

Originals

Gastric and oesophageal emptying in patients with Type 2 (non-insulin-dependent) diabetes mellitus

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Summary. Gastric emptying of a digestible solid and liquid meal and oesophageal emptying of a solid bolus were measured with scintigraphic techniques in 20 randomly selected Type 2 (non-insulin-dependent) diabetic patients receiving oral hypoglycaemic therapy and 20 control subjects. In the diabetic patients, the relationships between oesophageal emptying, gastric emptying, gastrointestinal symptoms, autonomic nerve function and glycaemic control were examined. The percentage of the solid meal remaining in the stomach at 100 min ($p < 0.001$), the 50% gastric emptying time for the liquid meal ($p < 0.05$) and oesophageal emptying ($p < 0.05$) were slower in the diabetic patients compared to the control subjects. Scores for upper gastrointestinal symptoms and autonomic nerve dysfunction did not correlate significantly ($p > 0.05$) with oesophageal, or gastric emptying. The

50% gastric emptying time for the liquid meal was positively related ($r = 0.58$, $p < 0.01$) to the plasma glucose concentration at the time of the performance of the gastric emptying test and the lag period, before any solid food emptied from the stomach, was longer ($p < 0.05$) in subjects with plasma glucose concentrations during the gastric emptying measurement greater than the median, compared to those with glucose concentrations below the median. These results indicate that delayed gastric and oesophageal emptying occur frequently in Type 2 diabetes mellitus and that delayed gastric emptying relates, at least in part, to plasma glucose concentrations.

Key words: Diabetes mellitus, stomach, oesophagus, gastric emptying, oesophageal emptying, autonomic nerve function.

Abnormal gastrointestinal motility is a well recognised complication of diabetes mellitus [1–20]. Gastric and oesophageal motor dysfunction in diabetic patients may result in significant upper gastrointestinal symptoms [2, 4, 5, 13–15], and delayed gastric emptying may contribute to poor blood glucose control [10]. A recent study demonstrated that oesophageal emptying of a solid bolus was delayed in 42%, and gastric emptying of either the solid or the liquid component of a meal was delayed in 56% of a group of 45 randomly selected Type 1 (insulin-dependent) diabetic patients [2]. No studies have adequately assessed the prevalence of abnormal oesophageal or gastric emptying in Type 2 (non-insulin-dependent) diabetes mellitus, although it has been assumed that disordered gastrointestinal motility occurs less frequently than in Type 1 diabetes mellitus [6]. We have used sensitive scintigraphic techniques to determine the prevalence of abnormal gastric and oesophageal emptying in 20 Type 2 diabetic subjects. The relationships between gastric emptying, oesophageal emptying, gastrointestinal symptoms, autonomic nerve function and glycaemic control have been examined.

Subjects and methods

The studies were performed in 20 patients (9 male, 11 female), mean age 60 years (range 42–77), mean body mass index (BMI) 27.8 (range 24.1–35.9) and mean body weight 75 kg (range 52–92), who were selected by random number from all the ambulant out-patients who were being treated with oral hypoglycaemic drug(s) (glibenclamide, gliclazide, tolbutamide and/or metformin) for Type 2 diabetes mellitus of at least 12 month's duration by two members (MH & PH) of the Endocrine Unit of the Royal Adelaide Hospital. Patients were not included in the study if they were taking any medication other than oral hypoglycaemic drugs, or there was a history of upper gastrointestinal surgery or peptic ulcer disease. The mean duration of known diabetes was 8 years (range 1–20), and the majority of the patients had other complications of diabetes mellitus including nephropathy, retinopathy and peripheral neuropathy. Some of the characteristics of the diabetic patients are shown in Table 1. Delayed gastric or oesophageal emptying due to organic obstruction was excluded by upper gastrointestinal endoscopy. Written informed consent was obtained in all cases, and the study was approved by the Ethics Subcommittee of the Royal Adelaide Hospital.

On one day, each diabetic patient underwent: (a) a subjective assessment of gastrointestinal symptoms, (b) an objective assessment of diabetic complications of autonomic neuropathy, peripheral neuropathy and retinopathy, (c) an assessment of glycaemic control, (d) measurement of gastric emptying of a mixed solid and liquid meal, and (e) measurement of oesophageal emptying of a digestible solid

