CLINICAL–ALIMENTARY TRACT

Epidemiology of Functional Dyspepsia and Subgroups in the Italian General Population: An Endoscopic Study

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BACKGROUND & AIMS: Population-based endoscopic studies are needed to assess the epidemiology of functional dyspepsia (FD) and the newly suggested subgroups of meal-related symptoms and epigastric pain. We evaluated the prevalence of, and risk factors for, FD in the Italian general population. **METHODS:** A total of 1533 inhabitants of 2 villages were invited to undergo symptom evaluation using a validated questionnaire, esophagogastroduodenoscopy, and ^{13}C-urea breath test; 1033 subjects (67.4%) took part. **RESULTS:** Of the 1033 subjects, 156 (15.1%; 95% confidence interval [CI], 12.9–17.3) had dyspepsia, and of these 114 (11%; 95% CI, 9.2–12.9) had FD. Of the 114 subjects with FD, 77 (67.5%) had meal-related symptoms (postprandial fullness and/or early satiation) and 55 (48.2%) had epigastric pain. Only 18 subjects (15.8%) had both meal-related symptoms and epigastric pain; this was fewer than expected by chance alone ($P < .001$). Unemployment (odds ratio [OR], 5.80; 95% CI, 1.56–21.60), divorce (OR, 2.76; 95% CI, 1.10–6.91), smoking (OR, 1.74; 95% CI, 1.11–2.70), and irritable bowel syndrome (OR, 3.38; 95% CI, 1.85–6.19) were significantly associated with FD. Unemployment, divorce, and irritable bowel syndrome were associated with both meal-related symptoms and epigastric pain, while smoking was associated only with meal-related symptoms. **CONCLUSIONS: FD is present in 11% of the Italian general population. Unemployment and divorce seem to increase the risk of FD, and smoking seems to be associated with meal-related symptoms. Two distinct subgroups of FD, as suggested by Rome III, seem to exist in the general population.**

Keywords: Epidemiology; Functional Dyspepsia; General Population.

Functional dyspepsia is a clinical syndrome characterized by chronic and recurrent gastroduodenal symptoms in the absence of any organic or metabolic disease that is likely to explain the symptoms.[1,2] The causes of functional dyspepsia remain uncertain and are likely to be multifactorial. Functional dyspepsia is associated with gastric motor sensitivity disorders and psychological factors, such as stress and depression, yet the role of these factors in the generation of symptoms remains unclear.[1–3] Functional dyspepsia is a common health and social problem. It dramatically reduces a patient's quality of life,[4] with an economic impact due to frequent clinical consultations, medication, and time off work.[5]

Data on the epidemiology of functional dyspepsia in the general population are sparse. A recent systematic review reported an estimated prevalence of functional dyspepsia of 12% to 15% in the community but highlighted the need for population-based endoscopic studies to examine the prevalence of documented functional dyspepsia.[6] The risk factors for functional dyspepsia, and in particular the association with sociodemographic and lifestyle factors, also remain poorly elucidated.[1–3]

A difficulty facing epidemiologic studies of functional dyspepsia is that the diagnosis of this condition is essentially a diagnosis of exclusion after endoscopy.[1,2] A number of population-based studies have provided data on the prevalence of, and risk factors for, functional dyspepsia, but the diagnosis of functional dyspepsia was based on symptom-defined criteria, and endoscopy was not performed.[7–11] Although most subjects with uninvestigated dyspepsia have functional dyspepsia, data extrapolated from such studies may be suboptimal, because subjects with organic dyspepsia had not been excluded.

Due to the difficulty associated with performing endoscopy in the community, to our knowledge, only 2 population-based endoscopic studies have been performed so far: the Sorreisa study in Norway[12] and recently the Kalixanda study in Sweden,[13] whereas only one, the Swedish study, used the Rome criteria to define functional dyspepsia. Two more endoscopic studies were performed in the community in the United States[14] and Taiwan[15]; however, they enrolled employed volunteers[14] or subjects receiving a self-paid physical checkup[15] instead of including a representative sample of the general population.

Abbreviations used in this paper: ^{13}C-UBT, ^{13}C-urea breath test; BMI, body mass index; CI, confidence interval; FD, functional dyspepsia; *H pylori*, *Helicobacter pylori*; IBS, irritable bowel syndrome; MICOL, Multicentre Italian Study on Cholelithiasis; OR, odds ratio.

0016-5085/10/$36.00
doi:10.1053/j.gastro.2009.12.057

Functional dyspepsia is most likely a heterogeneous condition consisting of different subgroups. Recently, the Rome III committee suggested patients with functional dyspepsia were divided into 2 subgroups, those with meal-related symptoms and those with epigastric pain, as the basis for clinical practice and research.[2] However, epidemiologic data on these 2 subgroups are sparse, and whether or not they are 2 distinct subgroups with different characteristics remains unclear.[16,17]

Further endoscopic studies in a representative sample of the general population are needed to improve the understanding of the epidemiology of functional dyspepsia and possibly of these new subgroups. Such studies may provide new insights into the management of patients with functional dyspepsia and may also be useful for clinical research.

