

Prevalence of metabolic dysfunction-associated fatty liver disease after pancreatic surgery in a historical Belgian cohort and review of the literature

V. D'Cruz^{1*}, A. De Zutter^{1,2*}, M. Van den Broecke^{3,4}, S. Ribeiro¹, L. Abreu de Carvalho⁵, P. Smeets³, C. Lecluyse³, E. Pape⁵, E. Callebaut¹, F. Berrevoet⁵, K. Geboes^{1,6}

(1) Ghent University Hospital, department of Gastroenterology, Ghent, Belgium; (2) Sint-Andriesziekenhuis, department of Gastroenterology, Tielt, Belgium; (3) Ghent University Hospital, department of Radiology, Ghent, Belgium; (4) Sint Vincentiusziekenhuis, department of Radiology, Deinze, Belgium; (5) Ghent University Hospital, General and HPB Surgery and Liver Transplantation, Ghent, Belgium; (6) Ghent University Hospital, Cancer Centre, Ghent, Belgium.

Abstract

Background and objectives: Metabolic dysfunction-associated fatty liver disease (MAFLD) has been reported as a complication after pancreatic surgery. The aim of this study is to assess this phenomenon in a Belgian population, specifically in a period in time when less perioperative chemotherapy was given.

Methods: We performed a retrospective monocentric cohort study with 124 selected patients who underwent pancreatic surgery – pancreaticoduodenectomy (PD), distal pancreatectomy (DP) or total pancreatectomy – between 2005 and 2014. Steatosis was assessed radiologically, using Hounsfield units on liver and spleen. Data on imaging, liver function, weight and other relevant parameters were gathered preoperatively as well as 2 and 6 months, 1 and 2 years after surgery.

Results: Thirty-eight (31%) out of 124 patients developed liver steatosis at least at one point in time in the two years following surgery, with a prevalence of 21.0% at 2 months, 28.6% at 6 months, 16.4% at 1 year and 20.8 % at 2 years. A statistically significant association with preoperative AST and ALT values, administration of pancreatic enzyme supplementation as a surrogate for pancreatic exocrine insufficiency (PEI) and weight loss at 2 years was detected.

Conclusion: MAFLD is seen in 31% of patients with PD or DP pancreatic resection in this retrospective analysis of a monocentric Belgian cohort. Both early and late onset of MAFLD was observed, implying that long-term follow-up is necessary. Clinical impact as well as a direct correlation with patients' weight and oral enzyme supplements needs to be further investigated. (*Acta gastroenterol. belg.*, 2024, 87, 373-380).

Keywords: Metabolic dysfunction-associated fatty liver disease, pancreatic surgery, pancreatic exocrine insufficiency.

Introduction

Metabolic dysfunction-associated fatty liver disease is a well-known condition characterised by intrahepatic accumulation of fat. MAFLD is associated with obesity, insulin resistance and metabolic syndrome (1). It comprises a spectrum ranging from liver steatosis to more serious non-alcoholic steatohepatitis (NASH) and liver cirrhosis (2).

The development of MAFLD after pancreaticoduodenectomy (PD) has been previously described (3-23). Different risk factors for the development of post-PD MAFLD have been suggested. The exact mechanism of this phenomenon has not yet been discovered. Increased uptake of fatty acids in hepatocytes, elevated lipogenesis, upregulation of peroxisome proliferator-activated receptor (PPAR) γ and interruption of the very low density lipoprotein excretion in the circulation are

possible mechanisms for steatogenesis after PD (23, 24). It has been suggested that obesity and metabolic syndrome are not risk factors for post-PD MAFLD, but rather exocrine insufficiency and malnourishment. Kang and Lee suggest that malabsorption of choline, an essential amino acid, can lead to decreased plasma levels of apolipoprotein B and, consequently, impaired hepatic export of triglycerides (24). Thus, PD not only alters the anatomy but also the gastrointestinal physiology, which can result in MAFLD.

