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DE DOCTEUR EN MÉDECINE

Influence de la sarcopénie préopératoire sur la variation de densité hépatique après duodénopancréatectomie céphalique pour adénocarcinome du pancréas

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Lexique :

- ASA : Amercian Society of Anesthesiologists
- BMI : Body Mass Index
- CCI : Charlson Comorbidity Index
- CI : Confidence Interval
- COPD : Chronic Obstructive Pulmonary Disease
- CT : Computed Tomography
- DPC : Duodénopancréatectomie Céphalique
- EWGSOP : European Working Group on Sarcopenia in Older People
- HAS : Haute Autorité de santé
- HU : Hounsfield Units
- IMC : Indice de Masse Corporelle
- INSEE : Institut National de Statistique et des Etudes Economiques
- LOS : Length Of Stay
- MRI : Magnetic Resonance Imaging
- NAFLD : Non Alcoholic Fatty Liver Disease
- NASH : Non Alcoholic Steato Hepatitis
- OR : Odds - Ratio
- PD : Pancreaticoduodenectomy
- PDAC : Pancreatic Ductal Adenocarcinoma
- PF : Pancreatic Fistula
- ROI : Region Of Interest
- SMI : Skeletal Muscle Index

Introduction :

La stéatose hépatique non alcoolique (NAFLD pour *Non Alcoholic Fatty Liver Disease*) représente aujourd'hui la première cause d'hépatopathie chronique, avec une prévalence estimée à 18,2 % en France (1). Il s'agit d'un terme général pour regrouper les maladies stéatosiques du foie non liées à la consommation d'alcool. Ces dernières pouvant aller de la simple stéatose à la *Non Alcoholic Steato Hepatitis* (NASH), se distinguant par son caractère inflammatoire.

Les patients atteints de NAFLD sont plus à risque de mortalité, notamment de causes cardiovasculaires (2), mais également de progression vers des maladies hépatiques plus agressives comme la NASH puis au stade le plus évolué, vers la cirrhose et le carcinome hépato-cellulaire. Il s'agit donc d'un enjeu de santé publique majeur justifiant une nécessité d'amélioration de nos pratiques.

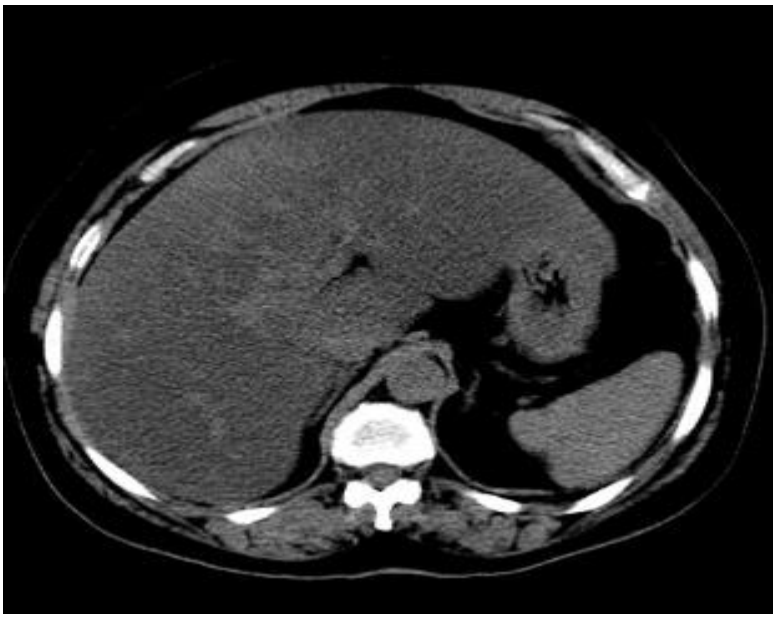

Figure 1 : Stéatose hépatique sur une coupe de scanner non injecté (hypodensité hépatique marquée)

Il est désormais démontré dans la littérature que la survenue de stéatose hépatique peut-être causée ou accélérée par une chirurgie du pancréas, et notamment après duodénopancréatectomie céphalique (DPC) (3) (4) (5) (6). Cette dernière consiste en une section de la tête du pancréas et du cadre duodénal en monobloc, puis une reconstruction dans le même temps avec triple anastomose : pancréatico-jéjunale (ou pancréatico-gastrique), bilio-digestive et gastro-jéjunale (figure 2). Elle est actuellement la seule intervention à visée curative pour les cancers de la tête du pancréas.

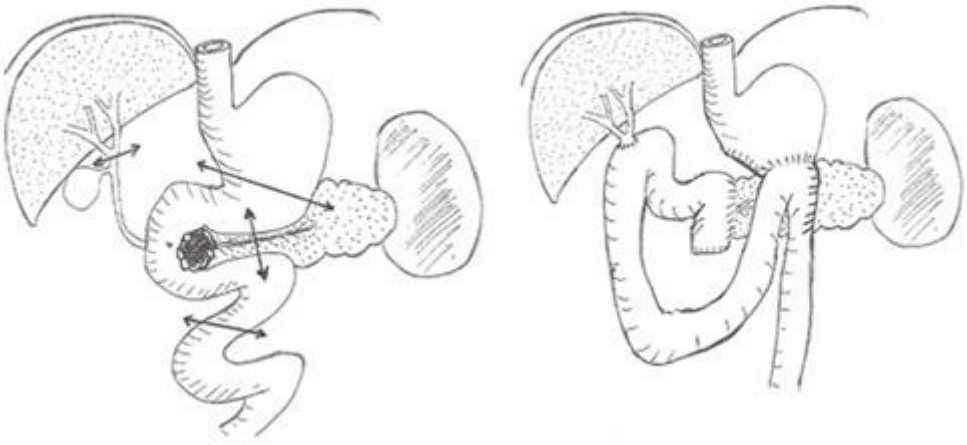

Figure 2 : Montage chirurgical d'une duodénopancréatectomie céphalique (reconstruction selon CHILD) (7)

En effet, le cancer du pancréas gagne du terrain avec une incidence en constante augmentation : 1,5 % de plus par an pour les hommes et 2,1 % pour les femmes, depuis 2010 en France (8). Il représente, en 2022, 15 895 nouveaux cas et 14 669 décès et représente par conséquent la quatrième cause de décès par cancer en

France (9) et la sixième dans le monde (figure 3). L'incidence de la stéatose hépatique après chirurgie du pancréas est variable selon les études mais elle se situe autour de 25 % (10). Certains travaux ont mis en évidence plusieurs facteurs favorisants comme l'Indice de Masse Corporelle (IMC), le sexe, l'insuffisance pancréatique exocrine induite ou encore la consommation d'insuline post opératoire (3) (11) (12).

