#### ORIGINAL CONTRIBUTIONS



# **Functional Gastrointestinal Disorders in Obese Patients. The Importance of the Enrollment Source**

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#### Abstract

*Background* Obesity is frequently associated to many functional gastrointestinal disorders. The aim of the present study was to assess the prevalence of functional gastrointestinal disorders in obese patients, according to their body mass index and their recruitment source.

*Methods* Five hundred ninety-six obese patients (body mass index (BMI)>30) filled out a standard questionnaire in order to evaluate the presence of functional gastrointestinal disorders. They were divided into four groups according to the Rome III criteria and their BMI: OF, obese patients from functional gastrointestinal disorder (FGID) enrollment; OO, obese patients from obesity management enrollment; MF, morbid obesity patients from FGID enrollment; and MO, morbid obesity patients from obesity management enrollment. Data analysis was performed using multivariate logistic regression.

*Results* Out of the 596 obese patients included in the present study, 183 (33 %) were complaining of FGIDs, while 413 (67 %) were consulting for obesity management. Compared to the OF group, the OO patients had a higher prevalence of females (P=0.008) and a younger age (P<0.001). Clinically,

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they reported a lower incidence of regurgitation (P=0.044), of chest pain (P=0.004), of irritable bowel syndrome (IBS; P= 0.035), and of functional diarrhea (P=0.030). Compared to the MF group, the MO patients had an older age (P=0.001), a higher BMI (P=0.013), and clinically by a high frequency of functional dyspepsia (P=0.006). There were symptoms that had similar prevalence in all groups (OF, OO, MF, MO) such as epigastric pain, postprandial distress, constipation, diarrhea, bloating, abdominal pain soiling, or nonspecific anorectal disorders.

*Conclusions* This study has shown that the recruitment source accounted for marked and specific differences in the prevalence of functional gastrointestinal disorders in obesity and morbid obesity. Symptoms with similar prevalence in all groups should be systematically detected in all patients.

**Keywords** Morbid obesity · Obesity · Functional gastrointestinal disorders · Rome criteria

#### Introduction

The World Health Organization (WHO) estimated that in 2008, 1.5 billion adults were overweight, with a body mass index (BMI) of 25 kg/m<sup>2</sup> or higher [1]. In France, the prevalence of overweight and obesity is relatively low in comparison with the USA [2, 3] but steadily increasing [4]. In France, in 2012, 32.3 % of the population was overweight and 15 % obese [3]. In comparison, the prevalence of overweight people in the USA in 2009–2010 was 69.2 %, and the prevalence of obesity was 35.9 % [2]. Overweight and obesity are responsible for an increase of type 2 diabetes, ischemic heart disease, and more deaths worldwide than underweight. In addition, obesity constitutes an economic burden on both public and private health services. Across all health services, per capita

medical spending for obese patients is US\$1,429 higher per year or roughly 42 % higher than the medical bills for a person of normal weight [5].

Functional gastrointestinal disorders (FGIDs) have a high prevalence among the general population: 20–40 % for esophageal disorders [6], 20 to 30 % for dyspeptic symptoms [7], 10–20 % for bowel symptoms, with a female predominance [8], 0.5 to 2 % for abdominal pain [9], and 2.2 to 15 % for anorectal disorders [10]. These disorders of unknown etiology are the origin of a symptom-based classification, used for clinical diagnosis, evidence-based management, and research: the Rome III criteria [11]. The somatic and psychosocial nature of these symptoms explains the complexity of the pathways of care. The absence of clear definition for such diseases leads to diagnostic delay and is the main reason for the difficulty to assess the cost of these pathologies [12].

The association between obesity and FGIDs, two common disorders, is often debated. Abdominal pain, irritable bowel syndrome (IBS), bloating, pyrosis, and gastro-esophageal reflux disease (GERD) symptoms are known to be significantly more prevalent in overweight patients [13–16], and BMI is associated positively with abdominal pain and diarrhea [17]. These studies were mainly performed on patients complaining of digestive symptoms [18, 19]. Other studies evaluating the relation between gastrointestinal symptoms and obesity are discordant. In a previous study on patients' eligible for bariatric surgery, we found a prevalence of 90 % of FGIDs with a high prevalence of functional bowel disorders [20]. In contrast, in a recent study on the relationship between FGIDs and BMI in patients complaining of FGIDs [21], we mainly found an increase of esophageal symptoms. The aim of the present study was to establish if the type of the enrollment can have an impact in the prevalence of FGIDs in obese patients and morbidly obese patients consulting for FGID or overweight management.