The reported incidence of MAFLD after PD ranges from 7.8 to 55% in studies with a follow-up between 3 months and 4.5 years (4,7-25). Most of these studies originate from Southeast Asia. Different techniques to assess steatohepatitis are used and time points for evaluation vary. Most publications are retrospective. Only 4 studies examine MAFLD after pancreatic surgery in a (mainly) Caucasian population: two North American, one Swedish and finally one Dutch study, focusing solely on pancreatic neuroendocrine tumours (10,13,18-19).

The aim of our study was to investigate if MAFLD occurs after extensive pancreatic surgery – pancreaticoduodenectomy (PD), distal pancreatectomy (DP) or total pancreatectomy – in a historical large Belgian cohort in a tertiary referral centre. We aimed to evaluate liver steatosis over time and to investigate the association with previously suggested risk factors.

Methods

The study is a retrospective monocentric cohort study in a tertiary academic referral centre starting from a database with 472 patients who underwent pancreatic surgery between January 2005 and December 2014. This period was chosen because we aimed to look into a historical cohort with adequate follow-up before the introduction of (neo)adjuvant folfirinix as treatment for adenocarcinoma, in order to have a sufficient

* Equal contribution.

Correspondence to: Geboes Karen, MD, PhD, Department of Gastroenterology, UZ Ghent. C. Heymanslaan 10, 9000 Ghent, Belgium.
Email: Karen.geboes@uzgent.be

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number of patients who did not receive chemotherapy. Pancreatic surgery included (non-)pylorus-preserving pancreaticoduodenectomy, total pancreatectomy and distal pancreatectomy with or without splenectomy. Data were collected for 2 years after surgery, whenever possible.

Exclusion criteria were: age under 18 at the moment of surgery, excessive use of alcohol (more than 7 units a week for females and more than 14 units a week for males), use of corticosteroids, known pre-operative liver steatosis (either mentioned in the medical history or by evaluation using the CT diagnostic criteria as described below), previous bariatric surgery, other known causes of liver disease (Wilson's disease, viral hepatitis, autoimmune liver disease, ...) and follow-up of less than 2 months.

This study was approved by the ethical committee of the Ghent University Hospital.

Out of 472 patients who underwent pancreatic surgery between 2005 and 2014, 244 patients were excluded because of lack of imaging data pre- and/or post-operatively. Another 104 were excluded because they met one or more exclusion criteria (Fig. 1). Most patients had other risk factors for steatosis, for instance clear alcohol abuse and 8 patients had a radiologic diagnosis of steatosis at diagnosis according to the methods used in our study. Finally 124 patients were eligible for analysis.

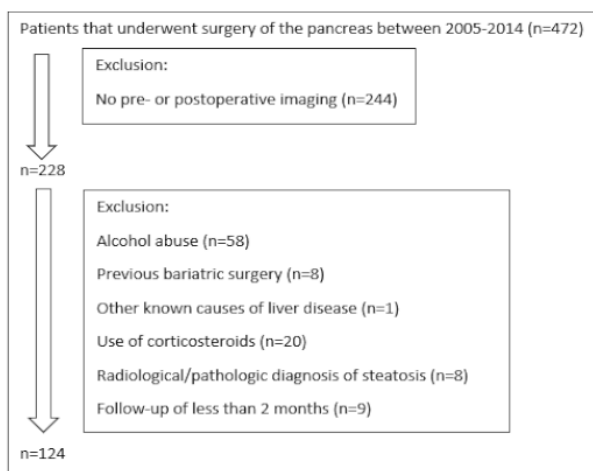


Fig. 1 — Flow diagram for exclusion.

Evaluation of MAFLD

The gold standard for the diagnosis of hepatic steatosis is a liver biopsy. Histopathologically, MAFLD is defined by the presence of steatosis in more than 5% of hepatocytes.

Due to the retrospective design of this study, we chose imaging parameters to define steatosis. CT diagnostic criteria for liver steatosis in an unenhanced CT are 1) absolute liver attenuation of less than 40 Hounsfield units (HU) or 2) liver attenuation at least 10 HU less than attenuation of the spleen or liver-to-spleen attenuation

ratio (L/M ratio) of less than 0.9 (25-28). This equals 30% of steatosis.

