Obesity Surgery (2019) 29:1195–1201
https://doi.org/10.1007/s11695-018-03641-2

ORIGINAL CONTRIBUTIONS

Long-term Results of Bariatric Surgery for Non-alcoholic Fatty Liver Disease/Non-alcoholic Steatohepatitis Treatment in Morbidly Obese Japanese Patients

Daisuke Uehara [1,2] · Yosuke Seki [3] · Satoru Kakizaki [2] · Norio Horiguchi [2] · Hiroki Tojima [2] · Yuichi Yamazaki [2] · Ken Sato [2] · Masanobu Yamada [1,4] · Toshio Uraoka [2] · Kazunori Kasama [3]

Published online: 12 December 2018

Abstract

Background Patients with morbid obesity are complicated with metabolic diseases and have a high incidence of non-alcoholic fatty liver disease (NAFLD), including non-alcoholic steatohepatitis (NASH).

Methods We report on a follow-up study of a cohort included 102 obese patients (55 males and 47 females, mean age 42.9 ± 10.6 years) undergoing bariatric surgery for the management of morbid obesity. Abdominal computed tomography was performed before and 1 year after surgery. Anthropometric and biochemical measurements were performed at 1, 3, and 5 years after surgery.

Results The mean body mass index (BMI) of the NAFLD patients improved from 42.5 ± 8.3 kg/m^2 to 28.5 ± 6.9, and 29.1 ± 5.7, 29.7 ± 5.5 kg/m^2 at 1, 3, and 5 years, respectively. The liver fat accumulation and visceral fat areas were significantly improved at 1 year after surgery. The decrease in the BMI, waist-hip ratio, body fat percentage, and basal metabolic rate remained decreased for at least 5 years after surgery. Blood test findings including AST, ALT, γ-GTP, uric acid, albumin, CRP, HDL cholesterol, LDL cholesterol, triglycerides, and homeostasis model assessment insulin resistance (HOMA-IR) were also still improved at least 5 years after surgery.

Conclusion Bariatric surgery is useful for ensuring the long-term treatment of NAFLD/NASH in morbidly obese Japanese patients. Bariatric surgery is a therapeutic option for patients resistant to conventional treatment.

Keywords Non-alcoholic steatohepatitis · Non-alcoholic fatty liver disease · Morbidly obesity · Bariatric surgery · Long-term treatment

Abbreviations

NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NAFL	Non-alcoholic fatty liver
LRYGB	Laparoscopic Roux-en-Y gastric bypass surgery
APMBSS	Asia-Pacific Metabolic and Bariatric Surgery Society
BMI	Body mass index
FPG	Fasting plasma glucose
FIRI	Fasting blood insulin
HOMA-IR	Homeostasis model assessment insulin resistance

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11695-018-03641-2) contains supplementary material, which is available to authorized users.

✉ Satoru Kakizaki
kakizaki@gunma-u.ac.jp

1 Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, Maebashi, Gunma 371-8511, Japan

2 Department of Gastroenterology and Hepatology, Gunma University Graduate School of Medicine, Maebashi, Gunma 371-8511, Japan

3 Weight Loss and Metabolic Surgery Center, Yotsuya Medical Cube, Tokyo, Japan

4 Department of Internal Medicine, Division of Endocrinology and Metabolism, Gunma University Graduate School of Medicine, Maebashi, Gunma 371-8511, Japan

Introduction

Morbid obesity predisposes to metabolic diseases, such as type 2 diabetes mellitus, hypertension, hyperlipidemia, and ischemic heart disease [1]. Patients with metabolic diseases and obesity have a high prevalence of non-alcoholic fatty liver disease (NAFLD), including non-alcoholic steatohepatitis (NASH). We previously reported that the prevalence of

NASH in Japanese morbidly obese patients was 77.5% [2]. Although the prevalence of morbid obesity in Japan is low compared with that in the USA, the prevalence of NASH in patients with morbid obesity is extremely high [2]. A high prevalence of NASH is also observed in Asian countries, such as Taiwan [3], relative to Western countries [4–6].

We also previously reported that racial differences exist in NAFLD/NASH in patients with morbid obesity [7]. Liver dysfunction among Japanese patients with severe obesity tends to be higher than in Caucasian patients, with equivalent body mass index [7]. We concluded that Japanese or Asian patients with morbid obesity must therefore reduce their body weight to a greater degree than Caucasian patients with the same BMI in order to avoid adverse health effects. Indeed, because Asians are reported to have obesity-related complications with a lower BMI than Caucasians, the Asia-Pacific Bariatric Surgery Group (APBSG) consensus meeting recommends bariatric surgery in Asian patients with a BMI > 37 or with a BMI > 32 and diabetes or ≥ 2 other obesity-related comorbidities [8].

