Gastrointestinal transit, appetite, and energy balance in gastrectomized patients

Mayra M Kamiji, Luiz EA Troncon, Vivian MM Suen, and Ricardo B de Oliveira

ABSTRACT

Background: Alterations in gastrointestinal tract physiology after gastrectomy may affect appetite and energy balance.

Objective: The objective of this study was to examine energy balance, appetite, and gastrointestinal transit in subjects with gastrectomy.

Design: Seven subjects with total gastrectomy (TG) and 14 subjects with partial gastrectomy (PG), who were free from signs of recurrent disease, and 10 healthy control subjects were studied. Resting energy expenditure (REE) was measured by indirect calorimetry and compared with REE predicted by the Harris-Benedict equation (mREE/pREE%). Gastrointestinal transit was measured by scintigraphy. Habitual food intake was assessed, and appetite was measured during scintigraphy after ingestion of a test meal (361 kcal).

Results: Body mass index was not different among the groups. mREE/pREE% was higher in patients with PG (P < 0.01) than in control subjects. The TG group showed higher energy intake (P < 0.05) than the PG group and control subjects. Gastric emptying was faster in the PG group than in control subjects, and gastrointestinal transit was accelerated in both PG and TG groups. An intense, precocious postprandial fullness and a relatively early recovery of hunger and prospective consumption sensations were seen in these patients.

Conclusions: Patients with PG or TG have higher than predicted energy expenditure, which in TG seems to be compensated for by increased energy intake. These patients have preserved postprandial appetite responses and precocious postprandial fullness, which seem to be associated with disturbances in gastrointestinal transit of the ingested meal and are likely to be independent of vagal fiber integrity or stomach-released ghrelin.

INTRODUCTION

In recent years, the rising epidemic of obesity has been associated with increased investigations aimed at elucidating the physiologic systems that regulate appetite and energy homeostasis (1). Appetite sensations are coordinated by complex mechanisms that involve peripheral mediators and the central nervous system (1–3). Several peptides released from the gastrointestinal tract, such as cholecystokinin (4), glucagon-like peptide-1, oxyntomodulin (5), and peptide YY3–36 (PYY3–36) (6), participate in this system, acting as satiation and satiety mediators either directly or via the peripheral neural pathway (1, 3). Although most gut peptides involved in energy balance regulation play a negative role, ghrelin stimulates food intake and fat mass (7). Because ghrelin is produced predominantly by oxyntic cells in the stomach (8), removal of the stomach or its acid-producing portion reduces plasma ghrelin concentrations in humans (7).

Gastrectomy also may cause disturbances in the regulation of food intake and appetite by several other mechanisms (10–12). Partial gastrectomy (PG), with the removal of the antrum and the pylorus, which is often associated with vagotomy, may lead to impaired gastric accommodation and abnormal gastric emptying (11). After total gastrectomy (TG), food immediately reaches the proximal small intestine, where satiation signal pathways to the brain are activated (10). Section of afferent vagal fibers, which participate in the negative feedback of the satiation process, also may contribute to deranged appetite and satiation sensation (12, 13).

Several studies that investigated the impact of gastrectomy on long-term quality of life and nutritional status yielded conflicting results (14–16). Although several studies investigated appetite and food intake in gastrectomy performed for obesity (17, 18), few studies involved patients after gastrectomy performed for either ulcer or cancer. The aim of this study was to evaluate appetite, food intake, gastrointestinal transit, and resting energy expenditure (REE) in patients who had undergone either PG or TG for ulcer or cancer in comparison with a control group of healthy volunteers.

SUBJECTS AND METHODS

Subjects

Subjects included 7 patients with TG for gastric cancer; 14 patients with PG for gastric ulcer (n = 4), duodenal ulcer (n = 4), or gastric cancer (n = 6); and 10 healthy volunteers (Table 1). In all TG patients, Roux-en-Y reconstruction was performed after gastrectomy. PG consisted of resection of gastric antrum plus a variable extension of gastric body. After antrum resection and selective vagotomy, a Billroth I (n = 3), Billroth II (n = 8), or Roux-en-Y procedure (n = 3) was performed for transit reconstruction. All patients underwent gastrectomy by the same surgical team at the Department of Surgery of the Ribeirão Preto Medical School University Hospital and attended hospital visits.
TABLE I  
Clinical characteristics of healthy subjects (control group) and patients with partial or total gastrectomy

