

## Clinical Study

# Changes in Erythrocyte Sedimentation Rate, White Blood Cell Count, Liver Enzymes, and Magnesium after Gastric Bypass Surgery

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**Background.** Roux-en-Y gastric bypass (RYGBP) is an established method for treatment of obesity, a condition of chronic inflammation with liver steatosis, characterised by increased erythrocyte sedimentation rate (ESR), white blood cell count (WBC), liver enzymes, and decreased magnesium (Mg). We investigated alterations, if any, in ESR, WBC, alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), and Mg after RYGBP. **Methods.** 21 morbidly obese nondiabetic patients who underwent RYGBP surgery were evaluated preoperatively (baseline), then 1 year (1st followup) and 3.5 years (2nd followup) after RYGBP and compared to an untreated control group. **Results.** Body mass index, ESR, WBC, ALT, and GGT were all significantly reduced at 1 year in the RYGBP group (30%, 35%, 20%, 45%, and 57%, resp.) while Mg increased by 6%, compared to control group ( $P = 0.001 - 0.009$ ). **Conclusions.** Obese patients treated by RYGBP show sustained reductions in ESR, WBC, ALT, and GGT possibly due to reduced liver steatosis and increased Mg.

## 1. Introduction

Bariatric surgery has become an effective treatment for obesity, also improving glucose tolerance, insulin sensitivity, lipid status [1–3], and reducing mortality [4, 5].

Obesity is a chronic condition [6, 7] characterised by elevated inflammatory markers such as erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), fibrinogen concentrations, and increased white blood cell (WBC) count [8–10]. Furthermore, these markers are correlated with central distribution of body fat, high blood pressure, hyperglycemia, dyslipidemia, and hyperinsulinemia, all well-known risk factors for cardiovascular disease [11, 12]. ESR, which measures the tendency of red blood cells to aggregate, has been identified as an independent predictor for myocardial infarction [13, 14] and coronary heart disease (CHD) [15, 16]. WBC has also been shown to predict CHD [17–19]. Bariatric surgical procedure such as adjustable gastric banding and RYGBP is associated with lowered WBC [20–23]. Corresponding information on ESR changes after RYGBP is scant.

Obesity is also associated with nonalcoholic fatty liver disease (NAFLD) [24, 25]. Serum alanine aminotransferase (ALT) and serum gamma-glutamyltransferase (GGT) are markers of NAFLD and of liver fat content [26, 27] and are found to predict the onset of type 2 diabetes mellitus (T2DM) [28] as well as CHD [29–31]. Dysmetabolic conditions like obesity and nonalcoholic steatohepatitis have also been associated with a low magnesium (Mg) status [32, 33].

The aim of this study was to assess changes, if any, in morbidly obese patients treated with RYGBP ( $n = 21$ ) after 1 year and after 3.5 years after surgery, regarding ESR, WBC, serum concentrations of ALT, GGT, Mg, and creatinine in comparison with a morbidly obese untreated control group.

## 2. Material and Methods

**2.1. Patients.** Twenty-one consecutive patients (three male, eighteen female), all Caucasians, with morbid obesity, without established diabetes, and on the waiting list for RYGBP

TABLE 1: Clinical characteristics for patients before RYGBP surgery and at followups 1 year and 3.5 years after surgery and for morbidly obese controls at baseline.

|   | Controls<br>baseline | RYGBP<br>baseline | RYGBP<br>1 year | RYGBP<br>3.5 years | <i>P</i> for<br>difference at<br>baseline | <i>P</i> for trend<br>RYGBP |
|---|----------------------|-------------------|-----------------|--------------------|---|-----------------------------|
| Gender (women/men)                            | 16/5                 | 18/3              | 18/3            | 18/3               | 0.429                                     | —                           |
| Age (years)                                   | 38.7 (7.5)           | 45.7 (9.7)        | —               | —                  | 0.013                                     | —                           |
| BMI (kg/m <sup>2</sup> )                      | 44.3 (5.1)           | 42.3 (5.2)        | 29.7 (4.6)      | 32.1 (5.3)         | 0.211                                     | <0.001                      |
| Weight (kg)                                   | 124.0 (17.3)         | 120.0 (16.4)      | 84.0 (13.6)     | 90.8 (16.0)        | 0.444                                     | <0.001                      |
| Height (cm)                                   | 167.2 (8.5)          | 168.4 (6.2)       | —               | —                  | 0.614                                     | —                           |
| ESR (mm/hr)                                   | 16 (10)              | 17 (7)            | 11 (7)          | 12 (8)             | 0.679                                     | 0.018                       |
| White blood cell count<br>( $\times 10^9/L$ ) | 7.5 (1.6)            | 7.0 (1.53)        | 5.6 (1.04)      | 6.0 (1.55)         | 0.300                                     | 0.006                       |
| S-ALT ( $\mu$ katal/L)                        | 0.57 (0.48)          | 0.62 (0.25)       | 0.34 (0.18)     | 0.24 (0.10)        | 0.691                                     | <0.001                      |
| S-GGT ( $\mu$ katal/L)                        | 0.69 (0.46)          | 0.65 (0.42)       | 0.28 (0.19)     | 0.31 (0.24)        | 0.815                                     | <0.001                      |
| S-magnesium (mmol/L)                          | 0.80 (0.06)          | 0.80 (0.06)       | 0.85 (0.08)     | 0.87 (0.07)        | 0.961                                     | 0.009                       |
| S-creatinine (mmol/L)                         | 81.8 (10.1)          | 75.9 (8.7)        | 75.3 (8.3)      | 73.6 (9.8)         | 0.051                                     | 0.704                       |

