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ORIGINAL ARTICLE

Fatty liver disease in living liver donors: a single-institute experience of 220 donors

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SUMMARY

We retrospectively reviewed 220 living liver donors, with a focus on the development of postoperative fatty liver. Data regarding demographics, comorbidities, imaging tests, operations and biopsies were obtained from medical records. We used unenhanced CT and USG to diagnose fatty liver. Donor candidates with fatty liver underwent weight loss intervention until imaging tests no longer demonstrated any features of fatty liver. Among 220 donors, 61 were diagnosed with preoperative fatty liver. The mean BMI of these 61 donors significantly decreased from 24.9 at the first visit to 23.6 kg/m^2 immediately before surgery ($P = 0.0386$). A multivariate analysis revealed the following significant risk factors for postoperative fatty liver: male sex ($P = 0.0033$), BMI immediately before surgery ($P = 0.0028$) and a history of treatment for preoperative fatty liver ($P = 0.0231$). Postoperative fatty liver was often refractory to weight loss intervention. No improvement was observed in 14 of the 32 donors who had been diagnosed with fatty liver postoperatively, and one of the 14 donors even developed NASH. In conclusion, special attention should be paid to prevent fatty liver after surgery in male donors who show a high BMI immediately before surgery and with a history of treatment for preoperative fatty liver, and lifelong follow-up is recommended.

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Key words
fatty liver disease, living donor liver transplantation, postoperative donor follow-up

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Introduction

Living donor liver transplantation (LDLT) was introduced in Japan in 1989, as a life-saving procedure for end-stage liver disease (ESLD) [1]. LDLT offers liver transplant candidates an alternative to a long wait for a liver from a deceased donor. However, LDLT poses risks to the donor—subjecting a healthy person to a major surgical procedure without any direct therapeutic benefit. The morbidity and mortality of living liver donors have been reported worldwide [2–7]. Thus, potential donors must be in good physical and mental health, and donor safety should be the top priority in any situation.

The use of steatotic grafts for liver transplantation is significantly associated with poorer outcomes in the recipient. Accumulating evidence indicates that steatosis in liver grafts increases the incidence of postoperative complications and primary graft nonfunction, and prolongs intensive care unit stay and hospital stay—

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consequently increasing the treatment costs [8]. Furthermore, long-term investigations show that donor steatosis is a risk factor for steatohepatitis and new-onset diabetes in recipients after LDLT [9,10]. Therefore, >30% macrovesicular steatosis is considered unacceptable in most transplant centres, and half of these centres prefer to include evaluations of macrovesicular and microvesicular steatosis when assessing graft suitability [11].

Steatosis in liver grafts could also have negative effects on donor outcomes after living liver donation. Studies have shown that steatosis is a risk factor for liver resection in general, demonstrating associations with an increased operative time, increased blood loss during transection, impaired hepatic regeneration and incidence of postoperative complications [12]. Thus, donors with steatosis may experience adverse outcomes after living liver donation. In fact, the only reported death of a living liver donor in Japan was related to nonalcoholic steatohepatitis (NASH) [7].

As the prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing worldwide, the pool of potential living liver donors is more frequently populated by individuals with fatty liver disease [13]. Donor candidates who have successfully ameliorated fatty liver through diet therapy are considered eligible. However, the long-term outcomes of such donors have not been fully evaluated. In the present retrospective study, we aimed to clarify the prevalence of and risk factors for postoperative fatty liver in living liver donors.

Patients and methods

Participants

Two hundred and thirty-three consecutive donors underwent donor hepatectomy in Osaka University Hospital between January 2000 and December 2015. Among them, six were excluded because they were lost to follow-up, and another seven were excluded because of the missing data. Thus, a total of 220 donors were enrolled in this study. The donors included 134 males and 86 females (mean age, 38 years [SD, ±11 years]). The study protocol was in accordance with the Declaration of Helsinki, and was approved by the Osaka University Clinical Research Review Committee.

Definitions

In this study, fatty liver was diagnosed by unenhanced computed tomography (CT) and ultrasonography (USG). The criterion for the diagnosis of fatty liver on unenhanced CT was a ratio of liver-to-spleen Hounsfield units <1.0. This ratio is reported to be useful in diagnosing cases of ≥30% steatosis [14]. The USG criteria were the presence of liver brightness and posterior attenuation, with stronger echoes in the hepatic parenchyma in comparison to the renal parenchyma and vessel blurring [15]. USG is also an accurate, reliable tool for detecting ≥20–30% steatosis, with a sensitivity and specificity of 84.8% and 93.6%, respectively [16].