<table>
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<th>Control (n = 10)</th>
<th>Partial gastrectomy (n = 14)</th>
<th>Total gastrectomy (n = 7)</th>
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</table>
| Age (y)                  | 38 ± 13
| Sex [F/M (n)]            | 5/5             | 6/8                         | 2/5                      |
| Body mass index (kg/m²)  | 25.6 ± 3.5      | 23.3 ± 4                    | 22.8 ± 4                 |
| Period after gastrectomy (y) | —              | 11 ± 13                     | 4 ± 3                    |

\(^1\) Mean ± SD (all such values).
\(^2\) P < 0.05 compared with the control group (Kruskal-Wallis test with Dunn’s multiple comparisons posttest).

for periodic examination from August 2005 to July 2006. Subjects with PG had undergone surgery a median of 6.0 y (range: 1.9–10) previously, and subjects with TG had undergone surgery a median of 3.5 y (1.0–8.8 y) previously. All patients were free from recurrent disease and had no history of other gastrointestinal surgery. All subjects had stable weight, defined as <5% weight change over the 3-mo period preceding the study. This information was obtained from patient medical records and confirmed at the time of the study. Ten gastrectomized subjects (6 PG and 4 TG) reported occasional symptoms. Among the patients with PG, occasional nausea was reported by 3 patients, abdominal distension was reported by 1 patient, cold sweats and dizziness after ingestion of sweets were reported by 1 patient, and mild diarrhea was reported by 1 patient. Among the patients with TG, cold sweats, dizziness, and weakness after ingestion of sweets were reported by 2 patients, and mild diarrhea was reported by 2 patients. Exclusion criteria for this study were recurrence of malignant disease, pregnancy, tobacco use, consumption of >2 alcoholic drinks/d, and aerobic exercise >30 min for 3 times/wk.

Study protocol

Outpatients with a history of TG or PG were enrolled in the study. Healthy volunteers were enrolled as a control group. The investigation was approved by the local ethics committee, and all patients provided written signed consent. Each subject was studied on 2 separate occasions. On the first occasion, indirect calorimetry was performed in standard conditions. On the second occasion, subjects underwent a scintigraphic assessment of gastric emptying and gastrointestinal transit, during which appetite sensations were assessed. Before this study, habitual food intake was determined. After scintigraphy, subjects were offered a buffet-style lunch, and food ingestion was recorded.

Energy expenditure measurement

REE was measured by indirect calorimetry (Vmax 29; SensorMedics Corporation, Yorba Linda, CA). Subjects were asked to arrive at the laboratory by automobile in the morning after an overnight fast (12 h) and refrain from alcohol consumption and intense physical activity for the 24 h preceding the testing session. The carbon dioxide and oxygen analyzers were calibrated before testing with 2 tanks of standard calibration gases (16% O₂ and 4% CO₂, and 26% O₂ and 0% CO₂) before each test. The flow meter was calibrated with a standard 3-L syringe. Subjects were instructed to relax and avoid sleeping during measurements. Each subject rested in the supine position for 30 min before testing. After this period, a canopy was placed over the subject’s head, and the calorimetric data collection was started. Oxygen consumption (VO₂), carbon dioxide production (VCO₂), respiratory quotient, and energy expenditure standardized for temperature, barometric pressure, and humidity were measured every minute for 30 min. REE was calculated according to Weir’s equation (19) and expressed per 24 h (20). Measured REE values were compared with the REE calculated with Harris-Benedict predictive equation, using current body weight. The ratio between measured REE (mREE) and predicted REE (pREE) was calculated and expressed as a percentage [mREE/pREE (%)].

Habitual food intake

Each subject’s habitual food intake was assessed by a nutritionist, who administered a 24-h food recall and a 3-d dietary record (21). In the latter, the subjects were requested to record their dietary intake during 2 weekdays and 1 weekend day. Measured values of energy, carbohydrate, protein, fat, and fiber intake and the number of meals for each subject were calculated. A diet and weight management software, Diet Pro software (version 4.0; Agromidia, Vicoso, Brazil), was used for the analysis. The ratio between daily energy intake and measured REE was calculated and expressed as percentage [kcal/mREE (%)].

