

# Apparent improvement of fatty liver by petite low carbohydrate diet (LCD) in patient with type 2 diabetes (T2D)

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## Abstract

The case is a 64-year-old female patient with type 2 diabetes (T2D), dyslipidemia, hypertension who has been taking the medicines Metformin, Linagliptin, Rosuvastatin, and Amlodipine. She continued the petite low carbohydrate diet (LCD) for the latest 2-3 years, and then clinical changes were found, including weight reduction of 3-4 kg, improvement of fatty liver by abdominal CT scan, and laboratory data of GOT 87 to 20 U/L, GPT 63 to 24 U/L, GGT 209 to 99 U/L, HbA1c 7.6 to 6.2%, and LDL 166 to 57 mg/dL. Though LCD is continued to a limited degree, it can contribute to the clinical improvement of T2D and metabolic dysfunction-associated steatotic liver disease (MASLD).

**Keywords:** Type 2 diabetes (T2D); Low carbohydrate diet (LCD); Metabolic dysfunction-associated steatotic liver disease (MASLD); Japan LCD promotion association (JLCDPA); Fatty liver index (FLI); Nonalcoholic fatty liver disease (NAFLD)

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## Introduction

For decades, various practices and research have been found concerning overweight, type 2 diabetes (T2D), the Diabetes Remission Clinical Trial (DiRECT), and metabolomics technologies [1]. Several biomarkers may be related to the diabetic pathophysiology of complications and clinical progress, such as LDL, triglyceride, branched-chain amino acids (BCAAs), and other metabolites. From the WHO global diabetes point of view, certain contexts of the growing burden of diabetes-related medical and health problems have attracted attention [2]. Among them, core target and metric levels for some UN members have been found. They include: i) at least 80% of possible diabetes would be diagnosed, ii) 80% of diagnosed diabetics have HbA1c below 8.0%, iii) 80% of diagnosed diabetics show BP below 140/90 mmHg, and iv) 60% of diagnosed diabetics take statins.

Combining adequate nutritional treatment and pharmacological agents, T2D patients would be treated in a more satisfactory manner than before [3]. From a diabetic treatment point of view, recent advances have been made in the detailed measurement of simultaneous glucose variability, effective oral hypoglycemic agents (OHAs), and injective agents for diabetes [4]. Furthermore, some agents show beneficial clinical effects for heart failure, blood pressure, and renal function, leading to a reduction in the risk of cardiovascular events. The medicine includes sodium glucose co-transporter 2 inhibitors (SGLT-2i), glucagon-like peptide-1 receptor agonists (GLP-1RA), newer glucose-dependent insulinotropic polypeptides (GIP), GLP-1

dual agonists, and others.

Concerning the related problems of diabetes and fatty liver, metabolic problems have been known for patients with nonalcoholic fatty liver disease (NAFLD). They include several clinically diseased states, such as fatty liver, diabetes, metabolic syndrome, and atherosclerotic cardiovascular disease (ASCVD). The multi-medical society consensus group proposed a novel nomenclature for metabolic dysfunction-associated steatotic liver disease (MASLD) [5]. Lots of NAFLD patients as diagnosed before seem to have been reclassified and also categorized as MASLD under the current nomenclature, and several associations and specific institutes have studied the difference and coincidence between NAFLD and MASLD using various data so far. Further, waist circumference would be adjusted according to the different races, ethnicities, or countries. Moreover, the increased risk of certain diseases, such as diabetes, can be clarified through detailed analyses [6].

Authors and collaborators have been involved in clinical nutrition therapy, the treatment of atherosclerotic cardiovascular diseases (ASCVD), and so on for a long time. Aside from them, we have initiated and developed a low-carbohydrate diet (LCD) in Japan through various activities of the Japan LCD Promotion Association (JLCDPA) [7,8]. We have announced 3 useful types of LCD, which are super LCD, standard LCD, and petite LCD, associated with carbohydrate calorie ratios of 12%, 26%, and 40%, respectively [9]. Several diseases included type 1 diabetes (T1D), slowly progressive insulin-dependent diabetes mellitus (SPIDDM), T2D, and dyslipidemia [10]. In our recent experience, we took care of an impressive female case and her characteristic aspects, and some

discussion will be presented in this article.

