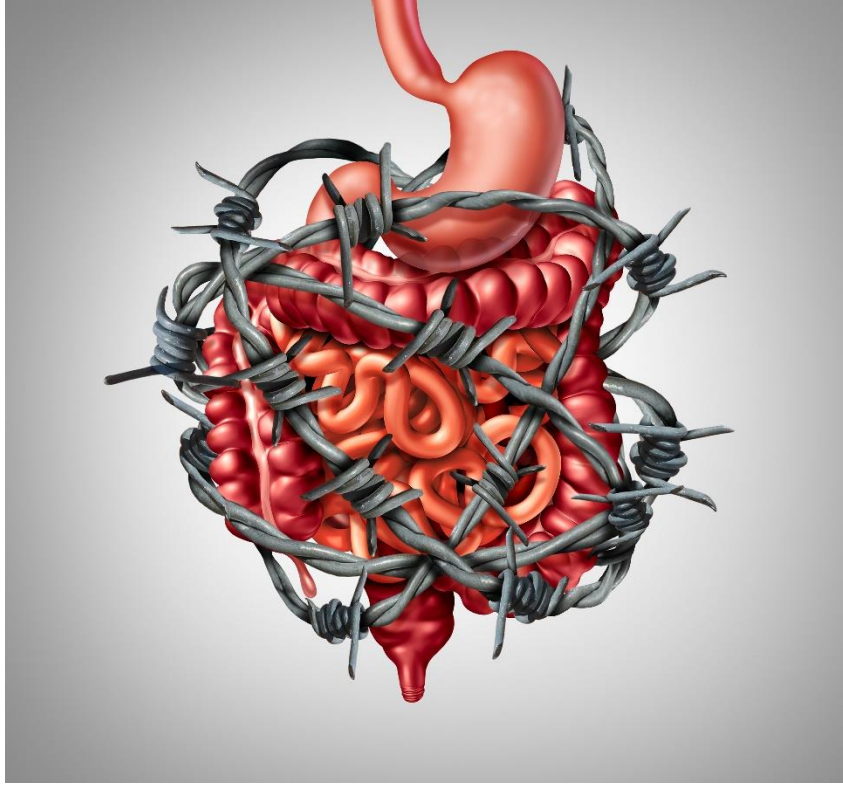
INSELSPITAL
Universitätsklinik für
Viszerale Chirurgie und Medizin

Diagnosis and Management of Gastroparesis



Bauchzentrum BERN

Bible Class 21.11.2018 / I. Linas

Case 1: 20 year old male

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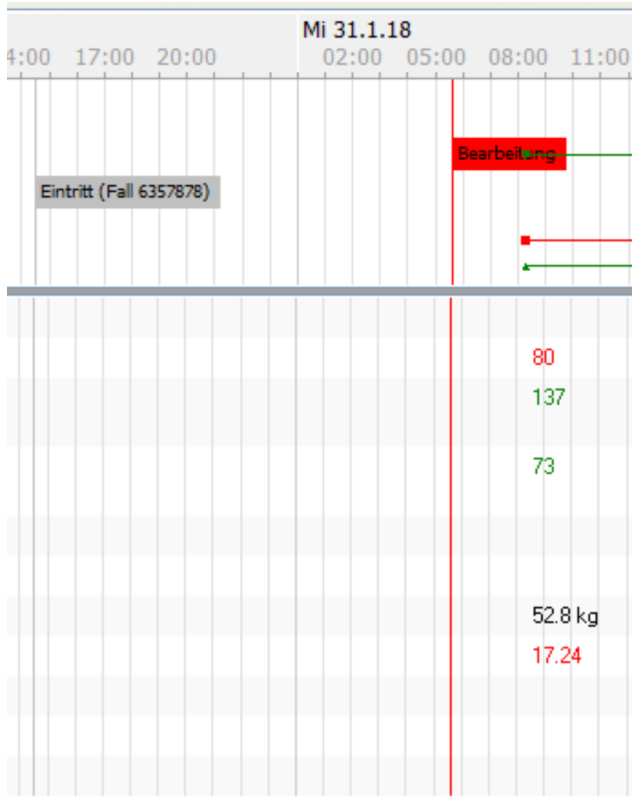
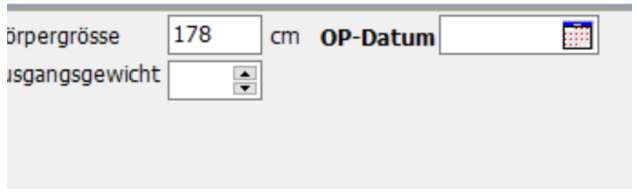
- Presents as an outpatient after a hospital stay in the internal medicine ward for unclear transient periumbilical pain
- Intermittent episodes of periumbilical pain (1x/2M) and
- Recurrent progressive postprandial fullness and vomiting for 8M with weight loss (8-10 Kg).
- Fatigue, cannot play football any more like before
- Otherwise healthy
- Normal western diet, no alcohol, no smoking
- Family history: Parents emigrated from Kosovo, otherwise unremarkable
- Current medications: Paracetamol, Metamizol as needed

Case 1: 20 year old male





Case 1: 20 year old male

Name	Einheit	Referenz	Wert
▼ **Blut: Elektrolyte**			
Natrium	mmol/L	136 - 145	141
Kalium	mmol/L	3.5 - 4.5	3.9
Chlorid	mmol/L	98 - 107	103
Calcium gesamt	mmol/L	2.15 - 2.50	2.29
Calcium korrigiert	mmol/L		2.24
Anorg. Phosphat	mmol/L	0.81 - 1.45	1.09
Magnesium	mmol/L	0.70 - 0.91	0.85
▼ **Blut: Metabolite**			
Glucose	mmol/L	4.11 - 5.89	4.99
Creatinin (P)	µmol/L	59 - 104	76
eGFR nach CKD-EPI	mL/min	> 59	> 90
Harnstoff	mmol/L	3.2 - 7.3	3.2
Protein total	g/L	64 - 83	78
Albumin	g/L	35 - 52	42
C-reaktives Protein	mg/L	< 5	< 3
Bilirubin gesamt	µmol/L	< 17	4
▼ **Blut: Enzyme**			
ASAT	U/L	< 50	30
ALAT	U/L	< 50	51 +
G-Glutamyltransferase	U/L	< 60	43
Lactat-Dehydrogenase	U/L	< 480	382
Pankreas-Amylase	U/L	13 - 53	39
▼ **Blut: Schilddrüsenparameter**			
TSH	mU/L	0.36 - 3.83	3.26
FT4	pmol/L	12.2 - 23.5	18.5
▼ **Blut: Anämieparameter**			
Vitamin B12	pmol/L	keine Referenzwert	437
Ferritin ECLIA	µg/L	20 - 250	121
▼ **Blut: Diabetesparameter**			
HbA1c (DCCT/NGSP)	%	4.8-5.9	5.3
HbA1c (IFCC)	mmol/mol	22 - 42	34
▼ **Blut: Erythrocytenparameter**			
Erythrozyten-Folsäure	nmol/L	1008 - 2426	798 -
▼ **Hämatogramm**			
Entnahmeart			venös
Leukozyten	G/L	3.00 - 10.5	8.67
Hämoglobin	g/L	135 - 168	144
Hämatokrit	L/L	0.40 - 0.50	0.40
Erythrozyten	T/L	4.20 - 5.70	4.80
MCV	fL	80 - 98	82
MCH	pg	27 - 33	30
MCHC	g/L	320 - 360	365 +
RDW	%	11.5 - 14.5	11.9
Thrombozyten	G/L	150 - 450	229
MPV	fL	6.7 - 11.0	10.7
Normoblasten maschinell	/100 Leuk.	0	0.00
▼ **Differenzierung maschinell**			
Neutrophile	G/L	1.60 - 7.40	5.27
Eosinophile	G/L	0.02 - 0.40	0.08
Basophile	G/L	0.00 - 0.15	0.10
Monozyten	G/L	0.20 - 0.93	0.71

Case 1: 20 year old male

- 21.08.2017 Sonografie Abdomen: keine akute Appendizitis, keine anderen Pathologien
  - 09.11.2017 Oesophago-Gastro-Duodenoskopie: Normalbefund im oberen Gastrointestinaltrakt.
  - 13.11.2017 Histopathologie Duodenal- und Magenschleimhaut: keine histopathologischen Veränderungen. Keine chronische oder aktive Entzündung.
  - 09.11.2017 Helicobacter pylori negativ.
  - 24.11.2017 Zöliakieabklärung: Gliadin(DP)-Antikörper IgG und IgA negativ, Antikörper gegen Transglutaminase IgA negativ.
  - 21. und 23.01.2018 Sonografie Abdomen: keine intraabdominellen Pathologien
  - 24.01.2018 Laboruntersuchung und Urinstatus: bland
  - 24.01.2018 CT Abdomen: keine relevanten Pathologien
  - 25.01.2018 Serologie: Hepatitis B und C Virus HIV negativ
  - 26.01.2018 Stuhlanalyse: Nukleinsäuresequenz für allgemeine Enteritis Erreger negativ, Mikroskopie ohne mikroskopisch nachgewiesenen Darmparasiten
  - 26.01.2018 Urinuntersuchung auf Porphyrie: keine Hinweise auf akute Porphyrie
  - 26.01.2018 Sonografie Abdomen: Keine Rektusdiastase. Keine Umbilikalhernie.
  - 29.01.2018 Koloskopie: kein Korrelat für die Beschwerden des Patienten. Biopsate, Ileum und Kolonschleimhaut ohne histopathologische Veränderungen.
- 30.01.2018 Toxikologisches Screening Urin: unauffällig

Does the patient have a gastroparesis? Why/Why not?