The aim of this study was to evaluate the prevalence of, and risk factors for, documented functional dyspepsia and the 2 subgroups of meal-related dyspeptic symptoms and epigastric pain in a representative sample of the Italian general population.

Materials and Methods

Study Population

The study population was recruited from 2 Italian villages, Loiano and Monghidoro, as part of the Multicentre Italian Study on Cholelithiasis (MICOL), a population-based study including 2 cross-sectional surveys for the evaluation of the prevalence and incidence of gallstone disease.[18] Details regarding sampling procedures of the population were reported elsewhere.[19] Briefly, in the first MICOL survey, performed between 1985 and 1987, all 3547 inhabitants of the 2 villages aged 18 to 69 years were identified from the electoral roll and invited to participate. Of these, 2357 subjects took part. Ten years later, in 1996, 129 had died and 72 had moved away, and the remaining 2156 individuals were invited to participate to the second MICOL survey. Of these, 1533 (71.1%) aged 28 to 80 years gave informed consent to undergo a ^{13}C-urea breath test as part of an additional study of *Helicobacter pylori*.[20] Between 2000 and 2004, these 1533 subjects, who had not been given the result of the ^{13}C-urea breath test, were invited to take part in the present study. They were sent an explanatory letter and contacted by telephone to arrange an appointment. All participants were asked to withdraw from treatment with proton pump inhibitors, H_2-receptor antagonists, and antibiotics at least 4 weeks before assessment. A total of 1033 individuals aged 32–84 years were enrolled, yielding a response rate of those eligible for investigation of 67.4%. The study sample of 1033 subjects (51.1% male; mean age, 58.7 years) was representative of the source population in terms of sex (total population of the 2 villages over 32 years, 5133; 51.2% male; mean age, 55.8 years) but was older by 2.9 years ($P < .001$) mainly due to individuals younger than 35 years, who were underrepresented in the study sample (2.5% of the study sample vs 6.8% of the source population aged 32–34 years).

This study was approved by the ethical committee of Policlinico Sant'Orsola in Bologna, Italy, on September 19, 2000.

Assessments

During a single visit, participants underwent symptom assessment, esophagogastroduodenoscopy with multiple gastric biopsies, and ^{13}C-urea breath test. Data were also collected on age, sex, education level, occupation, marital status, weight and height, cigarette smoking, consumption of alcohol and coffee, and use of nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, and corticosteroids. Additionally, participants were asked about previous *H pylori* eradication therapy as well as personal and family history of gastroduodenal diseases. Details regarding these characteristics of the study sample have been reported elsewhere.[19]

Symptoms

Before the endoscopy, physician interviewers completed a detailed symptom assessment using a validated gastrointestinal symptom questionnaire that has been found to be reliable and reproducible.[21] The questionnaire showed good intraobserver and interobserver correlation. The average symptom Spearman correlation coefficient for the intraobserver reporting was 0.62 and for the interobserver reporting was 0.60.[21] The questionnaire recorded the frequency and severity of upper and lower gastrointestinal symptoms that had occurred at least once a month for 3 months during the previous year.[22] The frequency and severity of symptoms were graded using separate 5-point scales. The frequency of symptoms was graded as follows: 1 = absent, 2 = less than 2 days per week, 3 = at least 2 days per week but not daily, 4 = daily, intermittent; 5=daily, almost continuous. The severity of symptoms was scored as follows: 1 = no problem, 2 = mild, 3 = moderate (bothersome), 4 = severe, 5 = very severe.[21]

Definition of Symptom Groups

Dyspepsia was defined according to the modified Rome II criteria[1,23] as the presence of one or more symptoms of epigastric pain, postprandial fullness, or early satiation that occurred at least 2 days per week regardless of severity, or less than 2 days per week with at least moderate severity, for 3 months over the past year. The modified Rome II criteria[1,23] exclude from the definition of dyspepsia the symptoms of nausea and upper abdominal bloating alone, which were considered by Rome II criteria as cardinal symptoms of dyspepsia,[22] although they may cluster with dyspeptic

Table 1. Diagnostic Criteria for Functional Dyspepsia and the Subgroups of Meal-Related Symptoms and Epigastric Pain Used in the Study

Functional dyspepsia
Presence of epigastric pain, postprandial fullness or early satiation:
At least 2 days per week regardless of the severity, or less than 2 days per week with at least moderate severity, for at least 3 months during the previous year
Concomitant reflux symptoms absent or nonprominent (reflux symptoms mild and less than 2 days per week)
No endoscopic evidence of structural disease that is likely to explain the symptoms
Meal-related symptoms subgroup
Subjects with functional dyspepsia who have postprandial fullness and/or early satiation
Epigastric pain subgroup
Subjects with functional dyspepsia who have epigastric pain (pain localized to the epigastrium) not relieved by defecation or passage of flatus