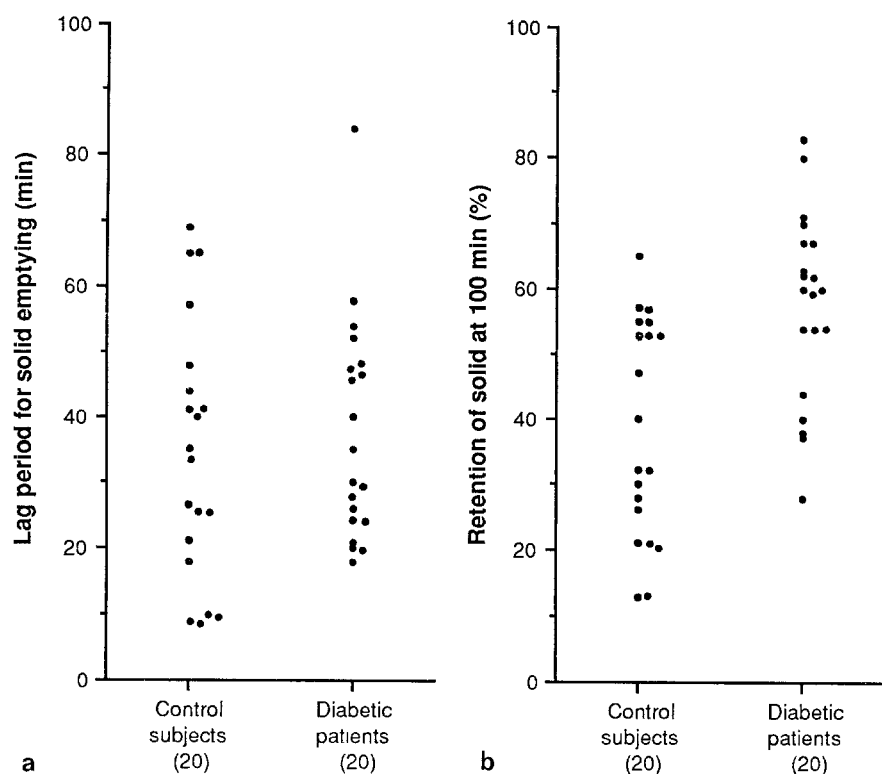


Fig. 1. Individual results for solid gastric emptying expressed as: **a** the lag period before food left the stomach and **b** the percentage of the solid meal remaining at 100 min in control subjects and in patients with Type 2 (non-insulin-dependent) diabetes mellitus. ($p < 0.001$)

bolus. On the study day, smoking was prohibited, and no patient took any medication until after the completion of the tests.

Gastric and oesophageal emptying measurements were also performed in 20 normal volunteers (mean body weight 65 kg, range 47–77) selected to be matched for sex and age (within 5 years) to each diabetic patient. All the control subjects were within 10% of ideal weight (mean BMI 22.7) (Metropolitan Life Insurance Criteria), non-smokers, on no medication and with no evidence of gastrointestinal disease. All the diabetic and control subjects were Caucasian.

The diabetic group was significantly heavier ($p < 0.01$) and had a higher BMI ($p < 0.01$) than the control group.

Assessment of gastrointestinal symptoms

Before the performance of the gastric and oesophageal emptying tests, gastrointestinal symptoms were assessed by a standard questionnaire [2, 4, 5]. Anorexia, nausea, early satiety, upper abdominal discomfort or distention, vomiting, abdominal pain ("gastric" symptoms), dysphagia, heartburn and acid regurgitation ("oesophageal" symptoms) were scored according to the following scheme: 0 = normal, 1 = mild (symptom could be ignored if the patient did not think about it), 2 = moderate (symptom could not be ignored, but did not influence daily activities), 3 = severe (symptom influenced daily activities). The maximum possible total score for the gastric symptoms was 18 and was 9 for the oesophageal symptoms.

The number of bowel actions each week, the consistency of bowel actions and the presence or absence of nocturnal diarrhoea and faecal incontinence were also noted. The patient was considered to suffer from constipation if less than three spontaneous bowel actions occurred each week [2, 4, 5].

Assessment of autonomic neuropathy, peripheral neuropathy and retinopathy

Autonomic neuropathy was assessed by standard cardiovascular reflex tests. Parasympathetic function was evaluated by the heart rate variation (R-R interval) during deep breathing and the immediate

heart rate response to standing (30:15 ratio). Sympathetic function was assessed by the fall in systolic blood pressure in response to standing. The result of each of these three tests was scored as 0 = normal, 1 = borderline, 2 = abnormal (for a maximum possible score of 6), according to criteria outlined by Ewing and Clarke [21]. A total score of ≥ 3 was taken to indicate definite autonomic nerve damage [2, 5].

Retinopathy was graded as none, background or proliferative on the basis of a recent ophthalmological assessment, which often included fluorescein angiography.

Peripheral neuropathy was diagnosed clinically when absent ankle reflexes were associated with either sensory or motor changes.

Assessment of glycaemic control

An indwelling venous cannula was used to obtain 5 ml blood samples 5 min before and at 30, 60, 90 and 120 min after the commencement of each gastric emptying test for measurement of the plasma glucose concentration.

Haemoglobin A_{1c} (HbA_{1c}) was measured (using the initial venous sample) by a modification of the fast protein liquid chromatographic assay described by Jeppsson et al. [22]. The HbA_{1c} results were expressed as a percentage; the range in normal subjects being 3.5–6.0%.