The number of bariatric surgeries performed to treat morbid obesity is gradually increasing in Japan. Evidence-based clinical practice guidelines for NAFLD/NASH drafted by the Japan Society of Hepatology (JSH) and the Japanese Society of Gastroenterology (JSGE) recommend bariatric surgery as the therapeutic option for the treatment of NASH in morbidly obese patients [9, 10]. However, there are still fewer bariatric surgeries performed in Japan than in European countries. We previously investigated the clinical characteristics of morbidly obese Japanese patients with NAFLD/NASH and reported the short-term outcomes of bariatric surgeries for NAFLD/NASH treatment [2]. However, there are no data concerning the long-term results of NAFLD/NASH treatment in morbidly obese Japanese patients.

The aim of the present study was to determine the long-term outcomes of bariatric surgery for NAFLD/NASH treatment in morbidly obese Japanese patients selected for bariatric surgery at a single center.

Patients and Methods

Study Design

This study followed-up the previously reported cohort [2] including 102 obese patients undergoing bariatric surgery for the management of morbid obesity. Consecutive obese subjects underwent bariatric surgery for the management of morbid obesity at a single center (Weight Loss and Metabolic Surgery Center, Yotsuya Medical Cube, Tokyo, Japan), and all were enrolled from October 2009 until July 2011 [2]. The exclusion criteria were a reported history of daily consumption of alcohol > 20 g/day, a clinical diagnosis of a liver disease of another etiology (including viral hepatitis, autoimmune hepatitis, primary biliary cirrhosis, drug-induced liver disease, hemochromatosis, biliary obstruction, and Wilson's disease), and severe complications, such as congestive heart failure. The patients who underwent a second bariatric surgery were also excluded. All subjects provided their written informed consent for participation [2].

As the indications for bariatric surgery, we followed the criteria established in 2005 by the Asia-Pacific Bariatric Surgery Group consensus meeting [8]. Patients underwent Roux-en-Y gastric bypass or sleeve gastrectomy, which was performed laparoscopically.

The standard clinical, anthropometric (weight, height, and waist and hip circumferences), and biochemical measurements, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyl transpeptidase (γ-GTP), uric acid, albumin, C-reactive protein (CRP), Fe, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, fasting plasma glucose (FPG), fasting blood insulin (FIRI), c-peptide, HbA1c, and cholesterol, were obtained before the bariatric surgery. All blood samples were collected after overnight fasting. The homeostasis model assessment insulin resistance (HOMA-IR) index was calculated using the following formula: glucose (mg/dL) × insulin (μU/mL)/405, and it was used as an index of insulin resistance. Computed tomography (CT) was performed, and subcutaneous and visceral fat areas were calculated. The liver/spleen Hounsfield unit ratio by CT (liver/spleen ratio) was calculated as a marker of steatosis [11]. The body fat percentage and basal metabolic rate were measured using the InBody570 instrument (InBody Japan Inc., Tokyo, Japan). During bariatric surgery, all patients underwent a needle liver biopsy under laparoscopic guidance with a 16-G Quick-Core biopsy needle (Cook Japan, Tokyo Japan) as described previously [2]. The diagnosis of type 2 diabetes was based on the Japanese Diabetes Society criteria [12]. Hypertension was diagnosed if the patient had a history of hypertension and was on antihypertensive medication or if the patient had a resting recumbent blood pressure of ≥ 140/90 mmHg on 2 repeated occasions.

The patient characteristics of this cohort are shown in Supplemental Table 1 (modified from ref. [2]) as described previously [2]. The patients were 55 males and 47 females. Eighty-four of the 102 patients (82.4%) were diagnosed with NAFLD. Seventy-nine patients were diagnosed with NASH, and five were diagnosed with non-alcoholic fatty liver (NAFL) [2]. The diagnosis of NASH was made histologically, as described in a previous report [2]. Supplemental Tables 2 and 3 show the characteristics of 84 NAFLD and 79 NASH patients, respectively.

The standard clinical, anthropometric, and biochemical measurements were compared before and at 1, 3, and 5 years after surgery. Abdominal CT findings were compared before surgery and at 1 year after surgery. The liver/spleen ratio and abdominal fat areas were compared before surgery and at 1 year after surgery.

This study was approved by institutional review board (IRB) of both Yotsuya Medical Cube (YMC-2009-3) and Gunma University Hospital (Gunma university-2017-005).

Statistical Analyses

All data are shown as the mean ± standard deviation (SD). Differences between groups were analyzed by Fisher's exact probability test and Mann–Whitney *U* tests, when a significant difference was obtained by the Kruskal–Wallis test. A value of $P < 0.05$ was considered to be significant.