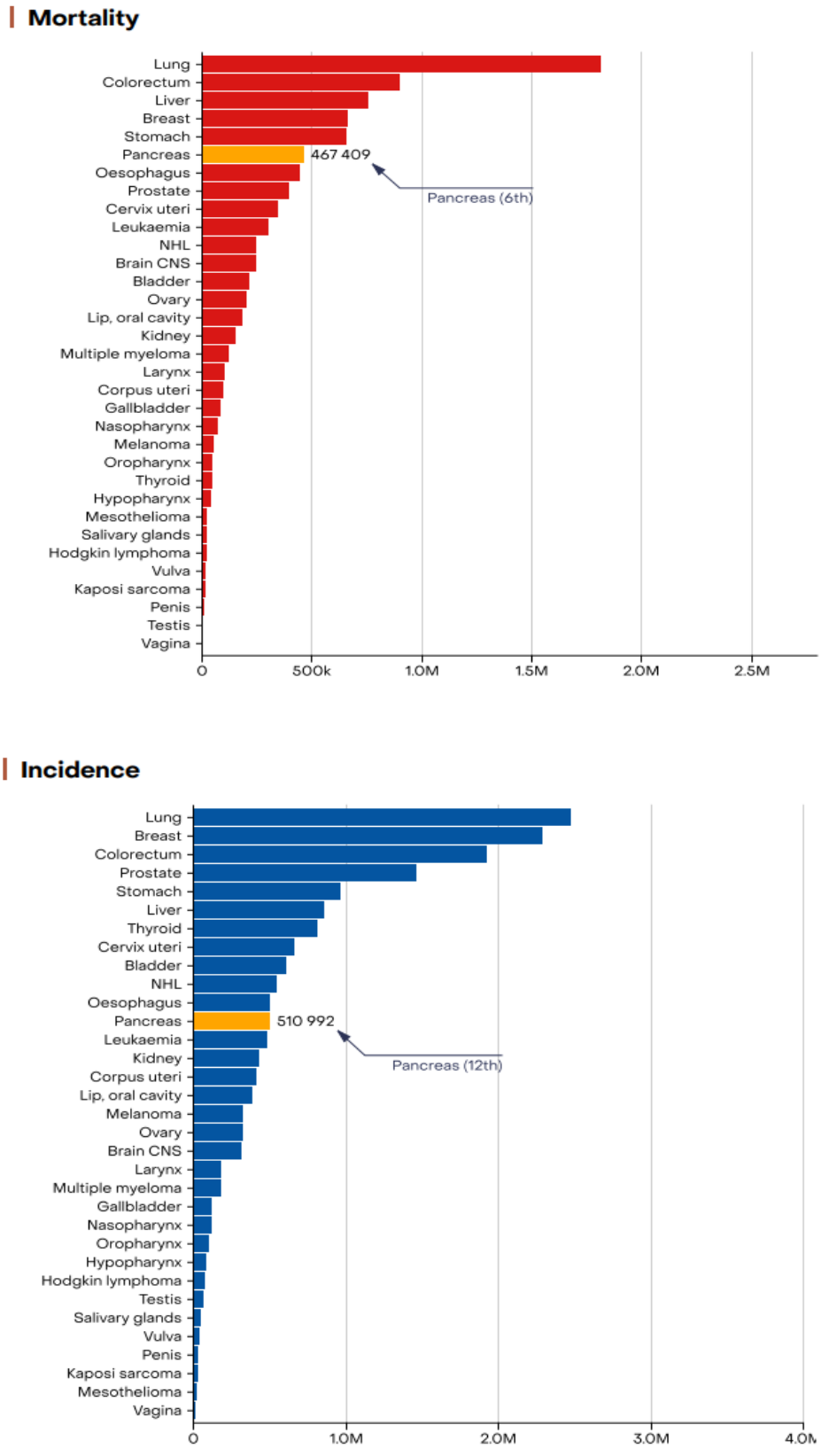

Figure 3 : Incidence et mortalité du cancer du pancréas dans le monde, GLOBOSCAN fact sheet (13)

Les explications physiopathologiques de l'apparition de cette stéatose après chirurgie pancréatique sont encore peu précises mais il s'agit d'une intrication de phénomènes, combinant insuffisance pancréatique endocrine et exocrine, inflammation et stress oxydatif (14) (15) (16) . Il existe également une altération du métabolisme lipidique entrainant une accumulation intrahépatique de lipides (17).

Par ailleurs, la sarcopénie, définie par l'*European Working Group on Sarcopenia in Older People* (EWGSOP) comme « une perte progressive et généralisée de la masse et de la force musculaire squelettique entraînant un risque d'effets indésirables tels qu'une incapacité physique, une mauvaise qualité de vie ainsi qu'une mortalité accrue » (18), est fréquente chez les patients atteints de cancer. Certaines études estiment une prévalence de la sarcopénie chez les patients atteints de cancer du pancréas entre 40 et 80 %. *El Amrani et al.* ont montré que l'incidence de la sarcopénie chez les patients opérés de pancréatectomie était d'environ 50 %. Cette sarcopénie est associée à une moins bonne survie ainsi qu'à une augmentation de l'incidence de complications postopératoires dans plusieurs cancers, y compris celui du pancréas (19) (20) (21) (22) (23).

Une relation entre sarcopénie et stéatose hépatique a été mise en avant dans plusieurs études avec un risque de NAFLD chez les patients sarcopéniques pouvant aller jusqu'à 5 fois celui des non sarcopéniques (14) (15) (16). En effet, ces deux phénomènes partagent certains mécanismes physiopathologiques comme la résistance à l'insuline ou le déficit en vitamine D (figure 4). Cette relation bien que

désormais démontrée, reste ambivalente raison pour laquelle il est difficile de se prononcer quant au rôle propre de l'une sur l'autre (24).