Measurement of gastric emptying

Details of this double isotope test, which measures both solid and liquid gastric emptying simultaneously, have previously been published [2, 4, 5, 23, 24]. The solid meal was 100 g of cooked ground beef containing 1.0–1.5 mCi of in vivo labelled ^{99m}Tc-sulphur colloid-chicken liver [23]. The liquid meal was 150 ml of 10% dextrose in water labelled with 0.75–1 mCi of ^{113m}In-DTPA. The test was performed at 10.00 hours (after the subject had fasted from solids from 19.00 hours and liquids from 24.00 hours the previous day). The study was performed in the sitting position with the scintillation camera behind the patient. The subject initially ate the solid meal over a 5 min

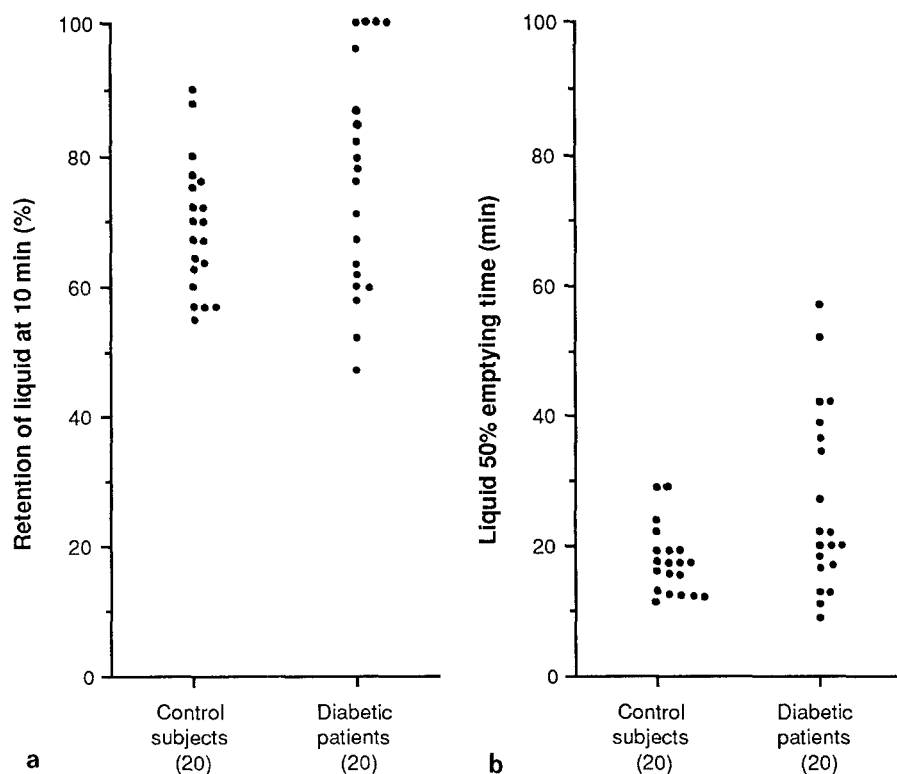


Fig. 2. Individual results for liquid gastric emptying expressed as: **a** the percentage of the liquid meal remaining at 10 min and **b** the time taken for 50% of the liquid meal to empty from the stomach in control subjects and in patients with Type 2 diabetes mellitus. ($p < 0.05$)

period and then immediately drank the dextrose solution. Time zero was defined as the time of meal completion, and then each study was continued for at least 2 h.

Data was corrected for patient movement, radionuclide decay, Compton scatter and gamma ray (tissue) attenuation using previously described methods [23, 24]. From the histograms of solid and liquid emptying (expressed as a percentage of the total meal remaining within the stomach vs time), several parameters were derived for subsequent analysis. For the solid component, these parameters were the lag period before food left the stomach and the percentage remaining at 100 min after meal completion.

The 50% emptying time for the solid meal was not used because some patients did not reach 50% emptying in the study period. Similarly, in some patients with markedly delayed emptying the linear emptying rate could not be determined accurately.

For the liquid component, the percentage remaining at 10 min after meal completion and the time for 50% emptying (T50) were obtained [2, 4, 5]. The percentage of liquid remaining at 10 min was used as an index of the early phase of gastric emptying.

Measurement of oesophageal emptying

This test, which measures the emptying of a solid bolus, has been described previously [2, 5]. Before the commencement of the gastric emptying test, after swallowing 5 ml of water as a lubricant, the seated subject swallowed a 10 g bolus of the solid meal and was then asked to swallow on command every 15 s. Cricoid movement was monitored during the performance of the test to ensure that no additional swallows were taken and the visual display of the gamma camera was used to confirm that the bolus had entered the oesophagus after the first swallow (using the level of the cricoid cartilage). The test was continued until the bolus was seen to enter the stomach, or until 20 swallows (= 300 s) had been performed. Analysis was performed by computer-drawn regions of interest corresponding to the oesophagus (cricoid to gastrooesophageal junction) and the stomach. The time for 95% of the radioactivity to enter the stomach was calculated [2, 5].

Statistical analysis

Data were evaluated using the Mann-Whitney U-test (unpaired data) and linear regression analysis.

