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Clinical Characteristics and Treatment Patterns among Patients Diagnosed with Gastroparesis in Europe (Finland and Spain) Using Real World Secondary Data

Executive Summary

Rationale and Background

Gastroparesis is a chronic motility disorder characterized by delayed gastric emptying in the absence of mechanical obstruction.¹ Gastroparesis is a serious disorder associated with impaired quality of life and a substantially increased risk of morbidity and mortality.²⁻⁴ Current pharmacological options for gastroparesis are notably limited.⁵ Moreover, given the sparsity of epidemiological data in Europe, there is a need to enhance our understanding of gastroparesis,⁶ both in terms of occurrence, and patient population characteristics. To address this gap, we conducted a bi-national, multi-database study employing real-world evidence to explore the natural history, prevalence, and incidence of gastroparesis in Finland and Spain.

Research Questions and Objectives

The primary study objectives include:

- To describe patients with gastroparesis in terms of characteristics and natural history of disease, including socio-demographic characteristics, etiologic factors, clinical characteristics, diagnostic practices, and treatment practices.
- To assess the incidence and prevalence of gastroparesis in the adult, pediatric and overall populations in countries of interest, i.e., Spain and Finland.

Study Design

This was an observational, bi-national cohort study using real-world data from multiple structured secondary databases in Finland and Spain and electronic medical records (EMR) in Finland. Cases of gastroparesis were defined based on available information on diagnosis codes and other clinical records, records of conducted tests and test results, and recorded pharmacological and non-pharmacological treatment (see case definition and analyses).

Setting

The study was based on routinely collected secondary data from large healthcare databases in Finland and Spain. In Finland, the study was conducted in a regional setting, based on EMR data from the Hospital District of Helsinki and Uusimaa (HUS, total population approximately 1.6 million) and the Hospital District of North Savo (PSSHP, total population 0.26 million), covering over 30% of the Finnish population. Regional hospital EMR data, including inpatient and specialist outpatient care data, were linked to the national administrative and health registers, to create a study-specific database. The

data sources in Spain included the IQVIA Longitudinal Health Search Database (LPD) and the Spanish Minimum Basic Data Set (MBDS). The LPD is a national database, covering primary care data for approximately 4% of the Spanish population (~2 million individuals). The MBDS is a national inpatient hospital discharge database with close to complete coverage (~95%) of hospital discharges in Spain.⁷⁻

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Case Definitions and Analyses

Three gastroparesis definitions, i.e., *definite*, *likely*, or *possible*, were designed according to the likelihood of true gastroparesis in the patients.

In Finland

- *Definite* gastroparesis: positive gastric emptying scintigraphy results with records of persistent main symptoms (i.e., records of at least 2 different symptom components that occurred on ≥ 2 different dates and ≥ 30 days apart, including abdominal pain, bloating, nausea and/or vomiting, prescriptions for the symptoms of gastroparesis [metoclopramide, domperidone, and antiemetics and antinauseant]).
- *Likely* gastroparesis: positive gastric emptying results without records of persistent main symptoms, or pyloric injections with records of persistent main symptoms.
- *Possible* gastroparesis: persistent main symptoms alone, or pyloric injection without persistent symptom records.

In Spain, in the LPD,

- *Likely* gastroparesis: recorded diagnosis codes of gastroparesis together with persistent main symptoms (i.e., records of at least 2 different symptom components that occurred on ≥ 2 different dates and ≥ 30 days apart, including abdominal pain, bloating, early satiety, nausea and/or vomiting, prescriptions for the symptoms of gastroparesis [metoclopramide, domperidone, and antiemetics and antinauseant]).
- *Possible* gastroparesis: records of persistent symptoms

In the MBDS,

- *Likely* gastroparesis: recorded diagnosis codes of gastroparesis together with persistent main symptoms (i.e., records of at least 2 different symptom components that occurred on ≥ 2 different dates and ≥ 30 days apart, including abdominal pain, bloating, early satiety, and nausea and/or vomiting).
- *Possible* gastroparesis: records of persistent symptoms alone, or treatment procedures (i.e., pyloric injection or gastric electrical neurostimulation) alone.
- International Classification of Diseases (ICD)-coded gastroparesis: any ICD diagnosis code of gastroparesis. which was added as a sensitivity analysis for the inpatient database.

Case dates were defined as the date when the corresponding case definition was met for the first time. Separate analyses including cases identified using each definition, including *definite*, *likely*, *possible*, and *ICD-coded* gastroparesis, were conducted. Descriptive analyses of the identified incident cases were reported before and after the case dates. Etiology of the incident case populations were assessed. As the case categories are hierarchical, separate analyses including cases with different minimum level of likelihood were conducted. Incidence rates and prevalence of the defined cases were estimated separately for each data source.