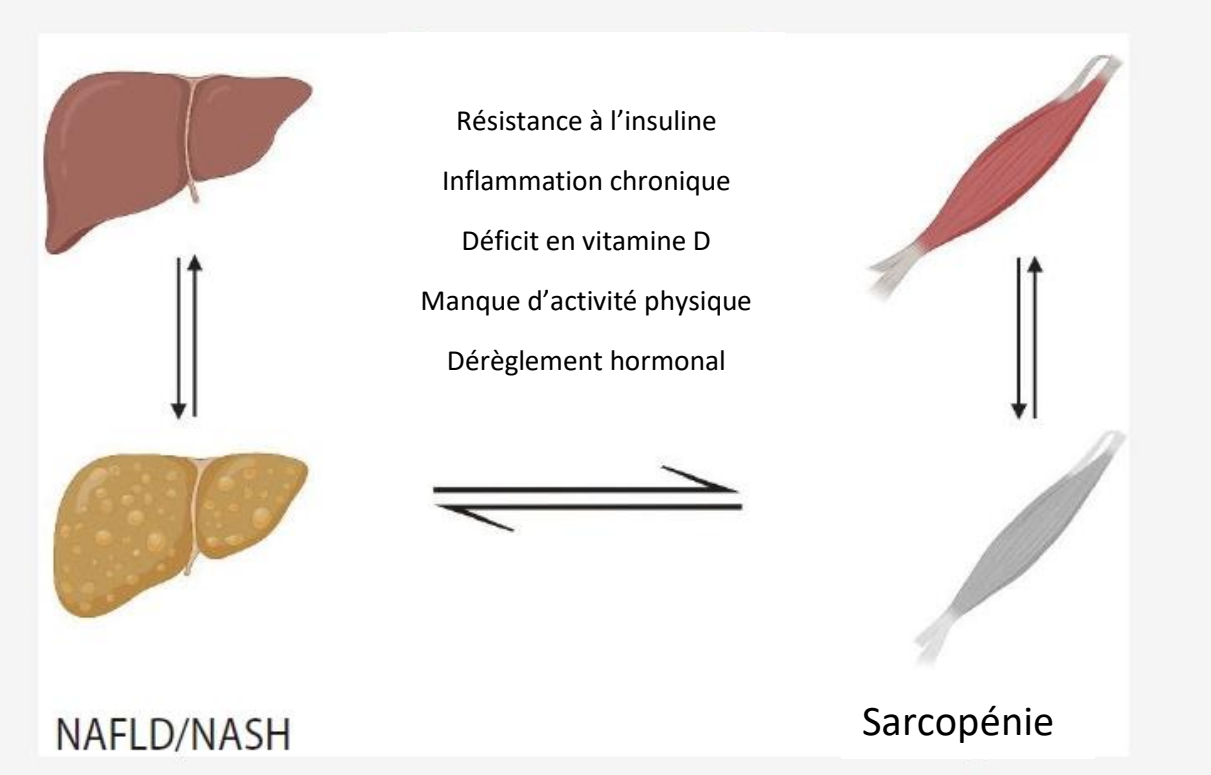

Figure 4 : Eléments physiologiques communs entre sarcopénie et NAFLD (16)

Nous nous sommes interrogés sur les implications que pourraient avoir une telle relation sur la prise en charge des patients opérés de cancer du pancréas. Etant donné l'amélioration constante des techniques chirurgicales, de la prise en charge post opératoire immédiate et du pronostic du cancer du pancréas (25), la question de la morbidité à long terme de ces chirurgies lourdes est légitime.

A la lumière de ces différentes observations, il n'existe à notre connaissance aucune étude analysant la corrélation entre sarcopénie pré opératoire et stéatose hépatique post opératoire dans le cadre d'une chirurgie du pancréas, et plus particulièrement de DPC.

Comprendre l’impact de la sarcopénie préopératoire sur la stéatose hépatique post-opératoire pourrait permettre de mieux identifier les patients à risque et de développer des stratégies préventives ciblées.

Nous nous sommes donc posé la question de l’influence de la sarcopénie pré opératoire sur la survenue de la stéatose hépatique après DPC pour adénocarcinome du pancréas.

ABSTRACT

Introduction: The relation between sarcopenia and hepatic steatosis is well established. However, to our knowledge, no study has explored this relationship in patients undergoing pancreatic surgery. The aim of this study is to determine whether pre-operative sarcopenia has an impact on hepatic density attenuation after pancreaticoduodenectomy (PD) for pancreatic ductal adenocarcinoma (PDAC).

Methods: All patients who underwent PD in Lille University Hospital between 2011 and 2020 were included. Pre-operative sarcopenia was assessed using Skeletal Muscle Index (SMI) measurements, cut-offs for the sarcopenic group were 38.9 cm^2/m^2 for women and 55.4 cm^2/m^2 for men. Hepatic steatosis was defined as mean hepatic density < 40 Hounsfield Units (HU). We measured liver density on pre- and post-operative Computed Tomography (CT) scans at 1-6 months and after 6 months. Liver density attenuation was compared between sarcopenic and non-sarcopenic groups.

Results: One hundred and nine patients were included. Sixty-six patients (61 %) were diagnosed with pre-operative sarcopenia and thirty-nine (36 %) presented post-operative hepatic steatosis within first 6 months. No significant difference was shown between the two groups in terms of liver density attenuation before and after surgery (p = 0.97). In the multivariate analysis, lower age (OR: 0.57, CI (0.36-0.89), p = 0.01) and higher Body Mass Index (BMI) (OR: 1.61, CI (1.02-2.57), p = 0.04) were risk factors for hepatic steatosis after PD for PDAC. Pre-operative sarcopenia and post-operative hepatic steatosis within the first 6 months had no impact on 3 years survival.

Conclusion: Pre-operative sarcopenia had no significant impact on liver density attenuation before and after surgery. Lower age and higher BMI are associated with

post-PD hepatic steatosis in patients with PDAC. Prospective studies should be considered to clarify these results.

Introduction:

Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic hepatopathy in France, with a prevalence of approximately 18 %. It can lead to Non-alcoholic steatohepatitis (NASH), characterized by inflammation, and in extreme cases to cirrhosis and hepatocarcinoma. Given its prevalence and complications, NAFLD represents a major public health concern and warrants attention for prevention and management.

Pancreatic ductal adenocarcinoma (PDAC) is a growing concern, with incidence rates raising by 1.5 % for men and 2.1% for women each year in France (8). It is now the 6th cancer-related cause of death worldwide, despite being the 12th most common cancer globally (13).

Pancreaticoduodenectomy (PD) remains the only curative surgical option for PDAC of the pancreatic head. PD has been associated with *de novo* post-operative NAFLD, in part due to exocrine and endocrine pancreatic insufficiency (3) (4) (5) (6). A higher pre-operative Body Mass Index (BMI) has also been shown to be a risk factor for post-operative hepatic steatosis (3) (12).

The European Working Group on Sarcopenia in Older People (EWGSOP) has defined sarcopenia as a “progressive and general loss of skeletal muscle mass and strength, causing adverse effects such as a poor quality of life, physical insufficiency and higher mortality”. Sarcopenia is highly prevalent amongst oncology patients (18).

Although numerous studies have demonstrated the link between sarcopenia and NAFLD, primarily through mechanisms such as chronic systemic inflammation or insulin deficiency, the causal relationship between the two remains uncertain (14) (15) (16).

To our knowledge, this is the first study focusing on this relationship in patients undergoing PD for PDAC. The primary objective of this study is to determine whether pre-operative sarcopenia had an impact on liver density attenuation within first 6 months after PD for PDAC. The secondary objectives were, first, to identify pre-operative risk factors for hepatic steatosis and, second, to evaluate the impact of sarcopenia and liver steatosis on survival after PD for PDAC.

METHODS

Study Population

All patients who underwent PD for PDAC between 2011 and 2020 in Lille University Hospital were retrospectively included. Inclusion criteria included: age > 18, open approach, and curative resection. Exclusion criteria consisted in: PD for other diagnosis than PDAC, other pancreatic resections, palliative derivation without resection, age < 18 years, and the lack of data. The study complied with French National Health guidelines on research involving human subjects.

Data Collection

Preoperative clinical data were collected including age, sex, American Society of Anesthesiologists (ASA) score, comorbidities according to Charlson Comorbidity Index (CCI) (stratified into two groups (CCI = 0 – 2 and CCI ≥ 3), biliary drainage before surgery and nutritional markers (albumin, pre-albumin, preoperative weight, weight loss between healthy weight and preoperative weight, undernutrition grade). Complications at 3 months postoperatively were collected and rated according to the Clavien – Dindo classification (26) with severe complications defined by a grade ≥ 3. Postoperative pancreatic fistula was defined according to the International Study

Group of Pancreatic Fistula (ISGPF) and classified into grades B or C (27). Bleeding and postoperative gastroparesis were graded according to the international consensus (28), and length of stay (LOS) was also assessed.

