

Natural History of Functional Dyspepsia



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Introduction

Dyspepsia is a common complaint, but the definition of dyspepsia has been evolving over the past 50 years.¹⁻⁵ Functional dyspepsia is a disorder characterized by the presence of chronic or recurrent symptoms of upper abdominal pain or discomfort in the absence of any known specific structural cause.⁴ Several consensus meetings have proposed standardized definitions for dyspepsia; however, there is no agreement, particularly about the overlap between heartburn and upper abdominal pain or discomfort.¹⁻⁴ Additionally, the term 'dyspepsia' is not often understood by patients.⁶

The reported prevalence for dyspepsia varies widely between different populations, possibly because most studies have focused on uninvestigated rather than functional dyspepsia.⁷⁻⁹ Furthermore, some of these studies may have included patients with reflux disease misclassified as functional dyspepsia; this makes interpretation of true prevalence difficult. Variations in the definition of dyspepsia and FD will also affect the prevalence. The prevalence of uninvestigated dyspepsia in India has been reported as 30.4% in a study from Mumbai.¹⁰

The annual incidence of dyspepsia has been estimated to range from 1% to 6%.⁹ There is a balance in the actual number of people reporting new symptoms and the number of people reporting symptom disappearance.

The symptoms of dyspepsia, gastroesophageal reflux and irritable bowel syndrome (IBS) overlap to a large extent. Some patients develop transition in symptoms from dyspepsia to IBS and vice versa, suggesting that the functional gastrointestinal disorders (FGID) are a spectrum of one disease. A dyspepsia subgroup classification is proposed for research purposes, based on the predominant symptom: (a) ulcer-like dyspepsia when pain is the predominant symptom, and (b) dysmotility-like dyspepsia when discomfort (not pain) is the predominant symptom.⁴ Unfortunately, the symptom profile is not specific for a particular physiologic disturbance. For example, early fullness, nausea, bloating, and upper abdominal discomfort may be associated with delayed gastric emptying, accelerated gastric emptying, or lack of gastric accommodation to a meal.³

Natural History

The natural history of functional dyspepsia (FD) is poorly defined.^{11,12} Symptoms often fluctuate and, in some cases, spontaneously disappear for long periods;^{11,12} In randomized-controlled trials, the placebo response in patients with FD is approximately 30% to 40%.¹³ This placebo response may partly reflect the natural fluctuations of upper gastrointestinal tract symptoms.¹⁴

Dyspepsia is a chronic disease in most patients. Approximately 30% to 50% of patients report improvement or resolution of their symptoms over a 5-year follow-up period.⁷⁻⁹ Most of this symptom resolution in community subjects is likely to represent spontaneous resolution, especially since no treatment has been found to give long-term relief.

Many longitudinal, population-based studies have evaluated the natural history of FD.

Olafsdottir and colleagues¹⁵ conducted a population-based study by mailing a questionnaire to the same age- and gender-stratified random sample of the Icelandic population aged 18–75 years in 1996 and again in 2006. Subjects were categorized into 4 subgroups of dyspepsia: frequent upper pain (more than 6 times per year), meal-related discomfort (discomfort related to eating), nausea or vomiting (once a week or more), and combination (>1 of 3 symptom complexes above); in addition, patients were classified as FD using a score. The FD criteria revealed a lower prevalence (14.0% in 1996, 16.7% in 2006) than the dyspepsia subgroup criteria (24.1% in 1996, 24.3% in 2006). FD was stable over the 10-year period; half of the FD patients continued to have the FD criteria and 22% had symptoms of IBS. FD was more common in young subjects and women.

