

## LEOPARD trial

**Reference:** de Rooij Tet *al.* Minimally Invasive Versus Open Distal Pancreatectomy ([LEOPARD](#)) A Multicenter Patient-blinded Randomized Controlled Trial. *Ann Surg* 2019; 269:2–9  
LEOPARD recruited 111 patients from 14 centres in the Netherlands.

**P:** All patients with an indication for elective distal pancreatectomy because of symptomatic benign, premalignant, or malignant left sided pancreatic tumours ( $\leq 8$ cm). Excluded were patients who had undergone radiotherapy for pancreatic cancer and those with chronic pancreatitis.

**I:** Minimally invasive distal pancreatectomy (MIDP, either laparoscopic or robotic)

**C:** Open distal pancreatectomy (ODP)

**O:** Time to functional recovery (days) after surgery, defined as all of the following: independently mobile at the preoperative level, sufficient pain control with oral medication alone, ability to maintain at least 50% daily required caloric intake, no intravenous fluid administration, and no clinical signs of infection when other criteria were met. Secondary endpoints included complications, feeding tube placement, percutaneous catheter drainage, surgical re-interventions, length of hospital stay, ITU admission, readmission, quality of life, and costs

The authors provided a link to their published [protocol](#) which contains detailed descriptions of the operative steps for both intervention and comparator.

### Results:

- Functional recovery was reached after a median of 4 days (IQR 3–6) for MIDP and 6 days (IQR 5–8) for ODP ( $p < 0.001$ )
- Moreover, every criterion of functional recovery was reached more rapidly after minimally invasive than ODP
- Operative time was longer after MIDP [217 (IQR 135–277) vs 179 (129–231) minutes;  $p = 0.005$ ], whereas blood loss was less [150 (50–350) vs 400 (200–775) mL;  $P < 0.001$ ]
- Length of initial hospital stay was 2 days shorter after MIDP [median 6 (IQR 4–7) vs 8 (IQR 6–9) days;  $P < 0.001$ ].
- Delayed gastric emptying [3 patients (6%) vs 11 patients (20%);  $P = 0.04$ ] and endoscopic feeding tube placement [4 patients (8%) vs 14 patients (25%);  $P = 0.02$ ] were less frequent after MIDP
- No differences were found for bleeding, surgical site infection, intensive care unit admission, surgical or radiological reintervention, and readmission
- MIDP was associated with better overall EQ-5D-3L health utilities than ODP

**Critical appraisal:** Overall low risk of bias. Relatively generalisable aside from detailed descriptions of the intervention and comparator.

<b>Internal validity (bias)</b>	Selection bias	Low – computer generated randomisation sequence
	Detection bias	Unclear – patients were blinded but primary outcome was measured by healthcare professionals
	Performance bias	Unclear – patients were blinded but healthcare professionals were not. Some standardisation of operative techniques but these were not measured during the trial
	Attrition bias	Low – no dropout in either group, only 1 crossover
	Selective outcome reporting	Low
<b>External validity (generalisability)</b>	P	Relatively wide inclusion criteria, few exclusions
	I	Published protocol contains detailed descriptions of how open and laparoscopic surgery should be performed.
	C	
	O	Although 'recovery' should be a patient-centred outcome, this definition encompasses quite surgeon-driven goals and the endpoint is very short
	O	14 centres in the Netherlands. The surgeons had to fulfil entry criteria to participate (>20 distal pancreatectomies and >5 minimally invasive pancreas resections) as well as submitting an operative video

#### How has this influenced practice?

There is a trend towards minimally invasive techniques for distal pancreatectomy in both the Netherlands and the UK. This RCT was grounded in existing evidence from earlier stage [IDEAL](#) work and was informed by a [national training programme](#) in minimally invasive pancreas surgery.

#### Other criticisms:

- Primary outcome is subjective and could therefore have been influenced by unblinded caregivers
- Is the primary outcome considered important to patients?
- Only a small number of patients with pancreatic ductal adenocarcinoma were included, which may hamper the evaluation of oncological outcomes. However, the radical (R0) resection rate and lymph node retrieval were similar in the 23 included patients between groups
- There is an overall worry about the lymph node yield during MIDP and this is the focus of an ongoing study in the Netherlands
- 14 centre study and although operative techniques were described in the protocol, adherence was not measured