Data given are arithmetic means ( $\pm$ SD).

BMI: body mass index, ESR: erythrocyte sedimentation rate, ALT: alanine aminotransferase, GGT: gamma-glutamyl transferase, S: serum.

were recruited from the Outpatient Clinic of Obesity Care, Uppsala University Hospital, Uppsala, Sweden.

Patients were investigated preoperatively (baseline), and then 1 year (1st followup) and 3.5 years (2nd followup) after RYGBP. Data from the RYGBP group were compared to that of a baseline matched morbidly obese control (MOC) group also recruited from the waiting list for RYGBP. Thus, this MOC group showed similar characteristics as compared to the RYGBP group; however, since the control group was recruited from the waiting list it was not possible to follow up longer than one year. The MOC group consisted of 21 morbidly obese patients (5 men, 16 women) who also did not have established diabetes and without pharmacological treatment for diabetes. Baseline characteristics of the subjects are shown in Table 1.

Exclusion criteria for participation were anaemia, liver disease, high alcohol consumption (>21 units per week, 1 unit = 8 g alcohol), use of hypoglycaemic agents, or lipid-lowering medication at baseline or followups.

The study was approved by the regional ethics review board at Uppsala University.

**2.2. RYGBP Surgery Procedure.** RYGBP excluded the stomach and duodenum from the passage of food. The flaccid part of the lesser omentum and the first gastric vessel on the lesser curvature was divided just below the fat pad, to create a small gastric pouch (2 cm by 3 cm). The pouch was then totally separated from the main stomach, which was left in the abdomen. The small bowel was divided 30 cm distal to the ligament of Treitz, and the aboral end was connected to the small gastric pouch. This jejunal limb, the so-called Roux limb, was made 70 cm long and placed behind the excluded stomach and transverse colon. The small bowel continuity was maintained by an enteroenterostomy between the Roux limb and the earlier divided proximal jejunum. This created the Y-shaped junction where the ingested food, via the Roux limb, and the gastric acid and bile are mixed.

All participants were given the same kind of dietary advice after surgery and were recommended to take a daily oral supplement containing vitamins and minerals (Vitamineral) which does not contain magnesium.

**2.3. Test Procedures.** All participants underwent physical examination and blood tests for ESR, WBC, ALT, GGT, Mg, and creatinine preoperatively (baseline) and at 1st and 2nd followups. Blood samples were collected from each patient following an overnight fast and analysed.

**2.4. Clinical Measurements.** Weight (kg) and height (m) were measured on standardised calibrated scales, and BMI (kg/m<sup>2</sup>) was calculated.

**2.5. Laboratory Analyses.** Serum concentrations of ALT, GGT, and creatinine were analyzed using routine methods for clinical chemistry at the Department of Clinical Chemistry at the University Hospital, Uppsala. Plasma ESR level (mm/hr) was assessed by Sedimatic 100 (Guest Scientific A.G., Cham, Switzerland). WBC was measured by a Cell-Dyn Sapphire (Abbott, Santa Clara, USA). Serum Mg was measured by spectrophotometric determination as previously reported [34].

**2.6. Statistics.** All analyses were defined a priori. Results are given as arithmetic mean with their standard deviation. ANOVA was used for trends over three and half years of followup. Changes between different time points were analysed using paired *t*-test. Tests were two-tailed, and a *P* value <0.05 was considered significant. Statistical software JMP 3.2 for PC (SAS Corporation, Cary, Tex, USA) was used.