Preoperative comorbidities of donor candidates that were considered in the present study included hypertension, diabetes mellitus and dyslipidaemia. These comorbidities were diagnosed based on the criteria of the Japan Society of Hypertension, the Japan Diabetes Society and the Japan Atherosclerosis Society. Hypertension was defined as a blood pressure of 140/90 mmHg or greater, or the use of any drug treatment for high blood pressure [17]. Diabetes mellitus was defined as a fasting plasma glucose level of ≥110 mg/dl from at least two assessments, a haemoglobin A1c (National Glycohemoglobin Standardization Program) value of >6.5%, or any drug treatment for diabetes mellitus [18]. Dyslipidaemia was defined as a total cholesterol level of ≥220 mg/dl, a low density lipoprotein cholesterol level of ≥140 mg/dl, a high density lipoprotein cholesterol level of <40 mg/dl, a triacylglyceride level of ≥150 mg/dl, or use of any drugs for the treatment of dyslipidaemia [19,20].

Donor evaluation

The preoperative evaluation included the complete history, a physical examination and laboratory tests, including blood count, blood chemistry, coagulation factors, hepatitis B virus, hepatitis C virus and serological profiles for other infectious disease. Donors also underwent chest and abdominal radiography, four-phase multidetector CT, drip infusion cholangiography-CT with three-dimensional reconstruction, and USG. Donor candidates were rejected if they were taking medications for any systemic disease, such as hypertension, diabetes mellitus, or psychiatric disease [21]. The requirements for living liver donation were an estimated remnant liver volume of >35% of the donor whole liver volume and an estimated graft volume of >35% of the recipient's standard liver volume.

Donor candidates who were diagnosed with fatty liver by unenhanced CT or USG were introduced to an experienced hepatologist to confirm the diagnosis and to receive a prescription for dietary and physical activity

intervention. After a period of intervention, they were re-evaluated by unenhanced CT and USG. We only accepted those whose findings were within the normal limits in both examinations (Fig. 1). It is our policy to avoid percutaneous liver biopsy in donor candidates, because this procedure can cause serious complications, such as bleeding. Preoperative liver biopsy is only indicated in cases where the hepatologist considers it is necessary.

Donor follow-up

In accordance with our LDLT protocol, donors were scheduled to visit the hospital for outpatient follow-up at 1, 3, 6 and 12 months postoperatively, and annually thereafter. Contrast-enhanced CT and laboratory tests were routinely performed during the first year of follow-up, while subsequent visits generally included physical examinations and blood tests, as well as weight measurement. We also questioned donors about their lifestyle every time and provided instructions to help donors develop or maintain a healthy lifestyle. Abnormal liver tests results and significant weight gain, prompted the suspicion of fatty liver. Donors with suspected fatty liver during follow-up were introduced to an experienced hepatologist. Unenhanced CT and USG was used to diagnose fatty liver after surgery, in the same manner as in the above-mentioned donor