Results

Follow-up Results at 1, 3, and 5 Years

The standard clinical, anthropometric, and biochemical measurements (AST, ALT, γ-GPT, uric acid, albumin, CRP, Fe, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, FPG, FIRI, c-peptide, HbA1c, HOMA-IR) of 85 NAFLD patients before and at 1, 3, and 5 years after surgery are shown in Fig. 1 and Table 1. The body weight, BMI, waist-hip ratio, body fat percentage, and basal metabolic rate were significantly decreased after surgery and remained decreased for at least 5 years after surgery. Blood test findings, including AST, ALT, γ-GPT, uric acid, albumin, CRP, HDL cholesterol, LDL cholesterol, triglycerides, FPG, FIRI, c-peptide, HbA1c, and HOMA-IR, were significantly improved at 1 year after surgery. The improvement in the body weight and blood test findings continued for at least 5 years after surgery. The platelet counts were significantly decreased at 1, 3, and 5 years after surgery.

The standard clinical, anthropometric, and biochemical measurements of 79 NASH patients before and at 1, 3, and 5 years after surgery are shown in Fig. 2 and Table 2. The trends in the results were the same across all NAFLD patients.

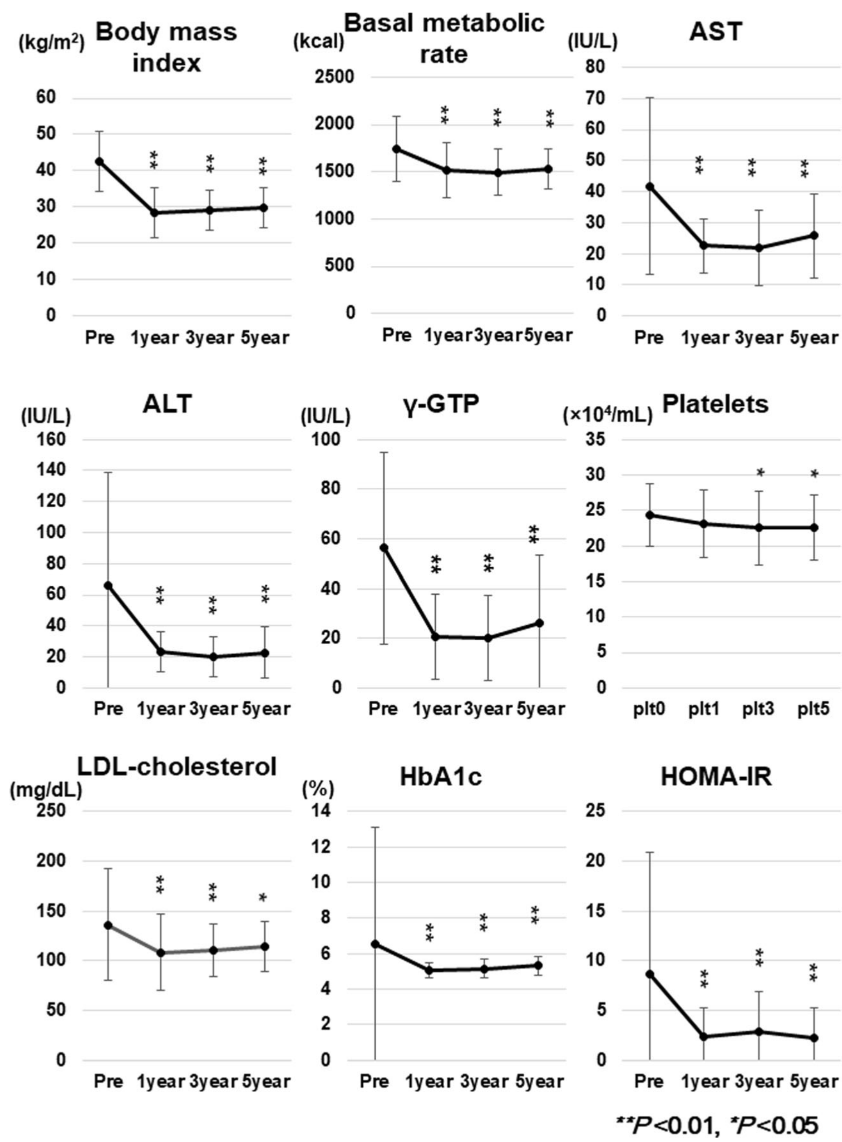

Fig. 1 Follow-up results of NAFLD patients at 1, 3, and 5 years

Abdominal CT Before Surgery and at 1 Year After Surgery

The liver/spleen ratio was calculated from the CT findings of NAFLD patients before and at 1 year after surgery (Fig. 3). Figure 3a shows the representative imaging before and at 1 year after surgery at the liver level. The mean liver/spleen ratio was 0.62 ± 0.31 before surgery and 1.04 ± 0.35 after surgery, indicating a significant improvement after surgery ($P < 0.01$).