Results

Gastric emptying

Solid emptying. In the control and the diabetic subjects, solid emptying was slower than liquid emptying and was characterised by an initial lag period, followed by an emptying phase that usually approximated a linear pattern. There was a significant delay of solid food emptying in the diabetic patients. The lag period was not significantly different from the control subjects (although it was grossly prolonged in one diabetic subject) (Fig. 1), but there was increased ($p < 0.001$) retention of solid food at 100 min. The percentage retention of solid food at 100 min was greater than the upper limit of the control range in 6 of the 20 diabetic subjects (30%) (Fig. 1).

Liquid emptying. The emptying curve for liquid was non-linear with a slope that decreased with time and usually approximated a monoexponential pattern in both control and diabetic subjects. The T50 for the liquid meal was slower ($p < 0.05$) in the diabetic patients than in the control subjects, but the percentage of the liquid meal remaining at 10 min was not significantly different between control subjects and diabetic patients.

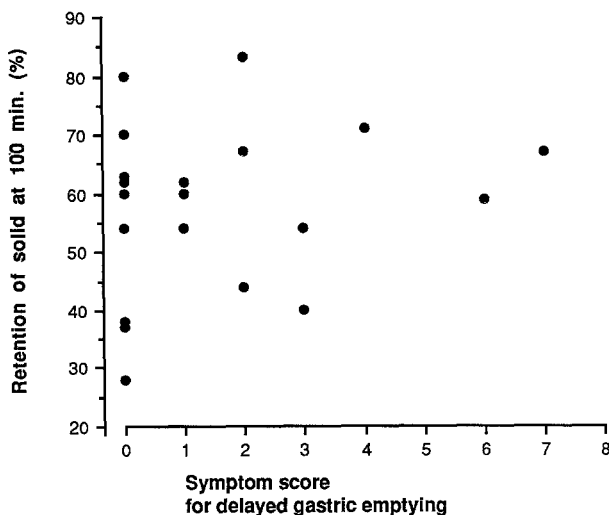
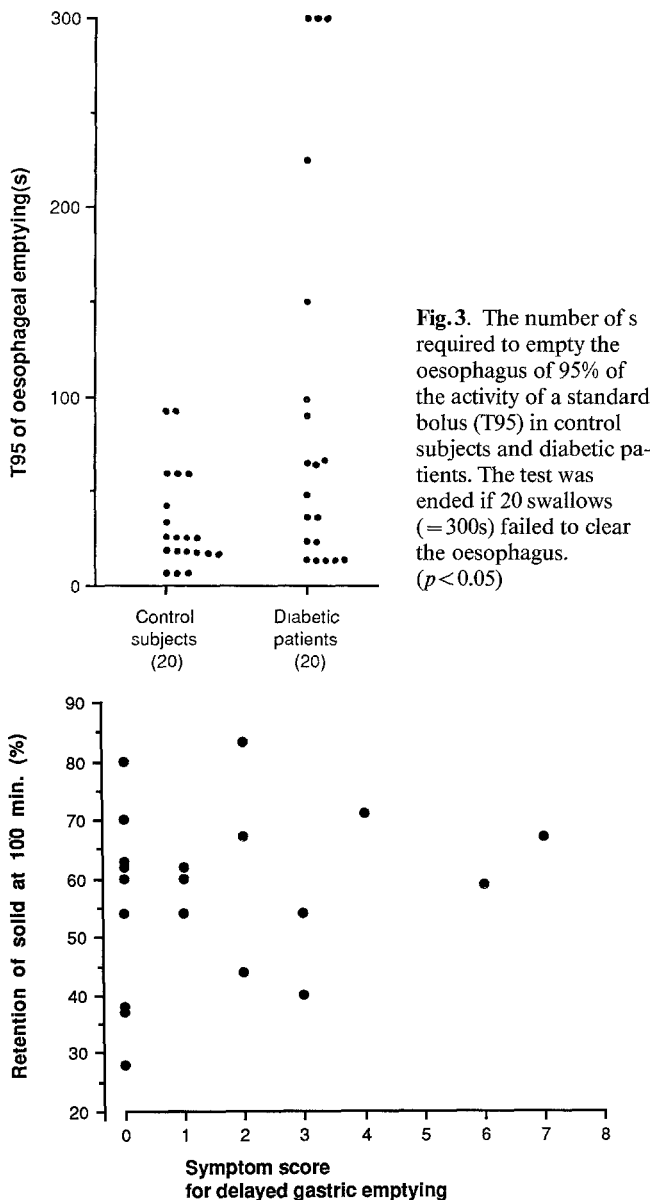


Fig. 4. The relationship between the symptom score for delayed gastric emptying and the percentage retention of the solid meal at 100 min ($r = 0.19$, NS)

The liquid T50 was greater than the upper limit of the control range in seven patients (35%) and less than the lower limit in two patients (10%). The percentage retention at 10 min was greater than the upper limit of the control range in five of the diabetic patients (25%) and less than the lower limit in two patients (10%) (Fig. 2).

