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ORIGINAL DATA

Esophageal Dysmotility is More Common Than Gastroparesis in Diabetes Mellitus and is Associated With Retinopathy

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■ Abstract

OBJECTIVES: Gastroparesis is a well-known complication of diabetes mellitus, both in symptomatic and asymptomatic patients. Esophageal dysmotility has also been described, but is not as well-characterized. The etiology and effect of these complications need to be clarified. The aim of the present study was to evaluate esophageal and gastric motility, complications, gastrointestinal symptoms, and plasma biomarkers in a cross-sectional study comprising patients with diabetes mellitus. **METHODS:** Patients with diabetes were consecutively asked to participate, and eventually 84 volunteers were included in the study. Esophageal manometry and the gastric emptying test were performed in all patients. Type of diabetes, symptoms, diabetic complications, body mass index (BMI), and biomarkers were recorded. Patients were interviewed about gastrointestinal symptoms. **RESULTS:** Esophageal dysmotility was present in 63% of patients and gastroparesis in 13% of patients. There was no difference in dysmotility between patients with type 1 and type 2 diabetes or between genders. Gastrointestinal symptoms did not correlate to objective findings. Age correlated negatively with gastric emptying rate ($p = 0.004$). Patients with esophageal dysmotility had longer duration of diabetes compared to those without dysmotility ($p = 0.043$). In logistic regression analysis, retinopathy was strongly associated with esophageal dysmotility, independent of duration ($p = 0.003$). **CONCLUSIONS:** Esophageal dysmotility is more common than gastroparesis in diabetes mellitus independent of gender, symptoms, and type of diabetes. There is a strong association between retinopathy and esophageal dysmotility.

Keywords: diabetes · gastroparesis · retinopathy · esophageal dysmotility · esophageal manometry · HbA1c · gastrointestinal tract · thyroid-stimulating hormone

Introduction

Diabetes often leads to late complications in different organs. Gastroparesis is a common complication in the gastrointestinal tract [1, 2]. Although some patients suffer from gastrointestinal symptoms, such as vomiting and abdominal fullness and bloating after eating, the association between symptoms and objective findings is poorly established [2-4]. The prevalence of gastroparesis is well-described in symptomatic and asymptomatic patients [5]. Some studies have shown that esophageal dysmotility is common in diabetic patients, but this dysfunction does not explain all symptoms [4, 6]. Motility impairment of the gastrointestinal tract may lead to delayed

and decreased glucose uptake after a meal, and may further affect glucose metabolism [3].

Normal physiology and pathophysiology of the gastrointestinal tract are still not fully understood. Likewise, the etiology of dysmotility is still unclear. Damage to interstitial cells of Cajal, loss of neuronal nitric oxide expression, hyperglycemia, vagal or autonomic neuropathy, and myopathy have been proposed as causes [7]. Abnormalities in plasma levels of several hormones have been described secondary to gastrointestinal dysmotility [8]. Thyroid dysregulation may also affect gastrointestinal motility [9]. Furthermore, other gastrointestinal diseases besides dysmotility disorders may affect patients with diabetes.

The aim of the present study was to examine consecutive patients with diabetes mellitus, independent of symptoms and type of diabetes, to describe esophageal and gastric dysmotility in these patients. Also, potential associations with possible causes or implications such as other diabetic complications, gastrointestinal symptoms, diabetes type, and plasma biomarkers were to be identified.

Patients and methods

This study was performed according to the Helsinki Declaration and was approved by the Ethics Committee of Lund University. All subjects gave written, informed consent before participating in the study.

Abbreviations:
AN - autonomous neuropathy
BMI - body mass index
CCK - cholecystokinin
CI - confidence interval
ED - esophageal dysmotility
HbA1c - glycated hemoglobin
IBD - inflammatory bowel disease
IBS - irritable bowel syndrome
IFCC - International Federation of Clinical Chemistry
IQR - interquartile range
LES - lower esophageal sphincter
MBq - megabecquerel
NGSP - National Glycohemoglobin Standardization Program
NS - not significant
OR - odds ratio
PN - peripheral neuropathy
ROI - region of interest
Tc - technetium
^{99m}Tc - technetium-99 isotope
SD - standard deviation
SSc - Systemic sclerosis
TSH - thyroid-stimulating hormone
w/v - weight per volume percentage

