# Reversal of NAFLD Fibrosis with a Medical Food

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## Introduction

Nonalcoholic fatty liver disease (NAFLD) includes steatosis, non-alcoholic steatohepatitis (NASH) and fibrosis. While steatosis alone is not a major concern, the development of NASH and fibrosis in NAFLD is a significant worldwide problem. NAFLD is associated with metabolic syndrome, obesity, type 2 diabetes, visceral fat, and insulin resistance. There are no effective medications for NAFLD. For obese patients weight loss of 10 percent, diet and exercise are recommended, but can be difficult to achieve. In the morbidly obese with NASH and fibrosis, bariatric surgery may be effective in approximately one third of cases but is invasive and expensive (1).

Nutrition and metabolism are inextricably linked. Nutritional requirements are defined as the amounts and types of nutrients needed to be derived from diet in order to maintain normal metabolism. Certain diseases are characterized by disruption to metabolism. When a disease disrupts a patient's metabolism their nutritional requirements may change. A medical food or food for special medical purpose (FSMP) may satisfy the distinctive nutritional requirements of patients with that disease.

Studies have established that patients with non-alcoholic steatohepatitis (NASH) experience disruption to a system of linked metabolic pathways that change their nutritional requirements. These disrupted pathways include choline/phosphatidylcholine metabolism (4,5), methionine/SAMe metabolism (2,3,4) and one-carbon metabolism (5).
Patients with NASH require greater amounts of diet-derived nutrients involved in these metabolic pathways than normal healthy people.

HepAssure has formulated a medical food that satisfies the distinctive nutritional requirements of patients with NASH.

Ingredients of this medical food are listed in Table 1. We describe a patient with NASH and fibrosis who was prescribed a medical food in an attempt to reverse his NAFLD.

**Case presentation**:

The patient is a 72-year-old male who first presented while awaiting CABG. At that time CT scan showed hepatosplenomegaly. He had been overweight for many years with an unhealthy diet. The patient denied excessive alcohol intake. He was not diabetic. Medications included: Atorvastatin 40 mg, Lisinopril 2.5 mg, Aspirin 81 mg, and Furosemide 40 mg qd.

Physical exam revealed weight 91.8. kg, height 178 cm, BMI 28.9, mild palmar erythema, and no notable hepatosplenomegaly. Laboratory data revealed platelets-112,000 x10E3/UL, bilirubin-1.4 mg/dL, AST–60 IU/L, ALT–65 IU/L, albumin-3.6g/dl (AST/ALT upper limit of normal 40/44 IU/L). Laboratory testing was negative for viral hepatitis, autoimmune liver disease, alpha1-antitrypsin deficiency, and iron overload. Liver biopsy was not performed.

Based on this evaluation it was concluded that the patient had cirrhosis, and this was likely due to NASH.

The patient underwent successful CABG and followed up in the office as an outpatient. He was enrolled in an IRB approved study to study the benefits of the medical food. The patient was sent for a fibroscan to the Mayo Clinic which revealed a score of 19.6 KP consistent with F4 fibrosis/cirrhosis. He was advised to lose weight, eat a lower fat, Mediterranean diet, exercise and start a medical food three times per day consisting of the ingredients listed in Table 1. This consisted of eight capsules taken three times daily. During this time the patient attempted to lose weight but was unsuccessful. He maintained a healthy diet and exercised more than his prior baseline.

He tolerated the medical food well and was followed with serial fibroscans over a period of 110 weeks. The patient's fibrosis score gradually dropped from F4 to borderline F1- F2. His last fibroscan score was 7.0 kPa (6.9 kPa and below is F0-F1). Scores are shown in Table 2 and are depicted in the graph in Figure 1.

Repeat lab data showed normalization of AST and ALT. Platelet count remained low at 97,000 x 10E3/uL.

**Discussion**

It is well established that patients with CLD experience disruption in choline, methionine and one-carbon metabolism (2,3,4,5). The medical food used in this study is designed to satisfy increased demand for specific diet-derived nutrients that are involved in those disrupted metabolic pathways. Depletion of these nutrients may contribute to increased severity of clinical manifestations including increased steatosis, oxidative stress, inflammation, stellate cell activation and progressive liver fibrosis. Successful reversal of liver fibrosis would indicate the medical food is effective in establishing homeostasis in these metabolic pathways, thereby causing down-regulation of profibrogenic activity and increase in fibrolytic activity (resorption of collagen).