# **Patients and Methods**

#### Subjects

All the patients were consulted in the gastrointestinal unit of Avicenne Hospital (Assistance Publique – Hôpitaux de Paris) for FGIDs or overweight management before the insertion of a gastric balloon or bariatric surgery and were subsequently referred to the Centre d'Exploration Fonctionnelle et de Rééducation Digestive (CEFRED). Five hundred and ninety-six patients (85 % females), aged 44.6±14.2 years (M±standard deviation (SD)), filled out a clinical questionnaire and were included in the present study (Fig. 1). A full evaluation failed to yield an organic cause for their complaint. This included morphological evaluations (endoscopy or radiology) and the ruling out of metabolic, endocrinologic, and neurologic

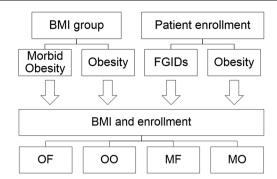


Fig. 1 Flow diagram of patient recruitment. Patients were divided according to the source of recruitment: functional gastrointestinal disorders (FGIDs) or obesity. Abbreviations: *OF* obese patients from FGID enrollment, *OO* obese patients from obesity enrollment, *MF* morbid obesity patients from FGID enrollment, *MO* morbid obesity patients from obesity enrollment

etiologies. None of these patients were using narcotics or had had any previous surgery of the gastrointestinal tract.

#### **Experimental Procedure**

#### Study Design and Group Definition

All the obese patients were divided into two groups according to their BMI:

- Obese (obesity class 1): BMI over 30 and under 35 kg/m<sup>2</sup>
- Morbidly obese (obesity class 2 and 3): BMI of 35 kg/m<sup>2</sup> or more

All patients were divided into two groups according to their main complain which was obesity or FGID treatment.

In order to study the effect of BMI and the type of enrollment, four groups were created:

- OF: obese patients from FGID enrollment
- OO: obese patients from obesity management enrollment
- MF: morbid obesity patients from FGID enrollment
- MO: morbid obesity patients from obesity management enrollment

The comparison of the groups of patients according to the origin of their recruitment was performed in a retrospective observational study.

#### Questionnaires

Patients filled out a standard clinical questionnaire based on questions to diagnose their FGIDs [20]. The interpretation was based on the functional disorders as defined by the Rome III criteria.

Functional esophageal disorders such as heartburn, chest pain of presumed esophageal origin, dysphagia, and globus were diagnosed in the absence of both gastro-esophageal reflux and histopathology-based esophageal motility disorders [6]. In addition to the above-mentioned symptoms, regurgitation was recorded.

Functional gastro-duodenal disorders such as dyspepsia, postprandial distress syndrome, epigastric pain syndrome, belching disorders, and aerophagia were diagnosed when there was no evidence of structural disease at upper endoscopy, abnormal behavior (self-induced vomiting, chronic cannabinoid use), central nervous system abnormalities, or metabolic diseases that could explain the symptoms [7].

IBS was diagnosed when recurrent abdominal pain or discomfort for at least 3 days per month in the last 3 months was associated with two or more of the following: improvement with defecation and onset associated with a change in frequency of stool or with a change in form (appearance) of stool. Subtypes of IBS (IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), mixed IBS (IBS-M), and unsubtyped IBS (IBS-U)) were defined according to the Rome III criteria [8]. Other functional bowel disorders (bloating, constipation, diarrhea, and unspecified) were diagnosed when the criteria for a diagnosis of IBS were insufficient or absent. Finally, nonspecific bowel disorders were diagnosed by default when patients did not meet the above-mentioned criteria.

As indicated by the Rome III criteria, establishing a diagnosis for functional abdominal pain syndrome includes all of the following: continuous or nearly continuous abdominal pain and no or only occasional connection between pain and physiological events (e.g., eating, defecation, or menses) associated with some loss of daily functioning [9]. We verified that patients did not present any symptoms that met the criteria for another functional gastrointestinal disorder that would explain the pain.

For functional anorectal disorders, the Rome III criteria were used for the diagnosis of functional fecal incontinence and functional anorectal pain, including levator ani syndrome, proctalgia fugax, and difficult defecation [10].

A questionnaire about urinary (urinary incontinence, dysuria) and sexual complaints (dyspareunia, impotence) was filled out by all the patients as previously described [22].

#### Statistical Analysis

Statistical analyses were carried out using IBM SPSS (IBM SPSS Statistics v20). The results are expressed as mean±standard deviation (SD). ANOVA with post hoc tests using Bonferroni correction was used for the analysis of the quantitative variables, and chi-square tests were used to analyze the qualitative variables.