Relationship between solid and liquid emptying in diabetic patients. There were significant correlations between the percentage retention of the liquid meal at 10 min and both the solid lag period ($r = 0.43$, $p < 0.05$) and the percentage retention of the solid meal at 100 min ($r = 0.49$, $p < 0.05$). The correlations between the liquid T50 and both the solid lag period ($r = 0.35$, NS) and the percentage retention of the solid meal at 100 min ($r = 0.34$, NS) were not statistically significant.

Of the 20 diabetic patients, 10 had delayed gastric emptying (values greater than the upper limit of the control range) for solid gastric emptying (percentage retention at 100 min), liquid gastric emptying (T50), or both.

Oesophageal emptying

In all subjects, the bolus of food entered the oesophagus after the first swallow, and no food was retained in the oesophagus after the consumption of the liquid meal. The diabetic group had significantly delayed ($p < 0.05$) oesophageal emptying; and in six of the 20 patients (30%), the time for 95% oesophageal emptying of the solid bolus was greater than the upper limit of the control range (Fig. 3). Visual inspection of the computer images demonstrated that in the diabetic patients with delayed oesophageal emptying, retardation of the bolus occurred in both the middle and distal parts of the oesophagus. There was no significant correlation between oesophageal emptying and either liquid or solid gastric emptying.

Gastrointestinal symptoms

There was considerable variation in gastrointestinal symptoms between patients (Table 1). Five of the 20 patients (25%) had a score for gastric symptoms of 3 or more out of a possible 18, and nine patients had no symptoms (Fig. 4). Oesophageal symptoms were also extremely variable, with a median score of 0.5 (range 0–8). Two patients suffered from dysphagia, and seven suffered acid regurgitation. Of the other gastrointestinal symptoms, one patient suffered from constipation; none had nocturnal diarrhoea; and two suffered faecal incontinence.

Diabetic complications

The autonomic neuropathy scores are shown in Figure 5 and Table 1. Eight patients had definite evidence of autonomic neuropathy (total score ≥ 3), and 16 (80%) had a score of 1 or more. The score for autonomic nerve dysfunction correlated significantly ($r = 0.45$, $p < 0.05$) with the age of the subject, but not with the duration of diabetes mellitus. Six patients clinically had peripheral neuropathy. Fifteen patients had no retinopathy, four patients had background retinopathy; and one patient had proliferative retinopathy.

Glycaemic control

Plasma glucose and HbA_{1c} concentrations varied considerably between patients (Fig. 6, Table 1). On the basis of the HbA_{1c} results, no patient was in the range for nor-

Table 1. See text

Patient number	Age	Sex	Duration of known diabetes mellitus (years)	Oral hypoglycaemic treatment	Glycosylated Haemoglobin (%)	Mean blood glucose (mmol/l)	Autonomic nerve function tests ^a			Upper gastro-intestinal symptom score		
							Parasympathetic	Sympathetic		Gastric	Oesophageal	Total
1	61	F	4	metformin	7.5	8.3	0	0	0	2	0	2
2	54	M	5	glibenclamide	11.4	17.6	1	0	0	0	0	0
3	64	F	9	glibenclamide metformin	8.8	17.7	1	0	1	7	2	9
4	66	F	15	tolbutamide	12.6	16.6	1	0	0	3	8	11
5	61	M	5	tolbutamide	6.6	8.5	1	1	0	0	0	0
6	48	F	4	glibenclamide	6.4	13.0	0	1	1	0	4	4
7	50	M	9	gliclazide metformin	8.7	12.6	0	0	0	0	1	1
8	75	F	2	tolbutamide	12.1	18.1	2	2	1	0	0	0
9	42	M	6	tolbutamide metformin	13.3	22.5	0	0	1	4	3	7
10	67	F	20	tolbutamide metformin	12.7	22.4	2	2	1	1	0	1
11	66	M	15	tolbutamide	15.7	22.2	2	2	1	2	0	2
12	62	F	5	tolbutamide	10.7	13.9	0	0	0	2	1	3
13	54	F	9	tolbutamide	16.0	21.5	2	2	1	1	1	2
14	55	F	1	tolbutamide	7.2	7.7	0	0	0	6	4	10
15	50	M	11	tolbutamide	11.3	11.3	1	0	0	0	0	0
16	61	F	9	tolbutamide metformin	9.2	11.6	2	2	2	3	1	4
17	61	M	17	glibenclamide	13.5	18.5	2	1	1	0	0	0
18	67	M	5	glibenclamide	10.9	10.0	1	0	0	0	0	0
19	77	M	6	tolbutamide	8.5	10.3	2	2	0	1	1	2
20	64	F	2	tolbutamide	11.1	13.4	2	2	1	0	0	0

^a 0 = normal; 1 = borderline; 2 = abnormal; DB = heart rate response to deep breathing; L/St = lying/standing heart rate; BP = systolic blood pressure response to standing

mal; seven patients were in the range 6.1–9.0%, six patients were in the range 9.1–12.0%; and seven patients had values > 12.0%. The plasma glucose concentrations (at -5, 30, 60, 90 and 120 min and the mean) were each directly related to the HbA_{1c} concentration ($r > 0.75$, $p < 0.001$) and all of the plasma glucose measurements taken during the gastric emptying test were directly related to each other ($r > 0.91$, $p < 0.001$).