After the triggering factor for liver injury is removed reversal of cirrhosis can sometimes occur and has been well described. After a sustained viral response with clearance of Hepatitis C, cirrhosis regression was observed in 61% and the collagen content decreased in 89% of patients at 61 months (6). In quiescent hepatitis B, histologic improvement has been seen in 87 percent of patients and 51 percent had regression of fibrosis at week 240 (7). Regression of fibrosis has been described in 33% of patients at 52 weeks post bariatric surgery and improvement of NASH in 85% of these patients (1).

This patient had improvement of his liver disease as demonstrated by normalization of LFTs and regression of fibrosis by fibroscan. Presumably there is some critical point in patients with more advanced liver disease beyond which liver injury cannot be normalized, but this patient likely had relatively early cirrhosis on presentation.

The patient did not have a pre-start nor a posttreatment liver biopsy. He declined invasive workup. Had a liver biopsy been performed this might have yielded important additional data. However, liver biopsy is subject to sampling error and medicine is moving away from its routine use. Fibroscan is considered a reasonable alternative to liver biopsy (8), especially in combination with non-invasive technologies (NIT) like blood test algorithms.

It is unlikely there was sampling error or fibroscan interpretation error given that the scans were repeated in the same Mayo Clinic lab with the same physicians and the curve moved consistently downward.
Weight loss is recommended in the treatment of NAFLD patients and we encouraged this in our patient. The patient was overweight but not obese. He attempted to lose weight but was unsuccessful**.** He followed the Mediterranean diet, exercised, and appeared to be compliant in consuming the medical food tid. The patient's improvement cannot be attributed to weight loss as there was none.

Regression of fibrosis can occur (1,6,7). In patients with NASH the trigger for liver fibrosis is ongoing (2,3,4,5). In this case we postulate the medical food addressed the metabolic disturbances (2,3,4,5) facilitating improvement. The improvement without weight loss underscores the hypothesis that the medical food possibly contributed to the regression of fibrosis.

The improvement in 110 weeks seemed physiologically appropriate. We did not expect faster resolution as the time frame was consistent with the

ranges described in the studies above (1,6,7).

## Conclusion

These data are encouraging, they indicate that the nutritional management of NASH patients may promote the natural regression of liver fibrosis up to early cirrhosis.

Obviously, one cannot draw too many conclusions from a single patient and the limitations of this case report are obvious.

There is a clear need for more studies to examine the role of nutrition and CLD. A double-blind randomized placebo controlled clinical trial is needed.

A successful clinical trial may establish the distinctive nutritional requirements of NASH patients and establish that HepAssure medical food satisfies them.

## Table 1

HepAssure medical food ingredients:

L-Lysine, L-Cysteine, L-Arginine, Polyenylphosphatidylcholine, Alpha Lipoic Acid, Vitamin C (as ascorbic acid & calcium ascorbate), N-Acetyl L-Carnitine, Betaine HCl, L-Glutamate (as L-glutamic acid),Turmeric (Curcuma longa), Grape Seed extract (95% Proanthocyanidins), Black Cumin seed (Nigella sativa), Magnesium (as

