Diagnosis and Management of Gastroparesis
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**

<table>
<thead>
<tr>
<th>Name</th>
<th>Einheit</th>
<th>Referenz</th>
<th>Wert</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blut: Elektrolyte</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Natrium</td>
<td>mmol/L</td>
<td>136 - 145</td>
<td>141</td>
</tr>
<tr>
<td>Kalium</td>
<td>mmol/L</td>
<td>3.5 - 4.5</td>
<td>3.9</td>
</tr>
<tr>
<td>Chlorid</td>
<td>mmol/L</td>
<td>96 - 107</td>
<td>103</td>
</tr>
<tr>
<td>Calcium gesamt</td>
<td>mmol/L</td>
<td>2.15 - 2.50</td>
<td>2.29</td>
</tr>
<tr>
<td>Calcium korrigiert</td>
<td>mmol/L</td>
<td>2.81 - 1.45</td>
<td>2.24</td>
</tr>
<tr>
<td>Anorg. Phosphat</td>
<td>mmol/L</td>
<td>0.81 - 1.45</td>
<td>1.09</td>
</tr>
<tr>
<td>Magnesium</td>
<td>mmol/L</td>
<td>0.70 - 0.91</td>
<td>0.85</td>
</tr>
<tr>
<td><strong>Blut: Anämieparameter</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>pmol/L</td>
<td>keine Referenzwert</td>
<td>437</td>
</tr>
<tr>
<td>Ferritin ECLIA</td>
<td>µg/L</td>
<td>20 - 250</td>
<td>121</td>
</tr>
<tr>
<td><strong>Blut: Diabetesparameter</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c (DCCT/NGSP)</td>
<td>%</td>
<td>4.8 - 5.9</td>
<td>5.3</td>
</tr>
<tr>
<td>HbA1c (FCC)</td>
<td>mmol/mol</td>
<td>22 - 42</td>
<td>34</td>
</tr>
<tr>
<td><strong>Blut: Erythrozytenparameter</strong></td>
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<td></td>
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<tr>
<td>Erythrozyten-Folsäure</td>
<td>nmol/L</td>
<td>1008 - 2426</td>
<td>798</td>
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<tr>
<td><strong>Hämatogramm</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>mmol/L</td>
<td>4.11 - 5.89</td>
<td>4.99</td>
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<tr>
<td>Creatinin (P)</td>
<td>µmol/L</td>
<td>59 - 104</td>
<td>76</td>
</tr>
<tr>
<td>eGFR nach CKD-EPI</td>
<td>mL/min</td>
<td>&gt; 59</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>Harnstoff</td>
<td>mmol/L</td>
<td>3.2 - 7.3</td>
<td>3.2</td>
</tr>
<tr>
<td>Protein total</td>
<td>g/L</td>
<td>64 - 83</td>
<td>78</td>
</tr>
<tr>
<td>Albumin</td>
<td>g/L</td>
<td>35 - 52</td>
<td>42</td>
</tr>
<tr>
<td>C-reaktives Protein</td>
<td>mg/L</td>
<td>&lt; 5</td>
<td>&lt; 3</td>
</tr>
<tr>
<td>Bilirubin gesamt</td>
<td>µmol/L</td>
<td>&lt; 17</td>
<td>4</td>
</tr>
<tr>
<td><strong>Blut: Enzyme</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>ASAT</td>
<td>U/L</td>
<td>&lt; 50</td>
<td>30</td>
</tr>
<tr>
<td>ALAT</td>
<td>U/L</td>
<td>&lt; 50</td>
<td>35</td>
</tr>
<tr>
<td>G-Glutamyltransferase</td>
<td>U/L</td>
<td>&lt; 60</td>
<td>43</td>
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<tr>
<td>Lactat-Dehydrogenase</td>
<td>U/L</td>
<td>&lt; 480</td>
<td>382</td>
</tr>
<tr>
<td>Pankreas-Amylase</td>
<td>U/L</td>
<td>13 - 53</td>
<td>39</td>
</tr>
<tr>
<td><strong>Blut: Schildrüsenparameter</strong></td>
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<tr>
<td>TSH</td>
<td>mU/L</td>
<td>0.36 - 3.83</td>
<td>3.26</td>
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<tr>
<td>FT4</td>
<td>pmol/L</td>
<td>12.2 - 23.5</td>
<td>18.5</td>
</tr>
</tbody>
</table>
Case 1: 20 year old male

- 21.08.2017 Sonografie Abdomen: keine akute Appendizitis, keine anderen Pathologien
- 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
- 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.

No! Not at this stage!


Let’s take a closer look


Delayed gastric emptying is traditionally considered a major pathophysiologic mechanism underlying symptoms in functional dyspepsia and idiopathic gastroparesis. 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


Most studies failed to find a convincing relationship between delayed gastric emptying and symptom pattern. 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, although a large multicenter study failed to find any association (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.
Let’s take a closer look


Furthermore, induction of delayed gastric emptying in healthy subjects by pharmacologic or dietary interventions is not associated with the occurrence of dyspeptic symptoms. These observations question the relevance of delayed emptying as a mechanism underlying dyspeptic symptoms.
Let’s take a closer look


- 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 barostat3,12 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 $y(t) = 1 - (1 - e^{-kt})^6$ 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, $k$.*

Case 1: 20 year old male

- Gastric emptying study
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

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.
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?

- Suspected Gastroparesis
- Confirm Diagnosis Testing for Cause
- Restoration of Fluids and Electrolytes Dietary Modifications Glucose Control
- Prokinetic Therapy qac Anti-emetics prn
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. Neurogastroenterol Motil 2004:16 765.73
Prucalopride

Gastric emptying after 7 days on prucalopride

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

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

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 fehlenden Kontraktionsbanden (jedoch bei erhaltener Kontraktionsfrequenz) als möglicher Hinweis auf eine Motilitätsstörung.
Interventional therapies

- 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.
### Table 4 Previous studies of gastric peroral endoscopic pyloromyotomy reported in the literature.

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

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.

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean GCSI score</td>
<td>3.3</td>
<td>0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean GES time, minutes</td>
<td>222.4</td>
<td>143.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean gastric retention at 2 hours, %</td>
<td>75.8</td>
<td>58.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean gastric retention at 4 hours, %</td>
<td>45.0</td>
<td>29.6</td>
<td>0.04</td>
</tr>
</tbody>
</table>

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

• G-POEM
• Intrapyloric Botox-injection
Intrapyloric Botox in patients with delayed gastric emptying

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