## Case Presentation

### History of present illness

The case is a 64-year-old female patient with T2D, dyslipidemia, hypertension, and reflux esophagitis (RE). She had an unremarkable past medical history until her 50s. She was pointed out to have elevated levels of LDL cholesterol about 6 years ago. Her clinical progress has been summarized in Table 1, including liver function, HbA1c, and lipid profile. It shows

elevated HbA1c and liver function for years. Her current medication has been stable for years: Metformin 500mg, Linagliptin 5mg, Rosuvastatin 2.5mg, Amlodipine 2.5 mg, and Esomeprazole Magnesium Hydrate 20mg per day. Her general situation and laboratory data have been almost stable for a few years.

She has continued the standard to a petite level of LCD so far. Her body weight has been slowly decreasing from 56kg to 53kg for the past 2–3 years. When she was 20 years old, her weight was 48kg. Her weight was gradually increased from 48kg to 56kg for 40 years (Table 1).

**Table 1:** Clinical progress for the case.

Year	2021	2022				2023		
Month	2	8	11	1	5	9	3	10
GOT (U/L)	69	84		87		20	25	19
GPT (U/L)	48	63		40		27	26	24
GGT (U/L)	142	189		209		170	99	155
HbA1c (%)	6.5	7.2	7.6	6.9	6.2	7	6.8	6.5
LDL (mg/dL)				166		133	87	57
HDL (mg/dL)				63		49	62	99
TG (mg/dL)				308		87	332	395
Weight (Kg)	56		55		54	53		52
Abd CT scan			*					*

### Physical exams

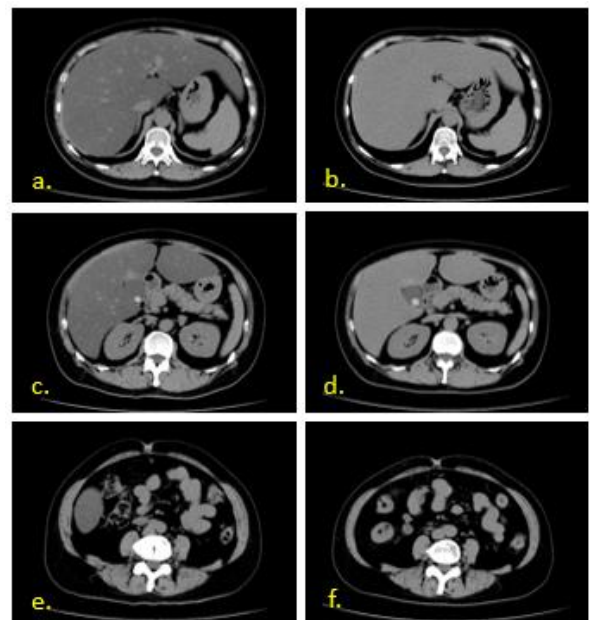
The case revealed unremarkable findings about physical status, vitals, lung, heart, abdomen, and neurological examination. Her body physique showed 150.5 cm in height, 55.6kg in weight, and 24.5 kg/m<sup>2</sup> in body mass index (BMI). As to diabetic complications, she does not have neuropathy, retinopathy, or nephropathy. Further, diabetic macroangiopathy was not detected as a cerebral vascular accident (CVA), ischemic heart disease (IHD), or peripheral artery disease (PAD). Chest X-P is negative, and the ECG revealed an ordinary sinus rhythm with no remarkable ST-T changes. For the examination of the pulse wave chart, the results showed CAVI 9.4/8.6 and ABI 1.16/1.18 in right and left, respectively, which are within normal limits for the age.

### Abdominal CT

Abdominal CT was conducted twice, in November 2021 and October 2023, with a 2-year interval. For the first CT scan, the right lobe of the liver was enlarged, and a higher degree of fatty infiltration in the parenchyma was observed (Figure 1, left). An obvious SOL was not found. One gallstone was detected in the gallbladder. No dilatation of the common bile duct was observed. In the parenchyma of the pancreas, there is a replacement of fat, and its density on the CT image seemed to be somewhat uneven.

For the second CT scan in October 2023, the density level of liver parenchyma decreased compared to the previous exam

(Figure 1, right). It indicates the improvement of the fatty liver. However, there is still moderate fatty infiltration in the liver. No obvious SOL was observed. One gallstone was found in the gallbladder. There was no dilatation of the common bile duct. Overall, the improvement in fatty liver has been detected in comparison with that two years ago.



**Figure 2:** Changes in abdominal CT,

Left (a,c,e) : Nov 2021,

Right (b,d,f): Oct 2023.

