

# The Role of Gut Dysfunction and Nutritional Factors In Liver Cirrhosis

## AKADEMISK AVHANDLING

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This thesis is based on the following publications:

- I. Evangelos Kalaitzakis, Magnus Simrén, Rolf Olsson, Pia Henfridsson, Irene Hugosson, Maria Bengtsson, Einar Björnsson. Gastrointestinal symptoms in patients with liver cirrhosis. Associations with nutritional status and health-related quality of life. *Scand J Gastroenterol* 2006. *In press.*
- II. Evangelos Kalaitzakis, Magnus Simrén, Hasse Abrahamsson, Einar Björnsson. The role of gastric sensorimotor dysfunction in gastrointestinal symptoms and energy intake in liver cirrhosis. *Scand J Gastroenterol* 2006. *In press.*
- III. Evangelos Kalaitzakis, Ingvar Bosaeus, Lena Öhman, Einar Björnsson. Altered postprandial glucose, insulin, leptin and ghrelin levels in cirrhosis: correlations with energy intake and resting energy expenditure. *Submitted.*
- IV. Evangelos Kalaitzakis, Jan-Erik Johansson, Ingvar Bjarnason, Einar Björnsson. Intestinal permeability in cirrhotic patients with and without ascites. *Scand J Gastroenterol* 2006;41:326-30



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# The Role of Gut Dysfunction and Nutritional Factors In Liver Cirrhosis

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## Abstract

Malnutrition is a common finding in patients with liver cirrhosis. Malnutrition has been shown to be associated with increased morbidity and mortality. Its pathogenesis remains unclear but both poor dietary intake and increased energy expenditure have been reported.

Spontaneous bacterial peritonitis is an important clinical problem in cirrhotics. It may occur as a consequence of repeated access of bacteria from the intestinal lumen (translocation) to the mesenteric lymph nodes. One of the mechanisms proposed to explain bacterial translocation in cirrhosis includes increased intestinal permeability.

The aims of the present study were to evaluate GI symptoms in cirrhotic patients and their possible relation to nutritional status, to assess whether gastric sensorimotor dysfunction or metabolic disturbances are associated with reduced food intake, and to investigate the role of ascites in intestinal permeability in patients with liver cirrhosis.

Gastrointestinal symptoms and health-related quality of life (HRQOL) were assessed with the aid of two questionnaires. Gastric sensorimotor function was measured by means of an electronic barostat. Food intake, as assessed with a food diary, was related to fasting and postprandial glucose, insulin, leptin, and ghrelin concentrations. Intestinal permeability was evaluated by a  $^{51}\text{Cr}$ -EDTA permeability test.

Cirrhotics were found to have increased severity of GI symptoms compared with reference values from the general population. A relationship between GI symptoms and compromised HRQOL as well as weight loss was observed.

Proximal stomach relaxation to a meal was increased in patients with liver cirrhosis as compared with healthy controls but the relation between gastric accommodation and energy intake was found to be disturbed in these patients. Gastric sensitivity to distension was shown to be related to GI symptom severity and to liver cirrhosis severity scores.

Patients with liver cirrhosis exhibited higher postprandial insulin and glucose concentrations compared to controls. Cirrhotics had higher fasting leptin that fell significantly postmeal and they showed an attenuated increase of ghrelin before the next expected meal. Altered glucose and hormonal levels in patients with cirrhosis were associated with poor food intake.

Only a few patients with cirrhosis had increased intestinal permeability, as assessed by a  $^{51}\text{Cr}$ -EDTA test, which was not influenced to a major extent by ascites.

**Conclusions:** In patients with liver cirrhosis GI symptom severity is high and it is associated with impaired HRQOL and weight loss. Gastric accommodation is not involved in the poor food intake observed in cirrhotics and gastric sensitivity seems to be a relevant factor for GI symptom generation in these patients. Altered postprandial glucose, leptin, and ghrelin levels are correlated to reduced energy intake in this patient group. Increased intestinal permeability is probably of limited importance in the pathophysiology of bacterial infections in patients with liver cirrhosis and ascites.

*Keywords:* liver cirrhosis; malnutrition; gastrointestinal symptoms; health-related quality of life; food intake; energy expenditure; gastric accommodation; gastric barostat; insulin resistance; leptin; ghrelin; intestinal permeability