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LETTER TO THE EDITOR

Crashing NASH in Patients Listed for Bariatric Surgery

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We read with great interest the publication of Ooi et al. describing the prevalence of NAFLD and NASH in a bariatric population [1]. They discussed the fact that there is a large variation in NASH prevalence in bariatric studies ranging from 7.3 to 56%. In their cohort, they found a NASH prevalence of 17.1%, which was lower than expected based on previous literature. This lower than expected NASH prevalence was in line with our observation. We intraoperatively collected liver needle and wedge biopsies from 20 obese patients undergoing bariatric surgery (Table 1). Patients with significant alcohol use (> 14 standard beverages a week for men and > 7 for women), secondary causes of hepatic fat accumulation, and chronic inflammatory diseases other than NASH were excluded. Strikingly, NASH, defined as the combined presence of steatosis, lobular inflammation, and hepatocyte ballooning, was not present in any of our obese patients, and the maximal NAFLD activity score was only 3 (Table 2).

Questions arise why none of our patients had NASH. We hypothesize that the absence of NASH in our cohort could be related to the preoperative low-calorie diet (so-called crash diet). All our patients received a 4-week food-based crash diet as part of standard clinical care. Crash diets have been shown to reduce liver volume by 12% and intrahepatic fat by 40%

Table 1 Patient characteristics

	Total group ($n = 20$)
Age (years)	51 (37.8–57.0)
Female gender	13/20 (65%)
BMI before crash (kg/m^2)	41.2 (40.1–42.5)
BMI after crash (kg/m^2)	38.6 (37.5–40.3)
Weight loss (kg)	8.0 (6.0–8.8)
Weight loss (%)	6.2 (5.3–7.6)
Hypertension	9/20 (45%)
Type 2 diabetes	4/20 (25%)
Dyslipidemia	6/20 (30%)
Obstructive sleep apnea	8/20 (40%)
Total cholesterol (5.0–6.4 mmol/L)	4.3 (4.0–4.6)
LDL cholesterol (3.5–4.4 mmol/L)	2.7 (2.2–2.9)
HDL-cholesterol (> 0.9 mmol/L)	1.0 (0.8–1.2)
Triglycerides (0.80–1.94 mmol/L)	1.3 (0.9–2.3)
ALT (F < 34, M < 45 U/L)	31.0 (19.0–39.8)
AST (F < 31, M < 35 U/L)	26.5 (19.0–30.8)
GGT (F < 38, M < 55 U/L)	22.5 (17.3–28.0)
ALP (F < 98, M < 115 U/L)	82.5 (73.3–96.8)
Fasting glucose (3.1–6.1 mmol/L)	5.4 (5.0–5.9)
HbA1C (25–44 mmol/mol)	35.0 (33.0–42.8)

Continuous variables are expressed as median (IQR). Categorical variables are expressed as number (percentage of the total group). *BMI*, body mass index; *ALT*, alanine aminotransaminase; *AST*, aspartate aminotransaminase; *GGT*, gamma-glutamyltransferase; *ALP*, alkaline phosphatase; *LDL*, low-density lipoprotein

Comment on
Ooi GJ, Burton PR, Bayliss J, Raajendiran A, Earnest A, Laurie C et al. Effect of Body Mass Index, Metabolic Health and Adipose Tissue Inflammation on the Severity of Non-alcoholic Fatty Liver Disease in Bariatric Surgical Patients: a Prospective Study. Obes. Surg. 2018.

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Table 2 Pathological analysis

Patient	Steatosis	Lobular inflammation	Portal inflammation	Ballooning*	Fibrosis	NAS	SAF
1	0	0	0	0	0	0	S0A0F0
2	0	0	0	0	0	0	S0A0F0
3	0	0	0	0	1	0	S0A0F1
4	0	1	0	0	0	1	S0A1F0
5	0	1	0	0	0	1	S0A1F0
6	0	1	1	0	0	0	S0A1F0
7	0	1	2	0	1	1	S0A2F1
8	1	0	1	0	1	1	S1A0F1
9	1	1	0	0	2	2	S1A1F2
10	1	1	1	0	0	2	S1A1F0
11	1	1	1	0	1	2	S1A1F1
12	1	1	1	0	1	2	S1A1F1
13	1	1	1	0	1	2	S1A1F1
14	1	1	2	0	1	2	S1A1F1
15	1	1	2	0	2	2	S1A1F2
16	1	1	2	0	2	2	S1A1F2
17	1	2	2	0	2	3	S1A2F2
18	2	1	0	0	1	3	S2A1F1
19	2	1	0	0	1	3	S2A1F1
20	2	1	0	0	1	3	S2A1F1

Steatosis: 0, < 5%; 1, 5–33%; 2, 34–66%; 3, > 66%. Lobular inflammation: 0, no foci; 1, < 2 foci/200× field; 2, 2–4 foci/200× field; 3, > 4 foci/200× field. Portal inflammation: 0, none; 1, mild; 2, moderate; 3, severe. Fibrosis: 0, none; 1, perisinusoidal or periportal; 2, perisinusoidal and portal/periportal; 3, bridging fibrosis; 4, cirrhosis. *Ballooning is scored using the SAF and Kleiner scoring system. In both, all biopsies scored 0. *NAS*, NAFLD activity score; *SAF*, steatosis, activity, and fibrosis score

[2]. The median amount of weight loss in our cohort after the 4-week crash diet was 8.0 kg or 6.2% of total body weight. Recently, it has been shown that this amount of weight loss (5–10% of initial body weight) can lead to improvement of lobular inflammation, hepatocellular ballooning, and NASH resolution in 84%, 64%, and 45% of the cases, respectively [3]. Although we cannot prove the presence of NASH *before* initiation of the diet, the presence of fibrosis in 14/20 (70%) patients is suggestive for burned-out NASH with resolution of hepatocyte ballooning after the dietary intervention [4]. A preoperative diet is prescribed in numerous bariatric centers in order to decrease liver volume, to diminish operation time, complexity, and postoperative complications [5, 6]. Although encouraged, preoperative weight loss is not obligated in all bariatric centers [7]. However, a survey among 99 Australian dieticians revealed that all dieticians provide bariatric patients with some form of nutritional intervention in the preoperative stage [8]. Therefore, our question to Ooi et al. is if a crash diet or another type of dietary intervention was prescribed before the operation.

Taken together, we hypothesize that large variations in NAFLD and NASH prevalence between different bariatric studies may be at least partly explained by the use of a preoperative crash diet. In addition, a crash diet may lead to bias in NASH biomarker and pathophysiology research. Therefore, we advocate that the application of a preoperative diet or other preoperative interventions should always be mentioned in bariatric NASH studies.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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