### 3. Results

**3.1. Baseline Data.** Clinical characteristics for patients at baseline, that is, before RYGBP surgery, are shown in Table 1.

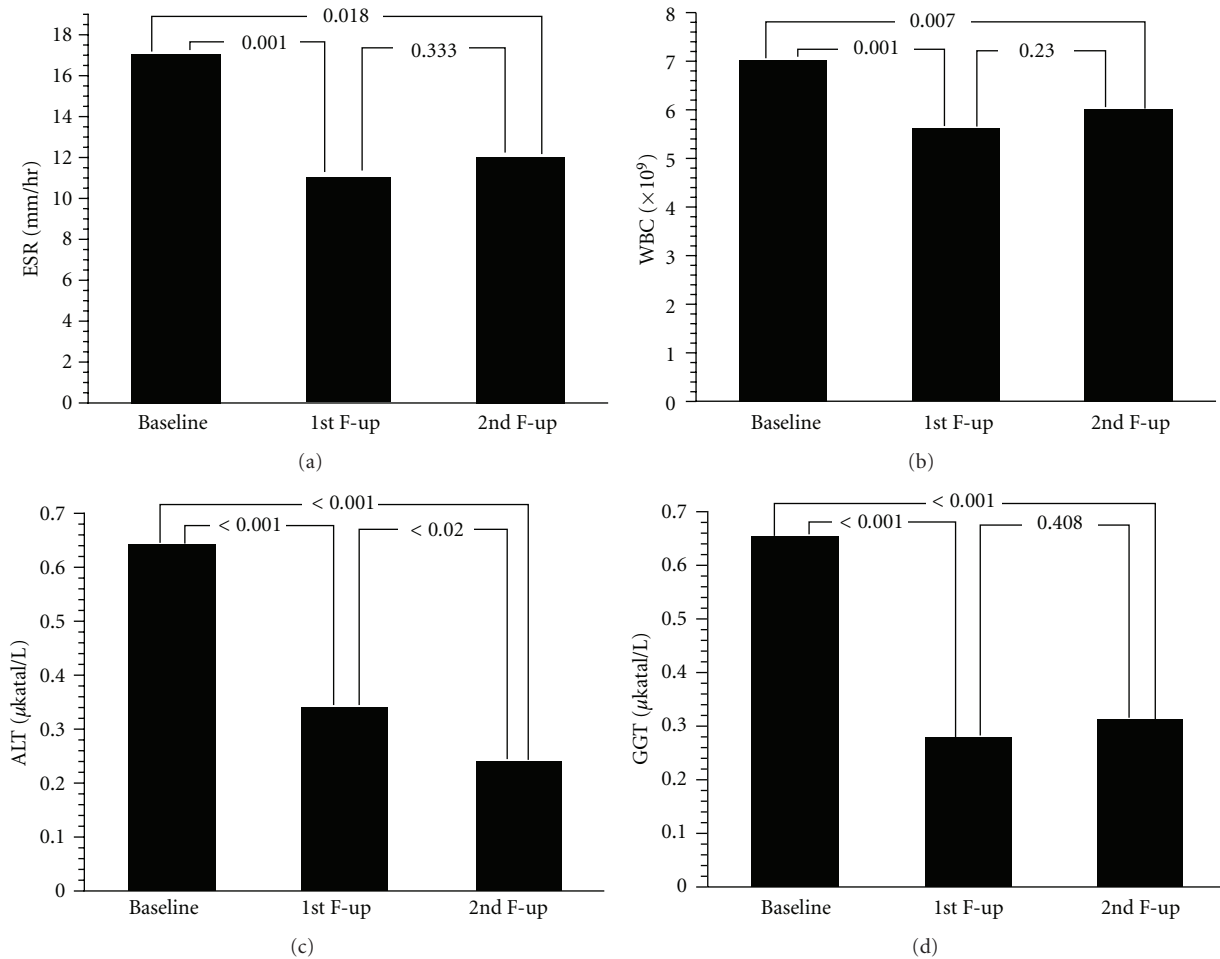


FIGURE 1: The changes in erythrocyte sedimentation rate (ESR) (a), white blood cell (WBC) count (b), serum alanine aminotransferase (ALT) (c), and gamma-glutamyl transferase (GGT) (d) concentrations are shown at baseline and at 1st followup (1 year) and 2nd followup (3.5 years) after Roux-en-Y gastric bypass surgery. Mean values are shown. Statistical significance indicated by  $P$  values. F-up denotes followup.