Logistic regression was used for data analysis that systematically included the groups as dependent variables and age, sex, and functional disorders as independent variables. For the analysis of the recruitment sources, a logistic regression model, with the FGIDs used as a reference group, was created for each symptom adjusted for age and BMI. The backwards selection procedure was used for model selection during the multivariate logistic regression. Statistically significant variables (P<0.05) remained in the adjusted model.

#### Results

# Patients' Characteristics According to the Importance of Their Obesity and the Type of Recruitment

The demographic and clinical descriptions of the subtypes of the obese patients defined by their type of recruitment and their body mass index are summarized in Table 1. Out of the 596 patients included in the present study, 183 (33 %) complained of FGIDs, while 413 (67 %) consulted mainly for obesity management.

The patients from the obesity recruitment group had higher BMI (41.8±6.5 vs 34.2±4.5; P<0.001), were younger (40.7± 12.2 vs 53.3±14.4; P<0.001), and mostly females (90 vs 73 %; P<0.001) than the obese patients from the functional disease recruitment. In the BMI group, the morbid obese patients had a higher BMI, were younger, and mostly females. The same patterns were observed in the OF, MF, OO, and MO groups (Table 1).

 Table 1
 Demographic of subtypes of obese patients defined by the type of recruitment and/or their body mass index

All patients		Recruitment	t	Body mass	index	Recruitmen	t and body ma	ass index	
		FGID	Obesity	Obese	Morbid obesity	OF	MF	00	МО
N (%)	596 (100)	183 (33)	413 (67)	185 (31)	411 (69)	132 (22)	51 (9)	53 (9)	360 (60)
BMI (kg/m <sup>2</sup> )	39.5±6.9	34.2±4.5	41.8±6.5**	32.2±1.4	42.7±5.8**	32.0+1.3	39.8+4.7	32.7+1.5	43.1+5.8**
Gender (% female)	500 (85)	132 (73)	368 (90)**	141 (77)	359 (88)*	91 (70)	41 (80)	50 (94)	318 (90)**
Age (years)	44.6±14.2	53.3±14.4	40.7±12.2**	49.6±14.8	42.3±13.3**	53.5+14.2	52.9+15.0	40.0+11.7	40.8+12.3**

*FGID* functional gastrointestinal disorders, *OF* obese patients from functional enrollment, *OO* obese patients from obesity enrollment, *MF* morbidly obese patient from functional recruitment, *MO* morbidly obese patients from obesity enrollment, *BMI* body mass index \*P=0.002, \*\*P<0.001

## Patient's Characteristics According to Their Recruitment

In the two populations, the prevalence of FGIDs was significantly different for many disorders, mainly for esophageal and anorectal disorders (Table 2). Figure 2 summarizes the significant difference in the frequency of FGIDs according to the two types of recruitment. However, many FIGDs including epigastric pain, postprandial distress syndrome, constipation, diarrhea, bloating, and soiling had similar prevalence regardless of the type of recruitment and presented no statistical difference.

After adjustment for sex, age, and BMI results remained practically the same, except for the odds ratio for defecation disorders and the mixed subtype of IBS (in the presence of very few cases) that were no longer significant. The odds ratio for sexual disorders showed a tendency for an increase after adjustment but was not statistically significant (odds ratio (OR); 2.024 95 % confidence interval (CI) [0.984–4.166], P=0.055).

# Comparison of the Obese Patient and the Morbidly Obese Patients According to Their BMI

The univariate analysis showed that morbidly obese patients reported fewer esophageal disorders, fewer occurrences of nonspecific dyspepsia, aerophagia, IBS diarrhea, IBS-M sub-type, more nonspecific bowel disorders, and fecal incontinence than the obese patients (Table 3).

The multivariate regression was adjusted for gender, age, and BMI and accounted for several confounding factors especially in the presence of few cases of reported FGIDs; only regurgitation remained significant. The other associations, statistically significant in univariate analysis, were no longer significant in multivariate analysis.

# Results of the Logistic Regression on the Groups of Obese Patients Defined by Their BMIs and Their Type of Recruitment

The patients were divided into four groups according to the importance of their BMI and their type of recruitment (OF, OO, MF, MO). The demographic characteristics of these four groups are shown in Table 1, while the clinical characteristics of these four groups are shown in Table 4.

The logistic regression showed, for each group, demographic and clinical characteristics.

• The OF group is associated with an older age (P<0.001) and a low prevalence of females (P=0.010). Clinically, this group is characterized by a higher prevalence of esophageal disorders: regurgitation (P=0.022) or chest pain (P=0.002). The OF group was used as the reference group for the logistic regression model.