In many patients only contrast-enhanced images were available. We used an absolute difference of twenty or more HU between liver and spleen (liver-spleen ≥ 20) in the venous phase as definition of liver steatosis (29-31).

For each patient, the average CT attenuation of four regions of interest (ROI) in the liver and two in the spleen were measured. Each ROI was a circular area with a diameter of 20 mm. Blood vessels, metastases and bile ducts were avoided as much as possible.

To follow the evolution over time, we measured liver and spleen attenuation whenever a CT scan was available: pre-operatively as well as 2, 6, 12 and 24 months post-operatively.

Description of associated factors

Evaluation of pancreatic exocrine function

Pancreatic exocrine function (PEI) was evaluated with a ^{13}C -labeled mixed triglyceride (MTG) breath test or a human pancreatic elastase measurement in stool (32-33).

Results were available for 27 patients. Both of these tests were not routinely carried out and only performed in symptomatic patients.

Evaluation of clinical factors

Pre- and postoperative variables that may be associated with the development of NAFLD after pancreatic surgery were chosen based on existing literature (3-23).

Preoperative factors included age, sex, underlying pathology, type of surgery, alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, CA 19.9, weight, and body mass index (BMI).

The remnant pancreatic volume (RPV) was measured using the formula $V = (AP(\text{tale}) + AP(\text{body}))/2 \times L(\text{body and tale}) \times CC(\text{body}) + (AP(\text{head})/2) \times 3.14 \times CC(\text{head})$. AP stands for anteroposterior distance, L for length, CC for craniocaudal distance (34).

The following clinical data were collected 2, 6, 12 and 24 months postoperatively, together with CT images if available: AST, ALT, albumin as well as the cumulative percentage weight loss relative to the preoperative weight. Patient files were checked for prescription of pancreatic enzymes and for faecal elastase and ^{13}C MTG breath test results.

Statistical analysis

All statistical analyses were performed using SPSS software version 25 (IBM Corporation, Armonk, NY). Clinical variables were expressed as numbers with percentage, means with standard deviation (SD) or medians with interquartile range (IQR). We used the Shapiro-Wilk and Kolmogorov-Smirnov-test with display via histogram and QQ-plots to decide whether a

variable is normally distributed or not. The Student's t-test was used to compare continuous variables with a normal distribution between groups with and without steatosis. If there was no normal distribution, the Mann-Whitney U-test was used. The Chi-square test was used to compare categorical variables.

Univariable logistic regression analysis was performed to determine risk factors for the development of NAFLD after pancreatic surgery. Variables that were statistically significant using univariable analysis or that were considered clinically important were used in the multivariable logistic regression analysis. Results were considered statistically significant when the p-values were less than 0.05.

Results

Patient characteristics

The mean age of the patients was 63 (range 26-86) years and the male-to-female ratio was 67/57 (Table 1). Diagnoses included adenocarcinomas (pancreas, ampulla and bile duct) (n= 82), neuroendocrine tumors (n=16), intraductal papillary mucinous neoplasms (IPMN) and

other less aggressive (pre)malignant conditions (n=10), inflammation (n=5), ampulloma/small bowel polyposis (n=5) and others (n=6). The group of others contained (metastasis of) non gastrointestinal tumor (n=3), small bowel carcinoma (n=2) and gastrointestinal stromal tumor (GIST) (n=1).

Pancreaticoduodenectomy was performed in 100 patients, total pancreatectomy in 10 patients, pancreatic body and tail resection in 9 patients of whom 3 also got a splenectomy, pancreatic tail resection in 4 and pancreatic body resection in one patient.

Thirty-eight of 124 patients (31%) developed steatosis at at least one time point in the follow-up period.

There is no significant difference in age, sex, weight and BMI between patients who develop NAFLD and patients who do not. The mean age in the NAFLD group is 60.6 and in the non-NAFLD group 63.7 years. There is also no significant difference in distribution of benign and malignant diseases, type of surgery or histopathological diagnosis (Table 2). There is a significant difference between both groups in preoperative value of ALT.