Assessment of gastric emptying and gastrointestinal transit

For gastrointestinal transit assessment, medications known to affect gastrointestinal motility were discontinued 48 h before testing; women were studied during the follicular phase of their menstrual cycle. All subjects were studied after an overnight fast ≥10 h (22) and reported to the nuclear medicine department by 0730. Gastric emptying and gastrointestinal transit were evaluated in all subjects after the ingestion of the same volume of a standardized liquid test meal consisting of 270 mL of water blended with 50 g of soy milk powder and 25 g of chocolate powder. The meal was labeled with 18 MBq (500 μCi) of [⁹⁹mTc]phytate (Instituto de Pesquisas Energéticas e Nucleares, São Paulo, Brazil). The caloric content of the test meal was 361 kcal, distributed as 51% carbohydrate, 34% fat, and 15% protein. Subjects were asked to ingest the meal continuously so that it was consumed within 2 min.

Immediately after test meal ingestion, subjects were placed upright in front of the low-energy, high-resolution, hexagonal hole collimator of a γ camera (DST; SMV America, Twinsburg, OH) connected to a dedicated workstation (POWERstation version 4.1.1; SMV, America). Serial images of the distribution of the ingested radioactivity over the anterior and posterior 2-min images were acquired every 5 min for the first 20 min and then every 10 min for 190 min (total of 210 min) (23). Time zero was defined as the time of meal completion. Before the test meal (baseline), immediately after meal completion (time zero), and at 30, 60, 90, 120, 150, 180, and 210 min, the subjects were...
asked to fill in 100-mm visual analog scales (VASs) on their feelings of hunger, fullness, and prospective consumption (24). During the test, subjects were allowed to walk quietly around the room, consume water ad libitum, and visit the toilet.

Data analysis for gastric emptying

Gastric emptying was analyzed in the PG group and in healthy volunteers but not in the TG group, because a well-defined small intestine portion that might be regarded as a “stomachlike” reservoir region could not be visualized in all patients. In healthy volunteers, a region of interest (ROI) corresponding to the total stomach was manually defined from the first anterior and posterior acquisitions, in which gastric accommodation was expected to be maximal. In the PG group, this gastric ROI was defined over the remnant stomach. Counts obtained from these regions throughout the study were recorded and stored. These data were then corrected for physical isotope decay, and the geometric mean of the anterior and posterior counts was computed to correct for posterior-anterior movement of the marker within the stomach [geometric mean counts = square root (anterior counts × posterior counts)] (23, 25).

In each frame, the geometric mean of the counts from the anterior and posterior gastric ROI was expressed as a percentage of that calculated for the anterior and posterior counts of total abdomen at time zero. An “activity-versus-time” curve for the stomach was then derived from these corrected counts for both control and PG groups. From this curve, the following gastric emptying variables were obtained for comparison between groups: the percentages of activity remaining in the gastric area at \( t = 0 \) and 30, 60, and 120 min after the meal, and \( t_{1/2} \), which was defined as the time taken for the activity in the gastric area to fall by 50% from the initial level.

Data analysis for gastrointestinal transit

Before meal ingestion, an external radioactive marker containing \(^{99m}\text{Tc}\) was taped to the skin at the midpoint between the umbilicus and the right iliac crest to serve as an approximate reference of the anatomic transition from terminal ileum to the cecum or ascending colon (23). ROIs for the anterior view of the proximal small intestine, the distal small intestine, and the cecum or ascending colon were defined on each image. These regions were delineated manually as described elsewhere (26). Briefly, the progression of the meal was initially assessed visually by replaying successive frames on the video monitor, a procedure that not only facilitated ROI definition but also allowed a qualitative assessment of gastrointestinal transit. Immediately after meal ingestion, the typical image of the stomach was seen on the first frames in PG and in healthy volunteers. As gastric emptying proceeded, activity was detected immediately below the gastric area (defined as proximal small intestine). From this region, the radioactivity moved to the right and downward to the pelvic area, where the ROI for distal small intestine was defined. Finally, the head of the meal moved upward and further to the right, toward the cecum or ascending colon, which was indicated by the external marker taped to the skin of the abdomen. In patients with TG, the ROI for the proximal small intestine was defined as a nearly round image formed immediately after ingestion of the meal on the first frames, before the meal started moving downward to the pelvic area. Radioactivity in each of the intestinal ROIs in every frame was expressed as a percentage of the total abdominal activity, from which the counts from the external mark were subtracted. Counts from these ROIs were used to draw activity-versus-time curves for each intestinal segment. Analysis of these curves provided data for assessing the progression of the front of the meal through the small bowel to the cecum and meal residence on each intestinal segment. The time of meal arrival at the proximal small bowel, distal small bowel, and cecum or ascending colon was defined as the time required for the first appearance of at least 10% of total abdominal activity in the corresponding ROIs (23). Meal residence in each intestinal segment was obtained from the area under the activity-versus-time curve (AUC) in the ROI corresponding to that segment, which was calculated by application of the trapezoidal rule. Values yielded by this method were divided by 210 min, and meal residence was expressed as activity per minute.