Study design

At the Department of Endocrinology, Skåne University Hospital, Malmö, and at one primary health care center in Malmö, consecutive patients with diabetes mellitus at least 18 years of age, were invited to participate in the study when scheduled for routine clinical follow-up. At the time of inclusion, the patients completed a questionnaire regarding 15 symptoms related to complications of the gastrointestinal tract (loss of appetite, swallow complications, meal-related cough, early satiety, nausea, vomiting, weight loss, abdominal fullness, bloating, regurgitation, constipation, diarrhea, evacuation incontinence, symptomatic postprandial hypoglycemia, and postprandial perspiration). The questionnaire has been used previously in this category of patients [3, 4]. Types and duration of diabetes and presence of diabetic complications were noted by physicians. Diabetic complications that were examined included retinopathy (based on fundus photography), angiopathy, microalbuminuria (measured as albumin/creatinin ratio), albuminuria, peripheral neuropathy (examined by patellar and achilles tendon reflexes, vibration sense, and monofilament), autonomic neuropathy according to established clinical criteria (sexual dysfunction, profound sweating, and orthostatic blood pressure), drug treatments, concomitant diseases, and body mass index (BMI).

Glycosylated hemoglobin (HbA1c) and thyroid-stimulating hormone (TSH) were analyzed at the Department of Chemistry, Skåne University Hospital, Malmö, according to routine clinical practice. HbA1c values were collected as Mono-S, and subsequently converted to the National Glycohemoglobin Standardization Program (NGSP) standard by use of the following algorithm: 0.923 x HbA1c (Mono-S) x 1.345 = HbA1c (NGSP) [10]. Percentage HbA1c values were converted to the International Federation of Clinical Chemistry (IFCC) standard in mmol/mol according to the following equation: IFCC (mmol/mol) = (NGSP (%) - 2.152) / 0.09148 [10].

The patients were referred to esophageal manometry and gastric emptying scintigraphy. Medications influencing gastric motility were ceased prior to examination. Further examinations were performed when clinically appropriate. Exclusion criteria were severe renal failure demanding dialysis or severe cardiac disease. The patients were allowed to participate in the study only if both manometry and scintigraphy were performed. Most withdrawals were due to an inability to swal-

Table 1. Clinical characteristics of patients

Parameter	Type 1 diabetes (n = 38)	Type 2 diabetes (n = 46)	p
Gender (m/f)	12/26	30/16	0.004
Age (yr)	51.3 ± 11.7	64.7 ± 10.9	< 0.001
Diabetes duration (yr)	26.4 ± 13.2	11.4 ± 10.1	< 0.001
BMI (kg/m^2)*	26.2 ± 5.6	30.3 ± 6.0	0.005
HbA1c (mmol/mol)	66.1 ± 9.9	58.8 ± 14.8	0.011
HbA1c (%)	8.2 ± 0.9	7.5 ± 1.4	0.011
TSH (mIU/l)	1.8 ± 1.2	2.1 ± 1.3	NS
ED (n)	25 (66%)	28 (61%)	NS
Gastric dysmotility (n)	6 (16%)	5 (11%)	NS
Retinopathy (n)	19 (50%)	28 (61%)	0.004
Angiopathy (n)	13 (34%)	9 (20%)	NS
Microalbuminuria (n)	3 (8%)	7 (15%)	NS
Macroalbuminuria (n)	3 (8%)	3 (7%)	NS
AN (n)	10 (26%)	6 (13%)	NS
PN (n)	20 (53%)	7 (15%)	< 0.001

Legend: Data are mean ± SD, or number (percentage). Student's *t*-test or Fisher's exact test were used for statistical calculations. AN: autonomous neuropathy. BMI: body mass index. HbA1c: glycosylated hemoglobin. ED: esophageal dysmotility. NS: not significant. PN: peripheral neuropathy. TSH: thyroid-stimulating hormone. $p < 0.05$ was considered statistical significant. * missing values in 16 patients.

low the manometry catheter (82%). Eighty-four patients out of 122 who agreed to participate (69%) completed the study, and were finally included in the statistical calculations.

Esophageal manometry

Standardized esophageal manometry was performed with an intra-luminal solid-state transducer system (Gaeltec Ltd, Isle of Skye, Scotland). Polygraph ID converter digitized the analog signal. The software was PolyGram NET (Medtronic-Synmed, Stockholm, Sweden). All pressure values were expressed in mmHg and referred to atmospheric pressure. The manometry catheter was introduced through the nose and fluoroscopically positioned in the distal esophagus with the patient sitting in an upright position. With the catheter in place, all participants were instructed to swallow 10 ml of a barium contrast medium (60% w/v). At least 5 barium swallows were recorded. The video fluoroscopic image and the manometry registration were mixed using a video output card (Medtronic) [4, 5].

Patients who fulfilled one or more of the following 5 criteria in esophageal manometry with abnormal results were considered to have esophageal dysmotility:

1. Absence of peristaltic contraction in the esophagus (aperistalsis >0%).
2. Mean peristaltic contraction amplitude <30 or >200 mmHg in the esophagus.
3. Percentage of simultaneous, non-propulsive peristaltic waves in the esophagus >10%.
4. Speed of the peristaltic wave <3 or >6 cm/s in the distal esophagus.
5. Resting pressure in the lower esophageal sphincter (LES) <10 or >30 mm Hg.

Normal peristaltic activity was defined as propulsive contraction waves with peak amplitudes between 30-200 mmHg and a speed between 3-6 cm/sec [11].

Gastric emptying scintigraphy

A test meal was prepared by adding tin colloid labeled with 30-50 MBq of ^{99m}Tc to an egg, which was whipped in a glass cup in a hot water bath until coagulated. The egg and a slice of toasted white bread were cut into pieces smaller than 1 x 1 cm, and served with 100 ml of 37°C water. The meal was ingested within 5 min. Immediately after this, a large-field double-headed gamma camera (Philips Skylight, Philips Medical Systems, Best, The Netherlands) was placed anteriorly and posteriorly parallel to the upper abdominal wall. The radioactivity was measured continuously (1-min frames) for 70 min, starting immediately after meal ingestion.

A region of interest (ROI) representing the stomach was created, and the activity of the first frame was taken as 100%. The gradual decreasing radioactivity, measured as the number of radioactivity decays per minute (counts/min), was plotted against time. The time elapsed to reach a 50% decrease of the activity in the ROI (T_{50}) was identified as the point at which this plot crossed the 50% value. The values of the radioactivity measured were corrected for the half-life of ^{99m} Tc and for attenuation by using the geometrical mean values of the decay curves obtained from the two gamma camera heads used. T_{50} >2 standard deviation (SD) of the value for healthy control subjects (70 min) was considered abnormal, and classified as gastric dysmotility [12].

Statistical analyses

All statistical analyses were carried out by SPSS 17.0 for Windows. All variables were analyzed for normal distribution by Kolmogorov-Smirnov test. Groupwise differences were tested by using unpaired Student's *t*-test and. If normality was rejected, Mann-Whitney *U*-test or Fisher's exact test were used. Correlations were calculated by Spearman's or Pearson's test. Multiple logistic regression analysis was performed to determine associations with esophageal dysmotility (dependent variable). Independent variables were age (years), gender (female/male), duration of diabetes (years), type of diabetes (1 or 2), HbA1c (mmol/mol), TSH (mIU/l), and existence of gastroparesis, angiopathy, peripheral neuropathy, autonom neuropathy, microalbuminuria, macroalbuminuria, retinopathy, labeled as yes or no. $p < 0.05$ was considered statistically significant. Values are expressed as median (interquartile range (IQR)) or mean ± SD.

Table 2. Prevalence of symptoms in diabetic patients

Symptom	Prevalence (n, %)
Loss of appetite	8 (11%)
Difficulties of swallowing	14 (19%)
Meal-related cough	10 (14%)
Early satiety	17 (23%)
Nausea	19 (26%)
Vomiting	2 (2%)
Weight loss	5 (6%)
Abdominal fullness	21 (29%)
Bloating	36 (49%)
Regurgitation	25 (34%)
Constipation	14 (19%)
Diarrhea	12 (16%)
Motion incontinence	3 (4%)
Symptomatic postprandial hypoglycemia	12 (16%)
Postprandial perspiration	8 (11%)

Results

Patient characteristics

Of the 84 enrolled patients (42 female) with diabetes, 38 patients (45%) had type 1 diabetes and 46 patients (55%) had type 2 diabetes. All patients with type 1 diabetes and 17 patients with type 2 diabetes were insulin-treated (n = 55). There were significant differences in clinical characteristics of age, gender, duration of disease, BMI, and HbA1c levels between patients with type 1 and 2 diabetes (Table 1). The only complication which differed between types of diabetes was retinopathy, which was more frequent in type 2 diabetes (Table 1).

Prevalence of esophageal or gastric dysmotility did not differ between type 1 and type 2 diabetes (Table 1). In esophageal motility variables, there was a higher mean amplitude of the peristaltic wave in patients with type 2 than in those with type 1 diabetes (70.0 (41.0-93.5) mmHg and 49.5 (23.0-69.2) mmHg, respectively, $p = 0.003$).

Besides diabetes, 3 patients had a history of hypothyroidism, one from thyreotoxicosis and one from atoxic adenoma. Sporadic cases of primary Sjögren's syndrome, celiac disease, Addison's disease, vitiligo, and pernicious anemia were observed.

Gastrointestinal symptoms and their relationship to esophageal and gastric dysmotility

The majority of patients (n = 73) had gastrointestinal symptoms, although they entered the study independently of symptoms. Abdominal bloating was the most prevalent symptom followed by regurgitation and abdominal fullness (Table 2). The only symptom that tended to correlate with gastroparesis was experience with postprandial hypoglycemia ($p = 0.054$). No symptom correlated with esophageal dysmotility (data not shown).

Patients were divided into cohorts according to presence or absence of different symptoms. It was apparent that patients with evacuation incontinence had an increased percentage of simultaneous contractions above the reference value (15.0 (0.0-30.0)%, $p = 0.03$). Patients with a history of excessive postprandial perspiration had a low LES pressure (7.5 (1.2-14.8) mmHg, $p = 0.013$). Among patients suffering from diarrhea (16%), further examination with colonoscopy and extended laboratory analyses could not diagnose either inflammatory bowel disease (IBD), microscopic colitis, or any other organic disease in these patients. Thus, diarrhea was classified as a secondary dysmotility complication. Of the 84 patients, 28 patients (33%) had normal motility and only 8 patients (10%) had abnormal motility in both esophagus and stomach. There was no association between esophageal and gastric dysmotility (Tables 3 and 4).

Table 3. Characteristics of patients with normal versus abnormal esophageal motility

Parameter	Normal esophageal function (n = 31)	Abnormal esophageal function (n = 53)	p
Type of diabetes (1/2)	13/18	25/28	NS
Gender (m/f)	13/18	29/24	NS
GE T_{50} (min)	41.0 (27.0-55.0)	45.0 (30.0-61.0)	NS
Age (yr)	58.0 ± 12.5	59.1 ± 13.4	NS
Diabetes duration (yr)	14.3 ± 13.1	20.7 ± 13.7	0.043
BMI (kg/m^2)*	27.5 ± 5.9	28.3 ± 6.2	NS
HbA1c (mmol/mol)	60.1 ± 13.6	63.3 ± 13.0	NS
HbA1c (%)	7.6 ± 1.3	8.0 ± 1.2	NS
TSH (mIU/l)	1.9 ± 1.2	2.0 ± 1.3	NS
Gastric dysmotility (n)	3 (10%)	8 (15%)	NS

Legend: Data are mean ± SD, or number (percentage), or median (interquartile range). Student's *t*-test or Fisher's exact test were used for statistical calculations. GE: gastric emptying. BMI: body mass index. HbA1c: glycosylated hemoglobin. TSH: thyroid-stimulating hormone. NS: not significant. $p < 0.05$ was considered statistical significant. * missing values in 16 patients.

Esophageal dysmotility

Fifty-three of the 84 patients (63%) had abnormal esophageal dysmotility, and differed from those with normal motility by a longer duration of diabetes, 20.7 ± 13.7 years compared with 14.3 ± 13.1 years, $p = 0.043$ (Table 3). The duration of diabetes correlated negatively with the mean amplitude ($r = -0.435$, $p < 0.001$), positively with the percentages of aperistalsis ($r = 0.232$, $p = 0.036$), and negatively with LES pressure ($r = -0.217$, $p = 0.051$). There was a non-significant correlation between BMI and percentages of aperistalsis ($r = -0.226$, $p = 0.063$) and mean amplitude ($r = 0.224$, $p = 0.066$), and a weak correlation between BMI and speed of peristaltic wave ($r = -0.285$, $p = 0.027$). There was a strong association between esophageal dysmotility and retinopathy determined by Fisher's exact test ($p < 0.001$). In contrast, other diabetes complications showed no associations (data not shown). Among the variables tested for an independent association with esophageal dysmotility, the presence of retinopathy was the only one which showed an association (OR = 10.15, 95% CI = 2.16-47.62), independent of disease duration and other risk factors ($p = 0.003$).

Gastric dysmotility

Only 11 of the 84 patients (13%) had a delayed gastric emptying rate, but this was not associated with esophageal dysmotility (Tables 3 and 4). There were no differences in patient characteristics between delayed gastric emptying and normal gastric emptying (Table 4). The gastric emptying rate correlated negatively with age ($r = -0.309$, $p = 0.004$). No measured variable was associated with gastric dysmotility (data not shown).

Table 4. Characteristics of patients with normal versus abnormal gastric emptying

Parameter	Normal gastric emptying (n = 73)	Abnormal gastric emptying (n = 11)	p
Type of diabetes (1/2)	32/41	6/5	NS
Gender (m/f)	38/35	4/7	NS
GE T_{50} (min)	40 (28-52)	104 (90-325)	< 0.001
Age (yr)	59.6 ± 12.6	51.9 ± 14.3	0.067
Diabetes duration (yr)	17.9 ± 14.3	20.6 ± 10.1	NS
BMI (kg/m^2)*	28.5 ± 6.2	25.6 ± 4.7	NS
HbA1c (mmol/mol)	62.0 ± 14.0	62.7 ± 6.8	NS
HbA1c (%)	7.8 ± 1.3	7.9 ± 0.6	NS
TSH (mIU/l)	2.0 ± 1.3	1.7 ± 1.1	NS
Esophageal functions			
Dysmotility (n)	45 (10%)	8 (73%)	NS
Aperistaltic swallowing (%)	0.0 (0.0-10.0)	0.0 (0.0-10.0)	NS
Mean amplitude contractions (mmHg)	55.0 (39.0-85.5)	75.0 (45.0-88.0)	NS
Simultaneous contractions (%)	0.0 (0.0-0.0)	0.0 (0.0-20.0)	NS
Mean peristaltic speed (cm/s)	3.5 (3.0-4.5)	3.4 (3.1-5.6)	NS
LES pressure (mmHg)	17.0 (11.0-20.5)	16.0 (11.0-22.0)	NS

Legend: Data are mean ± SD, or number (percentage), or median (interquartile range). Student's *t*-test or Fisher's exact test were used for statistical calculations. GE: gastric emptying. BMI: body mass index. HbA1c: glycosylated hemoglobin. TSH: thyroid-stimulating hormone. LES: lower esophageal pressure. NS: not significant. $p < 0.05$ was considered statistical significant. * missing values in 16 patients.

Discussion

The main finding of the present study was an unexpected high prevalence of esophageal dysmotility in an unselected population of patients with

diabetes mellitus, and its strong association to retinopathy. Furthermore, the majority of patients suffered from gastrointestinal symptoms, which were not associated with objectively measured dysmotility.

Previous diabetes research has focused on gastroparesis, whilst esophageal dysmotility has not been regarded as a major problem, although it has been described in several studies [3, 4, 6, 7]. In the present study, we found that esophageal dysmotility was far more common than gastroparesis (63% vs. 13%). In agreement with this research, several studies have described an association between retinopathy and gastrointestinal dysmotility [13]. Microangiopathy is the common etiology behind both retinopathy and renal failure in diabetes. Hypothetically, microangiopathy may be the etiology also in gastrointestinal dysfunction.

Systemic sclerosis (SSc) is a collagenous disease characterized by severe gastrointestinal involvement [14]. The esophagus is the most frequently affected section of the gastrointestinal tract in both SSc and diabetes. The pathophysiology of this entity is autoimmunity with vasculitis and widespread damage to small blood vessels, rendering destruction of the smooth muscle layer with fibrosis in the bowel wall [15]. To examine the gastrointestinal tract for microangiopathy, a full-thickness biopsy is needed, which requires laparoscopic surgery with anesthesia. However, ethical considerations do not justify this procedure. The current histopathological findings do not rule out microangiopathy as a possible pathogenesis [7, 16].

An earlier study described how esophageal dysmotility influenced glucose homeostasis, with a delayed increase of postprandial plasma glucose and absence of observable symptoms [3], and elevated basal plasma levels of cholecystokinin (CCK) [8]. These observations may depend on concomitant dysmotility in the small intestine, causing slower bolus passage with a delayed absorption of glucose and increased stimulation of CCK secretion [17]. There appears to be similar motility patterns in the esophagus and small and large intestine, depending on neural regulation. In contrast, the stomach is regulated differently, depending on smooth muscle regulation [18]. A concomitant prevalence of esophageal and intestinal dysmotility has been described in several other entities, e.g. SSc [14, 19], Hirschsprung's disease [20] and celiac disease [21]. Distinct esophageal and stomach physiologies, accompanied by different pathophysiology in esophageal dysmotility and gastroparesis, may explain the lack of association between the two complications. It may also be the reason why patients with gastroparesis have normal CCK levels in plasma and postprandial increase of plasma glucose in due time [3, 4, 8].

Esophageal dysmotility may be an underestimated factor in patients with dysregulated diabetes. This aspect should be taken into account when considering insulin administration in these patients. Furthermore, our observation of pathological values in esophagus manometry in patients with a history of excess postprandial perspiration (lower LES pressure) and evacuation incontinence (simultaneous contractions) suggests that esophageal dysmotility affects patients' health and quality of life. Acid reflux into the esophagus may provoke autonomous reflexes through vagal nerves causing perspiration. Previously, we described that patients with severe gastrointestinal dysmotility suffer from autonomic neuropathy with effects on body temperature and perspiration [22].

Contrary to our findings, an earlier study in diabetic patients with gastrointestinal symptoms showed that the presence of delayed gastric emptying was slightly more common than esophageal dysmotility [4]. This difference may be explained by the nature of patient recruitment, namely the inclusion of consecutive patients independent of symptoms, and a higher incidence of type 2 diabetes in our study. Previous studies have shown that gastroparesis is present in approximately 30-50% of diabetic patients [23]. As hyperglycemia prolongs gastric emptying, the lower prevalence of this symptom in the present study may reflect a better metabolic control of the patients [23]. The HbA1c levels in our patients indicated a good metabolic control.

In agreement with our work, other studies have found a high prevalence of gastrointestinal symptoms in patients with diabetes mellitus, also with poor correlations with objective findings [2, 24]. Many of the patients experienced abdominal fullness and bloating, symptoms that were earlier ascribed to gastroparesis [3, 4], although these patients had normal gastric emptying rates in the present study. These symptoms are very common in women with irritable bowel syndrome (IBS) [25]. Therefore, a thorough examination of gastric emptying is necessary before the diagnosis of gastroparesis can be established.

Patients with an autoimmune disease often have other autoimmune diseases, such as thyroid diseases. In accordance, 3 patients (4%) suffered from hypothyroidism. Hypothyroidism occurs in 0.1-2% of the general population, and subclinical hypothyroidism in 15% [26]. Gastrointestinal mo-

tility and serum thyroid hormone levels seem to be closely related [27]. Both patients with hypo- and hyperfunction of the thyroid gland suffer from gastrointestinal complications [9, 28]. In the present study, only a minority of patients suffered from thyroid dysfunction, and there were no correlations of TSH plasma values with measurements of the examinations.

Microscopic colitis is a common cause of chronic diarrhea among middle-aged women. In our study, none of the patients suffered from this disease, suggesting that this disorder was not overrepresented in patients with diabetes. Therefore, it cannot explain the gastrointestinal symptoms. This is in agreement with an earlier study, which showed that increased colon subepithelial collagen layer thickness in patients with diabetes did not relate to collagenous colitis [29].

Limitations of the study included the small sample size and the fact that examinations were only performed once. We know that gastrointestinal motility varies from day to day, and this may cause some uncertainty in the analyses [30]. Thus, the study needs to be repeated. The possibility of microangiopathy in the esophagus should be studied more intensively.

In conclusion, esophageal dysmotility is more common than gastroparesis in both type 1 and type 2 diabetes, and is closely related to retinopathy. The pathology behind this and the effect on glucose homeostasis of this dysmotility needs to be further clarified. This study points to the possibility that esophageal dysmotility is an underestimated factor in patients with dysregulated diabetes.

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