Definition of Gastroparesis

The diagnosis of gastroparesis is based on the combination of

- symptoms of gastroparesis,
- absence of gastric outlet obstruction or ulceration, and
- delay in gastric emptying.

Symptoms of gastroparesis?

Symptoms of gastroparesis?

- **early satiety,**
- **postprandial fullness,**
- **nausea,**
- **vomiting**,
- *bloating,*
- *upper abdominal pain*

Do symptoms correlate with gastric emptying?

- **early satiety,**
- **postprandial fullness,**
- **nausea,**
- **vomiting**,
- *bloating,*
- *upper abdominal pain*

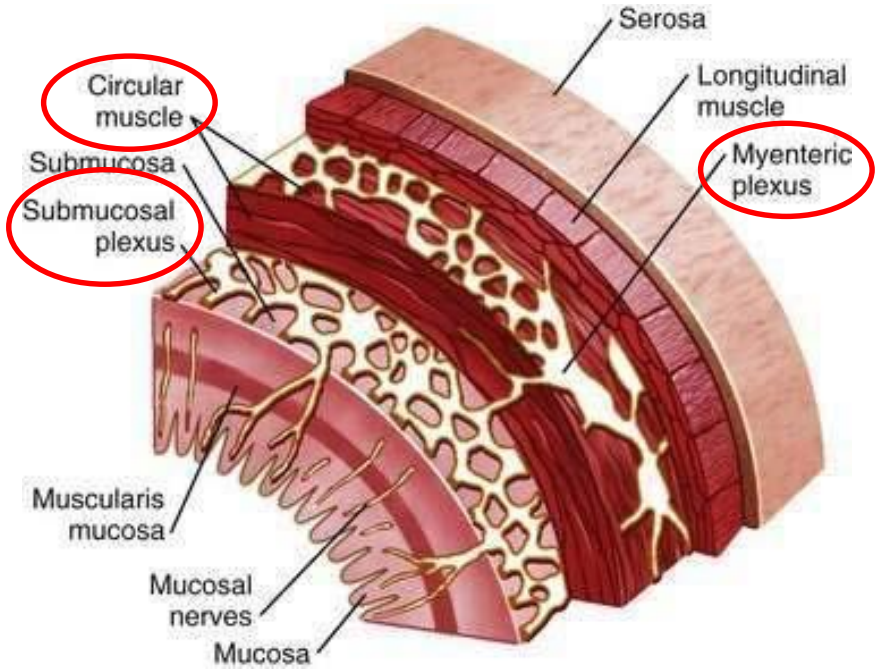
Case 1: 20 year old male

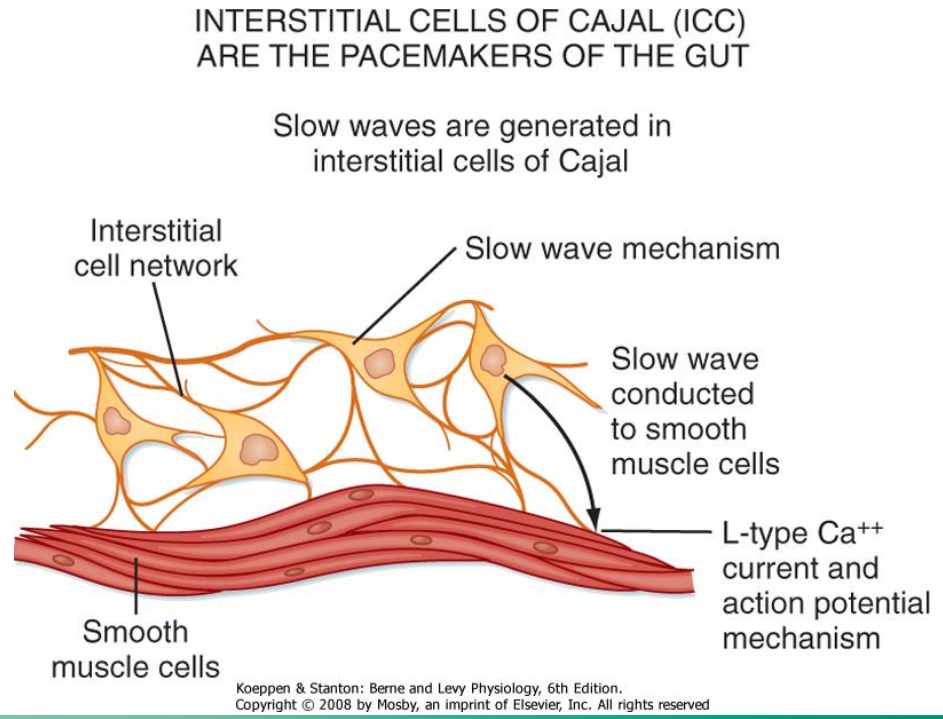
The diagnosis of gastroparesis is based on the combination of

- **symptoms of gastroparesis**
- **absence of gastric outlet obstruction or ulceration**
- delay in gastric emptying.

Normal gastrointestinal motor function

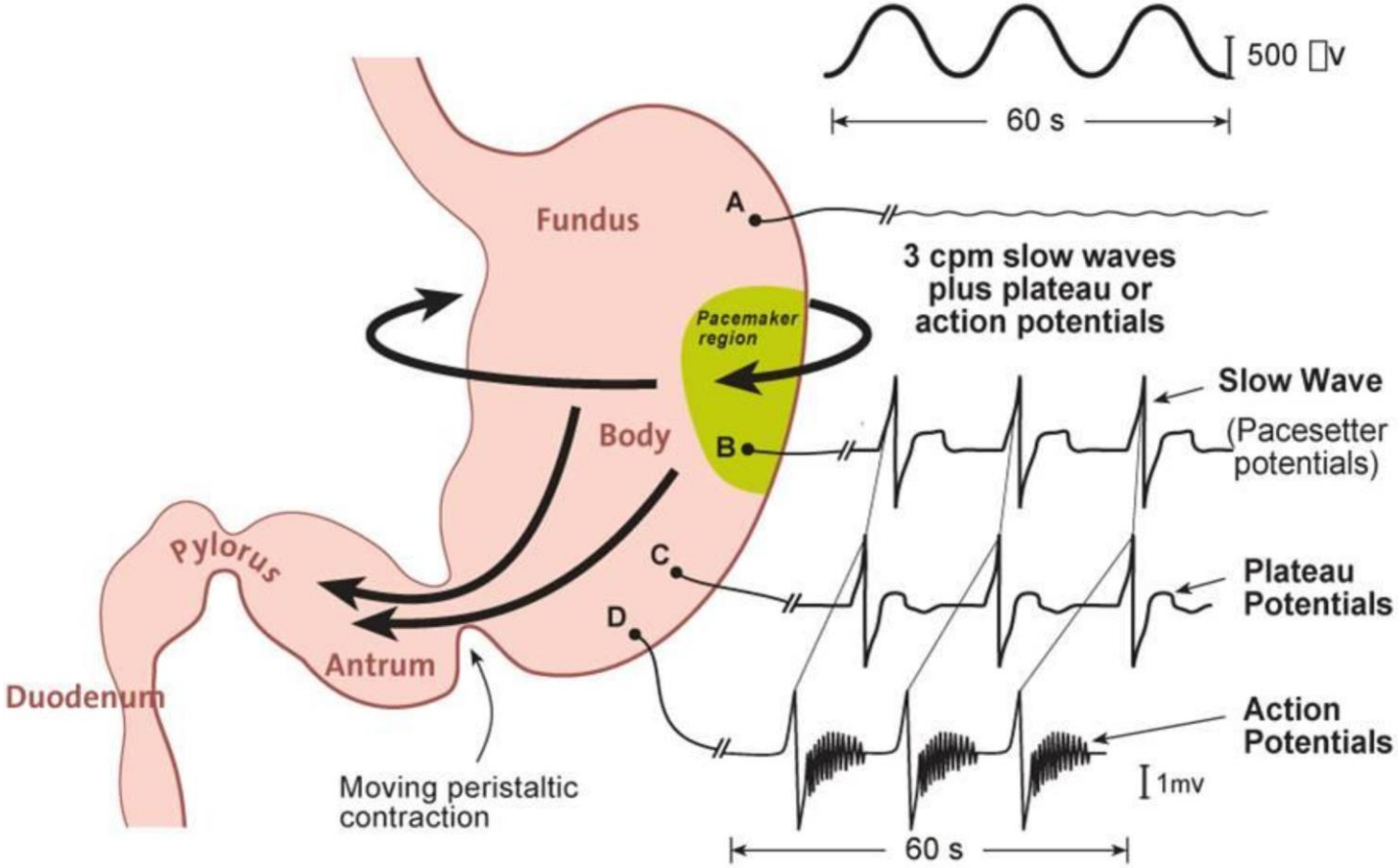
- Modulated through vagal (parasympathetic) and sympathetic stimuli, locally released transmitters and luminal input.
- Initiated by pacemaker cells (interstitial cells of Cajal)
- Spread to smooth muscle cells through the intrinsic (enteric) nervous system, which also serves as a communication network





Normal gastrointestinal motor function

- Proximal stomach: changes in tone in response to eating,
- Distal stomach: max 3cpm phasic contractions that propagate to the pylorus



Do we need to measure gastric emptying?

