The prevalence of NAFLD in morbidly obese subjects revisited

A.S. Meijnikman[1], N. Bosma[1], O. Aydin[1], M. De Brauw[2], H. Herrema[1], V.E.A. Gerdes[1], M. Nieuwdorp[1], A.K. Groen[1], Dutch Liver Pathology Panel, J. Verheij[1]

1 Department of Vascular Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands.

2 Department of surgery, Spaarne Gasthuis, Hoofddorp, the Netherlands.

INTRODUCTION

The global obesity epidemic is a driver for obesity-related complications such as non-alcoholic fatty liver disease (NAFLD). The active 'hepatitic' subtype of NAFLD is non-alcoholic steatohepatitis (NASH) and potentially leads to liver fibrosis and cirrhosis. It is estimated that the prevalence of NAFLD in the general population is approximately 25% but increases to over 90% in morbidly obese subjects[1,2]. It is important to validate the alarmingly high prevalence of NAFLD, including the occurrence of NASH, since these numbers are based on studies that differ in set-up (i.e. diagnostic tool, histological staging system).

AIM

The aim of this study was to determine the prevalence of NAFLD in a cohort of morbidly obese subjects scheduled for bariatric surgery.

METHOD

In this prospective cohort study, 149 morbidly obese subjects scheduled for bariatric surgery were included. A standard metabolic work-up was performed and body composition was assessed using bioelectrical impedance analysis. Liver biopsies were obtained perioperatively and were evaluated by a panel of liver pathologists. Histological diagnosis was based on Steatosis Activity Fibrosis (SAF) score. NAFLD was categorized into simple steatosis when steatosis was present in > 5% of hepatocytes without ballooning or NASH if ballooning and inflammation were both present in the biopsy.

RESULTS

No NALFD was seen in 43.6 %, simple steatosis in 47.7% and NASH in 8.7% of subjects. Subjects with NAFLD were older than subjects without NAFLD (48.7 ± 10.3 y. vs 42.7 ± 10.8 y; p <0.001), had higher prevalence of hypertension (38.0% vs 18.5%; p = .012), type 2 diabetes (32.4% vs 10.8%; p = .002) and dyslipidemia (29.6% vs 12.3%; p = .014.

Median (IQ range) BMI did not differ significantly: 38.0(35.2-40.5) vs 38.4(35.1-40.0) vs 38.5(37.1-40.9) in subjects with healthy liver, NAFLD and NASH, respectively.

Subjects with NAFLD had a lower percentage of total body fat (44.7 ± 5.5% vs 47.8 ± 4.8%; p = .005), and a higher fat-free mass (55.9 ± 5.5% vs 52.6 ± 5.4%; p = .002), than patients with a healthy liver.

Of interest, preoperative weight loss was equal in subjects with healthy liver, NAFLD and NASH.

Table 1. Baseline characteristics

	All patients (n = 149)	Healthy liver (n=65)	NAFL (n=71)	NASH (n=13)
Demographic				
Age at surgery (years), mean ± SD[a]	46.0 ± 10.9	42.7 ± 10.8*	48.7 ± 10.3*	47.4 ± 11.0
Female sex, n (%)[d]	112 (75.2%)	58 (89.2%)*^	47 (66.2%)*	7 (53.8%)^
Anthropometric				
BMI at start (kg/m²), mean ± SD[a]	41.6 ± 4.7	41.9 ± 5.2	41.3 ± 4.4	42.0 ± 3.4
BMI at surgery (kg/m²), mean ± SD[a]	38.7 ± 4.3	38.6 ± 5.2	38.6 ± 3.7	39.2 ± 3.2
Waist circumference (cm), mean ± SD[a]	122.7 ± 11.4	118.7 ± 10.3*^	125.3 ± 10.6*	132.4 ± 16.7^
Total body fat (%), mean ± SD[a]	46.1 ± 5.4	47.8 ± 4.8*	44.7 ± 5.5*	44.4 ± 5.3
Fat-free mass (%), mean ± SD[a]	54.1 ± 5.6	52.6 ± 5.4*	55.4 ± 5.5*	55.6 ± 5.3
Clinical				
Systolic BP (mmHg), mean ± SD[a]	132.0 ± 14.3	128.1 ± 14.1*	135.8 ± 14.3*	130.9 ± 10.5
Diastolic BP (mmHg), mean ± SD[a]	80.8 ± 10.6	78.7 ± 10.3	82.7 ± 11.0	80.9 ± 8.7
Laboratory parameters				
Fasting glucose (mmol/L), mean ± SD[a]	6.0 ± 1.3	5.6 ± 1.2*	6.2 ± 1.3*	6.3 ± 1.0
HbA1c (%), mean ± SD[a]	5.9 ± 0.9	6.0 ± 0.9	5.8 ± 0.8	6.2 ± 1.6
Fasting insulin (pmol/L), median (IQR)[b]	85.0 (57.0-133.0)	72.0 (46.8-100.8)*^	101.0 (66.5-156.0)*	120.2 (90.0-151.7)^
HOMA-IR, median (IQR)[b]	3.2 (2.2-5.3)	2.5 (1.6-3.5)*^	4.0 (2.4-6.6)*	4.6 (3.4-6.1)^
Total cholesterol (mmol/L), mean ± SD[a]	4.8 ± 1.1	4.9 ± 1.1	4.7 ± 1.2	5.0 ± 1.0
HDL-cholesterol (mmol/L), mean ± SD[a]	1.2 ± 0.3	1.3 ± 0.3	1.2 ± 0.4	1.1 ± 0.3
LDL-cholesterol (mmol/L), mean ± SD[a]	3.1 ± 1.0	3.2 ± 1.0	3.0 ± 0.9	3.5 ± 0.9
Triglycerides (mmol/L), median (IQR)[b]	1.4 (1.1-1.8)	1.2 (0.9-1.6)*	1.5 (1.2-1.9)*	1.6 (1.2-2.4)
ALAT (U/L), median (IQR)[b]	28.0 (21.0-41.0)	25.0 (19.0-35.0)*^	30.0 (22.0-42.0)*	38.0 (29.5-49.0)^
ASAT (U/L), mean ± SD[a]	25.9 ± 9.4	24.2 ± 8.5	26.6 ± 10.2	30.2 ± 9.0
γGT (U/L), median (IQR)[b]	25.0 (18.0-38.5)	22.0 (17.0-27.5)*	30.0 (22.0-42.5)*	24.0 (17.5-40.0)
AF (U/L), mean ± SD[a]	83.0 ± 21.8	84.5 ± 21.2	83.0 ± 22.7	75.6 ± 19.7
CRP (mg/L), median (IQR)[b]	3.2 (1.7-5.5)	3.2 (1.8-5.2)	3.1 (1.5-5.9)	3.8 (2.0-6.9)
Leukocytes (x 10⁹/L), mean ± SD[a]	7.4 ± 2.0	7.2 ± 1.6	7.8 ± 2.2	6.5 ± 1.8
Ferritin (µg/L), median (IQR)[b]	97.0 (48.0-172.0)	90.0 (49.0-151.0)	92.5 (43.0-182.5)	154.5 (82.3-203.5)