The fat area at the umbilical level was calculated from the CT findings of NAFLD patients before and at 1 year after surgery (Fig. 4). The total, visceral, and subcutaneous fat areas were calculated. All 3 fat areas at the umbilical level were significantly improved after surgery ($P < 0.01$).

Discussion

Bariatric surgery has been reported to be useful for the treatment of NASH in Caucasians [13]. Lassailly et al. evaluated 109 morbidly obese patients with biopsy-proven NASH who underwent bariatric surgery [13]. They reported that NASH had disappeared from 85% of the patients at 1 year after surgery. Compared with before surgery, patients had significant reductions in the BMI, ALT, γ-GTP level, and the insulin resistance index. Although we could not perform a follow-up biopsy at 1 year, the changes in the laboratory data in the present study were quite similar to their previous data.

Such long-term results with a large cohort are not well-established, even in European countries. Schneck et al. [14] reported the long-term histological remission of 9 morbidly obese women with NASH with a median follow-up of 55 months after bariatric surgery. They proved the long-lasting beneficial impact of such a treatment on hepatic steatohepatitis and hepatocyte death [14].

In the present study, the body weight, insulin resistance, liver fat accumulation, and visceral fat areas were significantly improved at 1 year after surgery. The improvement in the body weight and blood test findings continued for at least 5 years after surgery. This report is the first to describe the long-term results of bariatric surgery for Japanese morbidly obese patients complicated with NAFLD/NASH. Weight loss with a very low-energy diet is also reported to reduce the liver volume and visceral adipose tissue [15]. The reduction in the visceral adipose tissue by weight loss may help improve the insulin resistance and NAFLD/NASH.

A deceased platelet count is sometimes used as a predictor of progressing liver fibrosis [16]. In the present study, the platelet

Table 1 Follow-up findings for NAFLD patients at 1, 3, and 5 years

		Pre ($n = 84$)	1 year ($n = 82$)	3 years ($n = 62$)	5 years ($n = 47$)
Body weight	kg (mean ± SD)	119.6 ± 28.8 (76.3–217.8)	79.7 ± 22.4 (43.8–142.3)**	80.7 ± 17.8 (47.4–124.6)**	82.3 ± 17.7 (46.4–130.5)**
Body mass index	kg/m^2 (mean ± SD)	42.5 ± 8.3 (30.1–63.5)	28.5 ± 6.9 (16.9–51.4)**	29.1 ± 5.7 (16.0–51.2)**	29.7 ± 5.5 (17.5–45.2)**
Waist-hip ratio		1.14 ± 0.13 (0.89–1.48)	0.91 ± 0.12 (0.38–1.23)**	0.94 ± 0.09 (0.76–1.20)**	0.92 ± 0.09 (0.77–1.19)**
Body fat percentage	%	42.4 ± 6.8 (25.9–56.2)	27.7 ± 8.7 (13.4–47.8) **	29.5 ± 6.7 (15.4–42.4)**	32.8 ± 7.5 (16.5–51.2)**
Basal metabolic rate	kcal	1747 ± 345 (1059–2777)	1517 ± 297 (1061–2406)**	1496 ± 250 (1022–2072)**	1530 ± 213 (1168–1958)**
AST	IU/L	41.8 ± 28.5	22.6 ± 8.6**	21.9 ± 12.2**	25.7 ± 13.7**
ALT	IU/L	66.1 ± 73.0	23.1 ± 12.9**	20.2 ± 13.1**	22.9 ± 16.5**
γ-GTP	IU/L	56.4 ± 38.6	20.7 ± 17.3**	20.0 ± 17.1**	26.1 ± 27.2**
Uric acid	mg/dL	6.6 ± 1.6	5.7 ± 1.6**	5.6 ± 1.7**	5.7 ± 1.5**
Albumin	g/dL	4.1 ± 0.3	4.3 ± 0.2**	4.3 ± 0.4**	4.3 ± 0.2**
CRP	mg/dL	0.53 ± 0.50	0.28 ± 1.50**	0.10 ± 0.24**	0.07 ± 0.12**
Fe	mg/dL	104.7 ± 38.0	103.7 ± 41.9	94.6 ± 45.3	98.7 ± 57.5
Platelets	×10^4/mL	24.4 ± 4.4	23.1 ± 4.8	22.5 ± 5.3*	22.6 ± 4.6*
Total cholesterol	mg/dL	200.0 ± 40.1	193.4 ± 441.6	192.0 ± 33.1	195.7 ± 34.7
HDL cholesterol	mg/dL	47.0 ± 9.3	60.0 ± 13.2**	60.8 ± 15.7**	60.9 ± 16.5**
LDL cholesterol	mg/dL	136.1 ± 56.5	108.2 ± 38.6**	110.9 ± 26.7**	114.1 ± 25.3*
Triglycerides	mg/dL	147.6 ± 96.6	81.3 ± 48.4**	90.4 ± 58.5**	101.0 ± 86.0**
Fasting plasma glucose	mg/dL	125.0 ± 38.8	96.0 ± 15.3**	96.2 ± 13.4**	97.6 ± 12.7**
Fasting blood insulin	mU/mL	26.1 ± 22.8	9.7 ± 9.6**	11.2 ± 14.2**	8.9 ± 10.0**
C-peptide	ng/dL	3.9 ± 1.5	2.6 ± 1.5**	2.7 ± 2.1**	2.4 ± 1.6**
HbA1c	%	6.6 ± 1.2	5.1 ± 0.4**	5.2 ± 0.6**	5.3 ± 0.5**
HOMA-IR		8.7 ± 12.2	2.4 ± 2.8**	2.8 ± 4.0**	2.3 ± 3.0**