Do we need to measure gastric emptying?

Of course!

- accelerated gastric emptying and functional dyspepsia can also present similarly
- Documentation of delayed gastric emptying is necessary before selecting therapy with prokinetics agents or GES.

*Tack J , Bisschops R , Sarnelli G . Pathophysiology and treatment of functional dyspepsia . Gastroenterology 2004 ; 127 : 1239 – 55 .

*Bredenoord AJ , Chial HJ , Camilleri M et al. Gastric accommodation and emptying in evaluation of patients with upper gastrointestinal symptoms . Clin Gastroenterol Hepatol 2003 ; 1 : 264 – 72 .

No! Not at this stage!

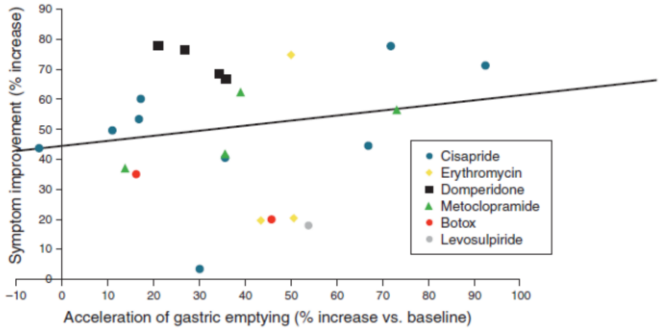
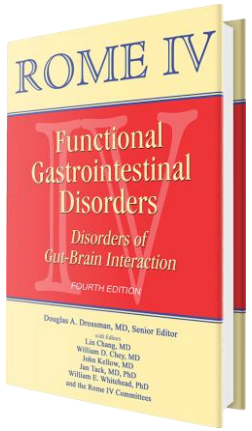
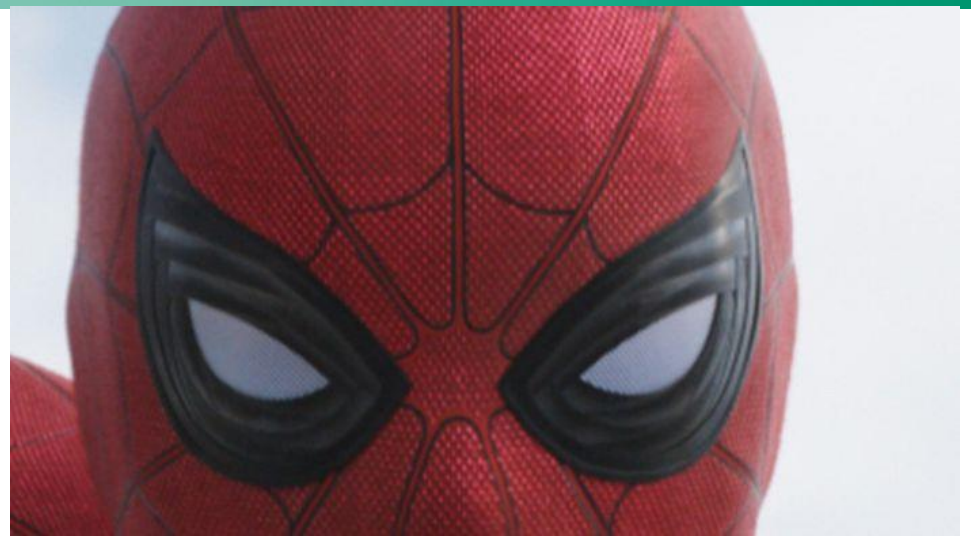


Figure 1. The relation between acceleration of gastric emptying and symptom improvement in gastroparesis patients after treatment with metoclopramide, domperidone, cisapride, erythromycin, botulinum toxin A (botox), and levosulpiride (11,16,22–26,13,35,43,46–54). A meta-regression analysis to evaluate the overall correlation between symptom improvement and GE resulted in a nonsignificant correlation (P=0.4).

Janssen P, Tack J et al. Am J Gastroenterol. 2013 Sep;108(9):1382-91



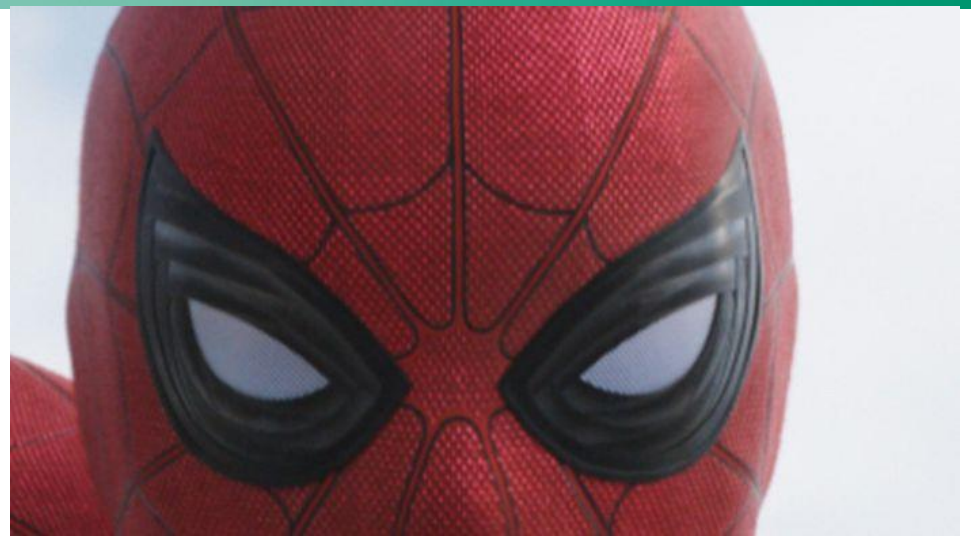
Let's take a closer look



Tack J , Bisschops R , Sarnelli G . Pathophysiology and treatment of functional dyspepsia . Gastroenterology 2004 ; 127 : 1239 – 55 .

Delayed gastric emptying is traditionally considered a major pathophysiologic mechanism underlying symptoms in functional dyspepsia and idiopathic gastroparesis.[7,11,20–29] Several studies have investigated the relationship between delayed gastric emptying and symptom pattern and severity. Depending on the study, the percentage

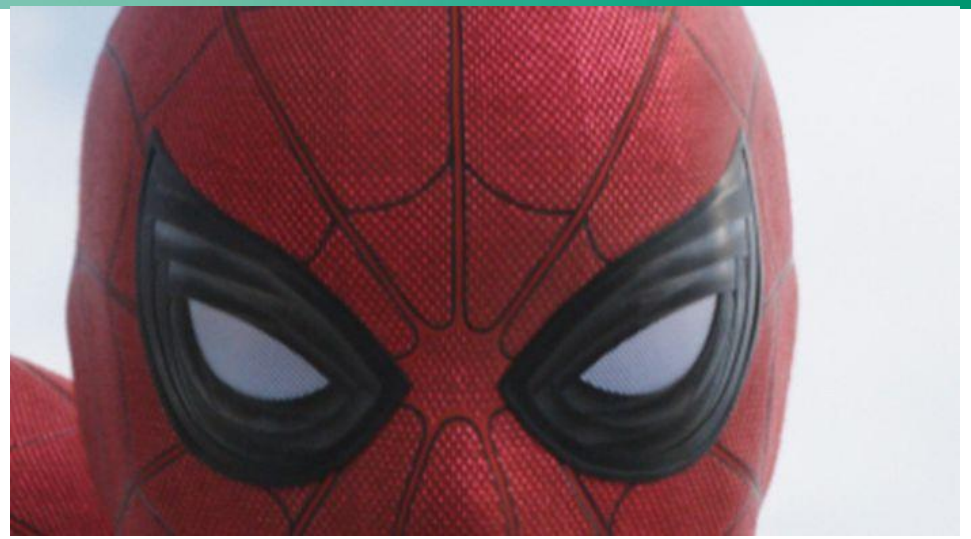
Let's take a closer look



Tack J , Bisschops R , Sarnelli G . Pathophysiology and treatment of functional dyspepsia . Gastroenterology 2004 ; 127 : 1239 – 55 .

Most studies failed to find a convincing relationship between delayed gastric emptying and symptom pattern.[20–22] More recently, 3 large-scale single-center studies showed that patients with delayed gastric emptying for solids are more likely to report postprandial fullness, nausea, and vomiting,[7,11,28] although a large multicenter study failed to find any association[29] (Table 2). Almost all studies focused on solid emptying rate only. A recent large-scale study suggested an association between delayed emptying for liquids and symptoms of postprandial fullness.[11]

Let’s take a closer look



Tack J , Bisschops R , Sarnelli G . Pathophysiology and treatment of functional dyspepsia . Gastroenterology 2004 ; 127 : 1239 – 55 .

