Prevalence of functional gastrointestinal disorders in a population of subjects consulting for gastroesophageal reflux disease in general practice

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SUMMARY

Aims — To establish the prevalence of functional gastrointestinal (GI) disorders in adult patients with symptoms of gastroesophageal reflux disease (GERD) and to assess the impact of GERD treatment on functional GI disorders in medical practice in France.

Methods — 3318 patients with GERD symptoms (mean age 53 yr; 1726 women and 1592 men) were involved in the survey. A questionnaire on demographic data, GERD features, presence of functional GI disorders and their features, and impact of GERD treatment on functional GI disorders was performed by the physician. The size of the different groups was compared using either a chi² test or a Mantel-Haenszel analysis, on a case by case basis.

Results — Seventy-two percent of patients with GERD had associated functional GI disorders, with a mean of 4.1 ± 1.9 functional digestive symptoms per patient. Gas, flatulence, transit disorders and abdominal distension were the most commonly reported symptoms. Among patients with functional GI symptoms, 27% had symptoms suggestive of irritable bowel syndrome (IBS), 16% were suggestive of dyspepsia while 57% had both upper and lower functional digestive symptoms. According to the patients, GERD treatment had a positive impact (significant to complete improvement) on their functional GI disorders in about one-third of patients particularly in those with dyspeptic-type symptoms.

Conclusions — Functional GI disorders are particularly common in adult patients suffering from GERD, with a three times higher prevalence than in the general population.

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Gastroesophageal reflux disease (GERD) and functional gastrointestinal (GI) disorders are two chronic digestive conditions particularly common in the general adult population.

GERD is characterized by symptoms and/or presence of reflux esophagitis. Heartburn and acid regurgitations are the most typical symptoms. GERD prevalence varies according to the frequency threshold to be considered: 7% to 10% of the general population report daily GERD symptoms, 14% to 20% at least weekly and 15% to 30% at least monthly [1-3].

Functional GI disorders include a range of chronic digestive symptoms for which no organic abnormality can be identified, at least by conventional investigation procedures. Different syndromes have been identified leading to Rome II criteria classification [4]. Non-ulcer dyspepsia (with symptoms dominated by pain or upper abdominal discomfort) and irritable bowel syndrome (IBS) (with symptoms dominated by pain or abdominal discomfort with transit disorders) are the most common. In the general population, the overall prevalence of functional GI disorders (with at least one functional digestive symptom during the last three months) varies from 54% to 69% depending on the definition criteria considered [5-9]; that of non-ulcer dyspepsia varies from 11% to 41% [6, 8, 10, 11] and that of IBS from 9% to 22% [5, 6, 8, 9, 12, 13]. There is a definite overlap between the different types of functional GI disorders, since at least 50% of patients have both IBS and functional dyspepsia [8]. The symp-
tom profile of patients may change in time from dyspepsia to IBS or vice versa [14].

In the general population, there is an independent association between IBS, dyspepsia and GERD [15]. The links between GERD and functional GI disorders have been studied mainly in IBS patients, in whom prevalence of GERD is higher than that observed in the general population and varies from 40% to 79% depending on the studies [8, 12, 15, 16]. However, only one study to date has been published on IBS prevalence in patients with GERD, which involved a small number of patients and reported an increased prevalence of IBS in this population [17].

The aim of this survey was to establish in primary care the prevalence of functional GI disorders in a large sample of patients suffering from GERD and to study the GERD features that may influence this prevalence and assess the impact of anti-reflux treatment on functional GI disorders.

Patients and methods

A total of 1600 French general practitioners (GP) were involved in the survey and filled in a questionnaire on patients consulting for symptoms of GERD during the survey period. Each physician could include 3 consecutive patients over a 6-week period, to avoid selection bias. Inclusion criteria were: age over 18 years, GERD diagnosis for at least 30 days, treated or not, absence of or low-grade (I or II) esophagitis. Demographic data, GERD data and information on possible functional GI disorders were collected. Only complete questionnaires were analyzed.

GERD and functional GI disorders diagnosis were established by the GP in his/her daily practice, by filling in a questionnaire concerning symptoms, without any specific selection criteria demanded for the study. GERD data included symptoms, time elapsed since diagnosis, frequency and treatment. Data on functional GI disorders included symptoms, time elapsed since diagnosis and treatment. Rome criteria were not required for inclusion in the survey.

Impact of GERD and functional GI disorders on quality-of-life was globally evaluated by patients on a 5-level scale, from absent to severe. Impact of treatment was evaluated by patients on a 5-level scale, from no impact to for inclusion in the survey.

The median time elapsed since the diagnosis of functional GI disorders was 36 months, and was similar to that of GERD, with a third of diagnoses having been made simultaneously, a third of functional GI disorders diagnoses made prior to that of GERD, and a third made after that of GERD. An impact of functional GI disorders on quality-of-life was reported by 92% of the patients, described as intense to severe by 26% of them. Nearly all patients with functional GI disorders had a specific treatment, the most common of which were antispasmodic drugs.