Malnutrition was assessed according to the *Haute Autorité de Santé* (HAS) criteria (29). Operative mortality was defined as death within 90 days of PD. The living status of all patients was verified using *the Institut National de Statistiques et des Etudes Economiques* (INSEE) database (30).

Outcome Measurements

Sarcopenia was measured using the Skeletal Muscle Index (SMI), which consists of the entire muscle surface on an L2-L3 Computed Tomography (CT) scan cross-section (figure 6), in cm^2, divided by the square height of the patient in m^2. To define sarcopenia, we used the cut-offs reported by *Mourtzakis et al.* of 38.9 cm^2/m^2 for women and 55.4 cm^2/m^2 for men (31).

Hepatic steatosis was measured using a mean of 5 Regions of Interest (ROI) in the liver parenchyma, on a non-injected CT scan section (figure 7). A measure below the cut-off of 40 Hounsfield Units (HU) was used to define hepatic steatosis (32).

Preoperative SMI and hepatic steatosis were assessed on the most recent preoperative CT scan using the MYRIAN software (33) and were measured within 6 months after PD and after 6 months.

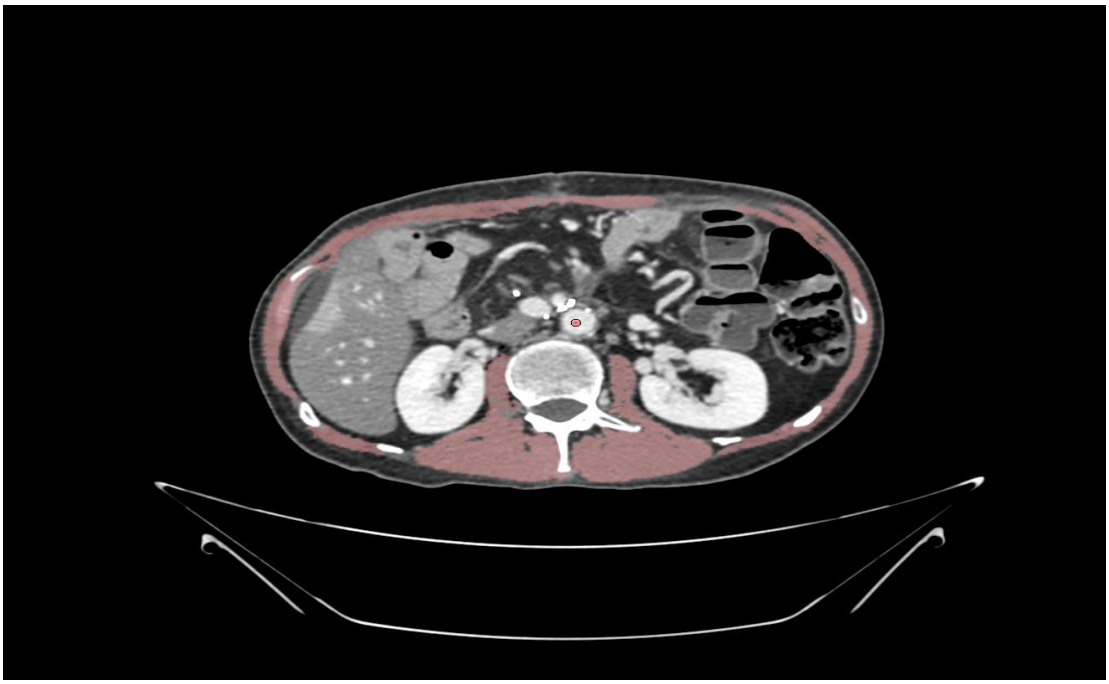

Figure 5: Total muscular surface on a L2-L3 CT section

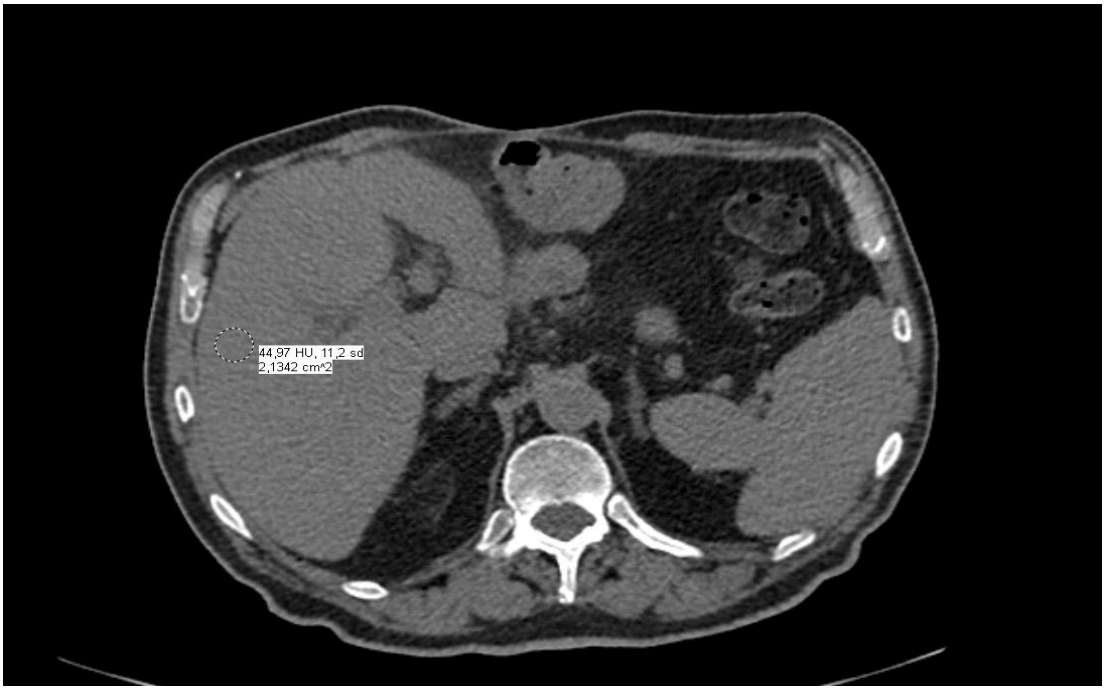

Figure 6: Example of an ROI in the liver parenchyma on a non-injected CT section

Statistical Analysis

Qualitative variables were described in terms of frequencies and percentages. Quantitative variables were described by the mean and standard deviation or by the median and interquartile range in cases of non-Gaussian distribution. The normality of the distributions was graphically checked and using the Shapiro-Wilk test. Patients survival was estimated using the Kaplan-Meier method. Patients characteristics and preoperative data were compared between patients with sarcopenia and those without using the Chi-square test (or Fisher's exact test when the expected count was < 5) for qualitative variables, and using the Student's t-test (or Mann-Whitney U test in cases of non-Gaussian distribution) for quantitative variables. The association between sarcopenia status and the change in liver density 6 months postoperatively was analysed using a mixed linear model (covariance pattern, with a compound symmetry covariance matrix) on liver density values, including a time effect in the model (6 months vs. preoperative), sarcopenia status, and the interaction term between sarcopenia status and time The mean difference in liver density variation 6 months postoperatively according to sarcopenia status was estimated from the interaction term. The model was adjusted for sex and preoperative liver density (including an interaction term with time). The normality of the model's residuals was verified. The association between sarcopenia status and different postoperative criteria was assessed using a logistic regression model for binary outcomes, a one-way analysis of variance (ANOVA) for quantitative outcomes, and a Cox proportional hazards model for survival. Effect sizes and their 95% confidence intervals were derived from the models (odds ratios (OR) for binary outcomes, mean differences for quantitative outcomes, and hazard ratios for survival). A sensitivity analysis adjusted for sex, CCI (categorized: 0+1+2 *vs*. 3+4 *vs*. >4), age, and BMI was performed for the primary