- The MF group was associated with an older age (*P*= 0.001) and a high BMI (*P*=0.013). Clinically, these patients reported frequently functional dyspepsia (*P*=0.006). Furthermore, they reported a higher incidence of urologic disorders (OR=2.86, 95 % CI [1.28–6.39]). The multivariate analysis has shown that the MF patients did not have different odds of reporting FGIDs compared to the OF group.
- The OO group was associated with a high prevalence of females (P=0.008) and a younger age (P<0.001). Clinically, these patients reported a lower incidence of esophageal disorders: regurgitation (P=0.044) or chest pain (P=0.004). They also had a low frequency of functional bowel disorders: IBS (P=0.035) and a low frequency of functional diarrhea (P=0.030). In addition, these patients report more sexual disorders (P=0.009). In the multivariate analysis, these patients reported less esophageal symptoms (globus (P=0.006), regurgitation (P=0.005), chest pain (P=0.001), heartburn (P<0.001), and dysphagia (P=0.020)) than the OF patients (Table 4). They also reported decreased rates of dyspepsia (P=0.012), increased rates of nonspecific bowel disorders (P=0.038), decreased rate of IBS (P=0.004), mainly IBS with diarrhea (P=0.040), and decreased rate of obstructed defecation than the OF patients.
- The MO group was associated with a younger age (P < 0.001) and a higher BMI (P < 0.001). Clinically, this group was characterized by a lower frequency of nonspecific dyspepsia (P=0.016) and a lower frequency of IBS-D (P=0.044). Moreover, these patients rarely reported urologic disorders (P=0.007). In the multivariate analysis, patients reported less esophageal disorders (globus (P=0.014), regurgitation (P=0.001), chest pain (P=0.001), heartburn (P<0.001), and dysphagia (P=0.006)) than the OF patients (Table 4). In addition, these patients also report decreased rate of dyspepsia (P=0.002), IBS with diarrhea (P=0.002), and increased rates of nonspecific bowel disorders (P=0.024), than OF patients.
- The prevalence of anorectal symptoms remained similar among and was independent of the recruitment after adjustment for BMI, age, and gender, except a lower rate of obstructed defecation in OO patients as compared to OF patients (*P*=0.033).

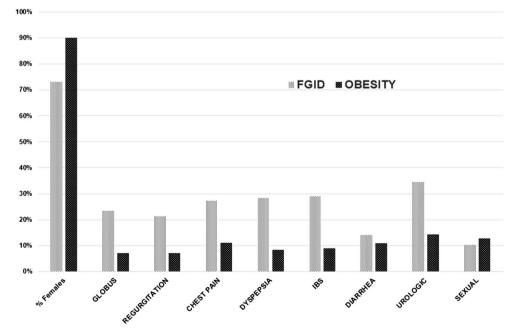
## Discussion

This study has showed that FGIDs found in obese patients can differ according to the origin of their enrollment and not with the importance of their obesity. Obese patients consulting for obesity management have different demographic characteristics than the obese patients consulting for FGIDs: they were