Postoperatively, there is a significant difference in the number of patients with diarrhoea (11 with/0 without diarrhoea in the NAFLD group vs 17 with/7 without in the non-NAFLD group, $p=0.045$) and the number of patients taking pancreatic enzyme supplementation (31 with/3 without in the NAFLD group vs 45 with/25 without in the non-NAFLD group, $p=0.004$). There is no significant difference in other postoperative variables (Table 2).

Prevalence and evolution over time

Out of thirty-eight patients that developed liver steatosis in the 2 years following surgery, twenty-eight only did so at one point in time. Thirteen patients had at least one radiological follow-up evaluation showing no more steatosis (Fig. 2).

Steatosis is seen more often early after surgery with a decreasing prevalence over time. Two months after surgery we report a prevalence of steatosis of 21.0% (13 of 62 patients with available data). After 6 months we note a prevalence of 28.6% (22/77), and after 1 and 2 years, we note steatosis in 16.4% (10/61) and 20.8% (10/48) patients, respectively.

Risk factors for the development of MAFLD after pancreatic surgery

Univariate analysis identified an association of the following variables with the development of NAFLD ($p<0.05$): preoperative ALT, preoperative AST, preoperative AST/ALT ratio, the use of pancreatic enzyme supplementation and relative weight loss 2 years postoperatively (Table 3).

In multivariate analysis using these five variables with $p<0.05$ and BMI, no significant independent risk factors for MAFLD were withheld.

Table 1. — Patient Demographics

Characteristics	Value
Age; Mean (range)	63 (26-86)
Sex ; M/F (%)	67/57 (54/46)
Histopathological diagnosis ; n (%)	
Adenocarcinoma	82 (66)
Pancreatic adenocarcinoma	66
Ampullary carcinoma	11
Bile duct carcinoma	5
Neuroendocrine tumor	16 (13)
IPMN and other PCN	10 (8)
IPMN	6
Solid pseudopapillary tumor	1
Serous cystadenoma	3
Inflammation	5 (4)
Ampulloma/ small bowel polyposis	5 (4)
Ampulloma	4
Small bowel polyposis	1
Others	6 (5)
(Metastasis of) other non-gastrointestinal tumor	3
Small bowel carcinoma	2
GIST	1
Operative procedure; n(%)	
Whipple	100 (81)
Total pancreatectomy	10 (8)
Pancreatic body and tail resection	9 (7)
Pancreatic tail resection	4 (3)
Pancreatic body resection	1 (1)
IPMN: Intraductal papillary mucinous neoplasm; PCN: Pancreatic cystic neoplasm.	