NOTE. The 2 subgroups of symptoms may overlap.

symptoms. Heartburn and/or acid regurgitation may coexist with dyspeptic symptoms if they were mild and occurred less than 2 days per week (nonprominent reflux symptoms).[1,2]

Functional dyspepsia was defined as dyspepsia without esophagitis, Barrett's esophagus, peptic ulcer, acute gastroduodenal erosions or malignancy, and no evidence of other structural disease that was likely to explain symptoms (Table 1).[1,2]

Subjects with functional dyspepsia were divided into 2 subgroups: (1) a meal-related symptoms subgroup, including subjects with postprandial fullness and/or early satiation, and (2) an epigastric pain subgroup, including subjects with epigastric pain (pain localized to the epigastrium) not relieved by defecation or passage of flatus. The 2 subgroups of symptoms may overlap (Table 1).

Gastroesophageal reflux disease was defined as the presence of heartburn and/or acid regurgitation that occurred at least 2 days per week regardless of severity or less than 2 days per week with at least moderate (bothersome) severity (prominent reflux symptoms).[1,2]

Irritable bowel syndrome (IBS) was defined as the presence of abdominal pain that was relieved with defecation and/or associated with at least 2 of the following bowel habit disturbances: abnormal stool frequency, urgency of evacuation, feeling of incomplete evacuation, passage of mucus, bloating, or feeling of abdominal distention (Rome I criteria).[24]

Esophagogastroduodenoscopy

Upper gastrointestinal endoscopy was conducted by 3 experienced endoscopists from the Gastroenterology and Endoscopy Unit of Saint Orsola Hospital who were blinded to the subject's symptoms. Endoscopists participated in training sessions and agreed on the standardized definition that would be used for upper gastrointestinal organic lesions.[19]

Esophagitis was graded according to the modified Savary–Miller classification; mucosal erythema of the esophagus was excluded from this definition.[19] Barrett's esophagus was diagnosed when biopsy specimens taken from any suspected area of columnar-lined esophagus were seen to contain specialized intestinalized epithelium.[19] Peptic ulcer was defined as a mucosal break >3 mm in diameter with depth in the stomach and/or duodenum.[25] Acute gastroduodenal erosion was defined as a mucosal break ≤3 mm in diameter without depth in the stomach and/or duodenum.[25]

H pylori

H pylori status was assessed using the rapid urease test, histology, and ^{13}C-urea breath test, as previously described.[19,20] *H pylori* status was defined as positive if 2 of the 3 assessments were positive. The presence of chronic gastritis was also assessed according to the updated Sydney System.[26]

Statistical Methods

The crude prevalence rates of functional dyspepsia and subgroups were calculated as proportions of the total number of respondents. The age- and sex-adjusted prevalence rates were calculated using the direct method of standardization with the 2005 census of the Italian general population as the reference.[27]

To evaluate if the 2 subgroups of functional dyspepsia were distinct, we calculated the expected overlap between the 2 subgroups by multiplying the corresponding marginal proportions. Then we compared the expected overlap with the observed overlap using the exact binomial test for proportions.

The association of functional dyspepsia and subgroups of functional dyspepsia with putative risk factors was evaluated using a multivariable logistic regression analysis. Risk was examined using subjects with no dyspeptic symptoms as the baseline group. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated following adjustment for age, sex, education level, occupation, marital status, body mass index (BMI) (calculated as weight in kilograms divided by the square of height in meters [kg/m^2]), cigarette smoking (ever having smoked, including past and current smokers, vs never having smoked), alcohol (none, weekly, or daily consumption of wine, beer, or spirits) and coffee consumption (none or any), use of medication (defined as use of NSAIDs, aspirin, or corticosteroids), *H pylori* infection, and presence of chronic gastritis and IBS. All analyses were conducted using Stata statistical software (Stata Corp, College Station, TX).

Results

Prevalence of Dyspepsia and Functional Dyspepsia

Of the 1033 subjects, 156 (15.1%; 95% CI, 12.9–17.3) had dyspepsia, while the remaining 887 subjects were classified as having no dyspepsia. Of the 887 subjects, 174 had dyspeptic symptoms but did not meet the criteria of dyspepsia due to the presence of concomitant prominent reflux symptoms.

Of the 156 subjects with dyspepsia, 114 (73.1%) had functional dyspepsia, while 42 (26.9%) had structural lesions including esophagitis (n = 13; 9%), Barrett's esophagus (n = 2; 1.3%), peptic ulcer (n = 14 [9%]; gastric ulcer, n = 3 [1.9%], duodenal ulcer, n = 11 [7.1%]), gastroduodenal erosions (n = 9; 5.8%), and gastric cancer (n = 4; 2.3%). One subject had both esophagitis and gastric cancer. The association between dyspeptic symptoms and organic lesions was reported elsewhere.[28]

The prevalence of functional dyspepsia in the study sample was 11% (114/1033; 95% CI, 9.2–12.9): 9.7% in men (51/528; 95% CI, 7.3–12.5) and 12.5% in women (63/505; 95% CI, 9.7–15.7).