One longitudinal population-based study¹⁶ in Olmsted County, Minnesota studied the natural history of IBS and its subgroups, as well as that of constipation, diarrhea, dyspepsia, and frequent abdominal pain over 12 years. Subjects were sent an initial GI symptom survey between 1988 and 1994, and then subsequently until 2003. Every subject received two surveys. The age- and sex-adjusted prevalence of dyspepsia increased slightly over 12-year follow-up, from 1.9% (95% CI: 1.5–2.4) to 3.3% (95% CI: 2.4 – 4.1). The increase was greater in females (2.0% to 4.2%) than in males. New-onset functional dyspepsia developed in 67 of 1323 (5.1%) over 12 years. In contrast 28 of 42 (66.7%) of subjects who had dyspepsia in the first survey had some resolution in their symptoms. Complete resolution of symptoms was reported only by approximately two-fifths of subjects; the majority continued to experience symptoms in some form 10 years later. The overall prevalence of each disorder was stable over time, but the turnover in symptom status was high. Many episodes of symptom disappearance were due to subjects changing symptoms rather than actual symptom resolution. In another population-based study from Finland,¹⁷ 201 subjects with dyspepsia were evaluated for fluctuation of GI functional symptoms including FD from 1993 to 2000. Approximately 37% of patients with ulcer-like, 20% of dysmotility-like, 22% of unspecified, 13% of reflux-like, and 34% of IBS-like dyspepsia had symptoms of the same subgroup as at baseline. Thus GI functional symptoms were unstable during prolonged periods of follow-up.

The majority of patients presenting in general practice with abdominal pain improve, with symptom resolution in 68% at 12 months. The functional diagnoses such as IBS and non-ulcer dyspepsia frequently overlap and are unstable, with patients moving from one functional diagnostic group to another over a 12 month observation period. Approximately 30% of people with dyspepsia will also report IBS symptoms.

In one systematic review,¹⁸ El-Serag and Talley identified 22 studies (1976–2002) which had examined the prevalence of dyspepsia. Only two studies provided information sufficient to calculate the prevalence of functional dyspepsia (11.5%–14.7%). The prevalence of uninvestigated dyspepsia ranged from 10% to 40%. When the definition of dyspepsia was restricted to participants with upper abdominal pain, the prevalence rate

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estimate was 5% to 12%. Thirteen studies (7 retrospective, 6 prospective) had evaluated the clinical course of FD. The follow-up duration was in the range 1.5-10 years for prospective studies and 5-27 years for retrospective studies; the median follow-up duration for all studies was approximately 5 years. Data on follow-up was obtained in 92.5–98.2% of prospective studies and in 67.7–82.2% of retrospective studies. All studies suggested that a proportion of patients will improve or go into symptom remission, but the rates of symptom disappearance varied widely between studies. A number of factors may influence these rates in addition to natural fluctuations of the disorder, including medical therapy.¹⁹ Unfortunately, uniform predictors of symptom change could not be identified from these studies.

Koloski and colleagues²⁰ followed up community subjects with either IBS or FD every 6 months for 18 months. They found that almost half of patients with FD had a change in their gastrointestinal symptom status during the follow-up, and that those patients without depression had more stable symptoms. This suggests that stratifying patients by psychiatric diagnosis may provide some prognostic information.

Patients with longstanding unexplained digestive symptoms are prone to develop reactive psychiatric disorders. Anxiety, depression, personality disorders, and a history of physical or sexual abuse are seen with increased frequency in these patients.²¹ One study found that psychotherapy led to reduction in symptoms over six years of follow up.²²

Dyspepsia and IBS are associated with anxiety, depression, medical consultation, sick leave and adverse effects on social life. In study from China, the degree of anxiety was an independent factor associated with health care utilization in patients with FD and IBS.²³

Kindt and colleagues²⁴ found that over 63 months, 22% of patients had disappearance of symptoms and 44% had an improvement; 5% were worse. Symptom disappearance was more likely in patients who were younger or who had less delayed gastric emptying.

Prognosis

Functional dyspepsia is not life-threatening and it has not been shown to be associated with any increase in mortality. Subgroups of functional dyspepsia play only a minor role in prediction of the long-term outcome, and usefulness of classification in clinical practice is hampered by subgroup instability over time.¹⁶ Though symptoms are unstable during prolonged periods of follow-up, only 2% of subjects develop a peptic ulcer over 7 years.¹⁷

Conclusions

Functional dyspepsia is a chronic disease and symptoms overlap with those of the functional gastrointestinal disorders. The symptoms of FD remain stable in some patients, but many patients have transition to symptoms of other FGIDs; approximately 10% develop spontaneous remission.

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