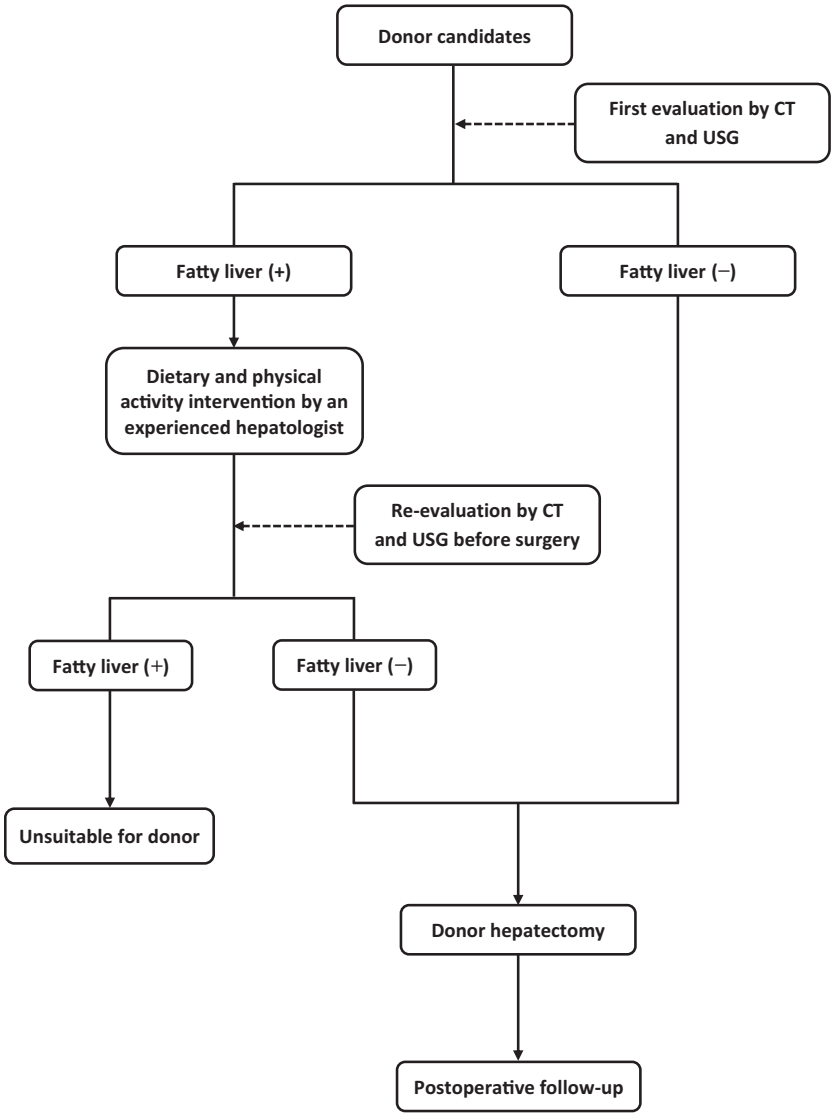

Figure 1 Donor evaluation protocol for fatty liver.

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evaluation, and percutaneous liver biopsy was indicated only in carefully selected cases. When donors were unable to visit the hospital, coordinators contacted the subjects via phone or mail, to ask about their recent physical condition. If the donors had received laboratory tests or abdominal imaging tests elsewhere, we asked for the results. Basically, we strongly recommended that all donors receive lifelong follow-up at our institute.

Data collection

Data regarding the donor demographics, preoperative comorbidities, imaging test results, operative factors and histological findings were collected from the hospital electronic medical records. Demographic data included sex, age at the time of surgery, height, weight and body mass index (BMI). In particular, we collected height and weight data at the first visit and immediately before surgery. The preoperative comorbidities included hypertension, diabetes mellitus and dyslipidaemia. Imaging tests included unenhanced CT and USG scans. Operative factors included the operative time, intraoperative blood loss and transfusion, graft type and postoperative complications. Histological findings refer to the intraoperative liver biopsy results regarding the extent of steatosis, with biopsy specimens obtained before graft harvest or after revascularization ("time zero biopsy" [22]) during surgery. Donors were encouraged to continue dietary and physical activity even after they had passed their re-evaluation. We therefore set a threshold of steatosis of intraoperative biopsy as low as 5% (the sum of macrovesicular and microvesicular steatosis) to evaluate the final level of preoperative donor management.

Statistical analysis

Data are presented as the mean ± standard deviation for continuous data, and as the number and percentage for categorical data. Comparisons between each pair of groups were performed using a Mann–Whitney *U* test for continuous variables, and either a chi-squared test or Fisher's exact test for categorical variables. Multivariate analyses were accomplished using logistic regression to calculate the independent risk factors for postoperative fatty liver, using variables found to be significant in a univariate analysis. All statistical analyses were performed using the JMP® 14 (SAS Institute Inc., Cary, NC, USA) software package, and P values of <0.05 were considered statistically significant.

Results

Donor characteristics

Table 1 summarizes the baseline characteristics of the 220 donors who were enrolled in this study. The BMI values at the two time-points did not differ to a statistically significant extent ($P = 0.3714$). At the preoperative donor evaluation, 61 donors were diagnosed with fatty liver by unenhanced CT and USG, while the remaining 159 were not diagnosed as such. Overall, 66 donors were diagnosed with dyslipidaemia, two were diagnosed with diabetes mellitus and 4 were diagnosed with hypertension—including one donor who had both hypertension and dyslipidaemia, and one who had all three comorbidities. The prevalence of dyslipidaemia was reduced to 46 donors through preoperative dietary and physical activity intervention. The most frequently used graft type was a left lobe graft, followed in decreasing order by a right lobe graft, lateral segment graft and posterior segment graft. A total of 57 donors experienced grade 1–3 postoperative complications, based on the Clavien–Dindo classification [23]; no donors experienced more severe complications (details not shown).