Eighty-five subjects (74.6%) with functional dyspepsia did not report reflux symptoms, while 29 (25.4%) reported concomitant although nonprominent reflux symptoms. Postprandial fullness and epigastric pain were the most frequent dyspeptic symptoms (Figure 1). Table 2 summarizes the frequency and severity of individual dyspeptic symptoms in the group of subjects with functional dyspepsia.

Of 114 subjects with functional dyspepsia, 77 (67.5%) had meal-related symptoms (postprandial fullness and/or early satiation) and 55 (48.2%) had epigastric pain, whereas 18 (15.8%) had both meal-related symptoms and epigastric pain. The prevalence of the 2 subgroups of meal-related symptoms and epigastric pain in the study sample was 7.4% (77/1033; 95% CI, 5.9–9.2) and 5.1% (55/1033; 95% CI, 4.0–6.9), respectively, while 1.7% of subjects reported an overlap of the 2 subgroups of symptoms (18/1033; 95% CI, 1.0–2.7).

Table 2. Frequency and Severity of Individual Dyspeptic Symptoms in 114 Subjects With Functional Dyspepsia

	Epigastric pain	Postprandial fullness	Early satiation
Frequency			
Absent	59 (51)	46 (40)	78 (68)
<2 Days/wk	10 (9)	13 (11)	3 (3)
≥2 Days/wk	24 (21)	32 (28)	14 (12)
Daily, intermittent	19 (17)	13 (11)	11 (10)
Daily, almost continuous	2 (2)	10 (9)	8 (7)
Severity			
Absent	59 (51)	46 (40)	78 (68)
Mild	11 (10)	17 (15)	6 (5)
Moderate	26 (23)	42 (37)	25 (22)
Severe	16 (14)	8 (7)	4 (4)
Very severe	2 (2)	1 (1)	1 (1)

NOTE. Numbers in parentheses represent column percentages.

Assuming that the 2 subgroups were independent, the expected number of subjects having an overlap of the 2 subgroups by chance was 37, calculated by multiplying the corresponding marginal proportions. We found that the observed number of subjects with overlap of the 2 subgroups was statistically significantly less than that expected by chance (18 subjects observed vs 37 subjects expected; $P < .001$, exact binomial test), indicating that the 2 subgroups may be distinct.

The prevalence of individual symptoms in the 2 subgroups of meal-related symptoms and epigastric pain is shown in Figure 2.

Table 3 shows the age- and sex-adjusted prevalence rates of functional dyspepsia and the subgroups of meal-related symptoms and epigastric pain in the adult Italian population. There was no difference between the crude and the age- and sex-adjusted prevalence rates.

Associations With Dyspepsia

Unemployment (OR, 3.92; 95% CI, 1.08–14.27), divorce (OR, 2.94; 95% CI, 1.34–6.46), cigarette smoking

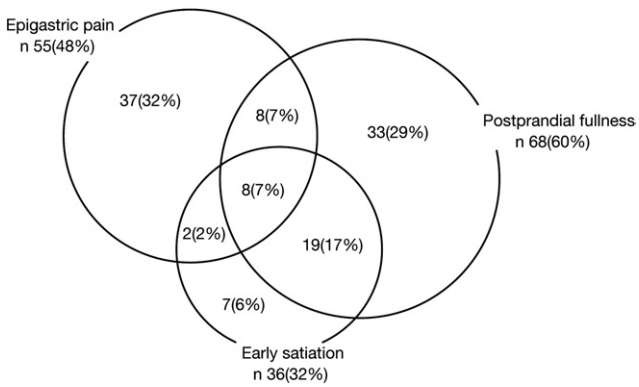

Figure 1. Prevalence of individual dyspeptic symptoms in subjects with functional dyspepsia.

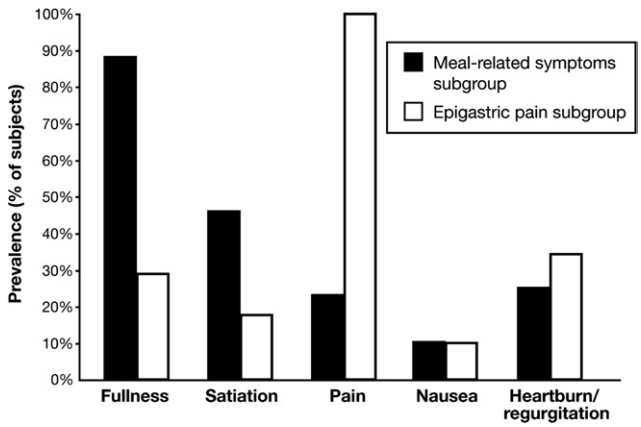

Figure 2. Symptom pattern in the subgroups of meal-related symptoms and epigastric pain. Note. Nonprominent heartburn/regurgitation.