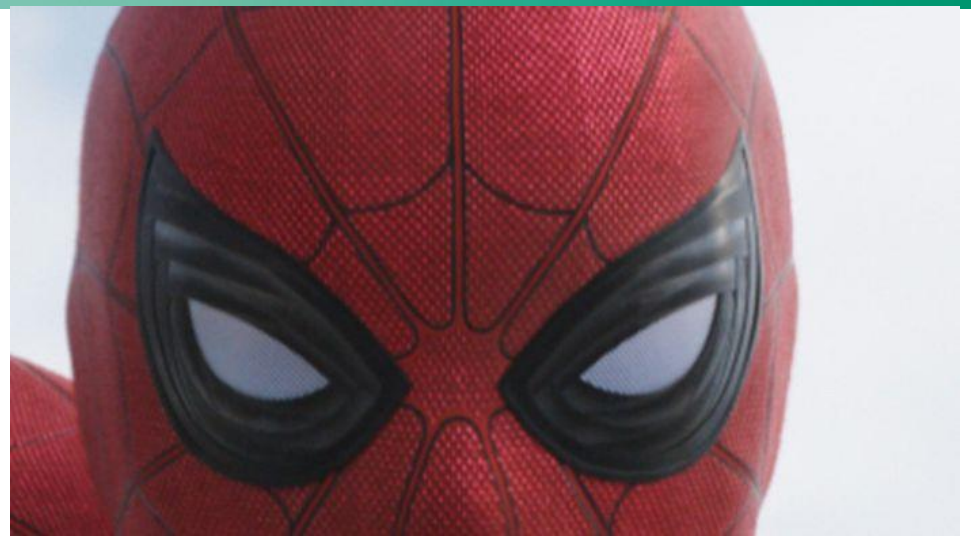
Furthermore, induction of delayed gastric emptying in healthy subjects by pharmacologic or dietary interventions is not associated with the occurrence of dyspeptic symptoms.[87] These observations question the relevance of delayed emptying as a mechanism underlying dyspeptic symptoms.

Let's take a closer look

Bredenoord AJ , Chial HJ , Camilleri M et al. Gastric accommodation and emptying in evaluation of patients with upper gastrointestinal symptoms . Clin Gastroenterol Hepatol 2003 ; 1 : 264 – 72

- *Retrospective study on 214 patients that underwent SPECT to assess gastric accommodation and 4h scintigraphy*

No significant differences in the symptoms reported by patients with normal, accelerated, or delayed gastric emptying (Figure 4) were noted. Although the frequency of vomiting was 20% higher in the diabetics with delayed gastric emptying, this difference was not statistically significant (Figure 4).



Our data in 151 patients with functional dyspepsia (i.e., abnormal gastric accommodation in 46.7%) confirmed 3 smaller previous studies documenting that gastric accommodation was impaired in approximately 45% of patients evaluated using barostat[3,12] or SPECT imaging.[4] SPECT assisted the identification of a motor abnormality potentially contributing to symptoms in 26% of the functional dyspepsia patients who had normal gastric emptying. Thus, our data suggested that SPECT may provide additional insight into the pathophysiology of symptoms in this patient population. If more specific therapies are identified to correct the variety of pathophysiologic disturbances contributing to dyspepsia, these data suggest that the tests would help identify patients for selective and potentially more effective therapy.

Methods of measuring gastric emptying?

Methods of measuring gastric emptying?

- **Solid meal 4-hour gastric emptying scintigraphy**
- Wireless motility capsule
- C-13 breath testing

- Medications that affect gastric emptying should be stopped at least 48 h.
- Hyperglycemia should be corrected before the test.

What about our method?

Gastric emptying T 1 / 2

Acceptable if

- imaging has been performed for 4 h or
- at least to 50 % emptying

*extrapolation to measure t 1 / 2 may be erroneous

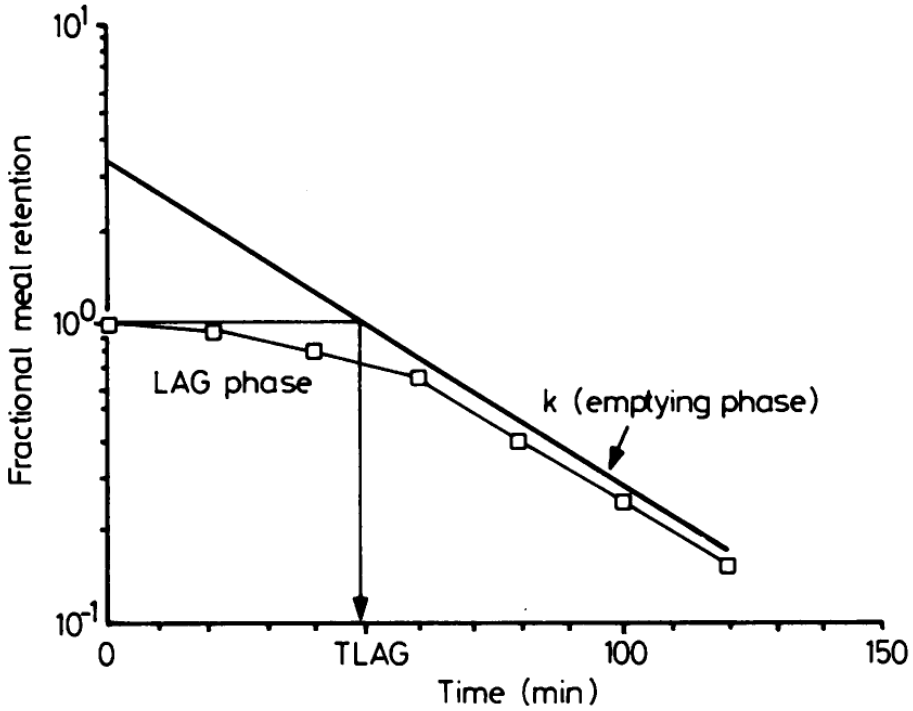


Fig. 1 *Fit of the function $y(t) = 1 - (1 - e^{-kt})^{\beta}$ to a typical solid emptying curve. Graph illustrates the two distinct portions of solid emptying, namely, the lag phase, as indicated by TLAG, and the emptying phase, which is characterised by the emptying rate, k.*

Siegel JA et al. Biphasic nature of gastric emptying . Gut 1988 ; 29 : 85 – 9

Case 1: 20 year old male

- Gastric emptying study

Magenentleerungsmessung fest vom 14.12.2017

Klinische Angaben

1. Rezidivierende Emesis unklarer Genese
   - Gastroskopie 11/2017: makroskopisch und histologisch unauffälliger Befund

Fragestellung

Gastroparese?

Untersucher: PD Dr. med. D. Pohl, Oberarzt m.e.V. (nicht anwesend)
L. Schnurre, Assistenzärztin (nicht anwesend)

Pflegefachpersonen: D. Jovanovic, MTA

Diagnose

1. Deutlich verzögerte Magenentleerung (fest)

Beurteilung und Procedere

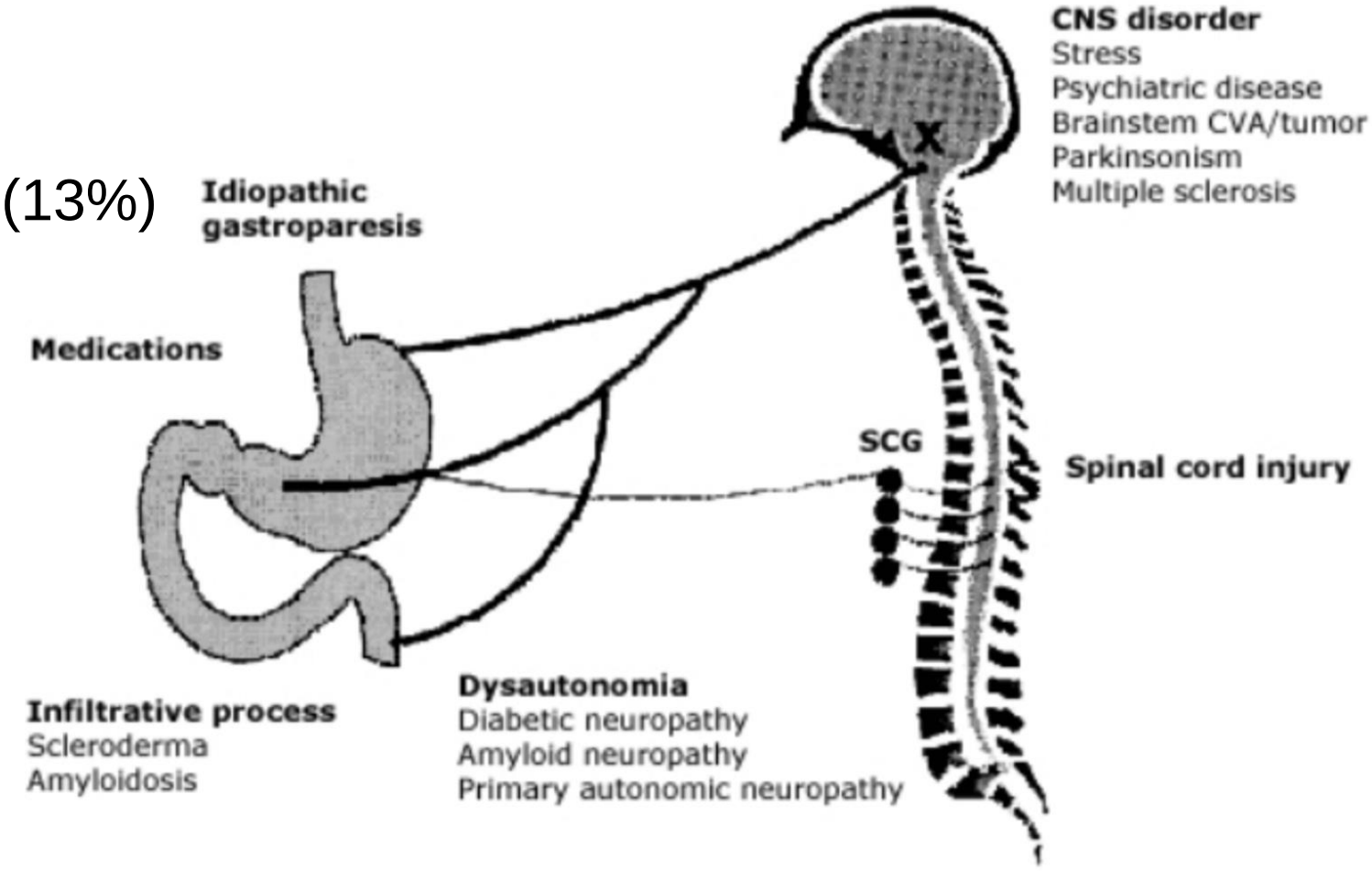
Die gemessene Magenentleerung ist mit einer Halbwertszeit von 212 Minuten deutlich verzögert, womit wir den Verdacht auf eine Gastroparese bestätigen können.

