



Modified Appleby: experience improves short-term results, but is it enough?

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The aim of this retrospective study (1) from one of the largest European centres of pancreatic surgery was to report the surgical and oncological results of a series of 71 distal pancreatectomies with monobloc resection of the celiac trunk (DP-CAR or modified Appleby) performed for locally advanced pancreatic cancer, over almost 20 years and comparing two periods: before 2013 (n=16) and after 2014 (n=55). They reported a mortality rate of 8.5% (6/71) and major morbidity of 32% (23/71), including 21.1% pancreatic fistulas and 14.1% gastric ischaemia. They performed 46% (33/71) sub-total distal pancreatectomies, extended in contact with the gastro-duodenal artery and 59% (42/71) multi-visceral resections and/or venous resections associated with pancreatic resection.

They showed that their results improved over time in terms of mortality on post-operative day 90 over the two periods studied (3.6% *vs.* 25%; P=0.02), while major morbidity remained similar (37.5% *vs.* 30.9%, P=0.62). Morbi-mortality were not increased when DP-CAR was combined with multi-visceral resection and/or venous resection. The number of DP-CAR performed without associated arterial anastomoses increased in the second period with a rate of ischaemic complications similar to those in series with arterial reconstructions (2) (after 2014, only 3.6% patients had arterial reconstruction *vs.* 31.2% before 2013, P<0.01). They concluded that this procedure

should be performed in an expert pancreatic surgery centre.

This is the largest single-center European series ever published. The multicenter European series (3) published in 2018 included 61 procedures in 20 centers. Some Asian single-center series have a substantial number of patients (4,5), notably the recent series by Wang *et al.* with 106 patients. The largest published series is the multicenter European series republished in 2019, supplemented by American and Asian data, reporting 191 patients (6). Despite these successive series, the modified Appleby still raises a number of questions: patient selection, the need for an arterial reconstruction, and the oncological risk/benefit ratio. While this series has the advantage of demonstrating that surgical expertise can reduce risks (very acceptable morbidity and mortality in the second period) and that it is possible and safe to avoid arterial reconstruction without ischaemic risk, a number of weaknesses can be noted.

With regard to patient selection, there is a lack of data on preoperative contact of the tumor with vascular axes (involvement of the celiac trunk, superior mesenteric artery and/or hepatic artery) confirming the locally advanced nature of resected tumors. The relatively low rate of neoadjuvant chemotherapy (based on which criteria?), the impact of the CA19-9 marker, and the value of positron emission tomography (PET)-scan as recommended by Truty's team (7) are not reported or discussed. The role of

neo-adjuvant radiotherapy combined with chemotherapy is also not mentioned in neo-adjuvant treatments or in the discussion, bearing in mind that in locally advanced tumors, it can increase the tumor response rate and improve resection margins (8). We are also surprised by the realization of this surgery in the case of metastases, which concerned 12.7% of the patients (9/71)!

We also had some concerns about technical data. While the problem of vascular reconstruction is well discussed, the description of the center's DP-CAR technique is succinct and refers to a technique that is explained in Klompmaker *et al.* (9), based on the experience of 7 centers. It is regrettable that no information is provided in the discussion on the local technical modifications that have led to improved outcomes for this procedure over the years.

Concerning the results, some surgical data should have been reported and analyzed. There was no mention of venous vascular complications (stenosis, thrombosis) despite the presence of a 44% rate of venous resections. There was no data on functional surgical results concerning possible endocrine and exocrine pancreatic insufficiencies. Finally, in the era of patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs), data on quality of life could have been interesting (10) although limited by the retrospective nature of the study.

Looking at the oncological results, the R0 rate was lower (58%) than other series, which are surprisingly not cited in the article (81–92%) (11,12). Despite this, overall survival at 3 years was 45.3% and at 5 years 19.4%, with a median overall survival of 28 months. These rates appeared acceptable compared with other series in the literature, and even higher than others European series (11). However, they are difficult to interpret due to the lack of data on neoadjuvant radiotherapy as mentioned above, but also adjuvant chemotherapy and recurrence rates. In the *Fig. S2*, it is surprising to see that there was no difference in overall survival at 3 years between patients having upfront surgery and those having surgery after neoadjuvant chemotherapy, with a trend towards better survival for patients with upfront surgery, which is in contradiction with the results already reported (4,5) showing increased survival after induction treatment. This maintains the debate about the selection of patients in this series, particularly in the second period studied where pancreatic cancers appeared to be more advanced according to *Tab. S1* (higher rates of invaded lymph nodes: N1, 38% *vs.* 19.7%; N2, 21.1% *vs.* 2.8%; $P < 0.01$; higher rates of stage III: 18.1% *vs.* 6.25%, $P < 0.01$). Finally, it would have been interesting to compare

survival data for DP-CAR alone with those for DP-CAR with multi-visceral resection and/or venous resection to analyze the oncological efficacy of such extensive resections for locally advanced tumors.

In conclusion, this study reported a large series of DP-CAR with satisfactory post-operative outcomes, confirming the clear improvement in the results of pancreatic surgery in recent years and justifying its use in expert centers. However, it is regrettable that such an experience cannot answer the final questions that can legitimately be raised about the modified Appleby: patient selection and therefore its risk/benefit ratio in terms of survival and quality of life.

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