Table 3. Age- and Sex-Adjusted Prevalence Rates of Functional Dyspepsia and the Subgroups of Meal-Related Symptoms and Epigastric Pain, Directly Standardized, in the Italian General Population

	Total	Male	Female
Functional dyspepsia (n = 114)	11.9 (10.2–13.6)	10.7 (8.5–12.9)	12.9 (10.4–15.5)
Meal-related symptoms subgroup (n = 77)	6.4 (5.0–7.8)	6.1 (4.2–7.9)	6.7 (4.6–8.8)
Epigastric pain subgroup (n = 55)	7.2 (5.9–8.5)	6.2 (4.8–7.7)	8.0 (6.0–10.1)

NOTE. 2005 Census of the Italian population.[27] Values are expressed as percent (95% CI).

(OR, 2.24; 95% CI, 1.51–3.32), and IBS (OR, 3.04; 95% CI, 1.74–5.33) were the only factors associated with uninvestigated dyspepsia (Table 4). No associations were found between age, sex, education level, BMI, alcohol or coffee consumption, use of medications (NSAIDs/aspirin or corticosteroids), or *H pylori* infection and uninvestigated dyspepsia.

Associations With Functional Dyspepsia and Subgroups

Functional dyspepsia. Unemployment (OR, 5.80; 95% CI, 1.56–21.60), divorce (OR, 2.76; 95% CI, 1.10–6.91), cigarette smoking (OR, 1.74; 95% CI, 1.11–2.70), and IBS (OR, 3.38; 95% CI, 1.85–6.19) were also associated with functional dyspepsia (Table 4).

We found that the prevalence of *H pylori* infection in subjects with functional dyspepsia was significantly lower than in those with no dyspepsia (OR, 0.50; 95% CI, 0.31–0.81). However, a history of previous successful eradication of *H pylori* was more frequently reported by *H pylori*–negative subjects with functional dyspepsia than those with no dyspepsia (23% [15/65] vs 13.5% [49/364]; OR, 1.93; 95% CI, 1.01–3.70). When we considered as *H pylori* negative those subjects with current *H pylori* negative status and no history of previous successful eradication (never *H pylori*), no associations were found between *H pylori* and functional dyspepsia (OR, 0.76; 95% CI, 0.46–1.25) (Table 4).

Age, sex, low education level, BMI, alcohol or coffee consumption, use of medications (NSAIDs/aspirin or corticosteroids), and presence of chronic gastritis were not associated with functional dyspepsia. No association was observed between BMI and functional dyspepsia even after stratification for overweight (BMI 25–29 kg/m^2: OR, 1.07; 95% CI, 0.67–1.70) and obesity (BMI ≥30 kg/m^2: OR, 0.54; 95% CI, 0.28–1.05).

Meal-related symptoms and epigastric pain subgroups. The multivariable logistic regression analysis showed that being unemployed or divorced was a risk factor for both meal-related symptoms (OR, 3.75; 95% CI, 1.57–8.95) and epigastric pain (OR, 3.04; 95% CI, 1.06–8.68) subgroups, while smoking was a risk factor for meal-related symptoms (OR, 1.98; 95% CI, 1.17–3.35) but not for epigastric pain (Table 5). IBS was associated with both the subgroups of functional dyspepsia (meal-related symptoms: OR, 4.07 [95% CI, 2.04–8.11]; epigastric pain: OR, 3.87 [95% CI, 1.82–8.22]). We also found that subjects with epigastric pain had a reduced BMI, although this was borderline statistically significant (OR, 0.91; 95% CI, 0.85–0.99) (Table 5).

Discussion

This study showed a prevalence of dyspepsia in the Italian general population of 16% with a prevalence of functional dyspepsia of 11%. We found that unemployment, divorce, cigarette smoking, and IBS were significantly associated with dyspepsia and functional dyspepsia. Unemployment, divorce, and IBS were associated with both meal-related symptoms and epigastric pain, while smoking was associated only with meal-related symptoms. We also found that the subgroup of subjects with epigastric pain had a reduced BMI, but not those with meal-related symptoms. No associations were found between age, sex, education level, increased BMI, alcohol or coffee consumption, use of medications (NSAIDs/aspirin or corticosteroids), *H pylori* infection, or chronic gastritis and functional dyspepsia.