The duration of known diabetes mellitus (but not age) correlated significantly with both HbA_{1c} ($r = 0.54$, $p < 0.05$) and mean plasma glucose ($r = 0.55$, $p < 0.01$). There were weak ($r = 0.43$, $p < 0.05$ for both) but significant correlations between HbA_{1c} and the mean plasma glucose and the score for autonomic nerve dysfunction.

Relationships between oesophageal and gastric emptying and other parameters in diabetic subjects

Age, sex and duration of diabetes mellitus. Oesophageal, gastric liquid and gastric solid emptying were not significantly related to age or the duration of known diabetes mellitus. No effect attributable to sex was seen for any of the parameters.

Gastrointestinal symptoms. There was no significant correlation between oesophageal, gastric or the total score for upper gastrointestinal symptoms and any pa-

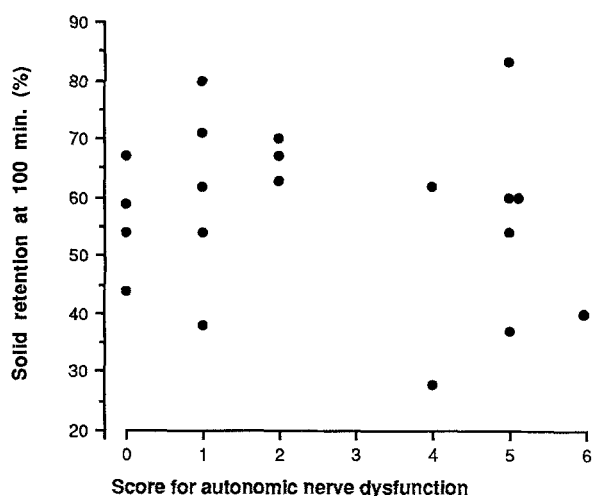


Fig. 5. The relationship between the percentage retention of the solid meal at 100 min and the score for autonomic nerve dysfunction in diabetic patients ($r = 0.19$, NS)

parameter of oesophageal or gastric emptying. Although there was a trend for patients with the higher gastric scores to have delayed gastric emptying, a number of patients with no or minimal upper gastrointestinal symptoms had delayed gastric emptying (Fig. 4).

Autonomic neuropathy. There was no significant correlation between the total score for autonomic nerve dysfunction, or the total score for parasympathetic nerve

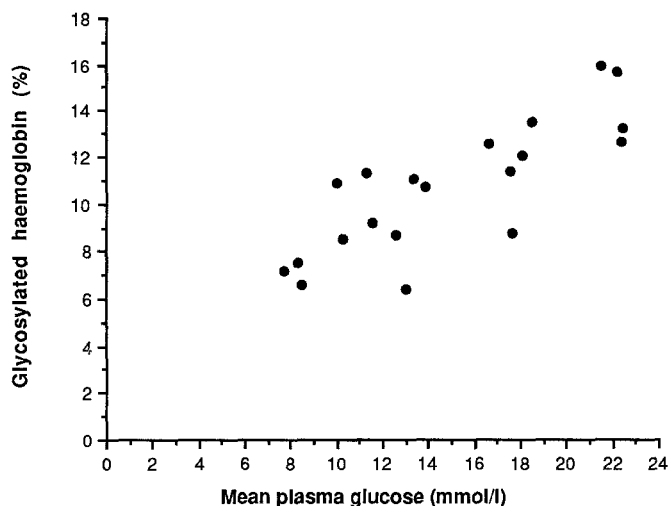


Fig. 6. The relationship between glycosylated haemoglobin (HbA_{1c}) and the mean plasma glucose concentration during the first 120 min of the gastric emptying test in diabetic patients ($r=0.82$, $p<0.01$)

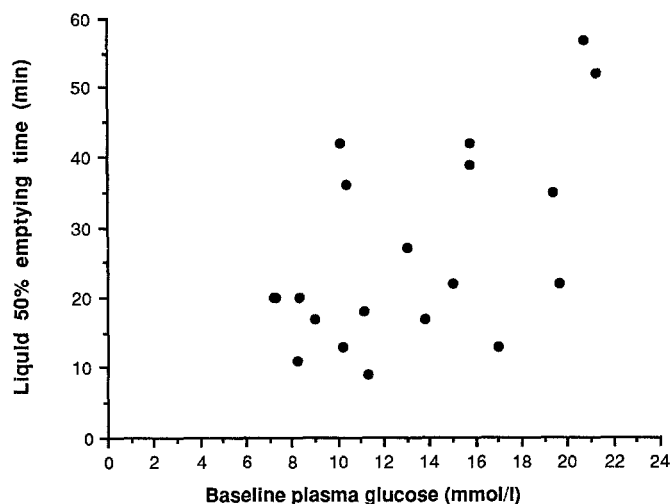


Fig. 7 The relationship between the 50% emptying time for the liquid meal and the plasma glucose concentration 5 min before the commencement of the gastric emptying measurement in diabetic patients ($r=0.58$, $p<0.01$)

dysfunction and any parameter of oesophageal or gastric emptying (Fig. 5).