Table 1. Living liver donor characteristics.

Characteristics	*N* = 220
Age in years, mean ± SD	38 ± 11
Male sex, *n* (%)	134 (60.9%)
BMI in kg/m^2, mean ± SD	
First visit	22.6 ± 3.3
Immediately before surgery	22.2 ± 2.8
History of treatment for preoperative fatty liver, *n* (%)	61 (27.7%)
Comorbidities in outpatient period, *n* (%)	
Hypertension	4 (1.8%)
Diabetes mellitus	2 (0.9%)
Dyslipidaemia	66 (30.0%)
Graft type, *n* (%)	
Left lobe graft	83 (37.7%)
Right lobe graft	69 (31.4%)
Lateral segment graft	56 (25.5%)
Posterior segment graft	12 (5.5%)
Operative time in minutes, mean ± SD	424 ± 82
Intraoperative blood loss in ml, mean ± SD	509 ± 478
Intraoperative blood transfusion, *n* (%)	0 (0%)
Histological findings by intraoperative liver biopsy, *n* (%)	9
<5% steatosis	177 (80.5%)
≥5% steatosis	43 (19.5%)
Postoperative complications, *n* (%)	57 (25.9%)

Risk factors for postoperative fatty liver

A total of 32 donors were postoperatively diagnosed with fatty liver, and the remaining 188 donors were not. Table 2 presents the results of the univariate and multivariate analyses of risk factors for postoperative fatty liver. Donors with postoperative fatty liver showed a significant male predominance, a significantly higher mean BMI immediately before surgery, a greater prevalence of preoperative comorbidities and a significantly more frequent history of treatment for fatty liver before surgery than the donors without postoperative fatty liver. Upon intraoperative liver biopsy, donors with postoperative fatty liver showed ≥5% steatosis significantly more frequently. Other factors, including donor age, did not significantly differ between the groups. A multivariate analysis revealed that male sex, BMI immediately before surgery and a history of treatment for preoperative fatty liver were significant risk factors for postoperative fatty liver.

The effect of preoperative fatty liver

As the history of treatment for preoperative fatty liver was identified as a significant risk factor in the multivariate analysis, we divided the donors into two groups based on the presence of a history of such treatment to compare various factors (Table 3). Donors with a history of treatment for preoperative fatty liver showed a significant male predominance, a significantly greater prevalence of preoperative comorbidities and a higher mean BMI at both time-points than the donors without a history of such treatment. Regarding the difference in BMI between the two time-points among donors with a history of treatment for preoperative fatty liver, their BMI was significantly reduced from 24.9 at the first visit to 23.6 kg/m^2 immediately before surgery ($P = 0.0386$). Donors with a history of treatment for preoperative fatty liver had a significantly longer interval between the first visit up until the day of surgery probably because of the preoperative dietary and physical activity intervention. As to the operative factors, although donors with a history of treatment for preoperative fatty liver had greater blood loss during surgery, there were no statistically significant differences in the operative time and frequency of postoperative complications. Donors with a history of treatment for preoperative fatty liver showed ≥5% steatosis upon intraoperative biopsy significantly more frequently than donors without a history of such treatment.

Table 2. Univariate and multivariate analyses of risk factors associated with postoperative fatty liver.