We found that the prevalence of functional dyspepsia in the Italian general population is similar to that reported by the endoscopic studies in Norway (13%) and Sweden (15%).[12,13] A relevant finding was that only 15% of subjects with functional dyspepsia reported an overlap of the 2 subgroups of meal-related symptoms and epigastric pain and that this overlap is unlikely to be due to chance. The Swedish study reported similar data with only 11% of subjects with functional dyspepsia having both meal-related symptoms (postprandial distress syndrome) and epigastric pain.[13] Previous attempts failed to define distinct subgroups of functional dyspepsia based on cluster of symptoms (Rome I) or on the predominant symptom (Rome II).[1] Our finding would support the Rome III suggestion that subjects with meal-related dyspeptic symptoms and those with epigastric pain may be 2 distinct subgroups of functional dyspepsia.[2]

To our knowledge, this is the first population-based endoscopic study to evaluate the relationship between functional dyspepsia and occupation and marital status. A number of population-based studies showed an association between unemployment and uninvestigated dyspepsia, suggesting, as most subjects with uninvestigated dyspepsia have functional dyspepsia, unemployment could be a risk factor for functional dyspepsia.[29,30] This study confirmed the results of such studies showing this

Table 4. Characteristics of Participants With Dyspepsia and Functional Dyspepsia in Comparison With Individuals With No Dyspepsia

	No dyspepsia (n = 877)	Dyspepsia (n = 156)		Functional dyspepsia (n = 114)	
	n (%)	n (%)	OR (95% CI)	n (%)	OR (95% CI)
Demographic factors					
Age (*y*)					
Mean (SD)	58.6 (13.1)	59.4 (13.1)	1.02 (0.99–1.04)	59.3 (13.1)	1.01 (0.99–1.04)
Sex					
Male	462 (52.7)	66 (42.3)	1.0	51 (44.7)	1.0
Female	415 (47.3)	90 (57.7)	1.38 (0.87–2.18)	63 (55.3)	1.06 (0.62–1.79)
Education level					
Above elementary	516 (58.8)	91 (58.3)	1.0	63 (55.3)	1.0
Elementary	361 (41.2)	65 (41.7)	1.06 (0.66–1.71)	51 (44.7)	1.32 (0.76–2.29)
Occupation					
Employed	442 (50.4)	73 (46.8)	1.0	53 (46.5)	1.0
Retired	319 (36.4)	50 (32.1)	0.75 (0.41–1.34)	35 (30.7)	0.71 (0.37–1.40)
Housewife	108 (12.3)	28 (17.9)	1.23 (0.65–2.33)	22 (19.3)	1.48 (0.72–3.04)
Unemployed	8 (0.9)	5 (3.2)	3.92 (1.08–14.27)	4 (3.5)	5.80 (1.56–21.60)
Marital status					
Married	687 (78.3)	122 (78.2)	1.0	90 (78.9)	1.0
Never married	113 (12.9)	15 (9.6)	0.89 (0.48–1.65)	11 (9.7)	0.78 (0.38–1.61)
Widowed	55 (6.3)	8 (5.1)	0.64 (0.28–1.46)	6 (5.3)	0.63 (0.25–1.61)
Divorced	22 (2.5)	11 (7.1)	2.94 (1.34–6.46)	7 (6.1)	2.76 (1.10–6.91)
Lifestyle factors					
BMI (kg/m^2)[a]					
Mean (SD)	26.5 (4.4)	26.0 (4.7)	0.97 (0.93–1.02)	25.9 (4.0)	0.97 (0.92–1.02)
Ever smoking					
No	477 (54.4)	68 (43.6)	1.0	56 (49.1)	1.0
Yes	400 (45.6)	88 (56.4)	2.24 (1.51–3.32)	58 (50.9)	1.74 (1.11–2.70)
Alcohol consumption					
None	316 (36.0)	71 (45.5)	1.0	47 (41.2)	1.0
Weekly	143 (16.3)	24 (15.4)	0.97 (0.56–1.67)	20 (17.5)	1.21 (0.66–2.22)
Daily	418 (47.7)	61 (39.1)	0.77 (0.49–1.21)	47 (41.2)	0.83 (0.49–1.39)
Coffee consumption					
No	174 (19.8)	42 (26.9)	1.0	27 (23.7)	1.0
Yes	703 (80.2)	114 (73.1)	0.69 (0.44–1.08)	87 (76.3)	0.82 (0.49–1.37)
Medication use[b]					
No	803 (91.6)	143 (91.7)	1.0	105 (92.1)	1.0
Yes	74 (8.4)	13 (8.3)	0.92 (0.48–1.76)	9 (7.9)	0.88 (0.42–1.88)
Other factors					
Current *H pylori* status[c]					
Negative	364 (41.5)	73 (46.8)		65 (57.0)	
Positive	513 (58.5)	83 (53.2)		49 (43.0)	N/A
Ever *H pylori*[d]					
No	315 (35.9)	56 (35.9)	1.0	50 (43.9)	1.0
Yes	562 (64.1)	100 (64.1)	1.13 (0.71–1.79)	64 (56.1)	0.76 (0.46–1.25)
Chronic gastritis					
No	164 (18.8)	28 (18.3)	1.0	24 (21.2)	1.0
Yes	706 (81.2)	125 (81.7)	0.78 (0.44–1.37)	89 (78.8)	0.81 (0.44–1.50)
IBS					
No	828 (94.4)	132 (84.6)	1.0	95 (83.3)	1.0
Yes	49 (5.6)	24 (15.4)	3.04 (1.74–5.33)	19 (16.7)	3.38 (1.85–6.19)

NOTE. OR and 95% CI interval calculated using a multivariable logistic regression model adjusted for all variables in the table except for current *H pylori* status.