#### Table 2 Clinical description of subtypes of obese patients defined by the type of recruitment

		Recruitment			Univariate analysis P	OR	95 % confidence interval	Multivariate analysis P
		All patients	FGID	Obesity			merva	anarysis 1
Esophagus	Globus	72 (12)	43 (23)	29 (7)	< 0.001	0.244	[0.125-0.478]	< 0.001
	Regurgitation	68 (11)	39 (21)	29 (7)	< 0.001	0.269	[0.135-0.535]	< 0.001
	Chest pain	96 (16)	50 (27)	46 (11)	< 0.001	0.251	[0.138-0.456]	< 0.001
	Heartburn	122 (20)	62 (34)	60 (15)	< 0.001	0.248	[0.143-0.429]	< 0.001
	Dysphagia	93 (16)	47 (26)	46 (11)	< 0.001	0.400	[0.218-0.735]	0.003
Gastro-duodenal	Epigastric pain	32 (5)	11 (6)	21 (5)	0.694	0.550	[0.213-1.420]	0.217
	Postprandial distress	64 (11)	26 (14)	38 (9)	0.085	0.743	[0.366-1.509]	0.412
	Nonspecific dyspepsia	87 (15)	52 (28)	35 (8)	< 0.001	0.224	[0.118-0.424]	< 0.001
	Aerophagia	103 (17)	50 (27)	53 (13)	< 0.001	0.398	[0.225-0.706]	0.002
Bowel	All IBS subtypes	90 (15)	53 (29)	37 (9)	< 0.001	0.225	[0.122-0.416]	< 0.001
	IBS constipation	5 (1)	3 (2)	2 (0)	0.172	0.559	[0.050-6.295]	0.638
	IBS diarrhea	38 (6)	24 (13)	14 (3)	< 0.001	0.170	[0.069-0.418]	< 0.001
	IBS mixed	11 (2)	7 (4)	4(1)	0.040	0.650	[0.134-3.164]	0.594
	IBS unspecified	36 (6)	19 (10)	17 (4)	0.005	0.338	[0.138-0.828]	0.018
	Constipation	141 (24)	35 (19)	106 (26)	0.095	1.163	[0.681-1.987]	0.580
	Diarrhea	71 (12)	26 (14)	45 (11)	0.273	0.658	[0.334–1.297]	0.227
	Bloating	20 (3)	7 (4)	13 (3)	0.631	1.627	[0.481-5.502]	0.434
	Nonspecific bowel disorders	114 (19)	19 (10)	95 (23)	< 0.001	2.272	[1.197-4.314]	0.012
Abdominal pain		37 (6)	14 (8)	23 (6)	0.332	0.726	[0.293-1.801]	0.490
Anorectal	Soiling	29 (5)	12 (7)	17 (4)	0.218	0.571	[0.207-1.578]	0.280
	Fecal incontinence	28 (5)	21 (11)	7 (2)	< 0.001	0.231	[0.071-0.750]	0.015
	Levator ani syndrome	16 (3)	13 (7)	3 (1)	< 0.001	0.107	[0.022-0.510]	0.005
	Proctaglia fugax	23 (4)	13 (7)	10 (2)	0.010	0.345	[0.112-1.065]	0.064
	Nonspecific anorectal disorders	17 (3)	7 (4)	10 (2)	0.423	0.856	[0.230-3.177]	0.816
	Obstructed defecation	163 (27)	63 (34)	100 (24)	0.013	0.659	[0.403-1.078]	0.096
Extra-digestive	Urologic disorders	122 (20)	63 (34)	59 (14)	< 0.001	0.409	[0.235-0.711]	0.002
	Sexual disorders	72 (12)	19 (10)	53 (13)	0.496	2.024	[0.984-4.166]	0.055

**Fig. 2** Significant differences of functional disorders according to the origin of enrollment



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		BMI group			Univariate analysis $P$	OR	95 % confidence interval	Multivariate analysis P
		All patients	Obese	Morbid obesity				
Esophagus	Globus	72 (12)	33 (18)	39 (9)	0.006	0.841	[0.384–1.845]	0.666
	Regurgitation	68 (11)	35 (19)	33 (8)	<0.001	0.415	[0.181 - 0.950]	0.037
	Chest pain	96 (16)	39 (21)	57 (14)	0.030	0.669	[0.336 - 1.334]	0.254
	Heartburn	122 (20)	51 (28)	71 (17)	0.006	0.550	[0.294 - 1.028]	0.061
	Dysphagia	93 (16)	40 (22)	53 (13)	0.010	0.543	[0.268 - 1.097]	0.089
Gastro-duodenal	Epigastric pain	32 (5)	8 (4)	24 (6)	0.557	1.374	[0.444 - 4.248]	0.581
	Postprandial distress	64 (11)	22 (12)	42 (10)	0.568	1.163	[0.519 - 2.610]	0.714
	Nonspecific dyspepsia	87 (15)	38 (21)	49 (12)	0.008	0.746	[0.362 - 1.538]	0.427
	Aerophagia	103 (17)	42 (23)	61 (15)	0.026	0.896	[0.459 - 1.746]	0.746
Bowel	All IBS subtypes	90 (15)	41 (22)	49 (12)	0.002	0.777	[0.380 - 1.586]	0.488
	IBS constipation	5 (1)	2 (1)	3 (1)	0.648	3.721	[0.200 - 69.293]	0.379
	IBS diarrhea	38 (6)	18(10)	20 (5)	0.030	0.468	[0.164 - 1.337]	0.156
	IBS mixed	11 (2)	8 (4)	3 (1)	0.005	2.156	[0.175–26.572]	0.549
	IBS unspecified	36 (6)	13 (7)	23 (6)	0.577	1.389	[0.482 - 4.001]	0.542
	Constipation	141 (24)	43 (23)	98 (24)	0.917	0.723	[0.398 - 1.312]	0.285
	Diarrhea	71 (12)	19 (10)	52 (13)	0.495	1.509	[0.688 - 3.310]	0.305
	Bloating	20 (3)	9 (5)	11 (3)	0.217	1.353	[0.322 - 5.694]	0.680
	Nonspecific bowel disorders	114 (19)	23 (12)	91 (22)	0.005	1.508	[0.772 - 2.946]	0.229
Abdominal pain		78 (14)	0.359	13 (7)	24 (6)	1.020	[0.356 - 2.925]	0.970
Anorectal	Soiling	29 (5)	8 (4)	21 (5)	0.838	1.321	[0.406 - 4.299]	0.838
	Fecal incontinence	28 (5)	14 (8)	14 (3)	0.035	1.664	[0.467 - 5.921]	0.035
	Levator ani syndrome	16 (3)	9 (5)	7 (2)	0.050	0.993	[0.184 - 5.364]	0.050
	Proctalgia fugax	23 (4)	11 (6)	12 (3)	0.105	0.568	[0.151 - 2.139]	0.105
	Nonspecific anorectal disorders	17 (3)	7 (4)	10 (2)	0.426	0.837	[0.184 - 3.814]	0.426
	Obstructed defecation	163 (27)	57 (31)	106 (26)	0.233	1.087	[0.618 - 1.909]	0.233
Extra-digestive	Urologic disorders	122 (20)	51 (28)	71 (17)	0.006	1.201	[0.626 - 2.302]	0.006
	Sexual disorders	72 (12)	24 (13)	48 (12)	0.684	1.197	[0.551 - 2.596]	0.684