Table 2. — Preoperative and postoperative characteristics

	NAFLD	No NAFLD	Number	p-value
PREOPERATIVE				
Age (year)*	60.6 (± 12.91)	63.7 (± 14.47)	124	0.173
Sex (male)	19 (50.0%)	48 (55.8%)	124	0.564
Weight (kg)**	74.0 (61.4-81.0)	68.8 (64.0-77.5)	107	0.438
BMI **	25.0 (21.1-29.1)	24.7 (22.7-27.2)	105	0.348
CA 19.9 (U/ml)**	110 (63-231)	51 (15-204)	68	0.114
ALT pre-op (U/L)**	93 (31-347)	38 (20-130)	111	0.016
AST pre-op (U/L)**	45 (23-129)	20 (20-63)	112	0.089
Pre-op AST/ALT ratio**	0.60 (0.41-0.87)	0.9 (0.59-1.06)	110	0.003
Alb pre-op (g/L)*	22.0 (±3.80)	38.5 (±7.65)	69	0.059
Malignant/benign	35/3	69/17	124	0.117
Diagnosis			124	0.307
Pancreatic adenocarcinoma	29 (76%)	53 (62%)		
IPMN	2 (5%)	8 (9%)		
NET	3 (8%)	13 (15%)		
Inflammation	1 (3%)	4 (5%)		
Ampulloma	0 (0%)	5 (6%)		
Others	3 (8%)	3 (3%)		
Type of surgery			124	0.397
Whipple	31 (82%)	69 (80%)		
Total pancreatectomy	3 (8%)	7 (8%)		
Pancreatic body and tail resection	3 (8%)	6 (7%)		
Pancreatic tail resection	0 (0%)	4 (5%)		
Pancreatic body resection	1 (3%)	0 (0%)		
POSTOPERATIVE				
ALT 2m (U/L)**	48 (31-71)	33 (19-52)	73	0.079
ALT 6m (U/L)**	43 (29-60)	40 (27-53)	60	0.433
ALT 1y (U/L)**	30 (24-38)	37 (26-62)	47	0.128
ALT 2y (U/L)**	45 (28-64)	30 (22-38)	38	0.071
AST 2m (U/L)**	43 (28-69)	26 (19-40)	75	0.004
AST 6m (U/L)**	37 (28-44)	34 (24-47)	59	0.405
AST 1y (U/L)**	30 (23-41)	32 (23-43)	47	0.869
AST 2y (U/L)**	37 (18-42)	30 (23-42)	39	0.701
Alb 2m (g/L)*	33.2 (± 7.83)	34.1 (± 7.73)	33	0.743
Alb 6m (g/L)*	37.3 (± 10.48)	36.3 (± 10.33)	20	0.456
Alb 1y (g/L)*	34.6 (± 9.05)	36.1 (± 9.79)	22	0.711
Alb 2y (g/L)*	34.8 (± 13.3)	40.6 (± 7.72)	11	0.374
Diarrhea	11/0	17/7	35	0.045
Pancreatic enzymes	31/3	45/25	104	0.004
Pancreatic exocrine insufficiency (MTG) (pos/neg)	9/0	15/3	27	0.194
Chemotherapy post-op (yes/no)	17/21	25/61	124	0.089
Weight 2m (kg)**	64.1 (52.0-73.5)	64.0 (60.0-74.0)	28	0.357
Weight 6m (kg)**	60.0 (53.0-75.5)	62.5 (55.8-73.3)	37	0.475
Weight 1y (kg)**	60.5 (52.5-72.3)	66.0 (59.8-76.8)	30	0.210
Weight 2y (kg)**	53.0 (45.5-79.0)	72.5 (61.2-84.5)	30	0.061
10% weight loss ever (yes/no)	13/13	22/31	79	0.318
RPV (cm ³)**	40.0 (18.5-49.1)	40.0 (22.4-62.0)	109	0.487
* not normally distributed with median (interquartile range); ** normally distributed with mean (± standard deviation). NAFLD =nonalcoholic fatty liver disease, ALT=alanine aminotransferase, AST=aspartate aminotransferase, Alb=albumin, AIPM=intraductal papillary mucinous neoplasm, NET=neuroendocrine tumor, MTG=ixed triglyceride breath test, RPV=remnant pancreatic volume.				