There were no statistically significant differences in gender, mean BMI, ESR, WBC, or serum concentrations of ALT, GGT, and Mg in the RYGBP group compared with MOC group. Mean age in the MOC group was lower.

**3.2. Follow-Up Data at 1 Year (1st Followup, RYGBP and MOC Groups) and 3.5 Years (2nd Followup, RYGBP Group).** BMI, ALT, GGT, ESR, and WBC were all decreased over the three and half years of followup after RYGBP while Mg was found to increase.

BMI was reduced by 30% in the RYGBP group, from 42.3 kg/m<sup>2</sup> at baseline to 29.7 kg/m<sup>2</sup> at 1st followup ( $P < 0.001$ ), and by 24%, from 42.3 kg/m<sup>2</sup> to 32.1 kg/m<sup>2</sup> at 2nd followup ( $P < 0.001$ ) implying a 6% gain (gain over the baseline BMI) between 1st and 2nd followups ( $P < 0.001$ ). In the MOC group BMI was unaltered between baseline and 1st followup (44.3 and 44.2 kg/m<sup>2</sup>, resp.;  $P = 0.920$ ). At 1st followup, the intergroup difference (between the RYGBP and MOC groups) was significant ( $P < 0.001$ ).

ESR decreased by 35% in the RYGBP group, from 17 mm/hr at baseline to 11 mm/hr at 1st followup ( $P = 0.001$ ) and to 12 mm/hr at 2nd followup ( $P = 0.018$ )

with no significant change between 1st and 2nd followups ( $P = 0.333$ ) (Figure 1(a)). In the MOC group, ESR was unchanged, 16 mm/hr at both occasions ( $P = 0.567$ ). The intergroup difference at 1st followup was significant ( $P < 0.001$ ).

WBC decreased by 20% in the RYGBP group, from  $7.0 \times 10^9$ /L at baseline to  $5.6 \times 10^9$ /L at 1st followup ( $P = 0.001$ ) and to  $6.0 \times 10^9$ /L at 2nd followup ( $P = 0.007$ ) with no significant change between 1st and 2nd followups ( $P = 0.230$ ) (Figure 1(b)). In the MOC group no change in WBC was observed between baseline and 1st followup (7.5 and  $8.3 \times 10^9$ /L, resp.;  $P = 0.0734$ ). The intergroup difference at 1st followup was significant ( $P < 0.001$ ).

ALT was markedly lowered by 45% in the RYGBP group, from 0.62  $\mu$ katal/L at baseline to 0.34  $\mu$ katal/L at 1st followup and to 0.24  $\mu$ katal/L at 2nd followup (both  $P < 0.001$ ). The further decrease of 29%, between 1st and 2nd followups, was also significant ( $P = 0.02$ ) (Figure 1(c)). In the MOC group, ALT was unchanged, 0.57  $\mu$ katal/L at both occasions ( $P = 0.842$ ). The intergroup difference at 1st followup was significant ( $P = 0.001$ ).

GGT was also markedly lowered by 57% in the RYGBP group, from 0.65  $\mu$ katal/L at baseline to 0.28  $\mu$ katal/L at 1st

followup ( $P < 0.001$ ) and to  $0.31 \mu\text{katal/L}$  at 2nd followup (both  $P < 0.001$ ) with no significant change between 1st and 2nd followups ( $P = 0.408$ ) (Figure 1(d)). In the MOC group an opposite trend was observed between baseline and 1st followup ( $0.69$  and  $0.81 \mu\text{katal/L}$ , resp.;  $P = 0.086$ ). The intergroup difference at 1st followup was significant ( $P < 0.001$ ).

Mg increased by 6% in the RYGBP group, from  $0.80 \text{ mmol/L}$  at baseline to  $0.85 \text{ mmol/L}$  at 1st followup ( $P = 0.009$ ) and further to  $0.87 \text{ mmol/L}$  at 2nd followup ( $P < 0.001$ ); however, the change between 1st and 2nd followups ( $P = 0.133$ ) was not significant. In the MOC group no change was observed between baseline and 1st followup ( $0.80$  and  $0.77 \text{ mmol/L}$ , resp.;  $P = 0.132$ ); however, the intergroup difference at 1st followup was significant ( $P < 0.014$ ).

No changes in creatinine levels were observed in the RYGBP group or in the MOC group.