AST, aspartate aminotransferase; *ALT*, alanine aminotransferase; *γ-GTP*, γ-glutamyl transpeptidase; *CRP*, C-reactive protein; *HOMA-IR*, homeostasis model assessment insulin resistance; *SD*, standard deviation; *NAFLD*, non-alcoholic fatty liver disease

*$P < 0.05$, **$P < 0.01$

counts were significantly decreased after surgery. If the liver fibrosis of patients had improved after surgery, the platelet counts would have been increased. On the other hand, the platelet counts increase by obesity or chronic inflammation [17, 18]. Because the platelet counts of the patients were within the normal range in this study, the deceased platelet counts may have reflected the improvement of chronic inflammation or obesity instead of liver fibrosis. An improvement of the chronic inflammation and obesity may have reduced the platelet counts.

One limitation associated with this study is that we were unable to perform a follow-up liver biopsy for all patients. Because the first liver biopsy was performed laparoscopically during surgery and was useful for a diagnosis, the burden on the patients was reasonable. However, the unreasonable burden expected with a routine but otherwise unnecessary follow-up liver biopsy prevented us from performing this procedure. We previously reported four cases with a follow-up biopsy [2]; while this is a relatively small number of cases, the mean NASH activity score was found to have significantly improved in this cohort [2].

Elastography and magnetic resonance (MR) elastography are non-invasive and sometimes used to estimate the liver stiffness or the extent of fibrosis in patients with liver disease, including NASH [19, 20]. Since elastography is performed percutaneously, a thick layer of subcutaneous fat hinders accurate measurements and sometimes leads to a misdiagnosis in obese patients. MR elastography is also difficult to perform in morbidly obese patients due to limitations concerning the size or ability of MR equipment to accommodate the patient. A safe, non-invasive, convenient diagnostic method for predicting the presence of fibrosis due to NASH in morbidly obese patients that can counter the above limitations is lacking. In the future, we plan to evaluate the improvement in NASH fibrosis in morbidly obese Japanese patients.