Causes of secondary gastroparesis?

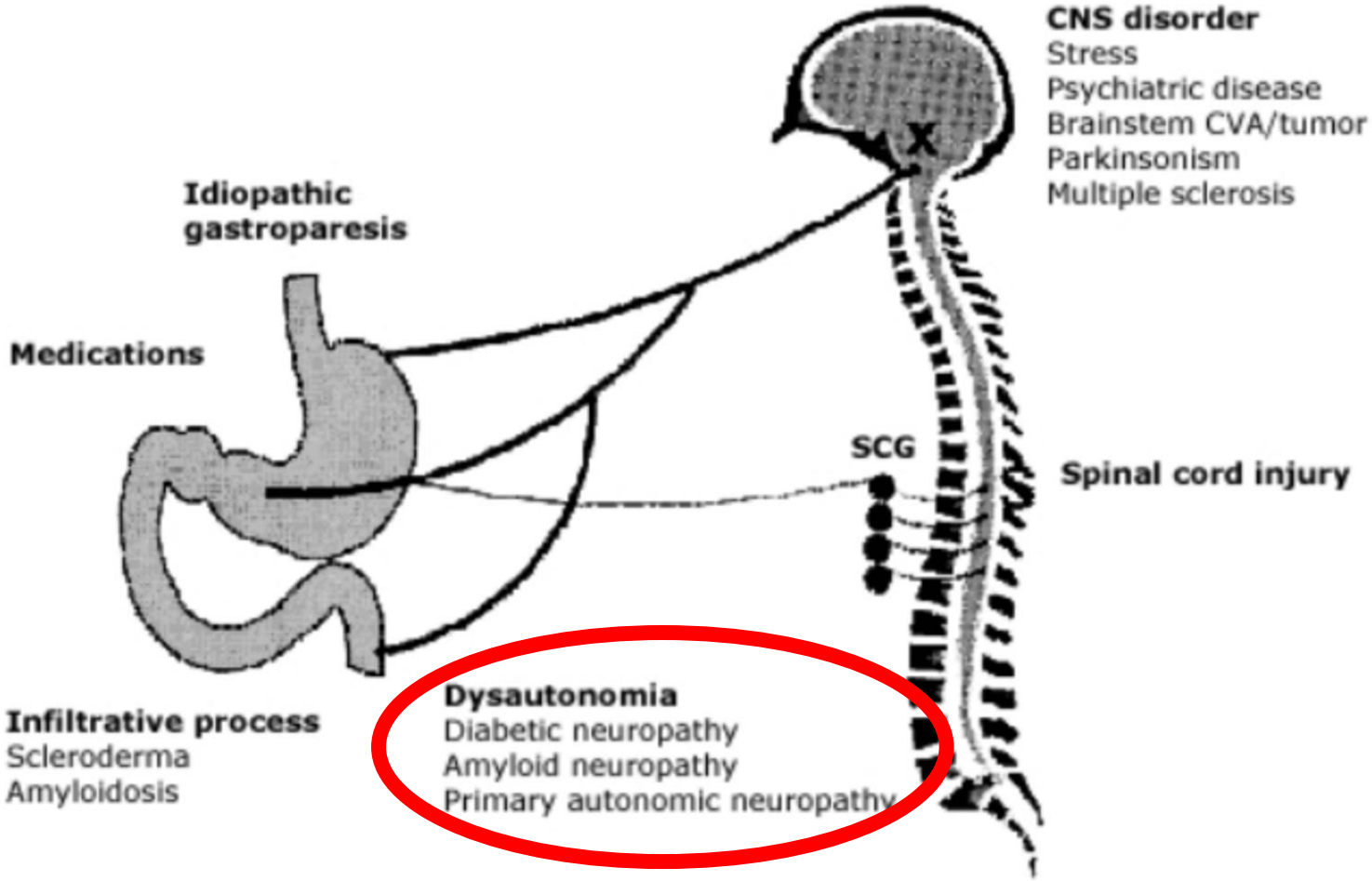
Causes of secondary gastroparesis

- Diabetes mellitus (30%)
- thyroid dysfunction
- neurological disease
- prior gastric or bariatric surgery (13%)
- autoimmune disorders

➢ **36% idiopathic**

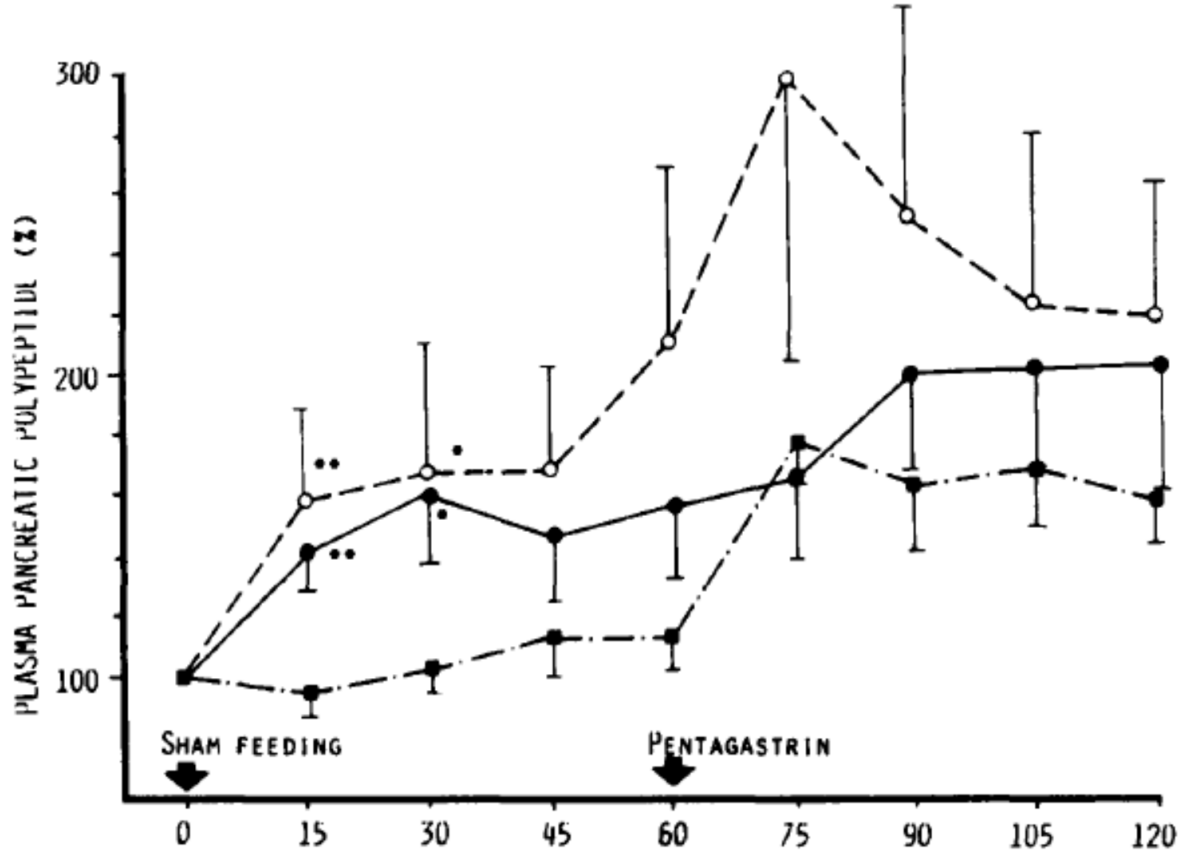


How to diagnose autonomic dysfunction?



