

## Liver failure caused by prolonged state of malnutrition following bariatric surgery

Willem J Lammers, Antonie JP van Tilburg, Jan A Apers, Janneke Wiebolt

Willem J Lammers, Department of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam 3015 CE, the Netherlands

Antonie JP van Tilburg, Department of Gastroenterology and Hepatology, Franciscus Gasthuis and Vlietland, Rotterdam 3045 PM, the Netherlands

Jan A Apers, Department of Surgery, Franciscus Gasthuis and Vlietland, Rotterdam 3045 PM, the Netherlands

Janneke Wiebolt, Department of Internal Medicine, Franciscus Gasthuis and Vlietland, Rotterdam 3045 PM, the Netherlands

ORCID number: Willem J Lammers (0000-0002-5455-5242); Antonie JP van Tilburg (0000-0002-3701-2879); Jan A Apers (0000-0002-6348-9697); Janneke Wiebolt (0000-0001-7825-7461).

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Correspondence to: Willem J Lammers, MD, PhD, Academic Fellow, Department of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam's-Gravendijkwal 230, Rotterdam 3015 CE, the Netherlands. [w.lammers@erasmusmc.nl](mailto:w.lammers@erasmusmc.nl)  
Telephone: +31-63-3343636  
Fax: +31-10-7035172

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### Abstract

Bariatric surgery is an effective tool in the treatment of patients with morbid obesity. In these case reports we describe 2 patients who developed liver failure after currently-practiced types of bariatric surgery, caused by a prolonged state of malnutrition provoked by psychiatric problems. Despite intensive guidance of a psychologist and dieticians after surgery, our patients deteriorated psychologically, resulting in a prolonged state of severe malnutrition and anorexia. Finally, a state of starvation was reached, passing a critical level of the liver capacity. Patients who present with signs of severe protein malnutrition after bariatric surgery should be closely monitored and checked for nutritional status. Specific attention should be given to patients who develop psychiatric problems post-bariatric surgery. If refeeding does not result in clinical improvement, reversal surgery should be considered in a timely manner.

**Key words:** Protein deficiency; Hyperbilirubinemia; Hyperammonemia; Liver failure; Urea cycle

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**Core tip:** Monitoring of patients after bariatric surgery is important. When psychiatric problems appear, you should be alert and treat your patients proactively. Unfortunately, these case reports show that psychiatric deterioration can lead to severe malnutrition and anorexia, although rarely resulting in liver insufficiency and failure.

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## INTRODUCTION

Morbid obesity is an increasing healthcare problem in the Western world, with development of important complications, such as diabetes, cardiovascular disease and fatty liver disease. Among morbidly obese individuals, nonalcoholic fatty liver disease is highly prevalent and a substantial number of patients may develop advanced liver fibrosis or cirrhosis over time<sup>[1,2]</sup>. Ultimately, these conditions will lead to liver failure and death.

Bariatric surgery provides an effective tool in the treatment of patients with morbid obesity and its comorbidity<sup>[3]</sup>. Short-term effects, such as significant weight loss and remission of diabetes, have been extensively documented<sup>[4]</sup>. Several clinical studies have shown that bariatric surgery has an important positive impact on the liver, with improvements of liver enzymes and liver histology<sup>[5,6]</sup>.

The development of liver failure after bariatric surgery has previously been described after jejunoileal bypass and biliopancreatic diversion (Scopinaro) surgery<sup>[7]</sup>, but is rare in modern bariatric surgery. A common idea is that nonuse of the bypassed intestine can lead to changes in the mucosa and bacterial flora. As a result of bacterial overgrowth hepatotoxic macromolecules are produced, passing the damaged mucosa and reaching the liver through the portal venous system and resulting in damage of hepatocytes.

In these case reports we describe 2 patients who developed liver failure after currently-practiced types of bariatric surgery, caused by a prolonged state of malnutrition provoked by psychiatric problems.