Questionnaire of appetite sensations

Before the test meal ingestion (baseline), immediately after meal completion (time zero), and at 30, 60, 90, 120, 150, 180, and 210 min, patients and healthy volunteers were asked to fill in 3 different 100-mm VAS forms concerning their feelings of hunger, fullness, and prospective consumption (24). Subjects were asked to indicate on the corresponding VASs how they felt at that very moment regarding hunger, satisfaction/fullness, and prospective food ingestion. This was prompted by the following questions, respectively: “How hungry do you feel? (I am not hungry at all, I have never been hungry); “How satisfied do you feel?” (I am completely empty, I feel totally full); “How much do you think you can eat?” (Nothing at all, a lot) (3, 24). Subjects were instructed to place a vertical mark at any point on each scale corresponding to their feelings. Hunger, fullness, and prospective consumption ratings were then determined by measuring the distance from the left side of the line to the mark.

The appetite ratings were then used for the following analysis: 1) within-group comparisons of appetite sensation ratings in the different moments, 2) between-groups comparison of fasting appetite ratings, and 3) between-groups comparison of change-from-baseline appetite (calculated by subtracting baseline data from the ratings at each time point after meal ingestion). For purposes of appetite analyses, the PG group was divided into 2 subgroups according to percentage of radioactivity at 5 min after ingestion of the meal. Subgroup A \((n = 8)\) included patients with \(\leq 25\%\) remaining in the stomach at \( t = 5 \) min; subgroup B \((n = 6)\) included patients with \( > 25\%\) remaining in the stomach at \( t = 5 \) min.

Statistical analysis

Results are expressed as means ± SD. Appetite scores were compared between and within groups by using a mixed linear model. In this model, appetite ratings were used as random effects, and both variables “group” (control, PG, or TG) and “time” were used as fixed effects. Results are expressed as means ± SD. Percentages of radioactivity were also compared between groups by using a mixed linear model. In this model, “age” and “sex” were used as control variables, percentage of radioactivity was used as random effect, and both variables group (control, PG, or TG) and time were used as fixed effects. Results of comparisons of percentage of radioactivity were adjusted for age and sex. The mixed linear models (random effects and fixed
Effects) were used for data analyses in which the assumption of a priori independence of observations was not adequate. Model adjustments were obtained by using the PROC MIXED of SAS software, version 9.1 (SAS Institute Inc, Cary, NC). Differences between groups regarding the mREE/pREE% ratio, measured REE, and predicted REE were analyzed by using a 2-factor analysis of variance (ANOVA), with “age” and “study group” (control, PG, and TG) as independent variables. This ANOVA was performed by using the GLM PROC of SAS software, version 9.1 (SAS Institute Inc). Dietary assessment and gastrointestinal parameters were compared by Kruskal-Wallis test with Dunn’s multiple comparisons test; and Mann-Whitney U test was used for 2-group comparisons. Within-group comparisons of REE were made by paired t tests.

RESULTS

Resting energy expenditure

The mREE/pREE% ratio was higher in the PG group (P < 0.05) than in the control group. Values for mREE were significantly higher (P < 0.0001) than pREE in the PG group (Table 2). In the TG group, mREE was higher than pREE and the mREE/pREE (%) ratio was higher compared with control group, although the differences showed only borderline significance (P = 0.06 and P = 0.07, respectively).

Food intake

Mean daily caloric intake (kcal · kg body wt$^{-1}$ · d$^{-1}$) and mean number of daily meals were higher in the TG group than in PG or control groups (Table 3). Habitual macronutrient and fiber daily intake were not different among the groups.

Gastric emptying

The gastric emptying curves for PG and control groups are shown in Figure 1. Gastric emptying was exceedingly rapid in the PG group, because the percentages of activity remaining in the gastric region at t = 0 and 30, 60, and 120 min after meals were all significantly lower than in controls. In healthy volunteers, gastric emptying at t1/2 was 43 ± 16 min (mean ± SD), whereas in the PG group the percentage of total radioactivity contained in the gastric ROI in the first image was already lower than 50% in 12 of the 14 patients. In the remaining 2 patients of the PG group, t1/2 values were 5 and 15 min.