Plasma pancreatic polypeptide response to sham feeding

- **Controls and diabetic subjects without AN**: significant mean 60% increase
- **AN:** no significant hPP response occurred

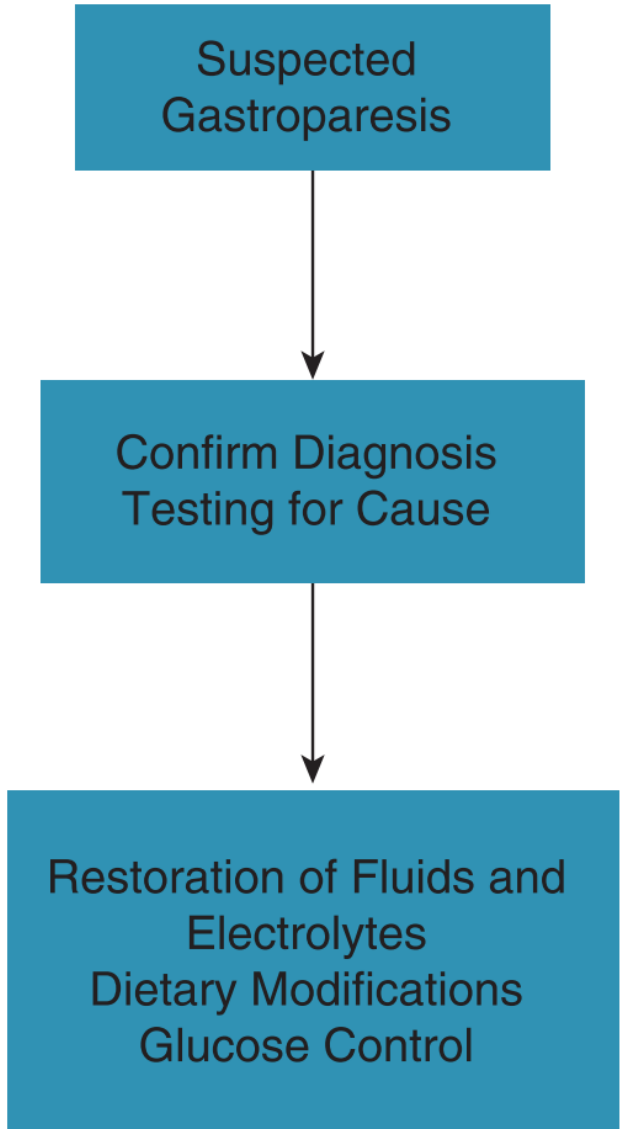


Buysschaert M, Donckier J, et al. Diabetes 1985; 34:1181-1185.

Management of Gastroparesis, first steps?

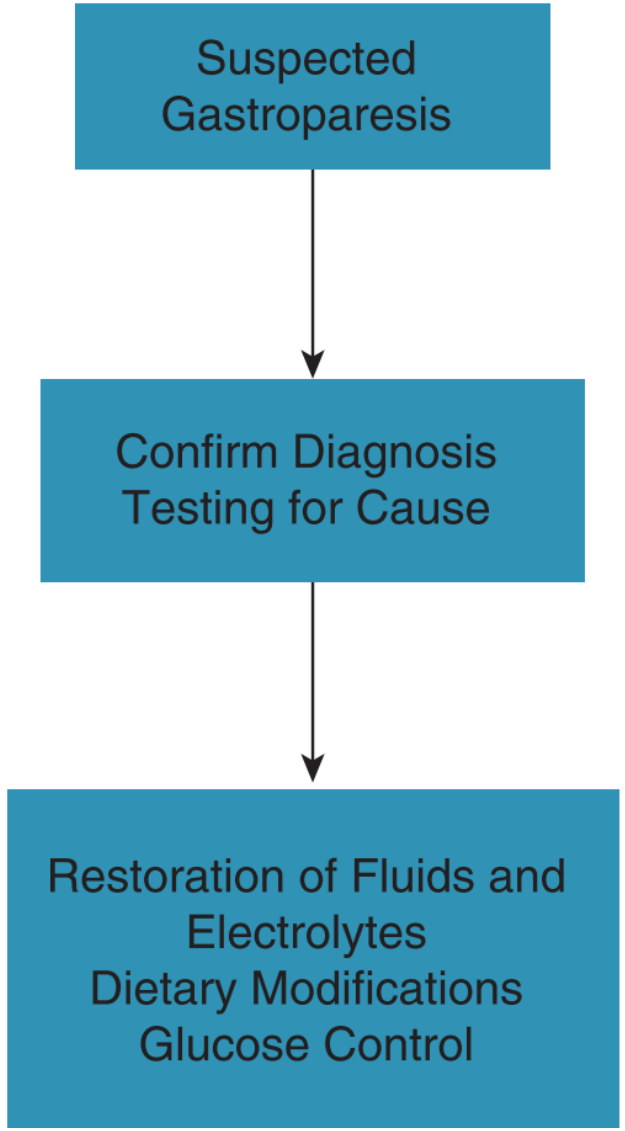
General measures

- restoration of fluids and electrolytes
- nutritional support
- *(optimization of glycemic control)*



General measures

- restoration of fluids and electrolytes
- **nutritional support?**
- *(optimization of glycemic control)*



Nutritional Support

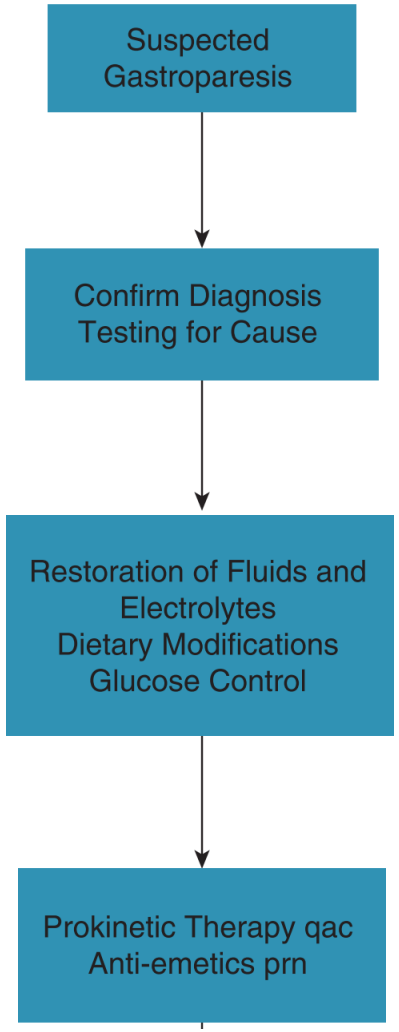
- Counseling from a dietician
- Frequent small volume meals
- Low in fat and soluble fiber.
- If unable to tolerate solid food, then use of homogenized or liquid nutrient meals is recommended.

- **If no oral intake -> NJS trial -> jejunostomy**
  - ➢ Loss > 10 % or more of the usual body weight during a period of 3 – 6 months
  - ➢ repeated hospitalizations for refractory symptoms.

Nutritional Support

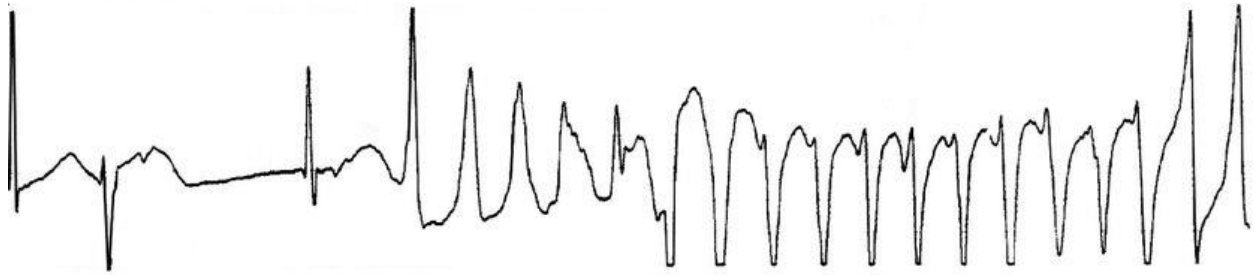
Inappetenz. Diese Beschwerden stehen in keinem Zusammenhang mit bestimmten Nahrungsmitteln, mit fetthaltigen Speisen oder anderen Faktoren, welche die gastrale Motilität reduzieren würden. Unter der hochdosierten Energie- und Proteinsubstitution ist das Gewicht stabil, jedoch nicht zunehmend. Der Patient nimmt 3 Fresubin-Drinks (1900-2000 kcal) pro Tag ein. Bei

Pharmacologic therapy?