Factors	Postoperative fatty liver (+) (n = 32)	Postoperative fatty liver (−) (n = 188)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	*P* values	OR (95% CI)	*P* values
Age in years, mean ± SD	36 ± 10	39 ± 12	0.98 (0.95–1.02)	0.3229		
Male sex, *n* (%)	30 (94%)	104 (55%)	12.11 (2.81–52.17)	**<0.0001**	11.17 (2.23–55.99)	**0.0033**
BMI immediately before surgery in kg/m^2, mean ± SD	24.5 ± 3.1	21.9 ± 2.6	1.37 (1.19–1.58)	**<0.0001**	1.31 (1.09–1.57)	**0.0028**
Preoperative comorbidities, *n* (%)	14 (44%)	35 (19%)	3.38 (1.53–7.44)	**0.0032**	0.83 (0.31–2.24)	0.7171
History of treatment for preoperative fatty liver, *n* (%)	21 (66%)	40 (21%)	7.06 (3.15–15.86)	**<0.0001**	2.95 (1.16–7.49)	**0.0231**
Right Lobe graft type, *n* (%)	9 (28%)	60 (32%)	0.83 (0.36–1.91)	0.6667		
≥5% steatosis by intraoperative liver biopsy, *n* (%)	15 (47%)	28 (15%)	5.04 (2.26–11.24)	**0.0001**	2.55 (0.97–6.71)	0.0582
Operative time in minutes, mean ± SD	426 ± 84	424 ± 82	1.00 (0.99–1.00)	0.8864		
Intraoperative blood loss in ml, mean ± SD	644 ± 580	486 ± 457	1.00 (0.99–1.00)	0.1063		
Postoperative complications, *n* (%)	8 (25%)	49 (26%)	0.95 (0.39–2.24)	0.8986		

When the p values are less than 0.05, they are indicated in bold.

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Table 3. Differences in donor factors between groups based on a history of treatment for preoperative fatty liver.

	Preoperative fatty liver (+) (n = 61)	Preoperative fatty liver (−) (n = 159)	P values
Age in years, mean ± SD	41 ± 12	37 ± 11	0.0745
Male sex, n (%)	48 (79%)	86 (54%)	**0.0008**
Preoperative comorbidities, n (%)	25 (41%)	24 (15%)	**<0.0001**
BMI in kg/m^2, mean ± SD			
First visit	24.9 ± 3.9*	21.8 ± 2.6	**<0.0001**
Immediately before surgery	23.6 ± 3.0*	21.7 ± 2.6	**<0.0001**
Days from first visit to surgery, mean ± SD	145 ± 179	102 ± 129	**0.0264**
Right Lobe graft type, n (%)	21 (34%)	48 (30%)	0.5442
Intraoperative blood loss in ml, mean ± SD	617 ± 549	468 ± 443	**0.0344**
Operative time in minutes, mean ± SD	429 ± 73	422 ± 86	0.3261
Postoperative complications, n (%)	17 (28%)	40 (25%)	0.6811
≥5% steatosis by intraoperative liver biopsy, n (%)	22 (36%)	21 (13%)	**0.0001**

*P = 0.0386.

When the p values are less than 0.05, they are indicated in bold.

We subsequently divided the 61 donors with a history of treatment for preoperative fatty liver into two groups based on the extent of steatosis on intraoperative biopsy: the ≥5% group (22 donors) and the <5% group (39 donors). The mean BMI of the <5% group significantly decreased from 24.6 ± 4.0 at the first visit to 22.9 ± 2.8 kg/m^2 immediately before surgery (P = 0.0349), while that of the ≥5% group did not (from 25.5 ± 3.6 to 24.8 ± 3.0 kg/m^2, P = 0.4304). Notably, 12 of the 22 (55%) patients in the ≥5% group were postoperatively diagnosed with fatty liver, in comparison to only nine of the 39 (12%) patients in the <5% group (P = 0.0130), suggesting that the extent of steatosis in the intraoperative biopsy specimen has a clinical implication during follow-up, despite the fact that it only showed marginal significance in the multivariate analysis.

Postoperative follow-up

Among the 32 donors who were postoperatively diagnosed with fatty liver, 21 donors with a history of treatment for preoperative fatty liver were diagnosed at a mean of 2.7 years after surgery, in comparison to a mean of 6.8 years in donors without a history of such treatment (P = 0.0007). Moreover, 10 of the donors with a history of treatment for preoperative fatty liver were diagnosed within one year after surgery, while no one was diagnosed within one year of surgery among the donors without a history of such treatment (P < 0.0001).

Regarding the outcomes of postoperative fatty liver, although we performed the same dietary and physical activity intervention as before surgery, this approach worked well in only seven of the 32 donors. The features of fatty liver disappeared on imaging tests, and the liver enzymes (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) also improved to the normal ranges. Eleven donors also showed improved levels of liver enzymes, but their imaging tests still revealed features of fatty liver. The remaining 14 donors had persistent abnormal values of liver enzymes, including one who had shown an ALT value of ≥100 IU/l several times and was eventually diagnosed with NASH by a liver biopsy.