outcome of liver density. The identification of risk factors for hepatic steatosis within 6 months postoperatively was conducted using univariate and multivariate logistic regression models. Odds ratios and their 95 % confidence intervals were derived from the models as a measure of effect size. Factors with a p-value < 0.20 in the univariate analysis were included in the multivariate logistic regression model. The association between hepatic steatosis within 6 months postoperatively and patient survival was assessed using a Cox proportional hazards model, with the origin date set as the date 6 months postoperatively (landmark at 6 months). The association between preoperative SMI and patient survival was also assessed using a Cox proportional hazards model. Hazard ratios and their 95 % confidence intervals (CI) were derived from both models as a measure of effect size. No statistical comparison was made for qualitative variables with a sample size < 8. The significance level was set at 5 %. Statistical analyses were performed using the SAS software (SAS Institute version 9.4).

RESULTS

A total of 185 patients who underwent PD for PDAC were identified. After exclusion of patients with missing data (n = 71), unclear pathological diagnosis (n = 2), extended resection (n = 2) and another tumor localization (n = 1), 109 patients were included.

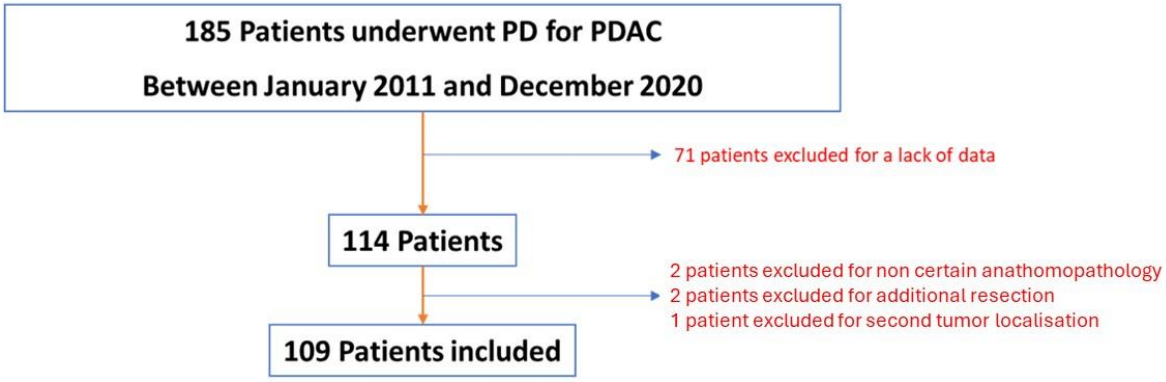

Figure 7: Flowchart of the study

Patient Characteristics

Demographic data are detailed in the table 1. Mean age of patients was 64.5 years with a majority being male. With regards to comorbidities, sixty patients (55 %) had a CCI ≥ 3, and 72 patients (69 %) had pre-operative malnutrition, including 42 % having moderate malnutrition. Overall, 61 % of patients had sarcopenia and the mean pre-operative SMI was 46.48 cm^2/m^2. Hepatic steatosis was present in 36 % of patients at 1 – 6 months

Table 1 : Patients characteristics

		All patients	Sarcopenia		p-value
			No (n = 43)	Yes (n = 66)	
Variable	N	n (%)	n (%)	n (%)	
Age (years)	109	64.5 ± 9.7	66.8 ± 8	63.1 ± 10.4	0.045
Sex ratio (M/F)	109	1.27	0.65	2	0.005
ASA score*		2.09 ± 0.67			
ASA 1 – 2	109	84 (77 %)	32 (74 %)	52 (79 %)	0.6
ASA 3 – 4	109	25 (23 %)	11 (26 %)	14 (21 %)	
Charlson Score	109	2.84 ± 2.58			
0 – 2		49 (45 %)	13 (30 %)	36 (55 %)	0.014
≥ 3		60 (55 %)	30 (70 %)	30 (46 %)	
Comorbidities					
High blood pressure	108	42 (39 %)	21 (50 %)	21 (32 %)	0.059
Ischemic heart disease	108	13 (12 %)	4 (10 %)	9 (14 %)	0.52
Heart failure	108	2 (2 %)	1 (2 %)	1 (2 %)	
Kidney failure	108	2 (2 %)	2 (5 %)	0 (0 %)	
COPD**	109	5 (5 %)	4 (9 %)	1 (2 %)	
Chronic pancreatitis	109	5 (5 %)	2 (5 %)	3 (5 %)	
Diabetes	109	31 (28 %)	12 (28 %)	19 (29 %)	0.92
Cirrhosis	102	1 (1 %)	1 (3 %)	0 (0 %)	
Malnutrition					
All	105	72 (69 %)	27 (64 %)	45 (71 %)	0.72
Moderate		44 (42 %)	16 (38 %)	28 (44 %)	
Severe		28 (27 %)	11 (26 %)	17 (27 %)	
Albumin	104	37.37 ± 5.43	37.83 ± 5.25	37.08 ± 5.56	0.49
Pre albumin	79	0.2 ± 0.07	0.2 ± 0.06	0.2 ± 0.07	0.98
Pre operative BMI***	109	25.32 ± 4.93	27.02 ± 5.52	24.22 ± 4.19	0.006
SMI					
Pre operative	108	46.48 ± 10.71	53.45 ± 10.23	41.86 ± 8.3	<0.001
1 – 6 months	109	34.61 ± 6.92	36.74 ± 7.67	33.23 ± 6.04	
> 6 months	88	36.57 ± 7.76	37.58 ± 8.24	35.87 ± 6.86	
Liver Density					
1 – 6 months	109	38.16 ± 23.79	37.77 ± 23.69	38.41 ± 24.03	
> 6 months	89	41.14 ± 25.47	43.63 ± 24.32	39.46 ± 26.32	
Hepatic Steatosis					
Pre operative	108	11 (10 %)	3 (7 %)	8 (12 %)	0.52
1 – 6 months	108	39 (36 %)	13 (30 %)	26 (40 %)	
> 6 months	89	26 (29 %)	9 (25 %)	17 (32 %)	
Post operative complications					
Clavien Dindo ≥ 3	109	20 (18 %)	10 (23 %)	10 (15 %)	
Anatomopathology					0.42
pT1 – pT2	106	48 (45 %)	17 (41 %)	31 (48 %)	
pT3 – pT4	106	58 (55 %)	25 (60 %)	33 (52 %)	
Chemotherapy					
Neoadjuvant chemotherapy	109	36 (33 %)	15 (35 %)	21 (32 %)	
Adjuvant chemotherapy	107	94 (88 %)	33 (81 %)	61 (92 %)	
Death					
1 year	109	16 (15 %)	6 (14 %)	10 (15 %)	
3 years	109	69 (63 %)	30 (70 %)	39 (59 %)	