Gastrointestinal transit

Qualitative analysis of the sequential scintigraphic images obtained from each subject and the activity-versus-time curves for the intestinal ROIs revealed distinct gastrointestinal transit patterns for each group. In healthy volunteers, the meal emptied regularly from the stomach, traveled rapidly throughout the proximal small bowel, and accumulated in the distal segment before reaching the cecum and ascending colon. In patients with PG, after exceedingly rapid gastric emptying, the meal traveled across the proximal small intestine more slowly, with significantly higher percentages of radioactivity in this ROI during the first 40 min after meal ingestion (Figure 1). In this group, the meal accumulation in the distal small bowel was earlier and greater than that seen in controls. The percentages of radioactivity in the ROI corresponding to the cecum or ascending colon were similar to those obtained in the TG group after the first 30 min after meal ingestion (Figure 1). Patients from the TG group

<table>
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<th>TABLE 2</th>
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<tr>
<td>Measured resting energy expenditure (mREE), predicted REE (pREE), and data obtained by indirect calorimetry in healthy volunteers (control group) and patients with partial gastrectomy (PG) or total gastrectomy (TG)$^1$</td>
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<tr>
<td>&amp; Control (n = 10) &amp; PG (n = 14) &amp; TG (n = 7)</td>
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<tr>
<td>mREE/pREE (%)$^2$ &amp; 104 ± 11 &amp; 117 ± 11$^4$ &amp; 118 ± 21</td>
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<tr>
<td>pREE (kcal/d) &amp; 1524 ± 164 &amp; 1340 ± 106$^d$ &amp; 1284 ± 184$^d$</td>
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<tr>
<td>mREE (kcal/d) &amp; 1380 ± 187 &amp; 1571 ± 187$^5$ &amp; 1493 ± 201$^6$</td>
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<tr>
<td>mREE (kcal/kg body wt) &amp; 23 ± 4 &amp; 26 ± 4 &amp; 25 ± 5</td>
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<tr>
<td>Fasting respiratory quotient &amp; 0.81 ± 0.05 &amp; 0.85 ± 0.06 &amp; 0.84 ± 0.06</td>
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<tr>
<td>VO$_2$ (L/min) &amp; 0.23 ± 0.03 &amp; 0.22 ± 0.03 &amp; 0.21 ± 0.03</td>
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<tr>
<td>VCO$_2$ (L/min) &amp; 0.18 ± 0.02 &amp; 0.19 ± 0.03 &amp; 0.18 ± 0.02</td>
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$^1$ Values are means ± SDs. VO$_2$, oxygen consumption; VCO$_2$, carbon dioxide production.
$^2$ mREE/pREE (%), ratio between measured resting energy expenditure (REE) and predicted REE expressed as percentage.
$^3$ Significantly different from control group, P < 0.05 (2-factor ANOVA with posttest).
$^4$ Significantly different from pREE, P < 0.0001 (paired t test).
$^5$ P = 0.06 compared with pREE (paired t test).

<table>
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<th>TABLE 3</th>
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<td>Habitual energy, macronutrients, and fiber intake and number of daily meals in healthy volunteers (control group) and patients with partial gastrectomy (PG) or total gastrectomy (TG)$^1$</td>
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<tr>
<td>&amp; Control (n = 10) &amp; PG (n = 14) &amp; TG (n = 7)</td>
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<tr>
<td>Habitual energy intake (kcal/d) &amp; 1811 ± 424 &amp; 1643 ± 479 &amp; 2021 ± 484</td>
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<tr>
<td>Habitual energy intake (kcal · kg body wt$^{-1}$ · d$^{-1}$) &amp; 27 ± 8 &amp; 27 ± 9 &amp; 34 ± 7$^6$</td>
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<tr>
<td>Energy intake/measured REE (%)$^3$ &amp; 113 ± 23 &amp; 106 ± 24 &amp; 138 ± 40$^7$</td>
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<tr>
<td>Carbohydrate (% of energy) &amp; 48 ± 8 &amp; 52 ± 5 &amp; 54 ± 8</td>
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<tr>
<td>Lipid (% of energy) &amp; 34 ± 6 &amp; 30 ± 5 &amp; 31 ± 6</td>
</tr>
<tr>
<td>Protein (g · kg body wt$^{-1}$ · d$^{-1}$) &amp; 1.2 ± 0.4 &amp; 1.3 ± 0.5 &amp; 1.3 ± 0.3</td>
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<tr>
<td>Fiber (g) &amp; 8 ± 4 &amp; 8 ± 6 &amp; 10 ± 0.3</td>
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<tr>
<td>Number of meals &amp; 4 ± 1 &amp; 5 ± 2 &amp; 6 ± 2$^2$</td>
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$^1$ Values are mean ± SD. REE, resting energy expenditure.
$^2$ P < 0.05 compared with both control and PG groups, Kruskal-Wallis test with Dunn’s multiple comparisons posttest.
$^3$ Ratio between habitual energy intake (kcal/d) and resting energy expenditure (kcal/d).
showed rapid transit through proximal and distal small intestine segments. At the end of the meal, most of the radioactive tracer had accumulated in distal small intestine segments, and transfer to the colon was initiated.