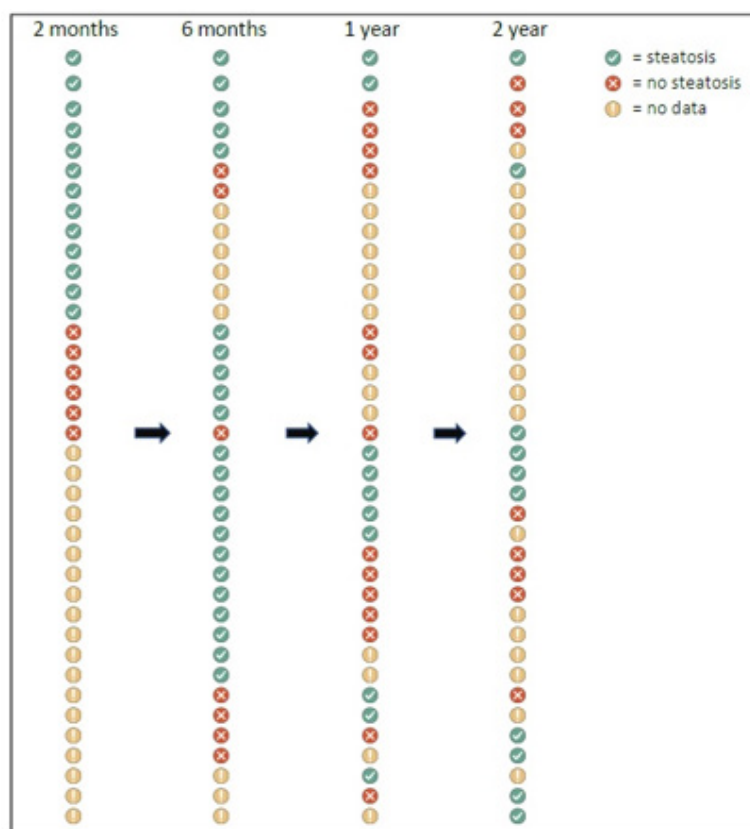


Fig. 2. — Time of onset of liver steatosis

Pancreatic exocrine insufficiency

PEI as shown by the ^{13}C -labeled mixed triglyceride breath test was not associated with the development of MAFLD after pancreatic surgery in univariate analysis. All patients in the group with MAFLD who performed a breath test, had PEI (<23% of ingested radioactive labelled carbon detected in exhaled air). As stated before, tests to diagnose PEI were not performed on a routine basis but only in symptomatic patients. Since we had no cases with normal results, it was not possible to perform a logistic regression. Whether pancreatic enzyme supplementation was taken or not, however, could be identified in 104/124 patients and this was clearly associated with the development of steatosis ($p=0.008$).

Discussion

We report an incidence of MAFLD after pancreatic surgery of 31%. This is comparable with what was found in other studies, mostly performed in southeast Asia (incidence between 7.8 and 55%) (4, 7-25). This wide range in literature can partially be explained by the differences in timing of evaluation, in the duration of follow-up and techniques or definitions used to diagnose MAFLD. There is no consensus in the existing literature about the time of onset of liver steatosis after pancreatic surgery nor about the ideal time for screening (7-25). In our study, the prevalence varies depending on the timing

of evaluation, between 16.4% at 1 year and 28.6% at 6 months.

The development of MAFLD after pancreatic surgery has not yet been studied extensively in Western populations. A Dutch study looked into MAFLD after pancreatic surgery for neuroendocrine tumours and reported an incidence of 20% over a median follow-up period of 54 months (13). The lower number may be due to the fact that in this study enucleation was considered, a surgical technique which spares more pancreatic tissue. A study performed in the USA examined MAFLD after pancreatic surgery by using a liver-to-muscle ratio on CT-images with IV contrast. They demonstrated a significant decrease in ratio after surgery, only in men. This definition of steatosis using liver/muscle-ratio has not been validated (10). Another USA-based study with no strict definition for MAFLD recorded an incidence of 14.3%, correlating with female gender, higher preoperative BMI, and shorter length of hospital stay (19). A fourth, Swedish study found an incidence of MAFLD of 17% during the first year after surgery (including PD, DP and total pancreatectomy). Here again, another definition is used to describe steatosis: a decrease of 20 HU in unenhanced scans and a decrease from 10 to 30 HU in the portal phase in contrast-enhanced scans. They are the only group using this definition (18).