Glycaemic control. There was no significant correlation between either plasma glucose or HbA_{1c} concentrations and oesophageal or gastric solid emptying. The T50 for gastric emptying of the liquid meal correlated significantly with plasma glucose concentrations at -5, 30, 60, 90 and 120 min and the mean plasma glucose ($r>0.50$, $p<0.05$) (Fig. 7) but not with HbA_{1c} ($r=0.19$, NS). There was no significant correlation between solid gastric emptying and either plasma glucose concentrations or HbA_{1c}. For the solid lag period, the correlation with mean plasma glucose was $r=0.37$ and with HbA_{1c} $r=0.15$. The solid lag period was, however, significantly ($p<0.05$) longer in diabetic patients with mean plasma glucose concentrations greater than the median level during the gastric emptying study (median T50 of

48 min) compared to those with plasma glucose concentrations below the median (median T50 of 30 min). There was no significant difference in the liquid T50 when the patients were divided similarly according to HbA_{1c} concentrations.

Discussion

Gastric emptying

This study is the first comprehensive evaluation of gastric emptying in patients with Type 2 diabetes mellitus, and the findings indicate that in this particular subgroup of Type 2 patients there is a high prevalence of gastric motor dysfunction, comparable to that demonstrated in patients with Type 1 diabetes mellitus [2, 15]. The majority of the patients had long standing diabetes mellitus, with variable glycaemic control, and there was a high prevalence of the complications autonomic neuropathy, peripheral neuropathy and retinopathy, but this population cannot be considered to be unusual. Our observations cannot be ascribed to the effect of aging on gastric emptying [25], and the slight but significant difference in body weight between the control and the diabetic groups is unlikely to be of importance [26]. There is no information to suggest that oral hypoglycaemic drugs may directly influence gastrointestinal motility, and such studies would be difficult to perform in normal subjects. In addition, as the last dose of oral hypoglycaemic drug(s) was given at least 15 h before the gastric and oesophageal emptying measurements, plasma drug concentrations would have been low. An effect of oral hypoglycaemic drugs on our findings, therefore, cannot be excluded but is unlikely. On the basis of previous results in patients with Type 1 diabetes mellitus, we would predict that the majority of Type 2 diabetic patients with slow gastric emptying of radioisotopically labelled meals would have a normal result with liquid barium sulphate [9, 20].

The normal stomach empties liquid, digestible solid and non-digestible solid meal components at different rates and with different patterns, but the motor mechanisms controlling this are poorly defined [27–29]. The gastro-duodenal pressure gradient, which is influenced by proximal gastric tone and pyloric and duodenal resistance, is of major importance in the control of liquid emptying [27, 29]. By contrast the grinding action of the antrum has a major influence in controlling gastric emptying of digestible solid food [27]. Our observations suggest that proximal stomach and antral motor activity is frequently diminished in patients with Type 2 diabetes mellitus, consistent with manometric [11–14] and scintigraphic [2, 4, 5, 8, 9, 15, 16] studies in Type 1 diabetic patients. Disordered pyloric motility may also contribute to delayed emptying [14].

The finding that gastric emptying is frequently delayed in patients with Type 2 diabetes mellitus is per-

haps not surprising [30]. Gastric bezoar has been reported in these patients [31] and abnormalities of gastric emptying have been demonstrated in two studies, which have measured gastric emptying in small numbers of selected patients with Type 2 diabetes mellitus [32, 33]. Leatherdale et al. [32] studied gastric emptying of a porridge meal in 10 patients with longstanding Type 2 diabetes mellitus and in 10 control subjects. The results of this study may be questioned because of probable technical inaccuracies [23, 24], but the time for 50% of the "peak content" of the meal to empty from the stomach was longer in the diabetic patients. Sasaki et al. [33] reported that gastric emptying of a water load was slower in a small group of obese Pima Indians with Type 2 diabetes mellitus compared to obese control subjects. In two of our 20 diabetic patients, gastric emptying of the liquid meal was faster than any control subject. This more rapid initial emptying has been demonstrated in Type 1 diabetes mellitus patients [2, 9, 15] and may reflect impaired proximal stomach accommodation to distension [34], or abnormal pyloric motility [14, 29]. The emptying of larger non-digestible solid particles, which is dependent on the integrity of phase 3 of the gastric interdigestive myoelectric complex, was not assessed in our study, but in symptomatic Type 1 diabetic patients gastric interdigestive myoelectric complexes are characteristically absent [11–13], and gastric emptying of non-digestible solid particles is markedly delayed [35].

