Exclusion criteria:
To minimize confounding effects of various comorbidities, specific exclusion criteria were applied for each test. Thus, participants were excluded from the oesophageal manometry, if they had previous oesophageal or gastric surgery, severe neurological diseases (e.g. Parkinson’s disease, multiple sclerosis), collagen vascular disease, untreated hypo- or hyperthyroidism, hypokalaemia and Crohn’s disease. Participants were excluded from the gastric emptying breath test, if they had previous gastric surgery, severe neurological diseases, collagen vascular disease, idiopathic gastroparesis, peptic ulcer, untreated hypo- or hyperthyroidism, hypokalaemia, Crohn’s disease, uraemia or were taking GLP-1 analogues or prokinetics. Finally, the exclusion criteria for the Diabetes Bowel Symptom (DBSQ) and the Gastroparesis Cardinal Symptom Index (GCSI) questionnaires included those of the $^{13}$C-octanoic acid breath test with the addition of the irritable bowel syndrome. In addition to these criteria, participants were allowed to decline their participation in certain examinations.

High-resolution oesophageal manometry
The catheter was inserted transnasally into the oesophagus and was positioned in a way that allowed visualization of the pressure topography of the full oesophageal length including the upper and lower sphincters. A series of 10 swallows with 5 ml of room-temperature water each followed. The topographical plots were analyzed using the software ViMeDat (Standard Instruments GmbH, Karlsruhe, Germany). The examiner reviewed each swallow in order to detect and correct any possible mistakes made by the software regarding the identification of anatomical landmarks. Each variable was measured ten times (once for each deglutition), and the average of these values was used as the final value of the variable. To determine the percentage of abnormal findings in each group, the reference values recently determined by Bogte et al. using the same technical equipment were applied [1].
Determination of gastric emptying

Gastric emptying was determined using a $^{13}$CO$_2$-breath test. At intervals of 15 or 30 min, breath specimens were sampled into gas-tight plastic bags and the $^{13}$CO$_2$-content was determined within 24 h using non-dispersive infrared spectrometry (Wagner Analysentechnik, Bremen, Germany).

Based on the excess $^{13}$C in the breath specimens, the time course of gastric retention was estimated using the Wagner-Nelson method, which corrects for the breath-test specific underestimation of gastric emptying [2]. Briefly, the emptying flow curve, i.e. the ratio between the cumulative amount of ingested $^{13}$C absorbed at time point t and ultimately $A(t)/A(\infty)$ was calculated from the percentage of dose recovery per hour (PDR) and the cumulative PDR (CPDR) as follows: $A(t)/A(\infty) = CPDR(t)/CPDR(\infty) = [1+((k_b/k_{el})-1)][1-exp(-kt)]^{k_b-1}$ with $k_{el} = 0.65\cdot h^{-1}$. Gastric retention, i.e. the percentage of labeled meal retained in the stomach at each time point was calculated as 100-$[1-A(t)/A(\infty)]$.

Key characteristics of the gastric emptying-time profile ($T_{1/2}$ and $T_{LAG}$) were calculated by taking advantage of the generalised linear regression model proposed by Lee et al. [3, 4]. The model predicts the scintigraphic gastric emptying estimates for $T_{1/2}$ and $T_{LAG}$ on the basis of the excess $^{13}$CO$_2$ production after meal ingestion. Using delta over baseline (DOB) values [o/oo], the $^{13}$C abundance in the Pee De Belenmitella (PDB) limestone standard (0,0112372) and an individual CO$_2$ production of 5 mmol·m$^{-2}$·min$^{-2}$ as estimated by Ghoos et al. [5], the exhalation of excess $^{13}$C [$\mu$mol·min$^{-1}$] was calculated. $T_{1/2}$ and $T_{LAG}$ were obtained by taking the reciprocals from the respective linear predictors [3]: $LP_{1/2} = 0.000853 + 0.006782 \times ^{13}$C (t=30 min) + 0.004668 $\times ^{13}$C (t=150 min), $T_{1/2} = LP_{1/2}^{-1}$, and $LP_{LAG} = 0.001546 + 0.017694 \times ^{13}$C (t=30 min) + 0.013779 $\times ^{13}$C (t=120 min), $T_{LAG} = LP_{LAG}^{-1}$, with $^{13}$C (t=30 min), $^{13}$C (t=120 min), and $^{13}$C (t=150 min) representing the exhaled amount of excess $^{13}$C [$\mu$mol·min$^{-1}$] at the specified time points.

Diabetes bowel symptom questionnaire

This questionnaire was introduced by Quan et al. in 2003 and consists of various parts that contain questions about upper and lower gastrointestinal tract symptoms [6]. Only parts A and B of the
questionnaire were used: Part A examines the presence and severity of abdominal pain/discomfort within the last 3 months and their relation to factors such as frequency of bowel movements, consistency of stool, meals and intake of milk. 13 questions were answered, with the score ranging from 1 to 5 for each question. If a participant did not experience any abdominal pain/discomfort within the last 3 months, the lowest score (1 point) was assigned. The maximum score was 65 points. Part B examines the presence and severity of upper gastrointestinal symptoms within the last 3 months. The symptoms examined are: early satiety, persistence of food in stomach, abdominal bloating, abdominal distension, loss of appetite, nausea, retching, vomiting, heartburn, acid regurgitation and dysphagia of solids and liquids. The 19 questions of this part were divided into 2 groups. The first group contained 11 questions concerning the frequency of symptoms while the second group consisted of 8 questions that had to do with the severity of symptoms. The score for each question ranged from 1 to 5 points for the first group and from 0 to 6 points for the second group. The minimum and maximum score was 11 and 55 points for the first group and 0 and 48 points for the second group of questions. Higher scores indicate higher frequency or severity of symptoms.

Additional references:


