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Overlaps with bladder pain syndrome and irritable bowel syndrome are associated with higher symptom burden and reduced quality of life in functional dyspepsia

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Abstract

Background: Functional dyspepsia and bladder pain syndrome are well-known to overlap with irritable bowel syndrome. Whether functional dyspepsia overlaps with bladder pain syndrome remains unknown. Our aim was to evaluate the presence of bladder pain syndrome in functional dyspepsia patients and its impact.

Methods: All consecutive patients with investigated dyspeptic symptoms in our tertiary care center between March 2015 and November 2018 were studied. Functional dyspepsia and irritable bowel syndrome were diagnosed according to Rome III and IV criteria while bladder pain syndrome was diagnosed using ESSIC criteria. Validated questionnaires were filled to assess quality of life (GIQLI), anxiety and depression (HADS), sleep (PSQI), and insomnia (ISI). Dyspeptic symptoms severity was assessed individually for eight dyspeptic complaints.

Key Results: Among 1453 patients with dyspeptic symptoms, 61.4% fulfilled Rome criteria for functional dyspepsia. Bladder pain syndrome was present in 16.0% of the patients not fulfilling diagnostic criteria for functional dyspepsia, 22.2% of patients with functional dyspepsia alone, and 36.4% of patients with overlapping functional dyspepsia and irritable bowel syndrome (p-values <0.0001). In patients with bladder pain syndrome overlapping with functional dyspepsia, dyspeptic symptoms severity, anxiety, depression, and insomnia levels were higher while quality of life and sleep quality were reduced (p-values <0.0001). These results were even more pronounced in case of overlap with irritable bowel syndrome (p-values <0.0001).

Conclusions and Inferences: Bladder pain syndrome is present in 26.9% of functional dyspepsia patients and is associated with higher gastrointestinal, psychological distresses, and sleep symptom burdens, and with reduced quality of life.

KEYWORDS
bladder pain syndrome, functional dyspepsia, irritable bowel syndrome, quality of life, symptom burden

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1 | INTRODUCTION

Overlap between functional gastrointestinal disorders, now called "disorders of gut-brain interaction" (DGBI), is frequent[1]. Functional dyspepsia (FD) and irritable bowel syndrome (IBS) are well known to overlap, both conditions being more prevalent in patients with the other one compared with the general population, which indicates an association between them[2,3]. FD-IBS overlap is associated with altered quality of life (QoL)[4] and impaired sleep[5], and those patients experience more severe gastrointestinal symptoms[6], have higher depression levels[7] and higher somatic symptom scores[8]. Similar results have been reported for the overlap with gastro-esophageal reflux disease (GERD)[9].

Bladder pain syndrome (BPS) and overactive bladder (OAB) are the main functional bladder disorders[10]. BPS is characterized by pelvic pain associated with lower urinary symptoms. BPS had successive definitions, including interstitial cystitis and interstitial cystitis/painful bladder syndrome (IC/PBS)[11]. BPS is currently diagnosed using the ESSIC criteria[12]. OAB is characterized by urinary urgency, with or without incontinence, in the absence of painful symptoms[13]. OAB and BPS remain therefore different entities that may coexist[14,15].

FD and BPS are both prevalent in the general population: 7.2% and 3.7%, respectively[16,17]. Previously, OAB has been shown to be common in FD patients, with a frequency of 20.5% in the disorder[18]. Likewise, dyspeptic symptoms are known to be a frequent complaint in patients with BPS[19]. However, the impact of the overlap with BPS and FD has never been assessed, neither on QoL, symptom severity nor other characteristics in FD patients. Therefore, the aim of our study is to assess the prevalence of BPS in FD patients and FD-IBS patients and to assess the symptom burden in these populations, including dyspeptic symptom severity, QoL, anxiety, depression, sleep quality, and insomnia.

Key messages

- Bladder pain syndrome is present in 26.9% of patients suffering from functional dyspepsia.
- Overlap with bladder pain syndrom (with or without overlapping IBS) is associated with higher dyspeptic symptoms severity, anxiety, depression, and insomnia levels, and with decreased quality of life and sleep quality in patients with functional dyspepsia.

2 | MATERIALS AND METHODS

This study is based on a retrospective analysis of prospectively acquired data from Rouen University Hospital. All patients had given written informed consent for data to be recorded and used for research, in accordance with the Declaration of Helsinki as revised in 2013[20]. Approval was obtained from the French data protection authority (Commission Nationale de l'Informatique et des Libertés, CNIL No 817.917), in compliance with French legislation. Ethical approval for the analysis of the data was obtained (CERNI No E2019-38).

2.1 | Patients

We analyzed retrospectively all patients referred between March 2015 and November 2018 at our center for chronic dyspeptic symptoms. All patients had normal endoscopy without *Helicobacter pylori* on the biopsies and normal routine blood tests. Patients who incompletely filled out the Rome questionnaire, diabetics, patients aged under 18 and patients with rumination, cyclic vomiting, and cannabinoid hyperemesis syndromes were excluded.

2.2 | Diagnostic criteria

FD, its subtypes postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS), and IBS were defined according to Rome III criteria[21,22] between March 2015 and end 2017, and according to Rome IV criteria[23,24] between end 2017 and November 2018. A post-infectious origin to dyspeptic complaints was evaluated by asking an history of acute gastroenteritis during the month preceding the onset of dyspeptic symptoms[25].

BPS was defined using an 8-item symptom-based self-questionnaire based on the ESSIC criteria published in 2008[12] (see Table S1). All patients should have at least three criteria to be diagnosed with BPS: (1) pain, pressure, or discomfort perceived to be related to the urinary bladder, (2) symptoms of at least 6 months, and (3) persistent or intermittent urge to void, pollakiuria (superior to eight mictions per day), or nycturia (at least one miction per night).

2.3 | Symptom questionnaires

The *GastroIntestinal Quality of Life Index* (GIQLI), a validated score in French[26], was used to measure QoL. This score is composed of 36 items concerning symptoms, physical state, emotions, and social impact. The score ranges from 0 to 144; the higher is the score, the better is the QoL.

Anxiety and depression levels were assessed, using the *Hospital Anxiety Depression Scale* (HADS) and its subscales (HADS-A and HADS-D, respectively)[27]. Each subscale includes seven items scored from 0 to 3; the higher is the score, the higher is the anxiety or depression.

Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI)[28]. The level of insomnia was defined by the Insomnia Severity Index (ISI)[29] questionnaire.

Eight individual symptoms (postprandial fullness, abdominal pain, bloating, regurgitations, nausea, early satiety, belching, and vomiting) were assessed using individual questions from the GIQLI

for all of them, except vomiting. Symptoms were graded from 0 to 4 during the 15 days preceding their appointment, with 0 corresponding to their absence and 4 to extremely severe symptoms. We defined two groups for each symptom: "absence of symptom" by a score lower or equal to 2, and "presence of symptom" by a score higher to 2 according to the 5-points Likert scale.

2.4 | Gastric emptying

Gastric emptying (GE) time was assessed in a subgroup of patients by ^{13}C-labeled octanoic acid breath testing as described elsewhere[30]. Briefly, patients ingested a 250-kcal test meal containing ^{13}C-labeled octanoic acid (Euriso-Top, Saint Aubin, France), with exhalations of air being collected before and every 15 min after the meal for 6–8 h. The presence of ^{13}C-labeled CO_2 was detected by infrared spectrometry (Kibion GmbH, Bremen, Germany) and gastric half emptying time could therefore be calculated using the software *InfraRed ISotope analyzer* (IRIS; Wagner/Analysen Technik, Bremen, Germany)[31]. Delayed gastric emptying was defined as a half emptying time ($T_{½}$) superior to 166 min according to Bromer et al.[32]

2.5 | Study design

Consecutive patients with dyspeptic symptoms were screened for FD, IBS, and BPS. Patients have been divided in five groups according to the presence and/or combination of FD, IBS, and BPS diagnostic criteria: "symptomatic controls" if no diagnostic criterium was present, FD alone, FD-IBS, FD-BPS, or FD-IBS-BPS. Our "symptomatic controls" are therefore composed of patients referred for dyspeptic symptoms but who did not fulfill Rome criteria for functional dyspepsia but also for IBS and BPS. Characteristics of the patients, QoL, anxiety, depression, sleep quality, and insomnia were compared between diagnostic groups.

A comparison of Rome III and IV cohorts was performed for quality control (Figures S3–S5).