 Table 3
 Clinical description of subtypes of obese patients defined by their body mass index

Functional disorders	ers	Groups				Univariate analysis	e analy:	sis	Odds ratio vs OF (OR [95 % CI])	% CI])
		OF	MF	00	MO	Р	OF	MF	00	МО
Esophagus	Globus	31 (23)	12 (24)	2 (4)	27 (8)	<0.001	1	0.942 [0.437–2.030]	0.118 [0.026-0.530]**	0.252 [0.135-0.470]***
	Regurgitation	32 (24)	7 (14)	3 (6)	26(7)	<0.001	1	0.456 [0.185–1.119]	$0.160 [0.045 - 0.569]^{**}$	$0.207 [0.110 - 0.390]^{***}$
	Chest pain	37 (28)	13 (25)	2 (4)	44 (12)	<0.001	1	0.865 [0.412–1.815]	$0.089 [0.020 - 0.392]^{**}$	0.317 [0.182-0.552]***
	Heartburn	46 (35)	16 (31)	5 (9)	55 (15)	<0.001	1	0.803 [0.400 - 1.613]	$0.159 [0.057 - 0.441]^{***}$	$0.286 [0.171 - 0.478]^{***}$
	Dysphagia	36 (27)	11 (22)	4 (8)	42 (12)	<0.001	1	0.690 [0.315–1.511]	$0.272 [0.088 - 0.837]^{*}$	0.444 [0.254 - 0.777] **
Gastro-duodenal	Epigastric pain	7 (5)	4 (8)	1 (2)	20 (6)	0.592	1	1.443 [0.401-5.187]	0.257 [0.030 - 2.224]	0.817 [0.314–2.131]
	Postprandial distress	19 (14)	7 (14)	3 (6)	35 (10)	0.248	1	0.923 [0.360–2.365]	0.428 [0.116–1.579]	$0.774 \ [0.397 - 1.509]$
	Nonspecific dyspepsia	35 (27)	17 (33)	3 (6)	32 (9)	<0.001	1	1.398[0.687 - 2.844]	0.202 [0.057 - 0.711]*	0.331 [0.184–0.597]***
	Aerophagia	37 (28)	13 (25)	5 (9)	48 (13)	<0.001	1	0.811 [0.386–1.704]	$0.236 [0.084 - 0.661]^{**}$	$0.362 [0.211 - 0.622]^{***}$
Bowel	All IBS subtypes	37 (28)	16 (31)	4 (8)	33 (9)	<0.001	1	1.136[0.561 - 2.304]	$0.191 [0.062 - 0.586]^{**}$	0.241 [0.135 - 0.430] * * *
	IBS constipation	1 (1)	2 (4)	1 (2)	1 (0)	0.048	1	4.569 [0.399–52.328]	3.165 [0.157–63.936]	0.465 [0.024-8.897]
	IBS diarrhea	17 (13)	7 (14)	1 (2)	13 (4)	<0.001	1	0.999 [0.385–2.591]	$0.117 [0.015 - 0.937]^{*}$	$0.237 [0.104 - 0.541]^{***}$
	IBS mixed	6 (5)	1 (2)	2 (4)	2 (1)	0.021	1	0.412 [0.048–3.554]	0.593 [0.102 - 3.459]	0.084 [0.015 - 0.473] **
	IBS unspecified	13 (10)	6 (12)	(0) 0	17 (5)	0.013	1	1.250 [0.445–3.515]	0.000 [0.000-0.000]	$0.454 \ [0.197 - 1.047]$
	Constipation	27 (20)	8 (16)	16 (30)	90 (25)	0.245	1	0.669 [0.280 - 1.599]	1.252 [0.586–2.675]	1.014 [0.597–1.721]
	Diarrhea	17 (13)	9 (18)	2 (4)	43 (12)	0.167	1	1.442 [0.595 - 3.499]	0.290 [0.063 - 1.344]	$0.984 \ [0.506 - 1.912]$
	Bloating	6 (5)	1 (2)	3 (6)	10(3)	0.548	1	0.410[0.048 - 3.505]	1.227 [0.267-5.628]	0.595 [0.190 - 1.863]
	Nonspecific bowel disorders	12 (9)	7 (14)	11 (21)	84 (23)	0.003	1	1.630 [0.600-4.425]	$2.748 [1.081 - 6.988]^{*}$	3.098 [1.555–6.174]**
Abdominal pain		11 (8)	3 (6)	2 (4)	21 (6)	0.646	1	0.763 [0.200–2.907]	0.434 [0.087 - 2.162]	$0.692 \ [0.292 - 1.640]$