*ASA: American Society of Anesthesiologists
**COPD: Chronic Obstructive Pulmonary Disease
***BMI: Body Mass Index
****SMI: Skeletal Muscle Index

Comparison between Sarcopenic and Non-Sarcopenic Patients

Non-sarcopenic patients were significantly older (66.8 years *vs*. 63.1 years, $p = 0.045$) and had a significantly higher male to female ratio (M/F) (2 *vs*. 0.65, $p = 0.005$), compared to sarcopenic patients. Regarding comorbidities, the CCI was significantly higher in the non-sarcopenic group ($p = 0.014$). Twenty-seven (64 %) and forty-five patients (71 %) were considered as malnourished in pre-operative course in non-sarcopenic and sarcopenic groups, respectively. Moreover, the pre-operative BMI was significantly higher ($p = 0.006$) in the non-sarcopenic group (27.02 kg/m²) compared to the sarcopenic group (24.22 kg/m²) (Table 1).

Correlation between Sarcopenia and Hepatic Steatosis

No significant difference ($p = 0.97$) was found between sarcopenic and non-sarcopenic patients regarding liver density attenuation after PD for PDAC after adjusting the analysis for patient's sex. The mean preoperative liver density was 52.98 HU in the non-sarcopenic group and 52.04 HU in the sarcopenic group. Liver density decreased to 37.77 HU in non-sarcopenic patients and 38.40 HU in sarcopenic patients after surgery (Figures 10 and 11). This result was similar after adjusting for sex, CCI, age and preoperative BMI ($p = 0.2$). Preoperative sarcopenia did not impact hepatic steatosis after 6 months (OR: 1.42, CI (0.55 – 3.67), $p = 0.52$), administration of adjuvant chemotherapy (OR: 2.96, CI (0.89 – 9.77), $p = 0.07$), and Clavien 3 and 4 complications (OR: 0.59, CI (0.22 – 1.56), $p = 0.29$).

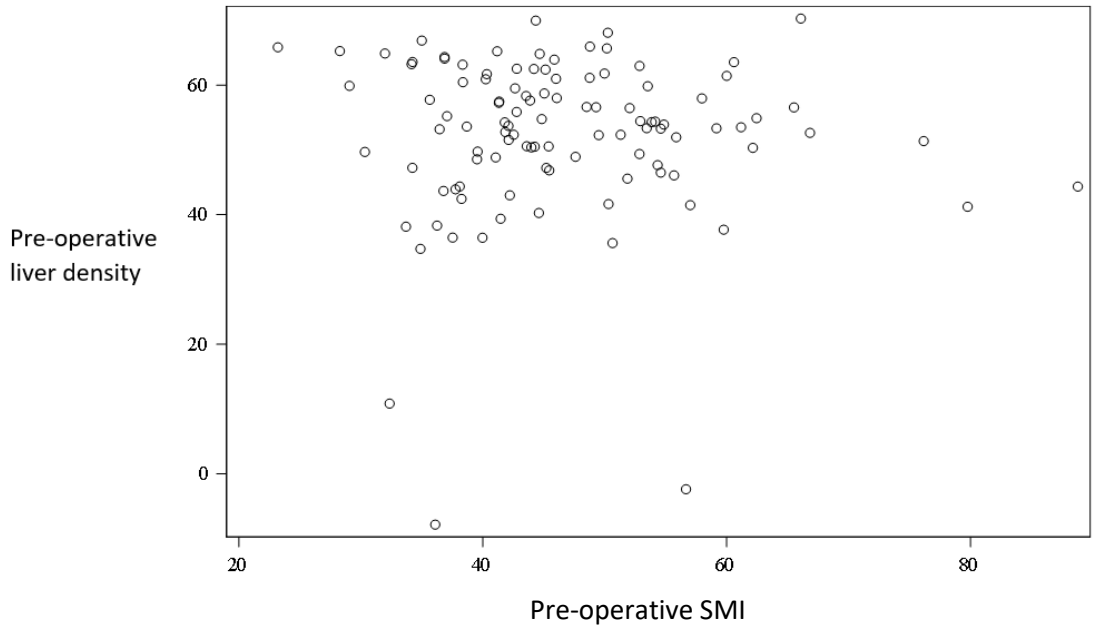

Figure 10: Scatter plot of Pre-operatives SMI and liver density

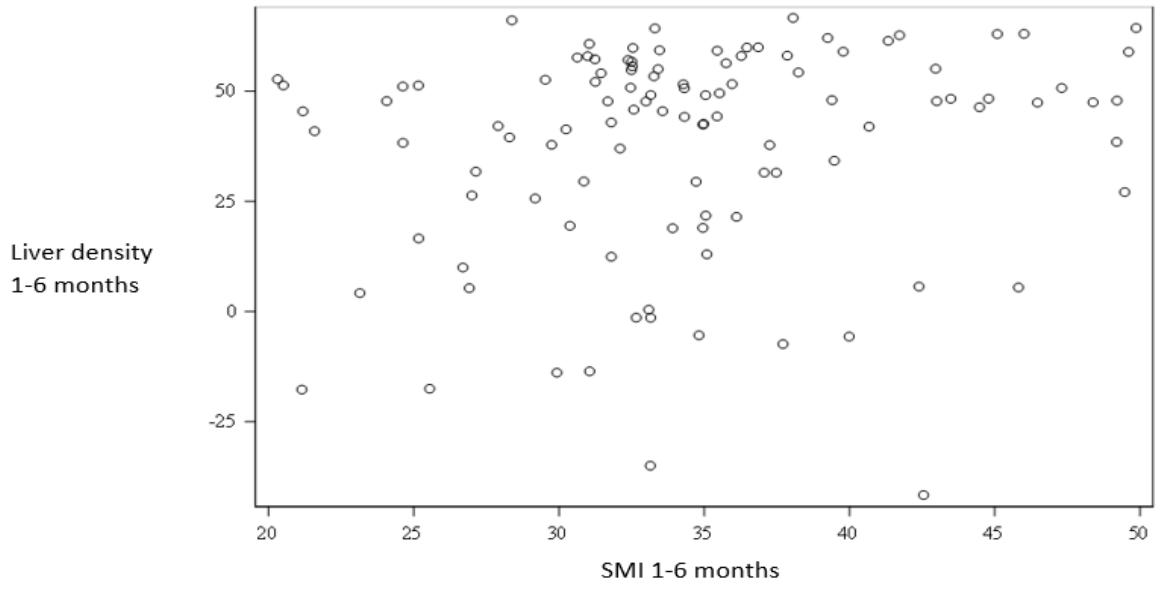

Figure 11: Scatter plot of 1-6 months liver density and SMI

Impact of Sarcopenia and Hepatic Steatosis on Survival after PD for PDAC

No significant difference was shown between sarcopenic and non-sarcopenic patients in terms of 3 years survival ($p = 0.54$). Furthermore, hepatic steatosis within 6 months after PD for PDAC had no impact on survival ($p = 0.9$).