[a]BMI was unknown in 7 subjects with no dyspepsia, 3 subjects with dyspepsia, and 2 subjects with functional dyspepsia.

[b]Defined as use of NSAIDs, aspirin, or corticosteroids.

[c]Forty-nine *H pylori*–negative subjects with no dyspepsia, 17 *H pylori*–negative subjects with dyspepsia, and 15 *H pylori*–negative subjects with functional dyspepsia reported previous successful eradication of *H pylori*.

[d]Never *H pylori* includes subjects with current *H pylori*–negative status and no history of previous successful *H pylori* eradication, and ever *H pylori* includes subjects with current *H pylori*–positive status and those with current *H pylori*–negative status but history of previous successful *H pylori* eradication.

Table 5. Characteristics of Subjects of the Subgroups of Meal-Related Symptoms and Epigastric Pain

	No dyspepsia (n = 877)	Meal-related symptoms subgroup (n = 77)		Epigastric pain subgroup (n = 55)	
	OR (95% CI)	n (%)	OR (95% CI)	n (%)	OR (95% CI)
Demographic factors					
Age (*y*)					
Mean (SD)	1 (—)	60.4 (12.8)	1.01 (0.99–1.04)	58.0 (13.3)	1.0 (0.97–1.03)
Sex					
Male	1 (—)	39 (50.6)	1.0	23 (41.8)	1.0
Female		38 (49.4)	0.98 (0.54–1.77)	32 (58.2)	1.39 (0.71–2.72)
Education level					
Above elementary	1 (—)	42 (54.5)	1.0	32 (58.2)	1.0
Elementary		35 (45.5)	1.26 (0.67–2.35)	23 (41.8)	1.32 (0.62–2.83)
Unemployed or divorced					
No	1 (—)	69 (89.6)	1.0	50 (90.9)	1.0
Yes		8 (10.4)	3.75 (1.57–8.95)	5 (9.1)	3.04 (1.06–8.68)
Lifestyle factors					
BMI (kg/m^2)					
Mean (SD)	1 (—)	26.4 (3.8)	0.99 (0.94–1.06)	25.0 (4.0)	0.91 (0.85–0.99)
Ever smoking					
No	1 (—)	34 (44.2)	1.0	28 (50.9)	1.0
Yes		43 (55.8)	1.98 (1.17–3.36)	27 (49.1)	1.43 (0.79–2.61)
Alcohol consumption					
None	1 (—)	31 (40.3)	1.0	21 (38.2)	1.0
Weekly		14 (18.2)	1.22 (0.60–2.50)	10 (18.2)	1.33 (0.58–3.04)
Daily		32 (41.6)	0.67 (0.36–1.25)	24 (43.6)	1.07 (0.52–2.18)
Coffee consumption					
No	1 (—)	19 (34.7)	1.0	12 (21.8)	1.0
Yes		58 (75.3)	0.80 (0.44–1.46)	43 (78.2)	0.85 (0.41–1.75)
Medication use[a]					
No	1 (—)	70 (90.1)	1.0	51 (92.7)	1.0
Yes		7 (9.9)	1.02 (0.43–2.38)	4 (7.3)	0.90 (0.30–2.67)
Other factors					
Ever *H pylori*[b]					
No	1 (—)	32 (41.6)	1.0	25 (45.5)	1.0
Yes		45 (58.4)	0.76 (0.42–1.36)	30 (54.5)	0.92 (0.45–1.89)
Chronic gastritis					
No	1 (—)	14 (17.1)	1.0	15 (25.9)	1.0
Yes		63 (82.9)	1.02 (0.48–2.19)	40 (74.1)	0.59 (0.26–1.37)
IBS					
No	1 (—)	63 (81.8)	1.0	44 (80)	1.0
Yes		14 (18.2)	4.07 (2.04–8.11)	11 (20)	3.87 (1.82–8.22)

NOTE. Subjects with no dyspepsia were used as the baseline control group. OR and 95% CI calculated using a multivariable logistic regression model adjusted for all variables in the table.

[a]Defined as use of NSAIDs, aspirin, or corticosteroids.

[b]Never *H pylori* includes subjects with current *H pylori*–negative status and no history of previous successful *H pylori* eradication, and ever *H pylori* includes subjects with current *H pylori*–positive status and those with current *H pylori*–negative status but history of previous successful *H pylori* eradication.

association and provided evidence that unemployment increases the risk of functional dyspepsia.