Data are given in mean ± SD, median (IQR), or n (%). All post hoc analyses performed with Bonferroni correction. Significance level .05.
*[a] One-way ANOVA; [b] Kruskal-Wallis test; [d] Chi-square or Fisher's exact test. * Significant difference between healthy liver and NAFL group; ^ Significant difference between healthy liver and NASH group.*

Table 2. Preoperative weight loss in patients with healthy liver, NAFL, and NASH

	Healthy liver (n=65)	NAFL (n=71)	NASH (n=13)
BMI at start (kg/m²), mean ± SD[a]	41.9 ± 5.2	41.3 ± 4.4	42.0 ± 3.4
BMI at surgery (kg/m²), mean ± SD[a]	38.6 ± 5.2	38.6 ± 3.7	39.2 ± 3.2
Start weight (kg), mean ± SD[a]	120.6 ± 17.4	124.3 ± 19.0	131.3 ± 20.4
Operative weight (kg), mean ± SD[a]	111.2 ± 16.5	115.9 ± 16.4	122.5 ± 18.4
Preoperative weight loss percent (%), mean ± SD[a]	7.7 ± 4.7	6.6 ± 3.3	6.6 ± 2.4
< 6 kg preoperative weight loss (kg), n (%)[d]	12 (18.5%)	15 (21.1%)	2 (15.4%)
6-8 kg preoperative weight loss (kg), n (%)[d]	16 (24.6%)	26 (36.6%)	4 (30.8%)
> 8 kg preoperative weight loss (kg), n (%)[d]	37 (56.9%)	30 (42.3%)	7 (53.8%)

Table 3. Prevalence of metabolic risk factors in patients with healthy liver, NAFL, and NASH

	Healthy liver (n=65)	NAFL (n=71)	NASH (n=13)
Hypertension, n (%)[d]	12 (18.5%)*	27 (38.0%)*	4 (30.8%)
Type 2 diabetes mellitus, n (%)[d]	7 (10.8%)*	23 (32.4%)*	4 (30.8%)
Dyslipidemia, n (%)[d]	8 (12.3%)*	21 (29.6%)*	1 (7.7%)
Metabolic syndrome, n (%)[d]	33 (50.8%)*^	53 (74.6%)*	12 (92.3%)^

Table 4. Insulin resistance in patients with healthy liver, NAFL, and NASH

	Healthy liver (n=55)	NAFL (n=62)	NASH (n=13)
Insulin resistance, n (%)[d]	21 (38.2%)^	33 (53.2%)~	12 (92.3%)^~
No insulin resistance, n (%)	34 (61.8%)	29 (46.8%)	1 (7.7%)

CONCLUSIONS

In sharp contrast to previous studies and to the general dogma that the prevalence of respectively NAFLD and NASH is 90% and 20% in subjects with (morbid) obesity, data from our large prospective Dutch cohort indicates that this prevalence is lower.

REFERENCES

1. Bedossa P, Tordjman J, Aron-Wisnewsky J, et al. Systematic review of bariatric surgery liver biopsies clarifies the natural history of liver disease in patients with severe obesity. Gut. 2017;66(9):1688-1696. doi:10.1136/gutjnl-2016-312238

2. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016;64(1):73-84. doi:10.1002/hep.28431

ACKNOWLEDGEMENTS

We thank J.C.M. Borger, D. Zwirs, the nursing staff and all patients for making this study possible.

CONTACT INFORMATION

Abraham S Meijnikman, MD, Department of Vascular Medicine, Amsterdam UMC, University of Amsterdam, Meibergdreef 9, 1105AZ, Amsterdam, the Netherlands.

E-mail: a.s.meijnikman@amc.uva.nl

Poster presented at: EASL The International Liver Congress 2019

DOI: 10.3252/pso.eu.ILC2019.2019

Metabolism, alcohol and toxicity

Abraham Meijnikman

THU-328

ILC2019