Anorectal	Soiling	8 (6)	4 (8)	(0) 0	17 (5)	0.250	1	1.393 [0.396-4.898]	0.000 [0.000 - 0.000]	1.055 [0.399–2.791]
	Fecal incontinence	14 (11)	7 (14)	(0) 0	7 (2)	<0.001	1	1.257 [0.459 - 3.440]	0.000 [0.000 - 0.000]	$0.274 \ [0.097 - 0.770]^{*}$
	Levator ani syndrome	6 (7)	4(8)	(0) 0	3 (1)	<0.001	1	1.255 [0.363-4.337]	0.000 [0.000 - 0.000]	$0.140 [0.034 - 0.586]^{**}$
	Proctalgia fugax	6 (7)	4(8)	2 (4)	8 (2)	0.048	1	1.015 [0.294–3.506]	0.525 [0.102–2.702]	$0.315[0.109-0.916]^{*}$
	Nonspecific anorectal disorders	5 (4)	2 (4)	2 (4)	8 (2)	0.728	1	1.083 [0.202-5.824]	1.214 [0.204–7.236]	0.691 [0.195–2.444]
	Obstructed defecation	47 (36)	16 (31)	10 (19)	90 (25)	0.049	1	0.795 [0.397–1.591]	$0.403 [0.180 - 0.903]^{*}$	0.593 [0.369 - 0.952]*
Extra-digestive	Urologic disorders	39 (30)	24 (47)	12 (23)	47 (13)	<0.001	1	2.044 [1.020-4.099]*	0.760 [0.343 - 1.686]	0.378 [0.219-0.653]***
	Sexual disorders	15 (11)	4 (8)	9 (17)	44 (12)	0.546	1	0.690 [0.216–2.197]	1.946 [0.747 - 5.070]	1.270 [0.636–2.538]

OBES SURG (2015) 25:2143-2152

\*P<0.05, \*\*P<0.01, \*\*\*P<0.001

*OF* obese patients from functional enrollment, *OO* obese patients from obesity enrollment, *MF* morbidly obese patient from functional recruitment, *MO* morbidly obese patients from obesity enrollment, *BMI* body mass index, *IBS* irritable bowel syndrome

vounger and more frequently females. In addition, the FGIDs were different according to the origin of their recruitment. Clinically, patients from the obesity recruitment reported esophageal disorders less frequently: globus, regurgitation, and chest pain. They also reported nonspecific dyspepsia, IBS, and functional diarrhea less frequently and had fewer urologic disorders and more sexual disorders. The second important information was that obese patients and morbidly obese patients consulting for obesity management have the same frequency of functional digestive disorders and extradigestive disorders. Thirdly, there were symptoms that had similar prevalence in all groups(OF, OO, MF, MO) like epigastric pain, postprandial distress, constipation, diarrhea, bloating, abdominal pain soiling, or nonspecific anorectal disorders (Table 2). These findings suggested that the abovementioned symptoms should be systematically detected in all patients since they do not represent an exclusive reason for seeking medical advice or treatment, and they are not modified by the type of enrollment in obese or morbidly obese patients.