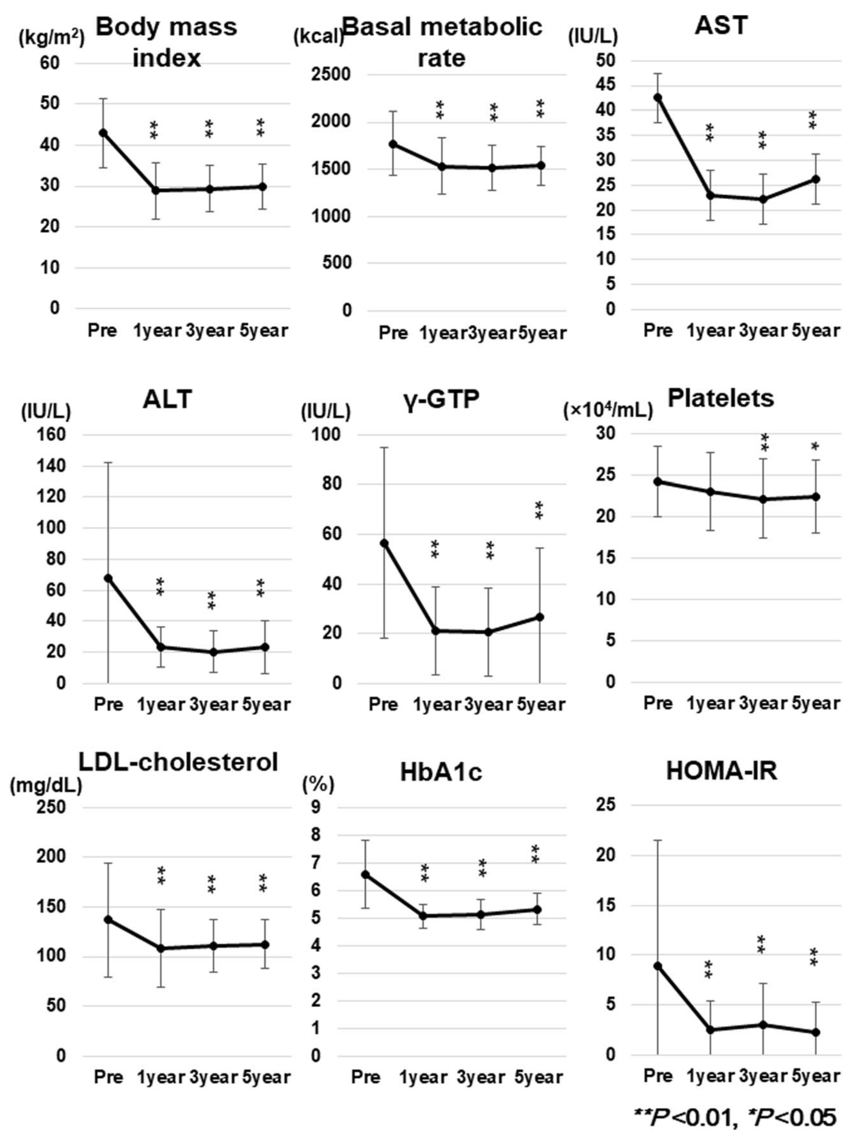

Fig. 2 Follow-up results of NASH patients at 1, 3, and 5 years

Table 2 Follow-up findings for NASH patients at 1, 3, and 5 years

		Pre ($n = 79$)	1 year ($n = 77$)	3 years ($n = 58$)	5 years ($n = 45$)
Body weight	kg (mean ± SD)	121 ± 28.7 (76.3–217.8)	80.8 ± 22.4 (43.8–142.3)**	81.8 ± 17.3 (47.4–124.6)**	82.8 ± 17.7 (46.4–130.5)**
Body mass index	kg/m^2 (mean ± SD)	42.9 ± 8.4 (30.1–63.5)	28.8 ± 6.9 (16.9–51.4)**	29.4 ± 5.7 (16.0–51.2)**	29.9 ± 5.5 (17.5–45.2)**
Waist-hip ratio		1.15 ± 0.13 (0.95–1.48)	0.91 ± 0.13 (0.38–1.23)**	0.94 ± 0.09 (0.76–1.20)**	0.92 ± 0.09 (0.77–1.19)**
Body fat percentage	%	42.7 ± 6.8 (25.9–56.2)	28.0 ± 8.8 (13.4–47.8)**	29.7 ± 6.8 (15.4–42.4)**	32.8 ± 7.7 (16.5–51.2)**
Basal metabolic rate	kcal	1770 ± 338 (1196–2777)	1533 ± 296 (1061–2405)**	1515 ± 241 (1022–2072)**	1536 ± 210 (1168–1958)**
AST	IU/L	42.5 ± 29.0	22.9 ± 8.8**	22.2 ± 12.6**	26.2 ± 13.9**
ALT	IU/L	67.5 ± 74.7	23.5 ± 13.2**	20.5 ± 13.5**	23.2 ± 16.8**
γ-GTP	IU/L	56.7 ± 38.4	21.1 ± 17.8**	20.6 ± 17.6**	26.6 ± 27.8**
Uric acid	mg/dL	6.6 ± 1.6	5.6 ± 1.6**	5.7 ± 1.7**	5.7 ± 1.4**
Albumin	g/dL	4.1 ± 0.3	4.3 ± 0.2**	4.3 ± 0.4**	4.3 ± 0.2**
CRP	mg/dL	0.51 ± 0.44	0.28 ± 1.55**	0.07 ± 0.12**	0.07 ± 0.12**
Fe	mg/dL	103.6 ± 38.5	103.9 ± 42.1	96.4 ± 44.7	108.8 ± 59.1
Platelets	×10^4/mL	24.2 ± 4.3	23.0 ± 4.7*	22.1 ± 4.7**	22.4 ± 4.4*
Total cholesterol	mg/dL	200.2 ± 41.1	192.9 ± 42.0	191.8 ± 33.1	193.6 ± 34.2
HDL cholesterol	mg/dL	46.3 ± 8.3	59.5 ± 13.2**	60.7 ± 15.4**	60.9 ± 16.6**
LDL cholesterol	mg/dL	136.8 ± 57.5	108.1 ± 39.1**	110.5 ± 26.2**	112.5 ± 24.9**
Triglycerides	mg/dL	149.7 ± 98.1	82.6 ± 49.2**	90.9 ± 58.4**	99.8 ± 86.6**
Fasting plasma glucose	mg/dL	125.7 ± 39.7	95.4 ± 14.9**	96.2 ± 13.8**	97.5 ± 12.9**
Fasting blood insulin	mU/mL	26.7 ± 23.3	10.0 ± 9.8**	11.7 ± 14.6**	8.6 ± 10.0**
C-peptide	ng/dL	4.0 ± 1.6	2.6 ± 1.5**	2.8 ± 2.1**	2.4 ± 1.6**
HbA1c	%	6.6 ± 1.2	5.1 ± 0.4**	5.1 ± 0.6**	5.3 ± 0.6**
HOMA-IR		9.0 ± 12.6	2.5 ± 2.9**	3.0 ± 4.2**	2.2 ± 3.1**