Results

Population characteristics

The survey was carried out between January and April 2003. Among 1600 GPs involved in the survey, 1500 returned between one and three questionnaires (median of 2.2 questionnaires per physician). Participating GPs came from all areas of France, from rural and urban areas, reflecting medical practices in France. Three thousand three hundred and eighteen complete questionnaires were analyzed. The patient population included 1592 men (49.1%) and 1726 women (50.9%) with a mean age of 53 years. Ten percent of the patients had a history of digestive surgery, mainly appendectomy and cholecystectomy.

The most common GERD symptoms were: heartburn in 84% of patients, regurgitation in 52%, substernal pain in 43% and cough in 33%; 2.5 different symptoms per patient were present on average. The median time elapsed since GERD diagnosis was 36.5 months. GERD symptoms were described as intermittent by 32% of patients, and occurred 2 to 3 times per week in 40% and regularly in 28%. Among the 2103 patients who underwent upper GI endoscopy, 13% had grade II esophagitis. GERD impact on quality-of-life was very common (reported by 89% of the patients) and scored as intense to severe by a quarter of them. Seventy-nine percent of patients were receiving proton pump inhibitors as GERD treatment, 35% an antacid, while lifestyle and dietary advice were adhered to 79% of the patients. Reflux symptoms improvement resulting from the treatment was considered significant to complete by more than 70% of the patients.

Prevalence of functional GI disorders and their features

A large majority of patients (72%) had functional GI disorders associated with GERD, with 4 different symptoms per patient on average. Gas and flatulence (81%), transit disorders (62%), abdominal distension (58%), upper abdominal pain (51%), spasms (50%), lower abdominal pain (44%) were the most commonly reported symptoms (figure 1). Transit disorders were most often alternating diarrhea and constipation (46%), or constipation (40%). According to the Rome II criteria, functional GI disorders symptoms reported by the patients could be classified as IBS (transit problems and/or lower abdominal pain) in 27% of the cases, functional dyspepsia (upper abdominal pain and/or early satiety and/or nausea) in 16%, and a combination of both upper and lower functional digestive signs in 57% (figure 2). The median time elapsed since the diagnosis of functional GI disorders was 36 months, and was similar to that of GERD, with a third of diagnoses having been made simultaneously, a third of functional GI disorders diagnoses made prior to that of GERD, and a third made after that of GERD. An impact of functional GI disorders on quality-of-life was reported by 92% of the patients, described as intense to severe by 26% of them.

Nearly all patients with functional GI disorders had a specific treatment, the most common of which were antispasmodic drugs.
(80%), antacids (34%) and laxatives (14%), while lifestyle and dietary advice were adhered to by 78% of the patients. Forty-one percent of patients took self-medication for their functional GI disorders.

**GERD features influencing prevalence of functional GI disorders**

Number of GERD symptoms was associated with an increased prevalence of functional GI disorders (P < 0.001). Prevalence of functional GI disorders increased from 66% in patients with only one symptom of GERD (N = 585) to 83.5% in patients with 5 symptoms or more (N = 141). Global level of GERD impact on quality-of-life reported by patients was also associated with an increased prevalence of functional GI disorders (P < 0.001). Prevalence of functional GI disorders increased from 67% in patients reporting low level (grade 1 on the 5-level scale) impact of GERD on quality-of-life (N = 577) to 85% in patients reporting severe impact (grade 5 on the 5-level scale) (N = 48).

On the contrary, the presence of grade II esophagitis did not modify the prevalence or type of functional GI disorders (72% of functional GI disorders in this sub-population of 272 patients). The frequency of onset of GERD symptoms did not influence the prevalence of functional GI disorders.

**Impact of GERD treatment on functional GI disorders**

According to patients, the treatment of GERD had a positive impact (significant to complete improvement) on the associated functional GI disorders in approximately one-third of the patients. A beneficial effect of GERD treatment was more often reported by patients with a functional dyspepsia profile (49% reported an improvement in dyspeptic symptoms as significant to complete) than by those with an IBS profile (only 21% reported an improvement in bowel symptoms as significant to complete) (P < 0.001). According to patients, the impact of GERD treatment was influenced by the greater number of GERD symptoms (P < 0.001) and the more severe global impact of functional GI disorders on quality of life (P < 0.001). Patients with one symptom of GERD (N = 378) following GERD treatment reported a significant to complete improvement of their bowel symptoms in 24% of cases and of their dyspepsia in 32% of cases, whereas the corresponding figures for patients with 5 symptoms of GERD (N = 90) were 30 and 39%, respectively. Among the 373 patients describing little impact of functional GI disorders on their quality-of-life, 33% reported a significant or complete improvement of their bowel symptoms and 41% of their dyspeptic symptoms with GERD treatment. Among the 38 patients with a severe impact significant or complete improvement in bowel and dyspeptic symptoms occurred in 34% and 34%, respectively. GERD treatment was less efficient for functional GI disorders in patients with grade II esophagitis (P < 0.001). The impact of GERD treatment on functional GI disorders did not correlate with the level of GERD impact on quality-of-life or the number of functional GI disorder symptoms.