Values for the time of meal arrival to the proximal small intestine, distal small intestine, and cecum or ascending colon were significantly lower in both PG and TG groups than those in the control group (Table 4). As shown in Table 4, meal residence (AUC) in the proximal small intestine was significantly higher in PG patients than in TG patients. AUC values were also significantly higher in the distal small intestine in TG patients than those in the control group. Meal residence in the cecum or ascending colon region was significantly greater in both PG and TG groups than that in controls.

Appetite sensations

Baseline hunger and prospective consumption ratings were not significantly different among the groups. Prospective consumption ratings decreased significantly ($P < 0.05$) immediately after meal ingestion ($t = 0$) in controls but not in PG or in TG groups. After meal ingestion, hunger and prospective consumption ratings increased gradually and became significantly different from the $t = 0$ rating at $t = 120$ min in the PG group, $t = 150$ min in the TG group, and $t = 180$ min in controls (Figure 2). Baseline fullness ratings were lower in PG and TG groups than in controls, and this difference attained significance for the TG group ($P < 0.05$). In controls, a slightly nonsignificant increase in fullness occurred during the first postprandial hour (Figure 2). Fullness ratings increased sharply immediately after meal ingestion in both PG and TG groups. In the PG group, a fullness sensation persisted for 120 min, whereas in the TG group the increase in fullness was transient.

In the PG group, appetite suppression after ingestion of the test meal was more evident in subgroup A than subgroup B. Subgroup A showed significantly higher fullness ratings at 30, 60, 90, 120, and 150 min than subgroup B ($P < 0.01$). Prospective consumption ratings in subgroup A also decreased significantly from baseline ratings at $t = 0$ and 30 min, which was not observed in subgroup B (Figure 3).

Changes from baseline appetite ratings

Change from baseline of hunger and prospective consumption sensation after completion of test meal ingestion until 210 min thereafter was not significantly different among the groups. Change of fullness feeling from baseline ratings was significantly higher in both PG and TG groups ($P < 0.01$) than that in controls at $t = 0$ and that at 30 min in the PG group ($P < 0.05$) compared with controls.
DISCUSSION

An important result of our study was that PG patients and TG patients—but not healthy volunteers—showed an mREE significantly higher than the REE as predicted by the Harris-Benedict equation. Although PG and TG patients were older than healthy volunteers, proper statistical analysis ruled out the possibility that