Subjects and Study Size

Analysis populations were extracted from the data sources. All individuals enrolled in the LPD during 2013-2020 were extracted. Individuals with any records of components in the case definitions of gastroparesis during 1997-2019 in the MBDS, and 2012-2020 in HUS and PSSHP were extracted. In the incidence analysis, 1,699,613 from the LPD, 1,322,700 from the MBDS, and 654,320 from Finland were extracted and included in the analysis populations. Individuals with gastrointestinal malignancies, inflammatory bowel disease, or celiac disease were excluded from the analysis. Additionally, for incidence analysis, prevalent cases before the study period were excluded and only new cases fulfilling case definitions for the first time during the study period were defined as incident cases.

Variables and Data Sources

The data sources in Finland included structured secondary care EMR data and information from national administrative and health registers covering primary and secondary care, linked on the unique national personal identification number available for all residents and citizens of Finland. The data sources in Spain included routinely captured data from, respectively, primary, and secondary care, organized in 2 separate databases. No linkage of other data sources was conducted in Spain.

Results

Due to the small sample size of definite Gastroparesis case definitions, results of incidence and prevalence are not shown, and only descriptive results are reported to ensure the integrity and robustness of our estimates remained intact.

The case populations for characterizing gastroparesis were *definite* or *likely* gastroparesis in Finland, *likely* gastroparesis in the LPD, and *ICD-coded* gastroparesis in the MBDS. These case definitions were selected considering the validity. The mean age at the case date of gastroparesis cases was 56.1 (standard deviation [SD] 17.7) years in Finland, 64.4 (SD 19.2) in the LPD, and 64.1 years (SD 20.3) in MBDS. In these populations, 62.8%, 64.3%, and 49.0% were female, respectively. Common comorbidities at baseline included chronic pulmonary disease (Finland 21.3%, LPD 40.5%, MBDS 10.0%), type 2 diabetes mellitus (Finland 27.7%, LPD 35.7%, MBDS 46.5%). Type 1 diabetes mellitus was reported in 19.1% of the patients in Finland and 13.5% in the MBDS, while it was less frequent (4.8%) in the LPD. Moderate/severe renal disease was commonly reported in the MBDS (26.7%). Cancer was reported in 35.7% of patients in the LPD, but only in 8.5% and 9.0% of patients in Finland and the MBDS,

respectively. Psychiatric disorders (of any type) were observed in 50.0%, 81.0%, and 23.6% of the cases in Finland, LPD, and MBDS, respectively, and this was largely driven by high proportions of mood disorders in Finland (40.4%) and the LPD (52.4%). In Finland, 44.7% of the patients had a history of gastro-esophageal reflux disease, and 23.4% had a history of ulcer disease, while in the LPD, 23.8% had history of gastro-esophageal reflux disease, and 57.1% also received diagnosis of functional dyspepsia. In Finland, 50.0% of the patients had a history of hernia. Other intestinal diseases were prevalent in patients in all 3 data sources, with 34.0%, 50.0%, and 20.8% of the patients having records in Finland, the LPD, and MBDS, respectively.

Frequently prescribed drugs were prokinetics (Finland 21.3%, LPD 73.8%), antidepressants (Finland 29.8%, LPD 50.0%), and opioids (Finland 36.2%, LPD 31.0%). Drugs with anticholinergic properties were also somewhat frequent, with 23.4% and 50.0% of cases having redeemed prescriptions for these in Finland and the LPD, respectively. Diabetic and idiopathic gastroparesis were the most common etiologies in all databases.

Common comorbidities in patients with gastroparesis before the case date included diabetes, chronic pulmonary diseases, renal diseases, and psychiatric disorders.

Discussion

The common patient characteristics and etiologies of gastroparesis aligned with previous database studies on gastroparesis.^{4,11,12} However, the frequent use of opioids and drugs with anticholinergic properties observed in this study raises a potential topic for future studies,¹³ given their known adverse gastrointestinal effects, especially on gastroparesis.^{14,15}

Additionally, emerging evidence suggests frequent misdiagnosis of gastroparesis in the US and controversies regarding gastroparesis' relationship with the differential diagnoses of functional dyspepsia remains.^{16–18} Despite very high frequencies of *possible* gastroparesis in the populations, a very small fraction of the cases was tested for and diagnosed with gastroparesis. Idiopathic gastroparesis was the main etiology in all databases when using the *possible* case definition, contrasting with what was seen for *definite* or *likely* gastroparesis, likely capturing gastrointestinal patient population with different underlying diseases than gastroparesis.

Conclusion

Diabetic and idiopathic gastroparesis are the most common etiologies of gastroparesis. Patients with gastroparesis are commonly comorbid with type 1 or type 2 diabetes, psychiatric disorders, and chronic pulmonary diseases. Prokinetics, antidepressant, and drugs that delay gastric emptying, including opioids and drugs with anticholinergic properties, are commonly prescribed in gastroparesis patients. However, considering that gastroparesis is commonly underdiagnosed and given the known limitations of the available data, there is likely an underestimation of the true occurrence of gastroparesis in the general population. More epidemiological studies are needed to further deepen the understanding of gastroparesis including the diagnosis criteria, the role of comorbidities in the course of gastroparesis, and effectiveness and safety of the common treatments used in gastroparesis, including opioids and drugs with anticholinergic properties.

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