**Discussion**

Our survey shows the high frequency of functional GI disorders in adult patients consulting with GERD in primary care, since 72% of these patients had functional GI disorders with a mean of 4 different symptoms per patient. Among these patients, 27% had symptoms suggestive of IBS, 16% of functional dyspepsia, while a majority of patients (57%) had mixed functional digestive symptoms with both upper and lower complaints. The global impact of functional GI disorders on their quality-of-life reported by the patients was as frequent as that of GERD (92% for functional GI disorders versus 89% for GERD) while the range of this impact was as significant as that of GERD. For both conditions, it was considered as intense to severe by a quarter of patients. Global impact of GERD on quality-of-life was more severe in patients with than without functional GI disorders, being scored as intense to severe by 26% and 21%, respectively (P < 0.001).

These results confirm those published by Pimentel et al. [17] related to US patients. In comparing the prevalence of IBS between 35 patients suffering from GERD and 49 control subjects unaffected by GERD, these authors demonstrated that the prevalence of IBS was 71% in patients with GERD versus 35% in control subjects (relative risk = 4.7; P < 0.01).

One of the interesting new aspects of our survey results from the large number of patients enrolled (3318 patients suffering from GERD) and the multicentric recruitment from widespread general medicine consultations (1 500 participating general practitioners representing all French areas). This avoided the bias of selective recruitment by specialized centres and provided an idea of real primary care in current medical practice. However, given that the diagnosis of GERD or functional GI disorders was made by GPs, there is a risk of including patients who did not really fulfill the Rome II criteria; on the other hand such recruitment offers the advantage of reflecting how these diagnoses are established in routine medical practice. In order to study a large number of patients the diagnosis of GERD, for practical reasons, did not rely on an abnormal esophageal pH measurement, as in the Pimentel study [17]. Therefore, the accuracy of a real diagnosis of GERD can be discussed. However, more than 84% of the patients reported heartburn which is a very specific GERD symptom allowing the diagnosis without any functional test [18]. In these patients, the description of 2.5 different GERD symptoms on average and a median duration of disease of 36.5 months is an important argument for a GERD diagnosis excluding the study of patients with only very episodic or transient GERD symptoms. Concerning functional GI disorders, Rome II criteria are very relevant in clinical trials for homogeneous population enrolment but it is now well recognized that these criteria select the most severe patients suffering with functional GI disorders [19-21]. According to the study design, the questionnaire was completed by the physician in the presence of the patient. Therefore, a possible bias could be that patient’s answers may have been influenced by the presence of the physician.
Quality-of-life was globally evaluated with a simple and short 5-level questionnaire, easy to use during a GP’s consultation. There were no available data on patients who refused to participate in the survey. For methodological reasons no control group with patients unaffected by GERD was available, in order to compare the prevalence of functional GI disorders in a general population recruited in the same conditions by the same GPs.

Another interesting aspect of this survey is patients’ own assessment of GERD treatment on outcome — especially when GERD was not associated with esophagitis — which resulted in satisfactory improvement (significant to complete) of their intestinal symptoms in 29% of the patients and of their dyspeptic symptoms in 38%. Patients with a “functional dyspepsia” profile were those who benefit the most from GERD treatment. However, this result needs to be interpreted with caution as 80% of patients also had a specific treatment for their functional GI disorders; it may have been difficult for them to distinguish between the impact of GERD and functional GI disorders treatments.

The particularly frequent association between GERD and functional GI disorders suggests a possible common pathophysiological mechanism, such as diffuse disorders of the smooth muscles and/or their innervation (altered visceral sensitivity or abnormal transmission) [22]. In the first studies on esophageal function in patients with IBS, the pressure of the lower esophageal sphincter was reduced and/or the esophageal peristalsis abnormal transmission) [22]. In the first studies on esophageal muscles and/or their innervation (altered visceral sensitivity or physiological mechanism, such as diffuse disorders of the smooth muscles systematically in patients presenting with GERD symptoms. This frequent association has not yet been identified, but these results may have been difficult for them to distinguish between the impact of GERD and functional GI disorders treatments.

In conclusion, this is the first epidemiological study involving a large population of patients recruited in general practice showing that the prevalence of functional GI disorders in patients suffering from GERD is high (72%). Functional GI disorders have a great impact on the patients’ quality-of-life. The common pathophysiological mechanism which could explain this particularly frequent association has not yet been identified, but these results should prompt clinicians to jointly assess functional GI disorders systematically in patients presenting with GERD symptoms.

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