



## Original article

# In nonalcoholic fatty liver disease, Roux-en-Y gastric bypass improves liver histology while persistent disease is associated with lower improvements in waist circumference and glycemic control<sup>☆</sup>

Katherine J.P. Schwenger, R.D., M.A.N.<sup>a,b</sup>, Sandra E. Fischer, M.D.<sup>c,d</sup>,  
Timothy Jackson, M.D.<sup>e,f</sup>, Allan Okrainec, M.D.<sup>e,f</sup>, Johane P. Allard, M.D.<sup>b,f,g,\*</sup>

<sup>a</sup>Institute of Medical Science, University of Toronto, Ontario, Canada

<sup>b</sup>Toronto General Hospital, University Health Network, Toronto, Canada

<sup>c</sup>Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada

<sup>d</sup>Division of General Surgery, University of Toronto, Toronto, Canada

<sup>e</sup>Division of General Surgery, University Health Network, Toronto, Canada

<sup>f</sup>Department of Medicine, University of Toronto, Toronto, Canada

<sup>g</sup>Department of Nutritional Sciences, University of Toronto, Toronto, Canada

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## Abstract

**Background:** In obese individuals undergoing Roux-en-Y gastric bypass (RYGB), nonalcoholic fatty liver disease (NAFLD) is seen in 75% to 100% of cases. This improves postsurgery, but some patients continue to have persistent NAFLD.

**Objective:** The purpose of this study was to determine the factors associated with persistent NAFLD at 12 months post-RYGB.

**Setting:** University Hospital, Canada, bariatric clinic.

**Methods:** This is a prospective cohort study of 42 patients who underwent RYGB. Liver biopsy, biochemical and clinical parameters were collected pre- and 12 months post-RYGB. Based on histology at 12 months, patients were separated in 2 groups, normal liver (NL) and persistent NAFLD.

**Results:** At baseline, NAFLD was diagnosed in 85.7% of patients and at 12 months post-RYGB, NAFLD was present in 19.1% of patients. Patients who had an NL at baseline remained with NL. RYGB resulted in significant decreases in body mass index, waist circumference, blood pressure, aspartate aminotransferase, alanine aminotransferase, fasting glucose and insulin, glycated hemoglobin, and triglycerides and significant increases in high-density lipoprotein cholesterol. Changes were similar in both groups except for waist circumference, which showed lower changes in those with persistent NAFLD. These patients also had significantly higher ( $P < .05$ ) fasting glucose and insulin with a higher proportion of patients having insulin resistance compared with those with NL.

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\*Correspondence: Johane P. Allard, Toronto General Hospital 585 University Avenue, 9-973, Toronto, ON M5G 2C4 T: 416-340-5159; F: 416-348-0065.

E-mail addresses: [Johane.allard@uhn.on.ca](mailto:Johane.allard@uhn.on.ca), [Dr.Johane.Allard@uhn.ca](mailto:Dr.Johane.Allard@uhn.ca) (J.P. Allard).

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**Conclusions:** RYGB resulted in significant improvements in liver histology, biochemical, and clinical parameters. However, despite similar weight loss, persistent NAFLD was associated with less improvement in waist circumference and worse glycemic control. (Surg Obes Relat Dis 2018;xxx:xxx–xxx.) © 2018 American Society for Bariatric Surgery. Published by Elsevier Inc. All rights reserved.

**Keywords:** Nonalcoholic fatty liver disease; RYGB; Bariatric surgery; Morbid obesity

Obesity is a significant health problem and is on the rise in today's society. As obesity rises, so do associated comorbidities, which include nonalcoholic fatty liver disease (NAFLD) [1]. Studies have found that as body mass index (BMI) increases, so does the prevalence of NAFLD [2]. In obese individuals undergoing bariatric surgery, NAFLD is seen in 75% to 100% of cases [1]. NAFLD includes a spectrum of liver abnormalities, which ranges from benign simple steatosis to nonalcoholic steatohepatitis (NASH), which in some cases progresses to hepatic cirrhosis [3]. Current management of NAFLD includes weight loss through lifestyle modifications, as well as pharmacologic treatment that targets NAFLD pathogenesis [4]. Nonetheless, in those who are obese, weight loss through lifestyle modification may be ineffective, and thus other weight loss strategies may be considered.

Current research suggests that bariatric surgery is effective at improving obesity-related co-morbidities as well as sustained long-term weight loss [5]. However, the effect on liver histology, specifically NASH and fibrosis, has shown conflicting results [6]. Also, for those with persistent NAFLD or NASH postsurgery, it is unclear what factors are associated with persistent histologic abnormalities. The purpose of this study will be to assess the impact of Roux-en-Y gastric bypass (RYGB) on NAFLD and related parameters after 12 months postsurgery and determine what are the factors associated with persistent histologic abnormalities.

## Methods

This is a prospective cohort study that was conducted from September 2013 to June 2017. It includes bariatric surgery patients from a University Hospital in Canada. The appropriate Research Ethics Boards approved this study protocol and conformed to the ethical guidelines of the 1975 Declaration of Helsinki. All participants gave their informed written consent.

## Subjects

Patients were approached and consented for research after the surgeons confirmed that the patients were suitable for bariatric surgery according to the criteria stated by the National Institutes of Health [7]. Study criteria also included age  $\geq 18$  years and alcohol consumption  $< 20$  g/day.

If known to have hyperlipidemia or type 2 diabetes, patients needed to be on a stable drug regimen for  $\geq 3$  months prior to study entry. Clinical and biochemical data were collected at baseline, prior to surgery, and at 12-months post-RYGB surgery. In preconsented patients, a wedged liver biopsy was performed intraoperatively and an ultrasound guided-needle biopsy was performed at 12 months post-RYGB. All RYGB were performed by 1 of 4 surgeons in a standard fashion at a single high-volume bariatric center. All procedures were performed laparoscopically in an antecolic fashion with linear stapled gastrojejunostomy. Standard pouch size is approximately 30 mL, biliopancreatic limb is 50 to 70 cm, and Roux limb 100 to 120 cm.

Patients were excluded from the study if they had liver disease of other etiology, medication known to precipitate steatohepatitis 6 months prior to study enrollment, regular intake of nonsteroidal anti-inflammatory drugs within the past 3 months prior to study entry, type 1 diabetes, smoking, or became pregnant or were breastfeeding during the year postsurgery. Figure 1 provides an overview of subject recruitment and study completion.

## Biochemical and clinical data

Patient's anthropometrics, blood pressure, and medication history were taken by a registered nurse before RYGB and 12 months post-RYGB. At 12 months post-RYGB, percent excess body weight loss (EBWL) was calculated ( $\%EBWL = 100 \times [\text{weight loss since RYGB/preoperative excess body weight}]$ ) using the Hamwi method [8].

Plasma and serum were collected after a 12-hour fast and analyzed by the hospital Laboratory Medicine Program using standardized methods. The homeostasis model (HOMA) for insulin resistance (IR) was also calculated using fasting serum glucose and insulin [9].

## Histology

The liver biopsies were preserved in 10% formalin within 15 minutes of collection, and later, were embedded in paraffin. A pathologist blinded to the study assessed the liver histology for the presence of steatosis, inflammation, ballooning of hepatocytes, and fibrosis using the Brunt system [10]. Additionally, the NAFLD activity score (NAS) was used to evaluate disease severity [11]. Simple steatosis was diagnosed if the liver had  $> 5\%$  steatosis and

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