AST, aspartate aminotransferase; *ALT*, alanine aminotransferase; *γ-GTP*, γ-glutamyl transpeptidase; *CRP*, C-reactive protein; *HOMA-IR*, homeostasis model assessment insulin resistance; *SD*, standard deviation; *NAS*H, non-alcoholic steatohepatitis

*$P < 0.05$, **$P < 0.01$

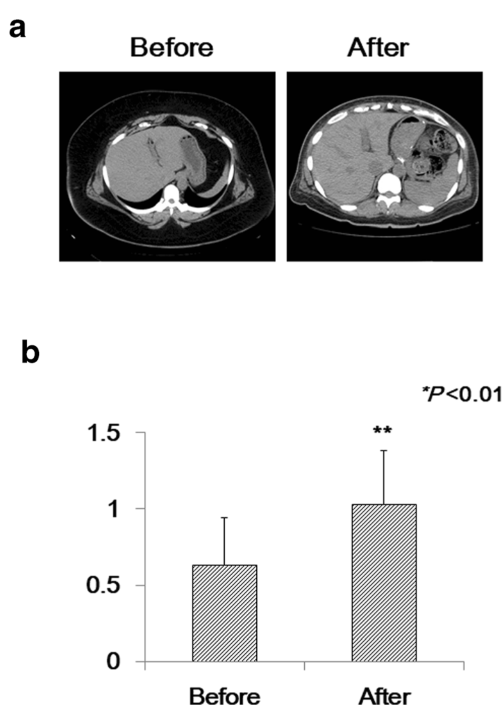

Fig. 3 Abdominal computed tomography of NAFLD patients at the liver level before and at 1 year after surgery. **a** Representative imaging before and at 1 year after surgery at the liver level. **b** The change in the liver/spleen ratio before and at 1 year after surgery

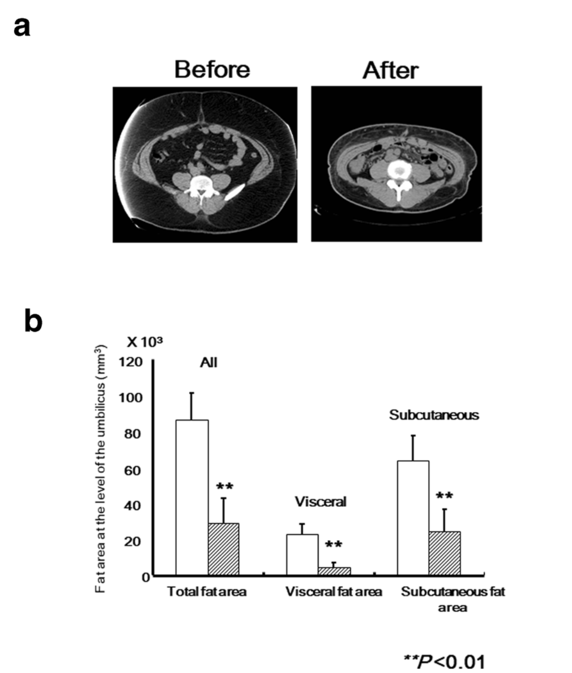

Fig. 4 Abdominal computed tomography of NAFLD patients at the umbilical level before and at 1 year after surgery. **a** Representative imaging before and at 1 year after surgery at the umbilical level. **b** The change in the fat area at the umbilical level before and at 1 year after surgery. Total, visceral, and subcutaneous fat areas were calculated

In conclusion, bariatric surgery is useful for ensuring the long-term treatment of NAFLD/NASH in morbidly obese Japanese patients. Bariatric surgery is a therapeutic option for patients resistant to conventional treatment.