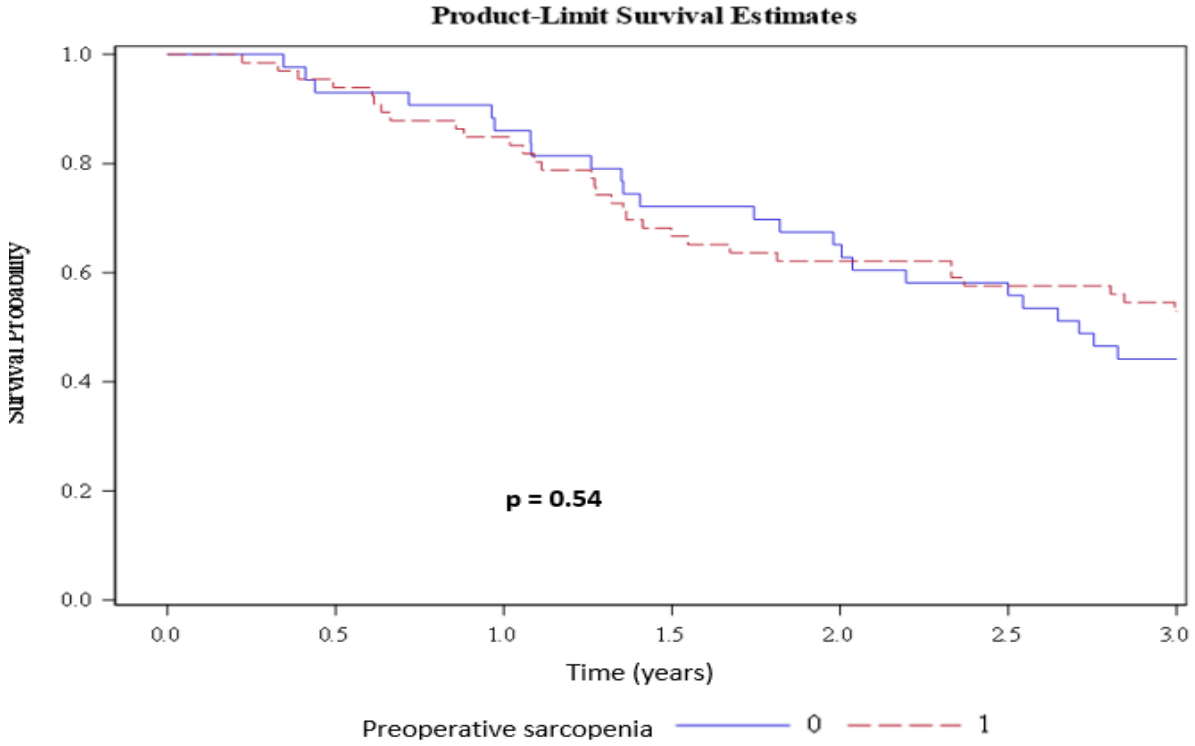

Figure 8: Overall survival of sarcopenic and non-sarcopenic groups at 3 years

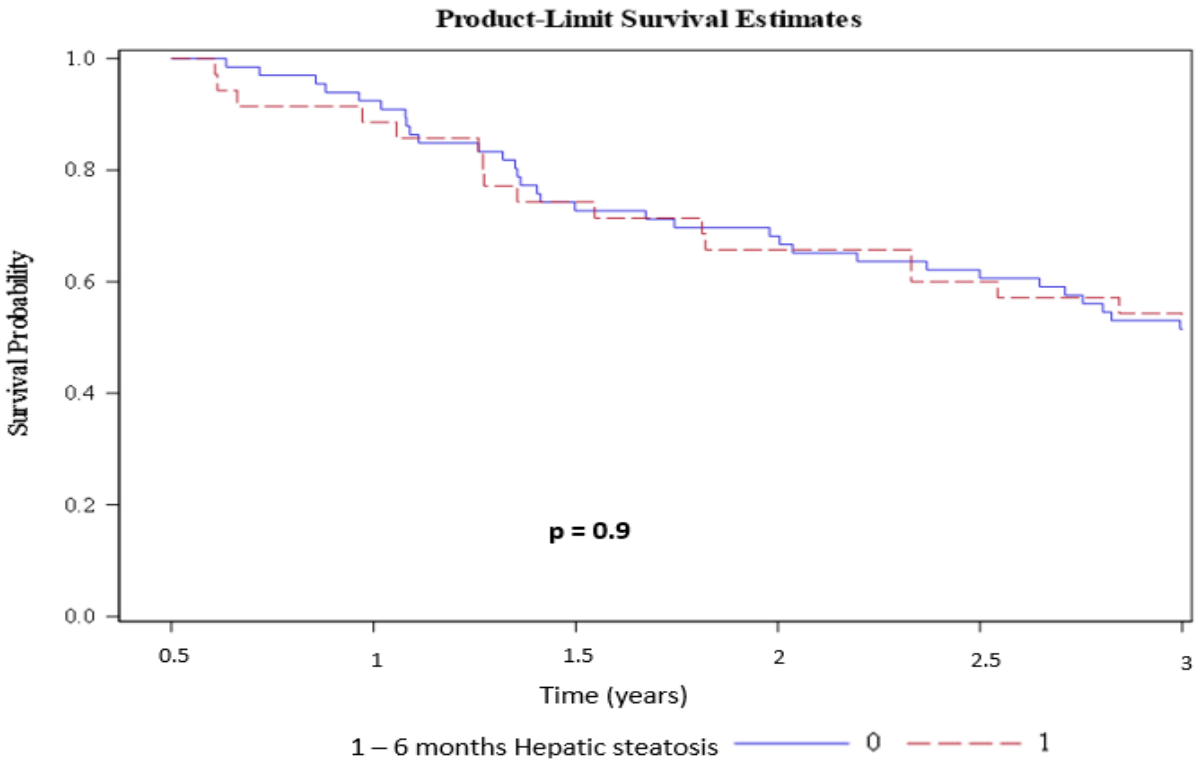

Figure 9: Overall survival of steatosis and non-steatosis groups at 3 years

Risk Factors for Hepatic Steatosis after PD for PDAC

We performed a univariate and multivariate analysis to assess for risk factors of hepatic steatosis within six months after PD (tables 2 and 3).