<table>
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<th>TABLE 4</th>
<th>Gastrointestinal transit variables in healthy volunteers (control group) and patients with partial gastrectomy (PG) or total gastrectomy (TG)(^d)</th>
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<tbody>
<tr>
<td>Control group (n = 10)</td>
<td>PG (n = 14)</td>
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<tr>
<td><strong>Proximal small intestine</strong></td>
<td><strong>Distal small intestine</strong></td>
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<tr>
<td>T10 (min)</td>
<td>37 ± 23(^d)</td>
</tr>
<tr>
<td>AUC (activity/min)</td>
<td>8.4 ± 5.9</td>
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<tr>
<td><strong>Time of meal arrival (T10) and meal residence (area under the time-activity curve for 210 min postprandially) were obtained for regions of interest determined for proximal small intestine, distal small intestine, and cecum or ascending colon. AUC, area under the time-activity curve.</strong></td>
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<tr>
<td>Mean ± SD (all such values).</td>
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<tr>
<td>(^d) P &lt; 0.01 compared with the control group.</td>
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<tr>
<td>(^\dagger) P &lt; 0.05 compared with the TG group.</td>
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<tr>
<td>(^\ddagger) P &lt; 0.05 compared with the control group, Kruskal-Wallis test with Dunn’s multiple comparison.</td>
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**FIGURE 2.** Within-group comparisons (mixed linear model) of hunger, prospective consumption, and fullness ratings (mean ± SEM) after meal intake in 10 controls (■), 14 patients with partial gastrectomy (PG; ▣), and 7 patients with total gastrectomy (TG; ▲). Baseline fullness ratings were significantly lower in the TG group than in the control group (\(P < 0.05\)). Hunger and prospective consumption increased significantly from time 0 at 180 min in controls (*\(P < 0.01\)), at 120 min in the PG group (\(^\ddagger\)\(P < 0.01\)), and at 150 min in the TG group (**\(P < 0.05\)). Peak of fullness occurred at time 0 in PG (\(^\ddagger\)\(P < 0.01\)) and TG (**\(P < 0.01\)) groups. In the PG group, fullness ratings continued to be higher (\(^\ddagger\ddagger\)\(P < 0.05\)) than baseline until 120 min and were significantly lower (\(^\ddagger\ddagger\)\(P < 0.01\)) than time 0 at 90 min. In the TG group, fullness ratings were significantly lower (**\(P < 0.01\)) than those at time 0 at 30 min. There was no significant change in fullness ratings over the observation period in the control group.
groups, and prospective consumption ratings decreased significantly from 90, 120, and 150 min than did subgroup B (rank test). Subgroup A showed significantly higher fullness ratings at 30, 60, and 90 min while subgroup B did not (mean ± SEM) after meal intake in subgroup A and subgroup B of the group of patients with partial gastrectomy. Fullness ratings increased at t = 0 in both groups, and prospective consumption ratings decreased significantly from baseline ratings (*P < 0.01, **P < 0.05, Wilcoxon’s matched-pair signed-rank test). Subgroup A showed significantly higher fullness ratings at 30, 60, 90, 120, and 150 min than did subgroup B (P < 0.01, Mann-Whitney test).

This result was caused by age differences. Because it is well established that aging itself is associated with a reduction in REE (28, 29), a low REE in TG would be shown if age were the determining factor. Although energy intake was higher in the TG group, body mass index (in kg/m²) was not significantly different among the groups. TG patients might require an increased daily energy intake to maintain a normal body weight. The high REE also may contribute to weight loss commonly observed in the first months postoperatively and difficulty in regaining weight, which is often associated with TG (15, 16, 30, 31). Gastric bypass, a procedure that shares some similarities with gastrectomy, has been associated with increased REE in rats (32).

Gastric emptying and gastrointestinal transit parameters results in healthy volunteers are similar to those of previous studies using the same scintigraphic technique (23, 25). Precipitous gastric emptying and rapid small intestine transit in PG subjects also have been reported (33). Because gastrointestinal transit seen in TG subjects is exceedingly rapid, with >55% of the test meal radioactive marker distributed between distal small bowel and colon 30 min after the ingestion, it is surprising that these patients presented only mild and occasional symptoms. Impairment of digestion or absorption may be caused by this fast transit pattern after gastrectomy (34, 35), so it is possible that our TG subjects have some degree of malabsorption, which may be compensated by the high caloric intake.

Our PG group was composed of patients with 3 different types of postoperative reconstructions, which may reflect a functional diversity not considered in our analysis. Gastric emptying rate and other functional characteristics of the gastrointestinal tract of PG patients are likely to be determined by the combination of reduction of gastric volume and loss of the antropyloric region and vagal innervation, however, which are features of all PGs, regardless of the reconstruction procedure used (36).

Although no significant differences were noted between the study groups in regard to fasting hunger and prospective consumption, fasting fullness ratings were lower in TG patients than in healthy volunteers. The explanation for this finding is uncertain but may suggest that stomach integrity is in some way necessary for fasting fullness perception in humans. Some other differences appeared when subjects were fed. In PG and TG subjects, the perception of fullness was intense and early, peaking at the end of the test meal, whereas in healthy volunteers it was only transitory (Figure 3). The presence of nutrients in the small intestinal lumen, which occurs after meals, is associated with increased fullness (37–40). This effect is probably mediated by several interrelated factors, including modulation of gastric emptying, gastrointestinal motility and transit (41, 42), and stimulation of gastrointestinal hormones. A likely explanation for our findings is that in both PG and TG subjects, rapid entry of substantial fractions of the meal into the small bowel immediately after ingestion caused abnormal distention of the bowel walls, which induced fullness. This interpretation is strengthened by the observation that among PG patients, subjects with the fastest gastric emptying rates had the most intense and the longest-lasting fullness ratings (Figure 3).

