July 2017 to December 2019 (1). A total of 702 patients were included, 566 PD of which 101 were at high risk of pancreatic fistula (HR-PD), 136 TP of which 86 were PD converted to TP (C-TP) for positive margin of pancreatic section for malignancy (49%), extensive vascular resection (14%) or technical reasons (27%) such as residual non-reconstructible pancreas/friable pancreas/microscopic Wirsung's duct, 10% for other reasons (bleeding.....) Patients in the HR-PD group received externalized stent of the Wirsung duct.

Pre-operatively, TP patients had more diabetes (37% *vs.* 19%, $P<0.01$) and received more neo-adjuvant treatment (38% *vs.* 26%, $P<0.01$) than patients in the PD group. Intraoperatively, there was more vascular resection (37% *vs.* 14%, $P<0.01$) and blood loss (20% *vs.* 13% bleeding $>1,000$ mL, $P<0.01$) in the TP group. Post-operatively there was no difference in 90-day mortality (4% *vs.* 3%, $P=0.6$), Clavien-Dindo morbidity ≥ 3 (19% *vs.* 19%, $P=0.9$), length of stay (10 *vs.* 9 days, $P=0.7$) or readmission rate (2% *vs.* 5%, $P=0.1$). However, there was a higher proportion of cardiac (23% *vs.* 5%, $P<0.01$), renal (10% *vs.* 3%, $P<0.01$) and pleural effusion (25% *vs.* 11%, $P<0.01$) events in the TP group. The rate of pancreatic fistula was 20% in the PD group.

Post-operatively, compared to the HR-PD group, the

C-TP group had fewer: post-operative collections (35% *vs.* 60%, $P<0.01$), abscesses (13% *vs.* 28%, $P<0.01$), chylous leakage (2% *vs.* 12%, $P=0.01$), post-operative bleeding (15% *vs.* 28%, $P=0.03$), ileus (16% *vs.* 34%, $P<0.01$), sepsis (10% *vs.* 31%, $P<0.01$) and surgical site infection (9% *vs.* 23%, $P=0.01$). The occurrence of Clavien-Dindo complications ≥ 3 was lower (19% *vs.* 31%, $P=0.05$) and the length of stay was also lower (10 *vs.* 21 days $P<0.01$). Mortality was comparable in both groups (3% *vs.* 4%, $P=0.6$).

All patients in the C-TP group developed postoperative diabetes while only 13% in the HR-PD group, and only 63% in the HR-PD group developed exocrine pancreatic insufficiency.

The study of quality of life at 30 months according to 5 questionnaires (EQ-5D, QLQ-C30, QLQ-PAN26, PAID and original questionnaires) reveals a difference on the questionnaire specifically assessing the psychological impact of diabetes, but does not reveal any significant difference in quality of life between the HR-PD and C-TP groups on the 4 other questionnaires, except for symptoms related to sexual relations which would be more present in the HR-PD group.

This study has the merit of asking a pertinent question: must TP be performed instead of TP in high-risk patients? Indeed, patients at high risk of pancreatic fistula according to the Alternative Fistula Risk Score have a risk of pancreatic fistula of around 39%. The originality of this study lies in the question asked, which is very relevant,

through the consideration of the quality of life at 30 months.

When TP is compared to PD, the post-operative follow-up does not differ in terms of length of stay, 90-day mortality or Clavien-Dindo 3 morbidity (19%). However, when comparing C-TP with HR-PD, it seems clear that the place of radical surgery deserves to be considered and this makes the article very interesting.

Obviously, this study suffers from biases: in the absence of randomization the patients are not entirely comparable, notably the greater presence of pre-operative diabetes in the TP group which tends to underestimate the impact on quality of life of post-operative diabetes.

C-TP patients had more frequent adenocarcinoma with neo-adjuvant treatment, vascular resections and more intraoperative bleeding than the HR-PD group. However, the postoperative follow-up after C-TP is favourable to C-TP, which reinforces the proof that TP is a surgery with less local morbidity. The study EVOQUE more renal and cardiac repercussions, perhaps because of extended vascular resections and associated bleedings in this group.

One of the strengths of this study is its monocentric nature, the patients were operated in the same context, by the same team, with large numbers, which makes the patients more comparable with each other.

Regarding quality of life, there was little difference in the responses to the questionnaires in terms of general quality of life or quality of life related to digestive symptoms. By category, there was a moderate difference in sexuality in the C-TP group and minimal differences between the C-TP and HR-PD groups with more diarrhea, ascites and adverse drug reactions in the C-TP group, and more concern about weight loss and insomnia in the HR-PD group. The study of the psychological impact of diabetes reflects a greater difficulty in managing insulin-requiring diabetes and the anxiety related to it.

Exocrine pancreatic insufficiency (EPI) is supplemented in all patients operated for TP, where it is considered that all suffer from EPI, whereas in the meta-analysis of the Dutch pancreatic cancer group (1) of 495 patients operated on for EPI, only 43.5% suffered from EPI and were substituted. The quality of life score according to the EORTC QLQ-C30 questionnaire was 64% (58–69%) in the Dutch group meta-analysis and 79% (64–95%) in the Verona group study (2-7).

In conclusion, the authors recommend TP for patients with pre-existing diabetes but do not routinely recommend this surgery for HR-PD with high risk of pancreatic fistula. Indeed, given a similar quality of life, length of stay and

survival, it is difficult to impose the sequelae of endocrine and exocrine pancreatic insufficiency in this indication without pre-existing condition.

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