## Ethical Considerations

The current article basically follows the ethical principles of the Helsinki Declaration. In addition, some comments were based on the Ethical Guidelines for Human Research. As to this study, the authors' et al. set up our ethical committee for adequate consideration. The committee is in the hospital with several specialists from different professions. They include the president of the hospital, physicians, registered nurses, nutritionists, pharmacists, and legal specialists. We have had a satisfactory meeting for the discussion, and the ethical affairs were recognized in a satisfactory manner. The informed consent was obtained from the patient as a document.

## Discussion

In this case, the fatty liver improved for 2 years by continuing the petite LCD. It implies a slight restriction of 40% carbohydrate involvement, whereas standard and super LCD imply 26% and 12% strict restrictions, respectively. Although weight reduction was mild for 3-4 kg for 2 years, apparent improvement was seen in blood tests and CT scans. Therefore, petite LCD can contribute to improving fatty liver disease. Thus, daily restriction of carbo would contribute to the improvement of diabetes, liver function, and a fatty liver.

Among these factors, the comparison of LCD and calorie restriction (CR) for MAFLD was investigated (n = 3961) [11]. In analyses by the tertile method, lower MAFLD was found for 0.63 vs. 0.64 in the LCD vs. CR groups, respectively. However, unhealthy CR groups (2 and 3)/(1) showed a higher risk of MAFLD of +49% and +77%, respectively. Further, two recent studies showed similar clinical effects in preventing MAFLD with LCD and CR [12,13].

Concerning the relationship between T2D and fatty liver, certain changes in their concepts have been observed. Formerly, Japan did not have so many cases of metabolic syndrome (Met-S), including obesity, T2D, NAFLD, nonalcoholic steatohepatitis (NASH), and related diseases. In recent years, however, Met-S has been acutely increased, and certain changes in some concepts have been found. NAFLD has been changed to MASLD for international societies. Similarly, the Japanese Society of Hepatology (JSH) and the Japanese Society of Gastroenterology (JSGE) announced the official name change in September 2023 [14]. The Japan Obesity Society (JOS) has presented recommendations about the latest situation of MASLD and/or NAFLD for the young generation [15]. The research was conducted for 322 university students associated with analyzing the behavioral questionnaire. As a result, MASLD/NAFLD was observed in 11% of cases, and certain misconceptions were detected concerning the body weights associated with the MASLD/NAFLD constitution. For detail analyses, MASLD showed associations with perceptions for weight and eating habits, whereas NAFLD showed associations with perceptions for constitution and weight. For an adequate

analysis of the results for eating behavior, graduated students may obtain an improvement in general understanding, leading to a reduction in MASLD/NAFLD.

For the comparison between NAFLD and MASLD, a study by cross-sectional method was conducted for Japanese NAFLD patients (n=3709). The difference was revealed as waist circumference for <94cm/<80cm (male/female) as the original criteria, compared with <85cm/<90cm (male/female) as the previous criteria. The results were as follows: a) for the original criteria, MASLD prevalence existed at 96.7% in NAFLD cases, ii) for the Japanese criteria, 96.2% of NAFLD cases were classified as MASLD. [16]. In the Sweden report, almost similar findings were found at 99% [17].

As regards MASLD, it was named for NAFLD and is not from alcohol consumption [18]. For its definition, MASLD means patients with hepatic steatosis (fatty liver) with plural cardiometabolic risk factors. They include overweight, obesity, T2D, abnormal markers such as blood pressure, glucose, waist circumference, triglycerides, HDL, HOMA-R, and so on. MASLD can be diagnosed using non-invasive methods, including CT scans, ultrasounds, and some biochemical factors. Recent novel indexes include the fatty liver index (FLI), which would suggest possible hepatic steatosis. These factors, r-GTP, TG, BMI, and waist circumference, can be calculated together. Elevated FLI may suggest a higher risk of diabetes, hypertension, and CKD [18]. Further, a novel category would be the MetALD for those with a high alcohol intake associated with overweight and obesity [19].

Certain limitations exist in this report. This is only one case with T2D and fatty liver for years. Petite LCD contributed to the improvement of fatty liver and liver function tests [20]. However, some other factors may be involved in her clinical progress. Paying close attention will be required for future changes from several points of view.

In summary, a 64-year-old female case with T2D and fatty liver was presented, along with some perspectives about the recent topic of NAFLD and MASLD together. It is expected that this article may become useful reference data for future clinical diabetology and hepatology.

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