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Diabetic visceral neuropathy is correlated to gastroparesis symptoms and glycaemic control in patients with type 2 diabetes

Aim: The study aimed to investigate the quantitative relation between gastric mucosal innervation and gastroparesis symptoms as well as functional parameters of gastric emptying.
Methods: 22 patients with type 2 diabetes (T2D) and gastroparesis symptoms (age 50 years and duration 6 years) and 25 age- and gender-matched healthy subjects were enrolled. Neuropathology with quantification of gastric mucosal innervation on endoscopic biopsy was performed. Specimens from the fundus, body and antrum of the stomach were obtained. Double-labelling immunofluorescence staining was applied on all specimens and innervation of the gastric mucosa (mucosal innervation density: MID in mm/mm^3) quantified using the stereology principle. All participants self-assessed their symptoms for the previous 2 weeks using the gastroparesis cardinal symptom index (GCSI). Gastric emptying scintigraphy (GES) was accomplished after a standardized test meal. Neurophysiological examinations encompassed nerve conduction studies of the lower limbs and quantitative sensory testing of thermal thresholds on the dorsum of the foot. Sudomotor testing as well as RR-interval variation (RRIV) were conducted at rest and during deep-breathing to investigate autonomic function.
Results: Patients with T2D mostly complained of stomach fullness and bloating as the most common GCSI symptoms. GES variables (half time and retention) were prolonged in the group with T2D [7 patients (32%)] and retention at 3 hours correlated with fasting blood glucose levels. Negative correlations of gastric emptying with RRIV and sudomotor function were found. Gastric MID of patients with T2D was significantly lower compared to healthy controls in all regions and was negatively correlated to total scores on the GCSI. A negative correlation between gastric MID of the fundus and HbA1c was found.
Conclusions: Reduced gastric mucosal innervation and prolonged gastric emptying scintigraphy parameters were proven in patients with T2D and both were correlated to gastroparesis symptoms and glycaemic control.

Comments. The study provides evidence that gastric mucosal innervation is reduced and gastric emptying is prolonged in patients with T2D and both are correlated to gastroparesis symptoms and glycaemic control. Previously, only limited reports focusing on type 1 diabetes and asymptomatic patients were available. In this study - although in a limited number of T2D patients and controls - comprehensive symptomatology, pathology and functional assessments were applied to get a multidimensional view on gastroparesis.
Additional negative correlation between gastric emptying and some measures of autonomic function were also found. One should add that GCSI symptom scores and gastric MID were not significantly different between diabetic patients with and without neuropathy. However, patients with neuropathy had more gastric retention at 2 hours. These partially conflicting results and the absence of associations between MID and GES might be a consequence of the complex pathogenesis of gastroparesis symptoms. Still, the study reaffirms that diminished mucosal innervation contributes to its pathophysiology. The authors suggest that gastric MID and GES characterize gastroparesis from a different aspect and MID and gastric retention at 2 hours could be the most sensitive and complementary markers for evaluating diabetic gastroparesis. Further studies are warranted to clarify the associations between anatomical and functional correlates of diabetic gastroparesis.
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Reference. Tseng PH, Chao CC, Cheng YY, Chen CC, Yang PH, Yang WK, Wu SW, Wu YW, Cheng MF, Yang WS, Wu MS, Hsieh ST. Diabetic visceral neuropathy of gastroparesis: Gastric mucosal innervation and clinical significance. Eur J Neurol. 2022 Jul; 29 (7): 2097-2108. doi: 10.1111/ene.15333. Epub 2022 Apr 3.
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