## CASE REPORT

### Case 1

A 43-year-old female underwent endoscopic gastric bypass surgery because of morbid obesity [body mass index (BMI) 59 kg/m<sup>2</sup>]. After 1 year, she underwent banded gastric bypass surgery because of insufficient

weight loss [BMI: 47 kg/m<sup>2</sup>, %excess weight loss (EWL): 34.9%, total body weight loss: 20%]. After surgery, she suffered from episodes of abdominal pain and dysphagia. Therefore, 1 year later the gastric band was removed with revision of the gastric bypass to a distal bypass (alimentary limb 735 cm, biliopancreatic limb 60 cm, common channel 100 cm). In the following period, additional weight loss was recorded (BMI: 32 kg/m<sup>2</sup>, %EWL: 79.4%, total body weight loss: 46%) with a relative good quality of life. Another year later, she became pregnant. Unfortunately, after 22 wk she gave birth prematurely, resulting in fetal death. In the following 6 mo, she was hospitalized four times with malnutrition, hypoalbuminemia (serum albumin 12 g/L), generalized edema and depression. During this period, she refused any involvement of psychiatrists.

At her final admission to the hospital, she had abstained from food for more than a week, with suspicion of anorexia. Common causes of hypoalbuminemia, such as protein-losing enteropathy and nephrotic syndrome were excluded. Enteral tube feeding was started with protein plus multi-fiber (protein: 95 g/L). However, on day 8 of admission, she developed a somnolent state caused by a hyperammonemic encephalopathy (serum ammonia: 224 μmol/L) and hypoglycemia, for which she was admitted to the intensive care unit (ICU). No urea cycle disorders were found. Liver test results are presented in Table 1. She was treated for hepatic encephalopathy with lactulose and rifaximin, and enteral feeding was changed to a low-protein diet. Additional imaging studies of the liver did not show parenchyma abnormalities or portal flow disturbance. Common causes of liver disease were excluded. No liver biopsy was performed due to coagulopathy. Unfortunately, she developed progressive liver failure in the following days, followed by aspiration pneumonia. Liver transplantation was deemed not feasible. On day 15, she died of multiorgan failure.

### Case 2

A 34-year-old female underwent gastric sleeve resection because of morbid obesity (BMI: 42 kg/m<sup>2</sup>), which was complicated by anastomotic leakage, abdominal sepsis and recurrent esophageal stenosis with stenting. Subsequently, after 5 mo, a gastric bypass (alimentary limb 150 cm, biliopancreatic limb 60 cm) was performed (BMI: 31 kg/m<sup>2</sup>, %EWL: 62.5%, total body weight loss: 25%). Unfortunately, she suffered from episodes of nausea and vomiting due to persistent gastrojejunal ulcerations distal of the esophageal stent. With regard to these complications, an esophageal-jejunostomy was performed 3 mo later. In the following 28 mo, she was admitted to the hospital 4 times for recurrent problems of malnutrition due to psychosocial problems and depression as a result of the aforementioned complications. During her hospitalization she refused psychiatric treatment.

Finally, she was hospitalized in the ICU in a malnourished (BMI 16 kg/m<sup>2</sup>, %EWL: 153%, total body weight

**Table 1 Results of liver test at presentation of hyperammonemic encephalopathy**

	Case 1	Case 2	Normal values
Albumin	12	10	> 35 g/L
Total bilirubin	53	9	< 17 $\mu$ mol/L
Alkaline phosphatase	103	149	< 120 U/L
AST	25	43	< 31 U/L
ALT	21	54	< 31 U/L
$\gamma$ -GT	76	55	< 35 U/L
Antithrombin III	10	20	> 80%
Thrombocytes	105	196	150-400 $\cdot 10^9$ /L
PT-INR	> 7 <sup>1</sup>	> 7 <sup>1</sup>	
Vitamin B12	1068	273	130-700 pmol/L
Vitamin B1	74	106	75-225 nmol/L
Vitamin B6	37	142	50-180 nmol/L
Vitamin D	17.4	< 10	> 50 nmol/L

<sup>1</sup>Under anticoagulant therapy. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase;  $\gamma$ -GT: Gamma-glutamyl transpeptidase; PT-INR: Prothrombin time-international normalized ratio.

loss: 62%) and somnolent state. She did not eat the days before hospitalization, likely due to psychiatric deterioration and suicidal ideation. She was diagnosed with a hyperammonemic encephalopathy (serum ammonia 86  $\mu$ mol/L) due to liver failure. Liver test results are presented in Table 1. The hepatic encephalopathy was treated with lactulose and rifaximin, and enteral feeding was started with Nutrison Protein plus Multifibre (Nutricia Medical, Dublin, Ireland). Despite these treatments, the patient's condition declined and 2 d after admission she died due to progressive liver failure.