Our definition using an absolute value < 40 HU, a decrease of 10 HU or a L/S-ratio of less than 0.9 in unenhanced CT scans and ≥ 20 HU in the venous phase

Table 3. — Univariate analysis

	OR	95% CI	p-value
Age (year)	0.977	(0.946-1.010)	0.174
Sex (male)	0.792	(0.368-1.702)	0.550
Weight (kg)	1.014	(0.986-1.043)	0.317
BMI	1.065	(0.965-1.174)	0.209
CA 19.9 (U/ml)	1.000	(0.999-1.001)	0.439
ALT pre op (U/L)	1.003	(1.001-1.005)	0.011
AST pre-op (U/L)	1.005	(1.000-1.010)	0.043
pre op AST/ALT ratio	0.181	(0.049-0.667)	0.010
Alb pre-op (g/L)	1.095	(0.993-1.207)	0.068
Malign/ benign	0.348	(0.095-1.268)	0.109
Pancreatic adenocarcinoma	2.006	(0.845-4.765)	0.115
Whipplel	1.091	(0.411-2.898)	0.861
ALT 2m (U/L)	1.005	(0.993-1.017)	0.449
ALT 6m (U/L)	1.012	(0.990-1.035)	0.279
ALT 1y (U/L)	0.980	(0.951-1.009)	0.178
ALT 2y (U/L)	1.010	(0.989-1.032)	0.355
AST 2m (U/L)	1.011	(0.997-1.025)	0.110
AST 6m (U/L)	1.008	(0.982-1.035)	0.544
AST 1y (U/L)	0.998	(0.984-1.012)	0.764
AST 2y (U/L)	1.002	(0.972-1.033)	0.900
Alb 2m (g/L)	0.984	(0.895-1.081)	0.734
Alb 6m (g/L)	1.011	(0.924-1.105)	0.815
Alb 1y (g/L)	1.020	(0.925-1.125)	0.695
Alb 2y (g/L)	0.936	(0.816-1.075)	0.349
Pancreatic enzymes (yes/no)	5.740	(1.593-20.688)	0.008
Chemotherapy post-op (yes/no)	1.975	(0.896-4.356)	0.092
Weight 2m (kg)	0.946	(0.868-1.030)	0.203
Δ kg 2m (kg)	0.981	(0.810-1.188)	0.844
Weight 6m (kg)	0.981	(0.926-1.039)	0.504
Δ kg 6m (kg)	0.996	(0.878-1.129)	0.947
Weight 1y (kg)	0.97	(0.920-1.024)	0.273
Δ kg 1y (kg)	0.948	(0.870-1.032)	0.215
Weight 2y (kg)	0.957	(0.910-1.007)	0.091
Δ kg 2y (kg)	0.859	(0.744-0.990)	0.036
RPV (cm ³)	0.991	(0.974-1.008)	0.289

ALT=alanine aminotransferase, AST=aspartate aminotransferase, Δ kg=difference between pre-operative weight and post-operative weight on stated moment, RPV=remnant pancreatic volume

in contrast-enhanced scans has been validated (11,25-28).

As in other cohorts, steatosis in our study is seen more often early after surgery with a decreasing prevalence over time. We generally saw an improvement over time and none of our patients showed a deteriorating evolution. It is important to mention, however, that case reports with complications and even fatal evolution of steatosis after pancreaticoduodenectomy have been published (35-37). Two months after surgery we report a prevalence of steatosis of 21.0%, rising to almost 29% at 6 months. A median time to detection of 5-6 months

was also described in the studies of Sato and Tanaka (6, 12). Steatosis occurred in 16.4% at 1 year in our study, comparable to what was published by Fujii, et al.: 12% at 1 month after surgery, 21% at 6 months and 15% at 1 year (17). Others also suggest that steatosis mainly occurs in the first six months and gradually decreases. In the Swedish trial for instance, steatosis after pancreatic surgery was seen as a self-limiting process (18).

The follow-up period in our study was longer and we found a higher prevalence of steatosis of 20.8 % at 2 years, challenging the idea of a self-limiting process.

Despite the frequent observation of MAFLD after pancreatic surgery, the pathogenesis has not yet been unravelled. It has often been suggested that steatohepatitis is caused by the administration of chemotherapy. However, MAFLD is also observed after surgery for benign tumors – in 23,9% of patients as described in a recent meta-analysis (38). Also, 42 (33% of) patients in our cohort received chemotherapy and this was not found to be a risk factor for the development of MAFLD.