2.6 | Statistical analysis

All results were expressed as mean ± standard deviation (SD). Quantitative data between groups of patients were compared using a non-gaussian unpaired t-test (Mann–Whitney test), whereas qualitative variables were compared using Fisher's exact test, both with 95% confidence interval (CI). Multiple groups comparisons were performed using Kruskal–Wallis test with Dunn's multiple comparison post-test to compare all pairs of columns, with significance level alpha of 0.05%. A multiple linear regression model was fitted to identify predictors of overlapping BPS in our cohort of FD patients using the following independent variables: age, body mass index (BMI), gender, GIQLI score, HADS, presence of IBS, and PSQI score. Multicollinearity was detected by using the variance inflation factor and correlated variables were removed from the regression model. Two-tailed p-value <0.05 was considered statistically significant. Factors used for the PCA were age, BMI, GIQLI, the eight dyspeptic symptoms individually, HADS-A and HADS-D subscales, and PSQI. We used all dimensions with eigen values superior to 1 to select principal components for analysis.

Data relied on spreadsheets using Microsoft® Excel® for Office® 365 version 1910 for Windows® (build 16.0.12130.20382, Microsoft Corporation®) and were analyzed using GraphPad® Prism® version 5.03 for Windows® (GraphPad Software, Inc.®, San Diego, California, USA, www.graphpad.com), except descriptive statistics which were performed with Microsoft® Excel®, univariate and multivariate analyses which were performed using SPSS® software version 27.0.0.0 (IBM® Corp. Released 2020. IBM® SPSS® Statistics for Windows®, Version 27.0. Armonk, NY, USA: IBM Corp) and mediation analysis and PCA which were performed using RStudio® software version 1.2.1335 (RStudio® Team [2016]. RStudio: Integrated Development for R. RStudio, Inc.®, Boston, MA, USA, www.rstudio.com), based on R software version 3.6.1 (R Core Team [2019]. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/), the psych package version 1.8.12[33] and the FactoMineR package version 1.34[34].

Venn diagrams were used to represent the proportions of subjects with different diagnoses, by using the Venn Diagram Plotter software (version 1.5.5228.29250 released April 25, 2014. PNNL, Richland, WA, USA, http://omics.pnl.gov/).

Other analyses included the investigation of factors associated with overlap with BPS using univariate and multivariate analyses, principal component analysis (PCA), GE study in a subgroup of patients, and comparison of Rome III and IV cohorts.

3 | RESULTS

3.1 | Patient characteristics

One thousand six hundred and fifty-five patients addressed for dyspeptic symptoms were identified in the eligible period. Patients who incompletely filled out the Rome questionnaire (n = 6), diabetics (n = 160), patients aged under 18 (n = 8), and patients with rumination, cyclic vomiting, and cannabinoid hyperemesis syndromes (n = 28) were not considered for further analysis. A total of 1453 patients were kept for analysis. Among them, 892 (61.4%) patients fulfilled criteria for FD, classified as PDS in 58.7%, EPS in 14.9%, and PDS-EPS in 26.4%; among them, 465 (52.1%) patients had FD-alone, 187 (21.0%) patients had FD-IBS, 133 (14.9%) patients had FD-BPS, and 107 (12.0%) patients had FD-IBS-BPS overlaps (Figure 1). Clinical and demographic characteristics of the overall population and "symptomatic controls" are presented in Table 1. Principal component analysis (PCA) was used to visualize graphically our data and assess the relationship between variables (Figures S1 and S2 and Table S2).