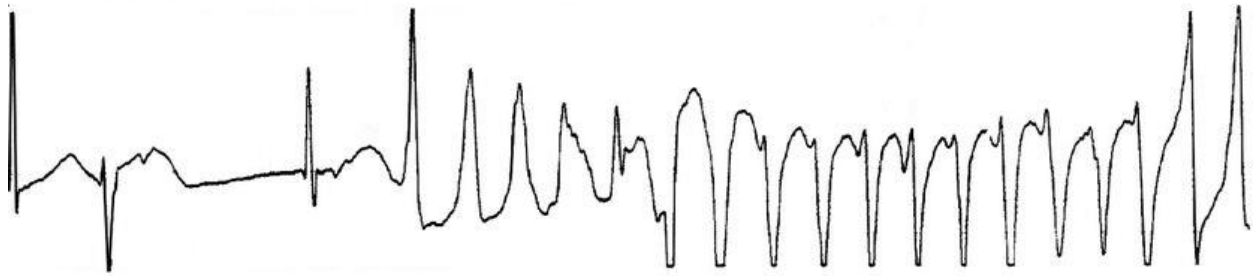
Pharmacologic therapy

- **Metoclopramide = Domperidone**



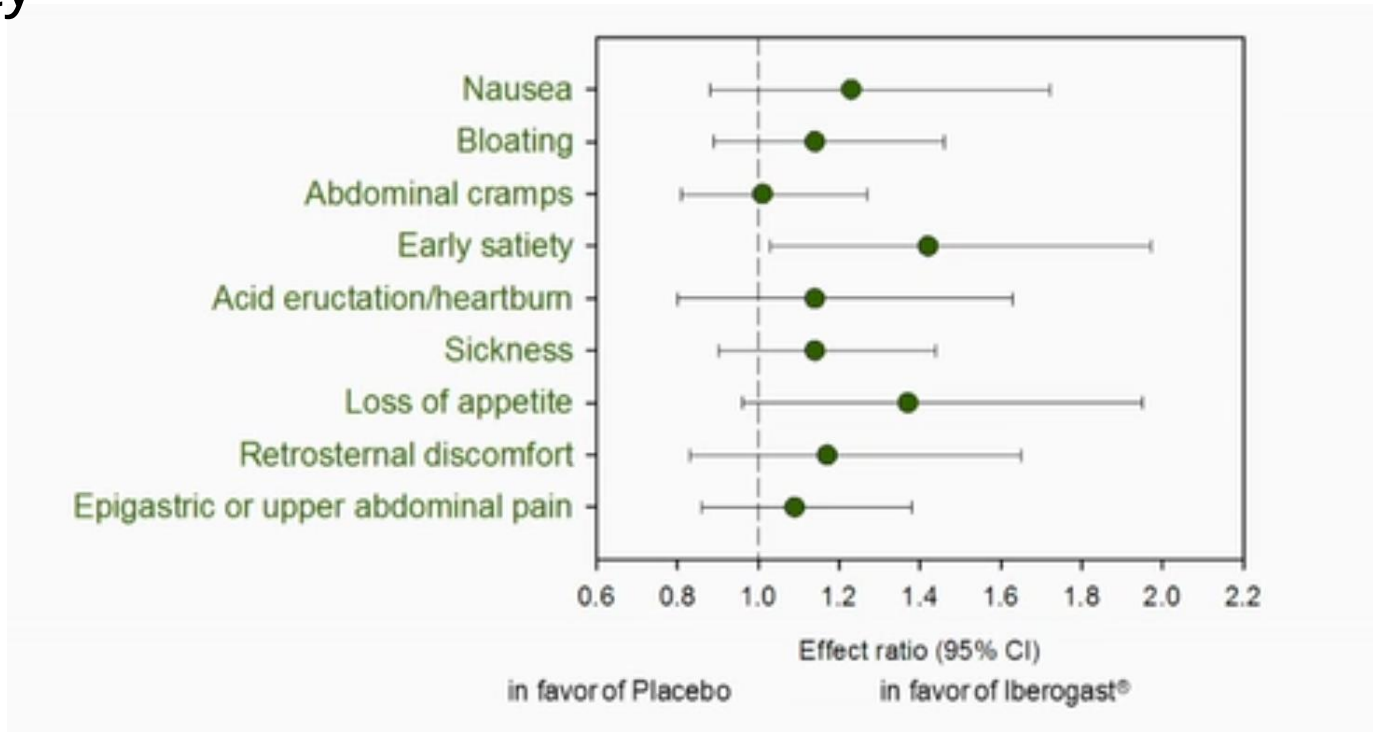
Pharmacologic therapy

- **Metoclopramide = Domperidone**
- **Erythromycin**
- **(Antiemetics)**
- **(TCAs)**



STW-5 (Iberogast)

- Relaxes Fundus and at the same time increases contractile waves in antrum
- Improves symptoms and motility
- 618 pat, UEGW 2018 (poster)
- Risks?



Hohenester B. et al. Neurgoastroenterol Motil 2004:16 765.73

Prucalopride

	n	GEt1/2min#	SBTT(min)#	GC4hr#	GC24hr##	ACt1/2hr##
placebo	14	117±6	210±20	0.6±0.1	2.3±0.3	13.1±2.3
pruc 2mg	13	105±5	151±13**	1.0±0.2	2.5±0.2	10.0±2.1
pruc 4mg	11	92±5*	134±16*	1.6±0.2*	3.2±0.4*	6.8±2.1*

Gastric emptying after 7 days on prucalopride

Prucalopride significantly accelerates gastric, small bowel and ascending colon emptying in patients with FD or C-IBS.

Bouras EP, Camilleri M et al. Gastroenterology. 2001 Feb;120(2):354-60.

No response to medical therapy

konservative Therapien eingesetzt (diätetische Massnahmen, Primperan, Motilium, Erythromycin, Antiemetika) und bei komplett fehlendem Ansprechen wieder abgesetzt. Vor der Evaluation einer

Datum:	02.11.2018
Untersuchung:	**Magenentleerungs- und Magenmotilitäts-Szintigraphie**
	- Dynamische Aufnahmen des Magens während 40 min.
Radiodiagnostikum:	89 MBq Tc-99m-MAA in einer semisoliden Testmahlzeit

Quantitative Auswertung:

Eliminationshalbwertszeit	40.5 min. (Norm 20 ± 3 min.)
Kontraktionsfrequenz	3.43/min. (Norm 3 ± 1/min.)
Kontraktionsamplitude	6.5% (Norm 28 ± 8%)

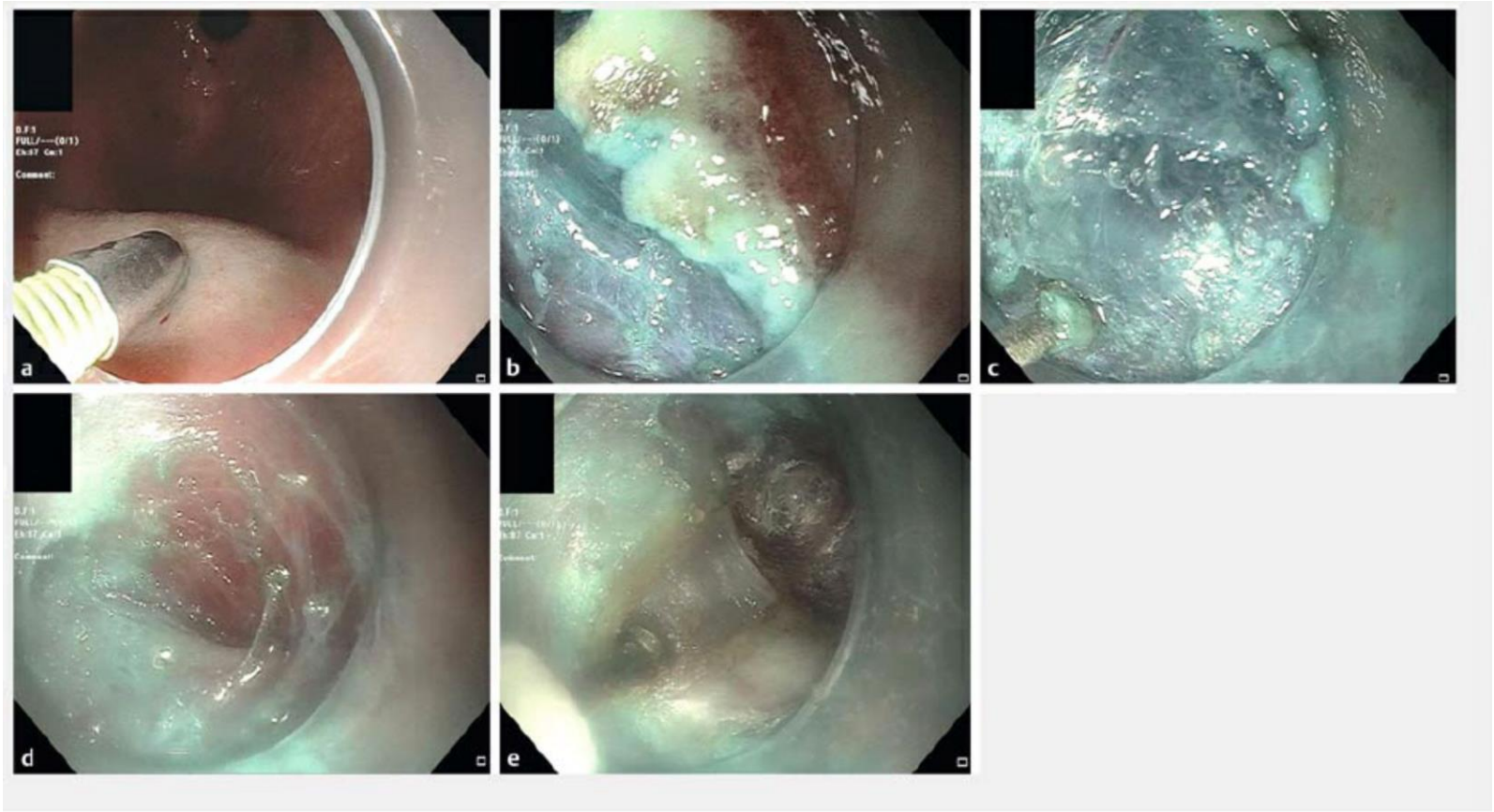
Beurteilung:

1. Erheblich verlängerte Eliminationshalbwertszeit und somit Bild einer Gastroparese.
2. Reduzierte Kontraktionsamplitude und fehelenden Kontraktionsbanden (jedoch bei erhaltener Kontraktionsfrequenz) als möglicher Hinweis auf eine Motilitätsstörung.