The possibility that the precipitous entry of contents in the small bowel causes fullness by exciting wall mechanoreceptors is supported by the finding that distention of the jejunum by saline infusion was shown to cause fullness in a volume-dependent manner (42). The presence of nutrients in the small intestine lumen, which occurs after meals, triggers the release of gastrointestinal hormones, however, including cholecystokinin (4, 12), glucagon-like peptide 1 (5, 9), and PYY (13, 17, 18), which in turn are associated with increased fullness. In this study, the exaggerated fullness sensation demonstrated by PG and TG subjects may have been caused by the rapid spread of the nutrients throughout the small intestine, because it has been shown that the magnitude of fullness elicited by nutrients in the bowel is proportional to the area of intestinal mucosa exposed (40, 41). The early arrival of substantial portions of the radioactive marker at the cecum-colon region in PG and TG subjects indicated that the rapid spread of the test meal occurred. The exaggerated increase in fullness perception in the TG group was transient, which might be associated with rapid emptying of the proximal small bowel. The perception of fullness was not impaired in our gastrectomized patients, who had also undergone vagotomy, which indicated that the integrity of vagal afferent innervation of gastrointestinal tract is not crucial for this sensation in humans. This finding was consistent with data from experimental studies that suggested that chyme-induced response of the proximal small intestine is responsible for satiation after gastrectomy and vagotomy (10, 12).

In the conditions of our study protocol, the time course of hunger and prospective consumption sensations had similar profiles in the PG and control subjects studied. After a slight reduction immediately after a meal, hunger and prospective...
consumption ratings increased gradually and eventually became significantly higher than the respective basal ratings. The same time course features were seen in TG subjects, except that prospective consumption tended to return earlier than in the other groups. Roughly, this pattern of variations keeps an inverse relation with the amount of the meal marker contained in the proximal gastrointestinal tract (stomach + small intestine) in the 3 groups, which is consistent with the notion that the inhibition of appetite sensations is under the influence of signaling from mechanoreceptors, chemoreceptors, or both located in that particular small bowel region (10, 12). On the other hand, because vagal fibers were severed in PG patients and TG patients are devoid of the main gastrointestinal source of ghrelin, the great similarity among the 3 groups of study regarding hunger and prospective consumption responses to the test meal strongly suggested that neither vagal afferents nor ghrelin released from the stomach exert relevant influences on these sensations in humans.

Our study had some weaknesses that should be acknowledged. One potential pitfall of this study occurred in the significant age difference between controls and gastrectomized subjects. Available evidence indicates that the influence of age on gastric emptying is small in comparison with that of gastrectomy; thus, the impact of age on gastric emptying should be negligible. Statistical analysis of the impact of age on REE was performed and revealed no significant effect. Another possible limitation of the study was pooling of subjects with different reconstruction procedures in the PG group. Gastrointestinal motility after gastrectomy was determined by features common to Billroth I, Billroth II, and Roux-en-Y procedures—namely, gastric volume reduction and resection of the antropyloric region (36). The relatively small sample size was a limitation because it led to the possibility of type II statistical errors; lack of significant associations should be interpreted with caution.

In conclusion, patients with partial or total gastrectomy have higher than predicted energy expenditure, which in TG seems to be compensated by increased energy intake. These patients also have a nearly normal postprandial response of hunger and prospective consumption sensations and an earlier and increased postprandial fullness, which seem to be associated with disturbances in gastrointestinal transit of the ingested meal and are likely independent of vagal fiber integrity or stomach-released ghrelin.

The authors’ responsibilities were as follows—MMK, LEAT, and RBO: conceived, designed, and conducted the study; MMK and VMMS: designed and measured resting energy expenditure and interpreted indirect calorimetry data; and MMK, LEAT, and RBO: wrote the manuscript. All authors were responsible for data interpretation. None of the authors had a conflict of interest.

REFERENCES