Discussion

Our results showed that fatty liver after donor hepatectomy was highly associated with male sex, BMI immediately before surgery and a history of treatment for preoperative fatty liver. The association with ≥5% steatosis upon intraoperative biopsy and preoperative comorbidities was significant in univariate analyses; however, in the multivariate analysis, ≥5% steatosis only showed marginal significance and the presence of comorbidities did not remain significant.

Male sex has been considered a risk factor for NAFLD [24]. The prevalence of NAFLD is reportedly higher in men than in women [25]. Additionally, men consume more alcohol than women worldwide [26], which may lead to the development of alcoholic fatty liver disease (AFLD). In our donor population, males comprised 48 (79%) of the 61 donors who were preoperatively diagnosed with fatty liver (Table 3). Moreover, the severity of NAFLD is also higher in men in comparison to women [25]. In our study, among the 61 donors

who underwent preoperative dietary and physical activity intervention, 22 donors showed ≥5% steatosis upon intraoperative liver biopsy. Notably, 20 of these 22 (91%) donors were male. We hypothesize that in comparison to female donors, male donors may have had a more severe degree of fatty liver before surgery, which made it more difficult for males to achieve complete improvement (<5% steatosis) within the limited time before surgery. Postoperatively, fatty liver was also more frequently diagnosed in males, as 30 of the 32 (94%) donors who were diagnosed with postoperative fatty liver were male (Table 2). Another possible reason is that male donors more frequently resumed drinking alcohol after surgery, which may have contributed to the development of fatty liver.

The relationship between fatty liver and BMI has been well documented, and hepatic steatosis is becoming more common in association with the worldwide increase in obesity [27]. Obesity is among the most common reasons of donor candidate disqualification early in evaluation, because of the increased likelihood of significant steatosis [13]. Within our study population, donors who were diagnosed with fatty liver after surgery had a mean BMI immediately before surgery of 24.5 kg/m^2, which was significantly higher than that of donors who were not diagnosed with fatty liver after surgery (21.9 kg/m^2). A BMI of 24.5 kg/m^2 is very close to the criterion of obesity class 1, as defined by the Japan Society for the Study of Obesity [28], which is a BMI of ≥25 kg/m^2. Moreover, based on the diagnostic criteria for the new nomenclature for fatty liver—metabolic dysfunction-associated fatty liver disease (MAFLD), which was recently reported by Eslam *et al.* [29], overweight is defined as a BMI of ≥23 kg/m^2 among Asians. The mean BMI of 24.5 kg/m^2 sufficiently fulfils this diagnostic criterion for MAFLD.

Weight loss through lifestyle modification, consisting of diet and exercise, is the current mainstay of therapy for NAFLD [30,31]. Guidance from the American Association for the Study of Liver Diseases suggests that a loss of at least 3–5% of body weight is necessary to improve steatosis [24]. Wong VW *et al.* [32] reported that half of non-obese patients (<25 kg/m^2) achieved remission of NAFLD with 3–5% body weight loss; however, the same could only be achieved in obese patients (≥25 kg/m^2) with 7–10% body weight loss. This highlights that weight loss is associated with the remission of NAFLD in a dose-dependent manner. In our study, the mean BMI was significantly reduced from 24.9 to 23.6 kg/m^2 in the 61 donors who received dietary and physical activity intervention before surgery (Table 3); the rate of body weight loss was 5%. Moreover, 39 of these donors who exhibited <5% steatosis upon intraoperative biopsy achieved a more significant reduction in BMI from 24.6 to 22.9 kg/m^2; the rate was approximately 7%.

When a donor candidate is diagnosed with fatty liver based on a preoperative evaluation, our hepatologist instructs the candidate to lose weight. The minimum requirement is the absence of fatty liver in a re-evaluation by unenhanced CT and USG. Therefore, mild steatosis could exist in donor candidates who fulfilled the minimum requirement, although a mild steatotic liver can generally be acceptable as a liver graft in LDLT [11]. The goal of our preoperative dietary and physical activity intervention is to achieve a BMI of 22 kg/m^2, which is the ideal BMI for Japanese individuals [28]. In principle, we instruct donor candidates to continue to lose weight even after they pass a re-evaluation by unenhanced CT and USG. Nevertheless, in practice, weight loss is difficult to achieve and sustain. Some donor candidates can barely achieve the minimum requirement through several months of effort. It is ideal to continue losing weight thereafter; however, in some cases, transplantation cannot wait because the recipient is usually in a state of ESLD. Moreover, some donor candidates may reduce their efforts after they fulfil the minimum CT and USG requirements. Therefore, it is crucial to strictly instruct donor candidates to sustain their weight loss, even after a successful re-evaluation.