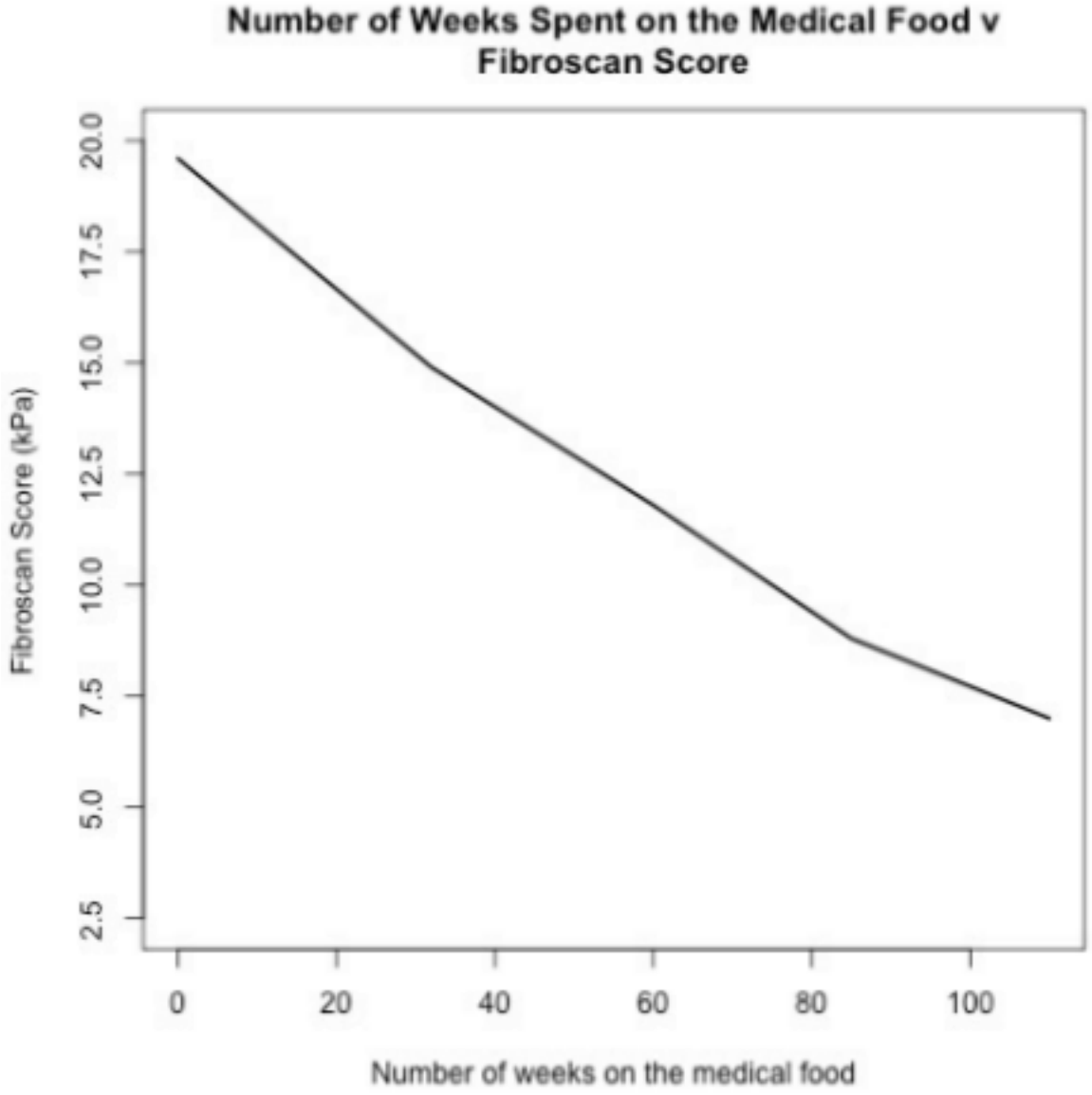
trimagnesium citrate), Artichoke (leaf) extract (Cynara scolymus), L-Glycine, Vitamin E (as D-alpha tocopherol acid succinate), Vitamin B1, Vitamin B2, CoQ10 (as ubiquinol), Calcium (as calcium citrate), BioPerine (Black pepper extract), Vitamin B3, Vitamin B6 (as pyridoxine HCl), Zinc (as zinc citrate), Vitamin A (Palmitate), Folate (as folic acid), Vitamin B12 (as methylcobalamin), Selenium (as selenate aspartate), Biotin, Pantothenic acid (as calcium pantothenate), Vitamin K2 (MK7), Vitamin D3 (as cholecalciferol)

Table 2

| Number of weeks on Medical food | Fibroscan score (kPa)* Mayo Clinic | Fibrosis Interpretation |
|---|---|---|
| 0 | 19.6 | F4 Cirrhosis -Stage 4 |
| 32 | 14.9 | F4 Cirrhosis-Stage 4 |
| 60 | 11.8 | F3 Fibrosis-Stage 3 |
| 85 | 8.8 | F2 Fibrosis-Stage 2 |
| 110 | 7.0 | F2Fibrosis-Stage 2 |

*Fibroscan score below 6.9 is considered normal-F0-F

**Figure 1**

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