The link with PEI has been suggested in the past and seems to be confirmed in our study (4,12). Unfortunately, diagnostic tests for PEI were not performed on a routine basis. The absence/presence of diarrhoea and steatorrhea is not routinely mentioned in all files. We therefore used the prescription of pancreatic enzyme replacement therapy (PERT) as a surrogate marker for PEI. Pancreatic enzyme supplements were not started on a routine basis postoperatively, except after total pancreatectomy. Enzyme supplementation is only initiated in case of a clinical suspicion of steatorrhea. The use of pancreatic enzymes shows a strong correlation with the presence of MAFLD ($p=0.008$). Patients using pancreatic enzymes were 5.74 more likely to have a diagnosis of liver steatosis at one of the established moments for evaluation in our study. We therefore hypothesize that the development of MAFLD is caused by malabsorption and recovers over time with adequate enzyme supplementation. Several authors stated before that the administration of pancreatic enzymes gives a recovery of steatosis, albeit not in all patients (12,13,15,39).

There was a difference in evolution of weight after surgery between the two groups: the steatosis group continued to lose weight, the non-MAFLD group regained weight. The average weight at 2 years in the MAFLD group was 60.3 ± 21.9 kg (median 53.0 kg) compared to 71.9 ± 13.6 kg (median 72.5 kg) in the non-MAFLD group, leading to a statistically significant association between relative weight loss at 2 years and development of steatosis ($p=0.036$). Again, this seems to be linked to the administration of pancreatic enzymes leading to an improvement in the nutritional status of the patient and an increase in weight. The link between postoperative development of steatosis and maldigestion/malabsorption because of PEI with continuing weight loss has been suggested before (40).

All our patients who underwent PD had a pancreaticojejunostomy. Nowadays, PD can be performed either with a pancreaticogastrostomy or a pancreaticojejunostomy. It is important to keep in mind that PEI has a higher prevalence with pancreaticogastrostomy (41).

Follow-up in our study was longer than average and we found some new cases of steatosis after 2 years. Future studies should include a longer follow-up in order to check whether steatosis can also only occur 2 years or later after pancreatic surgery and what the underlying risks may be.

This study has several limitations: first, the retrospective character of the analysis, with a high number of missing data leads to a lack of power: the lack of standardisation in postoperative follow-up, partly explained by the differences in histopathological diagnoses, surgical procedures and adjuvant treatments, creates a lot of missing clinical and radiological data. Also, we could not investigate the impact of performing a pancreaticogastrostomy or a pancreaticojejunostomy in this monocentric cohort. However, this historical cohort can provide important insights: currently both combination chemotherapy and PERT are given to all patients with a malignant diagnosis, making it hard to investigate the contribution of either one of those therapies to the development of steatosis.

Secondly, the use of imaging techniques for the detection of MAFLD is not the golden standard. However, follow-up with consecutive liver biopsies in a prospective trial does not seem feasible due to ethical reasons. In our study, contrast enhanced CT-images in the venous phase were used to diagnose steatosis according to a validated method, but other methods have been used by other investigators, hampering direct comparison. Standardization of scanning protocols and a consensus on the ideal imaging method are necessary if we want to draw solid conclusions. Biomarker-based screening tools like the Liver index (FLI) and Hepatic Steatosis Index (HSI) may be added as screening test for MAFLD (42,43).

Conclusion

MAFLD was found in 31% of patients that underwent extensive pancreatic surgery in a historical large Belgian cohort in a tertiary referral centre. The evolution over time and the association with the intake of pancreatic enzyme supplements in our study support a relationship with maldigestion/malabsorption. The prognosis of pancreatic cancer patients has increased since the introduction of adjuvant treatment with folfinirox. It is therefore important to also focus on supportive therapy, improving quality of life and preventing later secondary problems, such as MAFLD.

A long-term prospective study with a larger number of patients, standardized follow-up points and investigations, can help to better identify the risk of developing steatosis, the pathophysiology and possible contributing factors. A better follow-up of nutritional interventions, including dosing of pancreatic enzyme supplements, evolution of weight and steatosis is necessary.

COI Karen Geboes

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