Study protocol

Twenty years of pancreatic surgery in Iceland: a retrospective cohort study

Background:

Pancreatic surgery is often occasioned by cancer in the pancreas or periampullary region, where pancreatic ductal adenocarcinoma (PDAC) is the most common diagnosis. This disease has a dire prognosis and is projected to soon surpass breast cancer as the third leading cause of cancer death in the European Union. The overall 5-year survival rate is reported to be 10% in the US, to a large extent due to the fact that 80-85% of patients are inoperable at diagnosis.[1] Survival after resection is better but not high, reported to be between 20 and 25% 5 years after surgery.[1, 2] Periampullary tumors – including ampullary, duodenal and distal bile duct carcinomas – have a better survival with a postoperative 5-year survival rate of around 45%.[2] Apart from these diagnoses, pancreatic surgery is occasionally performed due to neuroendocrine tumors, chronic pancreatitis, metastases from renal cancer, and, increasingly, for premalignant cystic lesions such as intraductal papillary mucinous neoplasms (IPMN).[3, 4]

Pancreatic operations are large and complex procedures, with reported rates of severe complications (Clavien-Dindo ≥3a) after pancreaticoduodenectomy (PD) between 20 and 30% in modern data, and up to 38% after total pancreatectomy.[5, 6] Distal pancreatectomy (DP) is a smaller procedure where the most usual postoperative complication is leakage of pancreatic fluid from the divided pancreas.[7] Minimally invasive pancreatic surgery has come the furthest among distal resections, where three randomized controlled trials have now shown the safety of the technique both from a perioperative and an oncological perspective.[7-9] Recent international guidelines recommend minimally invasive distal pancreatectomy (MIDP) to be considered for benign, pre-malignant and malignant lesions alike in the pancreatic body or tail.[10]

The question of volume in pancreatic surgery has been a growing topic over the last decade, with many studies indicating an advantage in terms of rate of resections, rate of radical resections, short-term and overall mortality with increasing hospital volume.[11-13] Current international recommendations for training in minimally invasive pancreatic resections recommend an annual hospital volume of 50 PDs and 10 DPs to qualify for a training program.[14]

Iceland is a small country in a unique situation, with a population of 380 000 people and situated on the border of the North Atlantic and Arctic oceans.[15] There is one university hospital in the capital of Reykjavik, performing the majority of the surgery and all of the malignancy surgery on the island. As this is by necessity a low-volume hospital in terms of pancreatic surgery, there is a long tradition of specialists training overseas to gain sufficient experience and volumes to be able to maintain a good standard of care despite the isolated

conditions of the island. There is, however, limited information available on the outcomes of pancreatic surgery in the country.

The aim of this study is to investigate the outcomes of pancreatic surgery in Iceland over the last 20 years.

Study characteristics:

This is a retrospective cohort study with data accessed from patients' medical journals.

Patients:

All patients who have undergone pancreatic resection in Iceland between 2002-2022 will be included in the study. For the secondary outcome of duodenal cancer, patients with duodenal cancer who did not undergo resection in the same time span will also be included.

Primary outcome:

The primary outcome of the study is the rate of severe complications and short-term mortality after pancreatic resections in Iceland.

Secondary outcomes:

- Demographic, operative and postoperative data after pancreatic resections compared between operation methods.
- Oncological data and survival among patients with pancreatic and periampullary cancer.
- Outcomes after pancreatic surgery among patients who underwent resection for cystic lesions.
- Comparison of patients who underwent minimally invasive distal pancreatectomy during the study period to those who underwent open distal resection.
- Demographic and histopathological data as well as survival compared between patients with duodenal cancer who underwent resection and patients who did not.
- Trends over time in the usage of pancreatic and minimally invasive surgery as well as changes in outcomes.

Variables accessed from the medical journals of patients:

Preoperative data	*Operative data*	*Postoperative data*	*Histopathological data and survival*
Age	Operation date	Clavien-Dindo complication score[16]	TNM stage
Gender	Operation time	Postoperative pancreatic fistula[17]	Radicality
Body mass index	Type of operation	Delayed gastric emptying[18]	Lymph nodes acquired and positive
Comorbidities	Minimally invasive or open	Postpancreatectomy hemorrhage [19]	Histopathological diagnosis
Preoperative medicines including statins	Type of pancreatic anastomosis	Bile leak[20]	Oncologic treatment including details
ASA score	Blood loss	Postpancreatectomy acute pancreatitis[21]	Date of recurrence
ECOG performance status	Arterial or venous resection	Blood and drain amylase and bilirubin levels	Date of death
Unintended weight loss	Additional organ resection	Days with drain	
Smoking	Splenectomy	Radiologic drain placement	
Date of diagnosis		Intensive care and days	
Date of treatment decision		Reoperation and details	
Date of multidisciplinary conference		Wound dehiscence	
Preoperative biliary drainage		Wound infection	
Preoperative endoscopic ultrasound		Pneumonia	
Other preoperative intervention		Cardiovascular complications	
Preoperative blood tests: CEA, Ca 19-9, hemoglobin, bilirubin, albumin		Neurological complications	
Preoperative cyst fluid tests		Thromboembolism	
Preoperative biopsy		Length of hospital stay	
Preoperative TNM stage		In-hospital mortality	
Preoperative assessment (resectable, borderline, locally advanced or metastasized)		Textbook outcome[22]	
Neoadjuvant chemotherapy including details			

ASA, American Society of Anesthesiologists; ECOG, Eastern Cooperative Oncology Group; TNM, tumor, node, metastasis.

Time frame:

- Developing study protocol and seeking ethical permission: summer of 2023.
- Data collection: autumn of 2023 to spring of 2024.
- Data analyses and writing of manuscript: rest of 2024.
- Publication: 2025.

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