## DISCUSSION

In this case series, we present 2 patients who developed severe protein malnutrition after bariatric surgery, followed by hyperammonemic encephalopathy and liver failure provoked by psychiatric deterioration.

Both patients were hospitalized in a period of 1-3 years after bariatric surgery in a malnourished state with dehydration, severe protein deficiency and anasarca. Importantly, common causes of protein loss, such as nephrotic syndrome or protein-losing enteropathy, were excluded, and no clues of decreased synthesis capacity of the liver were observed as cause of hypoalbuminemia. Most likely, hypoalbuminemia was caused by post-bariatric malabsorption and/or self-induced food restriction.

In malabsorptive procedures, such as distal gastric bypass, malnutrition has been described and bariatric surgeons should be aware of this complication<sup>[8,9]</sup>. Macronutrient deficiencies after restrictive procedures, such as modern gastric bypass surgery, are very rare<sup>[10]</sup>. In the cases presented herein, hypoalbuminemia was enhanced by very poor intake due to psychosocial problems postoperatively, probably resulting in anorexia, despite successful psychiatric screening as part of the work-up prior to bariatric surgery. During repeated hospital admissions, intensive guidance of

psychologists and dieticians was provided. Despite these efforts, both patients remained critically malnourished, finally resulting in liver failure and death. From a clinical perspective it is of utmost importance to recognize patients at risk of psychiatric deterioration after bariatric surgery. Our cases underlined that even close monitoring by a psychiatrist does not guarantee a stable clinical course.

Liver insufficiency in our patients became manifest during hospitalization. Both patients developed somnolence caused by hyperammonemic encephalopathy. In our patients, urea cycle disorders as cause of hyperammonemia were unlikely and excluded. Liver insufficiency was present, as reflected by the laboratory results (Table 1). Common causes of liver disease, such as alcohol abuse, viral infection and autoimmunity, were excluded. Therefore, we consider it likely that our patients developed liver insufficiency due to a prolonged state of severe malnutrition and anorexia, which was not well recognized.

Liver insufficiency has been described after malabsorptive bariatric procedures, such as the Scopinaro procedures. Bacterial overgrowth with the production of hepatotoxic macromolecules was considered the main cause. Malnutrition as cause of liver insufficiency is rare and has been described in non-bariatric patients with anorexia nervosa. The following hypotheses have been proposed in the literature: Liver insufficiency may be caused by acute liver cell necrosis, the result of autophagy<sup>[11]</sup> or dehydration and hypovolemia with poor blood circulation through the liver<sup>[12]</sup>. We hypothesize that our patients developed anorexia following bariatric surgery, reaching a state of starvation and a critical level of the liver reserve capacity, finally resulting in a state of liver insufficiency and death.

In conclusion, liver failure due to severe malnutrition is a very rare but critical complication after bariatric surgery. Patients who present with signs of severe protein malnutrition after bariatric surgery should be closely monitored and checked for nutritional status. Specific attention should be given to patients who develop psychiatric problems post-bariatric surgery. If refeeding does not result in clinical improvement, reversal surgery should be considered in a timely manner.

## ARTICLE HIGHLIGHTS

### Case characteristics

Patients who underwent bariatric surgery in the past developed unconsciousness and liver failure after self-induced food restriction.

### Clinical diagnosis

Development of hepatic encephalopathy and hepatic failure.

### Differential diagnosis

Hypoglycemia or neurological disorders were excluded as the cause of unconsciousness. No viral, autoimmune or toxic agents were found to have caused the liver failure.

**Laboratory diagnosis**

Signs of severe hypoalbuminemia, liver failure and hyperammonemia.

**Treatment**

Lactulose and rifaximin to treat hepatic encephalopathy.

**Term explanation**

Hyperammonemia refers to high blood level of ammonia.

**Experiences and lessons**

Specific attention should be given to patients who develop psychiatric problems post-bariatric surgery. If refeeding does not result in clinical improvement, reversal surgery should be considered in a timely manner.

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