**3.3. Pearson's Product-Moment Correlation Coefficients.** A higher baseline BMI correlated with increased ESR ( $r = 0.41$ ,  $P = 0.012$ ) and with decreased Mg ( $r = -0.30$ ,  $P = 0.03$ ) but not significantly with WBC ( $r = -0.16$ ,  $P = 0.303$ ), ALT ( $r = 0.176$ ,  $P = 0.269$ ), or GGT ( $r = -0.02$ ,  $P = 0.198$ ).

## 4. Discussion

The main findings in this study were that ESR, WBC, and liver enzymes, ALT and GGT, decreased after RYGBP surgery. The sustained lowering of ESR and WBC, markers of inflammation, may indicate a long-term improvement regarding inflammatory status in obese subjects treated by RYGBP surgery along with a sustained lowering of both ALT and GGT, markers for liver steatosis and for metabolic and cardiovascular risk [30, 31]. Obesity is an inflammatory condition [6, 7] associated with elevated inflammatory markers such as ESR, CRP, fibrinogen, and WBC [8–10, 35]. It has been shown that CRP and other inflammatory biomarkers predict cardiovascular mortality [36]. Lowered CRP and WBC concentrations have been reported with at least 1 year's followup after RYGBP as well as after gastric banding [20]. Decreased ESR levels were also reported one and four years after gastric banding [21, 23]. RYGBP induces a larger weight loss than gastric banding, but data on ESR after RYGBP has been less complete. ESR has less intraindividual variation than CRP, which is influenced by minor infections, for example, common cold, and also by degree of physical activity. Our results show a decrease in ESR by 35% one year after RYGBP surgery which was sustained over time up to 3.5 years of followup. In contrast, no difference was observed in the control group.

In this study ESR was measured according to the principles of the Fåhræus-Westergren method [37, 38] which is considered the gold standard for determination of erythrocyte sedimentation rate. ESR is a widely available test and is used as a nonspecific marker of inflammation. It is higher in obesity and increases with age. The ESR value depends on the balance between factors promoting and factors resisting erythrocyte sedimentation. The promoting factors include fibrinogen (an acute-phase protein) and other proinflammatory cytokines. Levels of fibrinogen and the proinflammatory

cytokines are elevated in inflammatory conditions, their production by the hepatocytes being increased [39].

Hepatocyte production of these acute-phase proteins is in turn influenced by the degree of liver steatosis [40, 41]. Non-alcoholic fatty liver disease (NAFLD), of which liver steatosis is part, occurs in obesity and is associated with elevated fibrogen and liver enzymes [40, 42, 43]. Lowered liver enzymes such as GGT have been reported to predict the improvements in inflammation and fibrosis in the hepatocytes in NAFLD, two key prognostic features of this condition [27]. The lowered serum GGT, ALT, and ESR observed in this study after RYGBP might thus reflect decreased degree of liver steatosis. A similar pattern regarding fibrinogen, ALT, and GGT has previously been shown after gastric banding [23, 27]. Thus, it might be speculated that in the present study a decreased liver steatosis after RYGBP surgery has contributed to a reduced fibrinogen synthesis and lowered ESR.

WBC is increased in inflammatory conditions and is increased in obesity and correlates with central obesity [44, 45]. It is also associated with NAFLD regardless of the presence of classical cardiovascular risk factors and other components of metabolic syndrome [46]. The present study showed a decrease in WBC by 20% three and a half years after RYGBP which is in congruence with other shorter studies [20, 22]. Our results indicate that the lowered WBC may be sustained in the long term.

This study confirmed the findings from a previous study that noted increase in serum Mg one year after RYGBP [34] and further documented sustenance of this increase up to three and a half years. This increase is not thought to be due to impaired renal function as the serum creatinine did not change in the follow-up interval. The exact mechanisms have still to be explained.

Possible limitations to the study would be that the presence of concomitant minor infections was not documented. However, anaemia and renal impairment, factors which might influence ESR, were not observed in our study. We did not measure CRP for direct comparison with ESR. The control group was significantly younger than the RYGBP group, but since ESR increases with age it is unlikely that this had an influence on the ESR results. Body fat content and liver fat content measured by imaging techniques like Dual energy X-ray absorptiometry or ultrasonography would have been warranted to investigate if different fat distribution might influence the variables analysed in this study.

In conclusion, morbidly obese patients treated with RYGBP show a marked and sustained decrease in ESR, WBC, ALT, and GGT which may indicate improvements in general inflammatory status and particularly steatohepatitis. They also show sustained increases in Mg.

## Conflict of Interests

The authors declare that they have no conflict of interests.

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