Interventional therapies

- **G-POEM**

G-POEM



▶ **Fig. 1** Endoscopic views showing: **a** the submucosal bleb created by needle injection of the lifting solution (methylene blue and saline) 5 cm proximally to the pylorus; **b** a horizontal incision of 1 – 2 cm made at the 5- or 6-o'clock position to allow mucosal entry into the submucosal space; **c** submucosal tunneling performed with dissection of the submucosal fibers until the pyloric ring is seen; **d** the pyloric ring is seen at the end of the submucosal tunnel; **e** full-thickness myotomy is performed starting at the pylorus and proceeding proximally.

Kahaleh M et al. Endoscopy. 2018 Nov;50(11):1053-1058

▶ **Table 4** Previous studies of gastric peroral endoscopic pyloromyotomy reported in the literature.

Study	Total number of patients	Clinical success rates	Follow-up, months	Adverse event rate
Shlomovitz et al. [24]	7	85 % (symptom improvement); 80 % (normalization of GES)	6.5	14%
Khashab et al. [1]	30	86 % (symptom improvement); 47 % (normalization of GES)	5.5	6.7 %
Dacha et al. [25]	16	81 % (decrease in GCSI); 75 % (normalization of GES)	12	0%
Gonzalez et al. [3]	12	85 % (decrease in GCSI); 75 % (normalization of GES)	3	0%
Xue et al. [26]	14	61 % (decrease in GCSI); 83 % (decrease in GES)	2	0%

GES, gastric emptying scintigraphy; GCSI, gastroparesis cardinal symptoms index.

▶ **Table 3** Comparison of the primary outcomes before and after the gastric peroral endoscopic pyloromyotomy procedure.

	Preoperative	Postoperative	*P* value
Mean GCSI score	3.3	0.8	<0.001
Mean GES time, minutes	222.4	143.2	<0.001
Mean gastric retention at 2 hours, %	75.8	58.3	0.01
Mean gastric retention at 4 hours, %	45.0	29.6	0.04

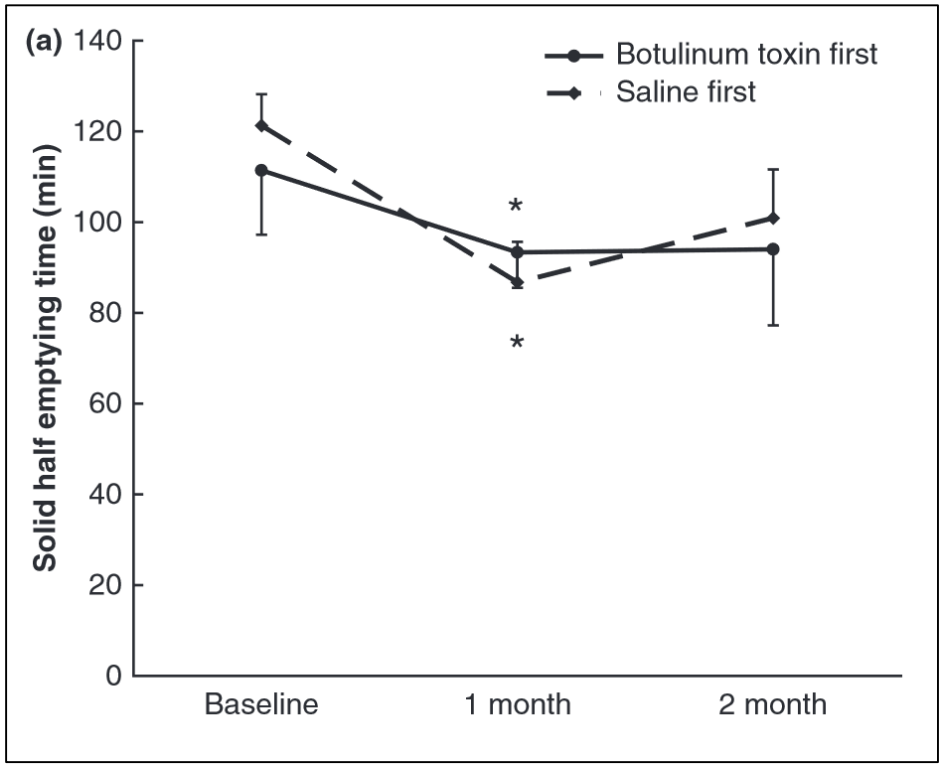
GCSI, gastroparesis cardinal symptoms index; GES, gastric emptying scintigraphy.

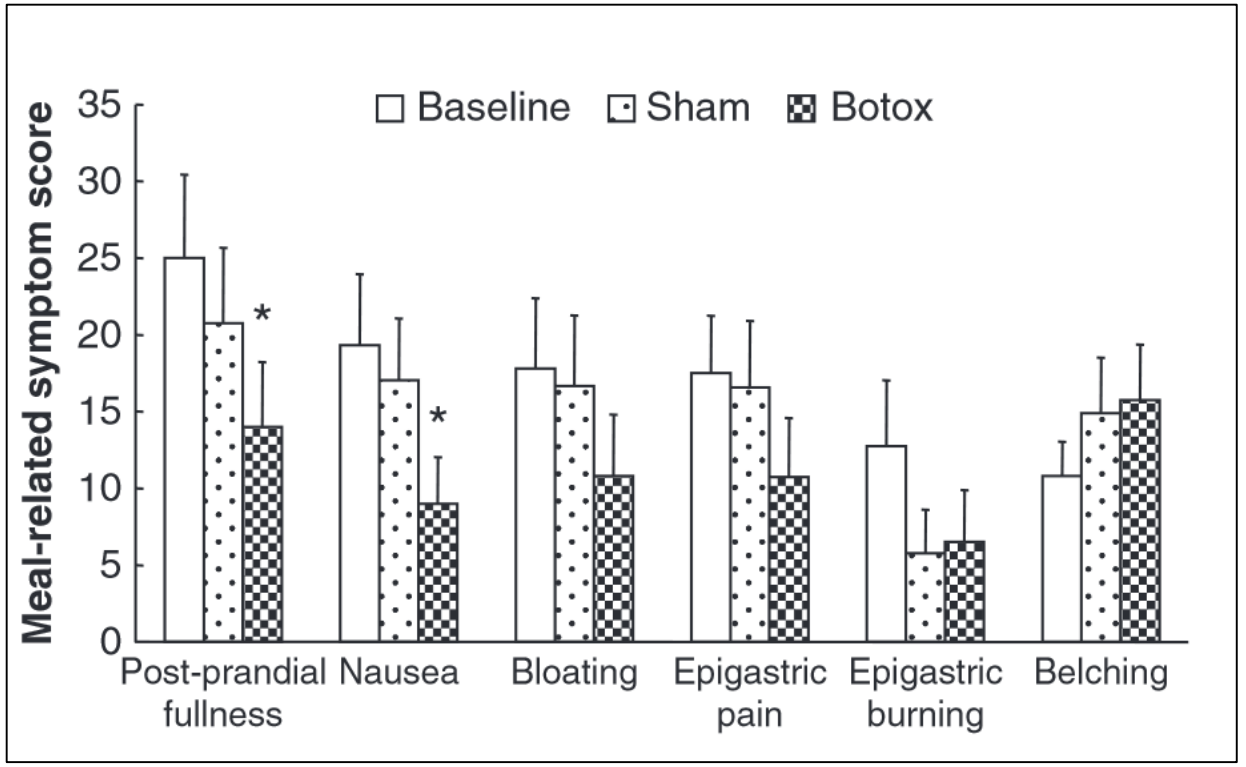
Kahaleh M et al. Endoscopy. 2018 Nov;50(11):1053-1058

Interventional therapies

- **G-POEM**
- **Intrapyloric Botox-injection**

Intrapyloric Botox in patients with delayed gastric emptying





Arts J et al. Aliment Pharmacol Ther. 2007 Nov 1;26(9):1251-8.

Interventional therapies

- **G-POEM**
- **Intrapyloric Botox-injection**
- **Gastric electrical stimulation**

Gastric electrical stimulation

- > 20 Trials, only 3 RCTs (4th coming?)
- 2 negative, 1 partly positive
- Diabetic > idiopathic
- No effect on gastric emptying
- Nonresponse, infection, electrode dislocation lead to explantation in up to 10%

Interventional therapies

- **G-POEM**
- **Intrapyloric Botox-injection**
- **Gastric electrical stimulation**
- **Surgery**
  - **Feeding jejunostomy + venting Gastrostopy**
  - **(Gastrojejunostomy)**
  - **(Gastrectomy)**

Thank you for your attention