As is well known, both unemployment[31,32] and divorce[33,34] are associated with psychological distress and depression, and this is most likely the link between these conditions and functional dyspepsia. A strong association between stressful life conditions and functional dyspepsia has been largely reported in patients seeking health care.[35,36] There is now increasing evidence that psychopathological factors are associated with functional dyspepsia, not only in subjects who seek health care but also in subjects in the general population.[13,37,38] If psychological distress and depression is the link between these conditions and functional dyspepsia, our study provides further, albeit indirect, evidence that psychopathological factors are likely to play a major role in the etiopathogenesis of functional dyspeptic symptoms. In Western countries, unemployment[27,39] and divorce[27,40] are increasing, and this may cause an increase of the prevalence of functional dyspepsia in the general population.

Very little is known about the association between smoking and functional dyspepsia, and although stopping smoking is recommended for patients with func-

tional dyspepsia, any strong evidence of an association has been lacking.[1,2] The Norway study showed that smoking was a risk factor for functional dyspepsia,[12] but the Swedish study[13] and a study on selected patients[41] did not confirm this. On the other hand, several population-based studies showed an association between smoking and uninvestigated dyspepsia.[29,30,42,43] Smoking is a risk factor for underlying organic lesions,[44] but this does not exclude also an association with functional dyspepsia. Our study showed that smoking is a risk factor for functional dyspepsia, but notably it only increases the risk of the meal-related symptoms, namely postprandial fullness and/or early satiation, and not the risk of epigastric pain. Experimental studies have shown that cigarette smoking may delay gastric emptying,[45,46] and this is a possible mechanism behind such an association.[47]

We found no association between obesity and functional dyspepsia. Some studies reported an association between obesity and dyspeptic symptoms, but subjects with gastroesophageal reflux disease may not have been excluded.[13,48] We found instead that subjects with functional dyspepsia, and in particular those with epigastric pain, had a statistically significant reduced BMI. Clinical studies have shown a sizeable and statistically significant association between functional dyspepsia and weight lost, and our result seems to be in line with these data.[49]

Finally, our study confirmed the presence of a significant overlap between IBS and functional dyspepsia and also showed that IBS was associated with both meal-related symptoms and epigastric pain. This finding is in agreement with clinical studies and supports the suggestion that, at least in a subgroup of patients, IBS and functional dyspepsia may be different manifestations of the same disorder.[50]

This is only the second study in a representative sample of the general population to evaluate the prevalence of, and risk factors for, functional dyspepsia using a recent Rome definition and applying endoscopy to exclude the presence of organic lesions. Functional dyspepsia was defined according with the modified Rome II criteria[1,23] because the study was performed before Rome III, but the functional dyspepsia subgroups of meal-related symptoms and epigastric pain were classified following the suggestion of the Rome III committee.[2]

We acknowledge that this study did not use all the specific criteria of Rome III for the definition of the subgroups of functional dyspepsia, but this is only a relative limitation. The main limitation of this study is that we do not have data on the characteristics of individuals who did not respond. A possible selection bias may be due to the requirement of an endoscopy procedure. This may skew sampling of volunteers by preferentially attracting more subjects with symptoms than without. However, in a similar study in Sweden, Aro et al showed that endoscopy was not a major, clinically relevant source of selection bias.[51] Furthermore, our study sample was similar to the general Italian population in terms of levels of obesity, alcohol use, and smoking, which suggests that the associations were not due to bias.[19] Another limitation may be the low number of subjects, in particular for the subgroups of functional dyspepsia. Both type I and II errors may occur and may bias some of our results. However, considering the paucity of data and the difficulty of performing a population-based endoscopic study, our results are still valuable.

In conclusion, functional dyspepsia is a common condition in the general population with a similar prevalence in northern and southern European countries. Unemployment and divorce seem to be associated with an increased risk of functional dyspepsia, suggesting a major role of psychopathological factors. Smoking is a risk factor for functional dyspepsia, although only for the subgroup of meal-related symptoms. Two distinct subgroups of subjects with functional dyspepsia with different risk factor profiles seem to exist in the general population, as indicated by the Rome III committee.

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Received September 11, 2009. Accepted December 29, 2009.

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Acknowledgments

The authors thank Drs D. Beretti, M. L. Bianchi, L. Ceroni, L. De Luca, S. Fossi, S. Maltoni, C. Martuzzi, G. Nicolini, P. Pozzato, and L. Ricciardiello for collaboration; Dr D. Panuccio, who was the head of the Unit of Internal Medicine of the Hospital of Loiano at the time of the study; and the primary care physicians of Loiano and Monghidoro—Drs De Stefano, L. Gaggioli, C. Gaggioli, and C. L. Navarra—for their help in coordinating the study.

Conflicts of interest

The authors disclose no conflicts.

Funding

Supported by a grant from the "Fondazione del Monte di Bologna e Ravenna," Italy.