Compliance with Ethical Standards

This study was approved by institutional review board (IRB) of both Yotsuya Medical Cube and Gunma University Hospital.

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

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Shuai X, Tao K, Mori M, et al. Bariatric surgery for metabolic syndrome in obesity. Metab Syndr Relat Disord. 2015;13:149–60.
2. Seki Y, Kakizaki S, Horiguchi N, et al. Prevalence of nonalcoholic steatohepatitis in Japanese patients with morbid obesity undergoing bariatric surgery. J Gastroenterol. 2016;51:281–9.
3. Liang RJ, Wang HH, Lee WJ, et al. Diagnostic value of ultrasonographic examination for nonalcoholic steatohepatitis in morbidly obese patients undergoing laparoscopic bariatric surgery. Obes Surg. 2007;17:45–56.
4. Dixon JB, Bhathal PS, O'Brien PE. Nonalcoholic fatty liver disease: predictors of nonalcoholic steatohepatitis and liver fibrosis in the severely obese. Gastroenterology. 2001;121:91–100.
5. Chisholm J, Seki Y, Toouli J, et al. Serologic predictors of nonalcoholic steatohepatitis in a population undergoing bariatric surgery. Surg Obes Relat Dis. 2012;8:416–22.
6. Harnois F, Msika S, Sabaté JM, et al. Prevalence and predictive factors of non-alcoholic steatohepatitis (NASH) in morbidly obese patients undergoing bariatric surgery. Obes Surg. 2006;16:183–8.
7. Kakizaki S, Takizawa D, Yamazaki Y, et al. Nonalcoholic fatty liver disease in Japanese patients with severe obesity who received laparoscopic Roux-en-Y gastric bypass surgery (LRYGB) in comparison to non-Japanese patients. J Gastroenterol. 2008;43:86–92.
8. Lee WJ, Wang W. Bariatric surgery: Asia-Pacific perspective. Obes Surg. 2005;15:751–7.
9. The Japanese Society of Gastroenterology. Evidence-based clinical practice guidelines for nonalcoholic fatty liver disease/ nonalcoholic steatohepatitis 2014. Tokyo: Nankodo; 2013.
10. Watanabe S, Hashimoto E, Ikejima K, et al. Evidence-based clinical practice guidelines for nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. Hepatol Res. 2015;45:363–77.
11. Sakitani K, Enooku K, Kubo H, et al. Clinical characteristics of patients with diabetes mellitus and fatty liver diagnosed by liver/spleen Hounsfield units on CT scan. J Int Med Res. 2017;45:1208–20.
12. The Japan Diabetes Society. Evidence-based practice guideline for the treatment for diabetes in Japan 2013. Tokyo: Nankodo; 2013.
13. Lassailly G, Caiazzo R, Buob D, et al. Bariatric surgery reduces features of nonalcoholic steatohepatitis in morbidly obese patients. Gastroenterology. 2015;149:379–88.
14. Schneck AS, Anty R, Patouraux S, et al. Roux-en-Y gastric bypass results in long-term remission of hepatocyte apoptosis and hepatic histological features of non-alcoholic steatohepatitis. Front Physiol. 2016;7:344.
15. Colles SL, Dixon JB, Marks P, et al. Preoperative weight loss with a very-low-energy diet: quantitation of changes in liver and abdominal fat by serial imaging. Am J Clin Nutr. 2006;84:304–11.
16. Lackner C, Struber G, Liegl B, et al. Comparison and validation of simple noninvasive tests for prediction of fibrosis in chronic hepatitis C. Hepatology. 2005;41:1376–82.
17. Furuncuoğlu Y, Tulgar S, Dogan AN, et al. How obesity affects the neutrophil/lymphocyte and platelet/lymphocyte ratio, systemic immune-inflammatory index and platelet indices: a retrospective study. Eur Rev Med Pharmacol Sci. 2016;20:1300–6.
18. Koca TT. Does obesity cause chronic inflammation? The association between complete blood parameters with body mass index and fasting glucose. Pak J Med Sci. 2017;33(1):65–9.
19. Yoshioka K, Hashimoto S, Kawabe N. Measurement of liver stiffness as a non-invasive method for diagnosis of non-alcoholic fatty liver disease. Hepatol Res. 2015;45:142–51.
20. Chen J, Talwalkar JA, Yin M, et al. Early detection of nonalcoholic steatohepatitis in patients with nonalcoholic fatty liver disease by using MR elastography. Radiology. 2011;259:749–56.