Postoperative follow-up of donors and continuous lifestyle instruction is very important. In our study, donors with a history of treatment for preoperative fatty liver frequently developed fatty liver again after surgery. In general, NAFLD patients are more likely to have an unhealthy lifestyle [33], and it is reported that long-term sustained weight loss is only achieved by 3%–6% of subjects [30]. Thus, it is necessary to see donors regularly at an outpatient clinic after surgery, to monitor their body weight and to educate them on refraining from unhealthy lifestyle habits, including excessive alcohol consumption. Furthermore, the outcomes of postoperative fatty liver in living liver donors were unsatisfactory, probably because of the lack of incentive to save the life of a beloved person. Almost half of the donors (14 of 32) who developed fatty liver after surgery did not show any improvement in either liver enzymes or imaging tests. One among them even developed NASH, which could make him a liver transplantation candidate in the future. NASH is rapidly becoming one of the leading causes of liver transplantation in much of the world, especially the United States [27,34]. Thus, preventing the development of fatty liver in living liver donors after surgery is more important than treatment.

A transplant centre reported that they obtain a preoperative liver biopsy specimen as a routine procedure in donor evaluation [35]. However, this is not a usual procedure worldwide [11]. Our policy is to avoid percutaneous liver biopsy in donor candidates. Ratziu *et al.* reported that considerable sampling variability could exist between two samples from the same liver, which could result in a substantial rate of misdiagnosis and staging inaccuracy in individuals with NASH [36]. In a retrospective study, Guba *et al.* reported a case in which preoperative liver biopsy failed to demonstrate steatohepatitis, and this ultimately led to the abortion of donor hepatectomy [37]. Furthermore, percutaneous liver biopsy can cause complications, including bleeding and pain [38]. In our institute, preoperative liver biopsy is only performed in cases where the hepatologist considers it is necessary for a definite diagnosis, such as donor candidates who present no features of fatty liver on CT or USG, but who show an elevated serum ALT level, or in whom other liver diseases are suspected. In contrast, intraoperative liver biopsy not only avoids the risk of a percutaneous procedure, but can also more accurately quantify the steatosis in the donor liver graft. This is a routine intraoperative procedure that is performed in most liver transplant centres to check for the ischemia/reperfusion injury. The extent of steatosis can be assessed at the same time. Although ≥5% steatosis in the intraoperative biopsy specimen showed marginal significance in the multivariate analysis, it could be useful for assessing the risk of postoperative fatty liver, especially among donors with a history of treatment for preoperative fatty liver.

This study was associated with several limitations. First, this study was a retrospective analysis that relied on data from medical records, and some data were missing. Second, since this was a single-centre study, further investigations are needed to assess the generalizability of our findings to other donor populations. Third, this was a 15-year retrospective study of 220 cases. Over this time period, there were a few changes to both our donor evaluation protocol and the diagnostic criteria for comorbidities. Fourth, the preoperative and postoperative diagnosis of fatty liver was based on unenhanced CT and USG. Liver biopsy was avoided whenever possible because we consider that donor safety comes first. Since selective liver biopsy is the usual practice for donor evaluation worldwide [11], the results of the present study could have clinical significance.

Our results showed that the risk factors for postoperative fatty liver in living liver donors were male sex, the BMI immediately before surgery and a history of treatment for preoperative fatty liver. Ideally, several donor candidates would exist, which would allow those with such risk factors to be excluded. However, the number of living donor candidates for a given recipient is usually very limited, and we are forced in such cases to select a less-than-ideal candidate as a living donor. Careful attention is required for these donors, because of the high possibility of fatty liver development after surgery, and lifelong follow-up is recommended.

Authorship

WF: designed study, collected data, performed study, analysed data, wrote the paper. MN: designed study, collected data. KG: performed study, analysed data, wrote the paper. YM: designed study, performed study. TN: performed study. SK: performed study. YD: performed study. HE: performed study. KU: designed study, performed study, analysed data, wrote the paper.

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Conflicts of interest

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