Previous studies on FGIDs in adult obese patients have shown discordant results about the prevalence of FGIDs in these patients. For example, GERD was associated with an increased BMI in some studies [23-25], while other studies reported no association [26, 27]. Thus, there was no clear relationship between FGIDs and obesity. The present study underlines the importance of the enrollment source to define the association between BMI and FGIDs. In fact, independently of the country of origin, previous studies associated BMI and organic or functional digestive disorders in cohort patients from different types of enrollment: functional disease recruitment [28], weight loss programs [29], bariatric surgery [20], endoscopic evaluation [27, 30], or epidemiological studies [31, 32]. In addition, some studies could include control groups [33] but did not separate obese patients according to their BMI [34]. However, the meta-analyses previously published did not take into account the presence of recruitment bias for GERD [35–38], pelvic floor symptoms [39], or all the FGIDs [40].

One main difference between patients from the two sources of recruitment was their demographic characteristics. The obese patients were younger and more frequently females. In our previous study, the patients before bariatric surgery [20] were  $40\pm12$  years old, which is similar to the age of the morbidly obese group in the present study ( $40.9\pm12.3$ ) and younger that the MF group (P<0.001).

One important result of the present study is the importance of the recruitment source to characterize the FGIDs in obese patients. While the clinical characteristics of the patients according to the importance of their obesity yielded no significant result in the multivariate analysis, the analysis based on the recruitment source showed significant results. The OF patients reported esophageal disorders (globus, regurgitation, and chest pain), nonspecific dyspepsia, IBS, and functional diarrhea more frequently. In a meta-analysis [40], a weak association between increasing BMI and reflux symptoms was found. Nevertheless, a large amount of heterogeneity was found in the results of the selected studies. The results of the present study show an increase of chest pain and heartburn in the group of obese patients (OF) as opposed to the morbidly obese patients (MF).

Obese and morbidly obese patients from the same recruitment did not exhibit significant differences regarding the frequency of their FGIDs after multivariate analysis. This approach underlined the relevance of studies where the BMI is cut off at 30 kg/m<sup>2</sup> without distinguishing morbid obese patients from the obese patients [39, 40]. Another example of an unexpected association is the presence of nonspecific bowel disorders as a major complain in the MO (23 %) and OO (21 %) groups compared to the MF (14 %) or the OF group of FGIDs (9 %; Table 2). Constipation was also more prevalent in the OO and MO groups compared to patients from FGID enrollment (Table 2). Although we cannot exclude that some FGIDs may naturally increase with increasing BMI, we have recently published the presence of a specific U-shaped relationship between BMI and dyspepsia [31]. Our findings suggest that there is a specificity of symptoms related to different BMI groups that is not linear and can be influenced by the gender [31].

The objective of our work was to personalize the evaluation of patients in a systematic way with the use of the ROME III criteria. The frequency of each type of FGID can have a strong variation from one study to another, and the present study showed that the type of enrollment is an important predictor for the frequency and the type of complains in obesity or morbid obesity patients.

We think that the presence of unusual BMI related symptoms should drive to further investigations, i.e., reported dysphagia in obese patients. Epigastric pain and postprandial distress are painful FGIDs with a similar prevalence among groups; this point should be taken in consideration in bariatric surgery candidates. In the presence of these symptoms, the choice of bariatric surgery should avoid worsening the existing symptoms, i.e., adjustable gastric banding. A purely restrictive method and probably should be avoided in these cases.

In conclusion, symptoms that had similar prevalence in all groups should be systematically detected in all patients. This study has shown that the recruitment source accounted for specific differences in the prevalence of functional gastrointestinal disorders in obesity and morbid obesity. This factor can induce a significant recruitment bias, and patients should not be pooled together.

#### Statements

**Contributorship** MB performed the research, contributed to the design of the study, revised the article content, and finally approved the version to be published.

MF interpreted the data, drafted the article, revised the article content, and finally approved the version to be published.

CJ interpreted the data.

GA participated in the selection of patients and the design of the study. JMC, GR, and RB contributed to the design of the study, revised the article content, and finally approved the version to be published.

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Ethical Approval For this study, formal consent is not required.

**Informed Consent** Informed consent was obtained from all individual participants included in the study.

**Role of the Funding Source** No funding sources had any role in study design, collection, analysis, and interpretation of data or writing of the report. The corresponding author had full access to all the data of the study and had final responsibility for the decision to submit it for publication.

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