TABLE 2. Univariate Analysis of predictive factors for Hepatic steatosis at 1 – 6 months

Variable	OR*	CI	*P*-value
Denutrition Grade 1	0.91	(0.36 – 2.32)	0.84
Denutriton Grade 2	0.73	(0.25 – 2.10)	0.84
Pre operative Biliary drainage	1.44	(0.64 – 3.24)	0.38
Neo-adjuvant chemotherapy	0.50	(0.20 – 1.21)	0.12
Age	0.57	(0.37 – 0.84)	0.01
Pre-operative BMI	1.43	(0.94 – 2.16)	0.08
Pre-operative Albumin level	0.96	(0.64 – 1.43)	0.84
Pre-operative Prealbumin level	1.04	(0.63 – 1.70)	0.88

** OR: Odds-Ratio*
***CI: Confidence Interval*
****BMI: Body Mass Index*

In the univariate analysis, a lower age was significantly associated with the occurrence of hepatic steatosis. As shown in the table 2, increased age was significantly associated with decreased liver steatosis after PD for PDAC (OR = 0.57, p = 0.01, $CI_{95\%}$ [0.37 – 0.84]). This tendency was confirmed in the multivariate analysis (Table 3). Additionally, the multivariate analysis showed that preoperative BMI was significantly associated with postoperative liver steatosis (OR = 1.61, p = 0.04, $CI_{95\%}$ [1.02 – 2.57]).

TABLE 3. Multivariate Analysis of predictive factors for Hepatic steatosis at 1 – 6 months

Variable	OR*	CI**	*P*-value
Neo-adjuvant chemotherapy	0.58	(0.22 – 1.53)	0.27
Age	0.57	(0.36 – 0.89)	0.01
Pre-operative BMI***	1.62	(1.02 – 2.57)	0.04

**OR: Odds-Ratio*
***CI: Confidence Interval*
****BMI : Body Mass Index*

DISCUSSION

To our knowledge, this study is the first to assess the correlation between preoperative sarcopenia and postoperative hepatic steatosis in the context of pancreatic surgery. Similarly to previous studies, 36.1 % of patients had hepatic steatosis (11) and 61 % had sarcopenia (19).

Our analysis showed no significant difference in terms of hepatic density attenuation between sarcopenic and non-sarcopenic patients (p = 0.97) while previous studies reported a correlation between sarcopenia and NAFLD (15). This could be explained by the fact that physiological and physical changes induced by PD may mask the effects of pre-operative sarcopenia on hepatic steatosis. Physiological mechanisms of sarcopenia and hepatic steatosis should be further explored to determine the risk factors for these two conditions.

Our results revealed no significant difference in 3 years survival between sarcopenic and non-sarcopenic or between steatosis and no steatosis groups. Previous research have suggested a poorer prognosis for patients with postoperative hepatic steatosis or pre-operative sarcopenia (19) (34). Our results could be explained by a limited sample size, resulting in insufficient statistical power. Conducting a multicentric study could help to address this limitation and provide more robust conclusions on the survival outcomes.

Similarly to previous studies, our multivariate analysis revealed that BMI was significantly higher in patients with post-operative steatosis. *Patel et al*. showed, in an analysis of 136 patients, an OR of 1.19 (1.02 – 1.4), p = 0.03 for the occurrence of hepatic steatosis following PD (3). BMI was also an independent risk factor for hepatic steatosis after total PD in *Kato et al*.'s study, a retrospective multicentric study of 148 patients (12). Similarly, *Sato et al.* found a significantly higher BMI in 120 patients with

steatosis after PD (35). The multivariate analysis also showed that decreasing age was significantly associated with the occurrence of post-operative steatosis after PD for PDAC. To our knowledge, no study has previously reported this postoperative finding. A higher age is considered as a risk factor for the occurrence of hepatic steatosis after pancreatectomy in previous publications (36). Further research is needed to elucidate this correlation.

The present study has some limitations. First, the retrospective nature may be a source of potential bias. Second, data about exocrine and endocrine pancreatic insufficiencies were not available although they may contribute to the occurrence of liver steatosis (11) (12) (34) (37). Third, the definition of sarcopenia and liver steatosis were only focused on imaging data, making these measures very restrictive. Other strategies such as Magnetic Resonance Imaging (MRI) or liver biopsy could be considered (32) (38). Finally, all patients in this study were treated in the same center which limits the external validity of our findings.

CONCLUSION

No correlation was found between sarcopenia and liver steatosis after PD for PDAC. Further investigations are needed to clarify these findings, and a prospective multicentric study would be beneficial to standardize data collection and enhance the robustness of these results**.**

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Date de soutenance : 4 Octobre 2024

Titre de la thèse : Influence de la sarcopénie préopératoire sur la variation de densité hépatique après duodénopancréatectomie céphalique pour adénocarcinome du pancréas

Thèse - Médecine - Lille 2024

Cadre de classement : *Médecine*
DES + FST/option : *Chirurgie viscérale et digestive*
Mots-clés : Sarcopenia, pancreatic adenocarcinoma, duodenopancreatectomy, hepatic steatosis

Résumé :
Introduction: Pancreatic Ductal Adenocarcinoma (PDAC) is the 6th cause of cancer mortality worldwide, 4th in France, with numbers increasing each year. On the other hand hepatic steatosis, a well know surgical complication after pancreatic surgery is becoming a public health issue, with Non Alcoholic Fatty Liver Disease (NAFLD) being now the first chronic hepatopathy in the world, which may lead to Non Alcoholic Steato Hepatitis (NASH) and in extreme cases, cirrhosis and hepatocarcinoma. Sarcopenia, which consists in lower muscle mass, especially frequent in patients with oncological pathologies shares multiple physiopathological mechanisms factors with hepatic steatosis. To our knowledge no study has been made about the imbrications between sarcopenia and hepatic steatosis in pancreatic surgery.This is why we wanted to determine whether or not pre-operative sarcopenia before Pancreaticoduodenectomy (PD) for PDAC had an impact on liver attenuation before and after surgery.
Methods: We included 109 patients, from Lille University Hospital, who underwent PD between 2011 and 2020. Pre-operative sarcopenia was assessed using Skeletal Muscle Index (SMI) measurements, and cut-offs for the sarcopenic group were 38.9 cm^2/m^2 for women and 55.4 cm^2/m^2 for men. We measured liver density on pre and post-operative CT scans at 1-6 months and after 6 months. Liver density attenuation between pre-operative and 1-6 months CT scans was compared between our sarcopenic and non sarcopenic groups.
Results: No significant difference was shown between our two groups in terms of liver density attenuation before and after surgery (p = 0.97). We also used univariate and multivariate analysis to try and determine risk factors for post-operative hepatic steatosis (mean hepatic density < 40 HU), a lower age was a risk factor for hepatic steatosis in both analysis (OR: 0.571, CI (0.36-0.89), p = 0.01, in the multivariate analysis) and a higher BMI was a risk factor for hepatic steatosis in the multivariate analysis (OR: 1.617, CI (1.02-2.57), p = 0.04), which is consistent with previous studies.
Conclusion: Pre-operative sarcopenia had no significant impact on liver density attenuation before and after surgery in our study. Further studies especially prospective ones should be considered to precise our results.

Composition du Jury :

Président : Pr Stéphanie TRUANT

Assesseurs : Dr Mathilde VERMERSCH, Dr Julien BOURRY

Directeur de thèse : Dr Mehdi EL AMRANI