This study demonstrates that the poor correlation between gastrointestinal symptoms and gastric emptying in Type 1 diabetic patients [2, 15] also exists in Type 2 diabetes mellitus patients. Although some patients with gastrointestinal symptoms had delayed gastric emptying, it also occurred in asymptomatic patients. The relatively high prevalence of gastrointestinal symptoms is not unexpected [1, 2, 15], and it is probable that gastrointestinal complications represent a generally underestimated cause of morbidity in both forms of diabetes mellitus.

A high prevalence of autonomic nerve dysfunction in Type 2 diabetes mellitus patients has been reported [36, 37], and it is well documented that abnormal autonomic nerve function tests precede the development of symptomatic autonomic neuropathy [36]. The absence in this study of a significant relationship between gastric emptying and the severity of autonomic nerve dysfunction differs from findings in Type 1 diabetes mellitus patients [2, 8, 15] and has several possible explanations. Only 4 of the 20 patients had no evidence of autonomic neuropathy, and it is possible that minimal abnormalities in cardiac autonomic nerve function are associated with disordered gastric motility. In addition, the relative impairments in sympathetic vs parasympathetic gastric innervation are likely to influence gastric emptying [13]. It is also possible that in the diabetic autonomic neuropathy syndrome gastric and cardiac systems may be affected differently [38], and

that vagal gastric damage may not necessarily be inferred from cardiac vagal dysfunction, but this hypothesis conflicts with the demonstration of a strong association between gastric acid output impairment and cardiac autonomic neuropathy [39].

The observation that the liquid T50 and the solid lag period are related to plasma glucose concentrations in Type 2 diabetic patients is consistent with our observations in Type 1 diabetes mellitus patients [2], although not with those made by other workers [16]. Induced hyperglycaemia in normal subjects slows gastric emptying of nutrient-containing liquid meals [40, 41] and decreases fasting antral contractility and gastric phase 3 activity [42]. The poor reproducibility of gastric emptying that has been observed in Type 2 diabetic patients [32], and the variable observations on liquid gastric emptying in Type 1 diabetic patients [2, 9, 15, 16, 20] may possibly be partly ascribed to variations in plasma glucose concentrations. The mechanism(s) responsible for the inhibitory action of hyperglycaemia on gastric motility is not known. Hyperglycaemia may suppress vagal nerve activity [43] and be an important factor in the aetiology of autonomic nerve dysfunction [44]. Alterations in gastrointestinal hormone secretion (such as motilin, pancreatic polypeptide, somatostatin, glucagon, gastrin and gastric inhibitory polypeptide) may be important [30]. Although plasma glucose and glycosylated haemoglobin concentrations correlated closely in our study, there was no significant relationship between gastric emptying and glycosylated haemoglobin. This latter observation suggests, but certainly does not prove, that delay in gastric emptying is more closely linked to acute, rather than chronic hyperglycaemia.

Oesophageal emptying

Recent studies suggest that tests measuring oesophageal radionuclide transit using liquid or solid boluses are as sensitive as manometric techniques in detecting oesophageal motor dysfunction, particularly in those disorders characterised by disorganised contractions [45, 46]. Our results indicate that there is a high prevalence of oesophageal motor dysfunction in patients with Type 2 diabetes mellitus; the time for 95% of a solid bolus to empty from the oesophagus was greater than the control range in six of the 20 diabetic patients. Delayed transit correlated poorly with symptoms of oesophageal dysfunction. These results are consistent with previous radiologic, radio-isotopic and manometric studies [2, 3, 7, 10, 47] in Type 1 diabetes mellitus patients. The manometric abnormalities which have been reported in Type 1 diabetic patients include a reduction in the primary peristaltic wave, frequent spontaneous contractions, reduced lower oesophageal sphincter pressure and multiphasic, multi-peaked peristaltic pressure wave complexes [3, 47]. Although we were unable to demonstrate a significant correlation,

delayed oesophageal emptying in Type 2 diabetic patients is likely to reflect autonomic nerve impairment [2, 7]. It should, however, be noted that a correlation between oesophageal motility abnormalities and neuropsychiatric status in diabetic patients has been reported [48].

Relationship of observations to glycaemic control

In patients with Type 1 diabetes mellitus, alterations in gastric emptying are likely to adversely affect glycaemic control [19]. If the same applies to Type 2 diabetes mellitus, and this has yet to be shown, our results suggest that diabetic gastroparesis may also be an under-emphasised contributor to poor glycaemic control in those patients with Type 2 diabetes mellitus. Furthermore, hyperglycaemia may itself lead to delayed gastric emptying and also gastrointestinal symptoms. Type 2 diabetic patients with unexplained poor glycaemic control should possibly be screened for gastric emptying abnormalities and gastrokinetic drugs may have a role in such patients by reducing variations in gastric emptying [5]. Our results provide a further rationale to improve and avoid major fluctuations in plasma glucose levels in Type 2 diabetic patients. While delayed oesophageal emptying in diabetic patients is usually relatively asymptomatic, these patients are at risk for delayed oesophageal transit of capsules and tablets (such as oral hypoglycaemic drugs) with the consequent risks of localised mucosal ulceration and delayed drug absorption [49].

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