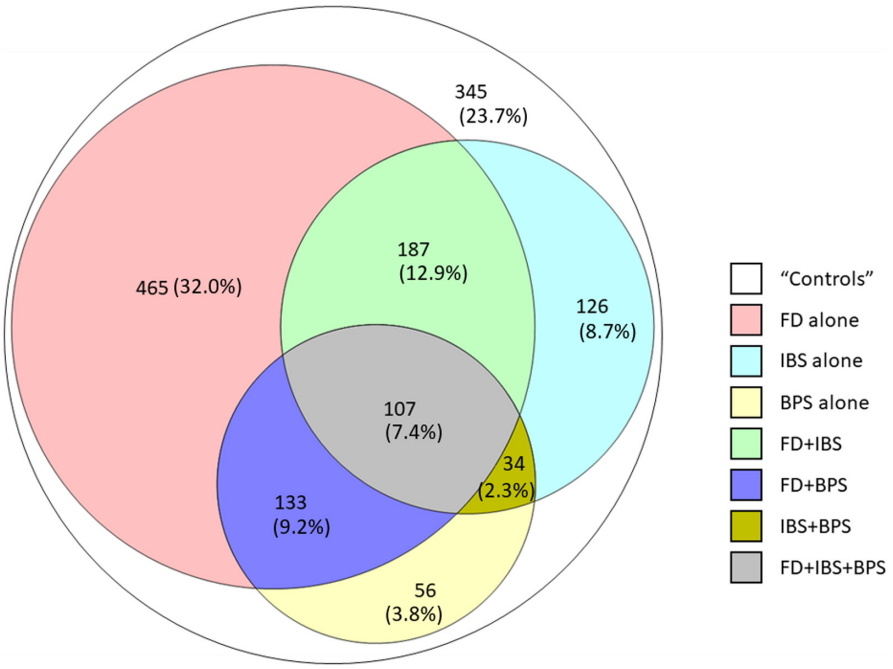


FIGURE 1 Venn diagram of the study population Venn diagram summarizing overlap syndromes. The numbers of subjects within each diagnostic group are shown, with areas of the circles being proportionate to the number of patients. "Controls" stands for "symptomatic controls" in the legend. BPS, Bladder Pain Syndrome; FD, Functional Dyspepsia; IBS, Irritable Bowel Syndrome

3.2 | Prevalence of BPS in FD patients

Bladder pain syndrome was found in 16.0% of patients not fulfilling Rome criteria for FD, 22.2% of FD alone patients, and 36.4% of FD + IBS patients. BPS was therefore more prevalent among patients with FD diagnosis compared with those not fulfilling Rome criteria for FD in the entire cohort (26.9 vs. 16.0%, respectively, $p < 0.0001$). BPS was also more prevalent among patients overlapping FD and IBS compared with those with FD alone (22.2% of those with FD alone versus 36.4% of those with FD-IBS overlap, OR: 2.00 [95% CI: 1.47–2.72], $p < 0.0001$).

In multivariate analysis, factors independently associated with overlapping BPS in FD patients were altered QoL and overlap with IBS and explained 6% of the variance, while other factors (age, psychological distress, BMI, sleep quality, and gender) were not. Results are shown in Table S3.

3.3 | Differences between diagnostic groups

Overall results are presented in Figure 2 and detailed in Table 1. Groups differed in age, BMI, sex ratio, QoL, anxiety-depression, and sleep quality ($p < 0.05$ for all). Female predominance increased with increasing number of diagnostics ($p < 0.0001$). QIGLI score in "symptomatic controls" was 97.0 and decreased to 84.1 in FD alone patients ($p < 0.0001$). The GIQLI decreased while insomnia and the HADS increased with the number of diagnostics. Similar results to those with HADS were shown for anxiety and depression subscales separately (Table 3). The alteration of sleep quality increased with the number of diagnostics.

There was a difference between all groups for symptoms of postprandial fullness, abdominal pain, bloating, nausea, and belching between groups ($p < 0.005$ for all), with increased scores when the number of diagnostics increased, but not for regurgitations, early satiety and vomiting ($p = 0.39$, 0.18, and 0.35, respectively). Data concerning symptoms are presented in Figure 3.

3.4 | Subgroup analysis of gastric emptying

Gastric emptying was available for 227 FD patients. Among FD alone patients, 70 (48.3%) out of 145 patients had delayed GE, with a mean GE half time of 176.8 min (SD: ±84.9). Likewise, 37 (45.1%; $p = 0.67$) out of 82 FD patients with either BPS and/or IBS overlap, with a mean GE half time of 186.9 min (SD: ±110.5) ($p = 0.61$).

4 | DISCUSSION

In the present study, we reported for the first time an association between FD and BPS. We showed BPS to be present in 26.9% of all FD patients, and even 36.4% of patients with FD-IBS overlap, in our cohort, while it was only 6.1% in patients referred for dyspeptic symptoms but who did not fulfill Rome criteria. Overlap with BPS was associated with reduced QoL, higher anxiety and depression levels, and altered sleep quality in FD patients. The impact of this overlap is even greater when considering IBS as an additional overlap diagnosis. Furthermore, we did not find any association between overlap diagnostics, including BPS, and GE half time.

Our results are in accordance with other publications in the field[35]. The proportion of overlap with IBS in our FD population is similar to the 38.3% found recently in a large Danish study using Rome III criteria for FD[36]. OAB is common in FD patients, with a prevalence of about 20%[18]; since OAB and BPS may share urinary symptoms[14], a large prevalence of BPS in FD patients was expected. However, the diagnosis of BPS is probably underestimated in clinical

TABLE 1 Patients' characteristics in the overall dyspeptic population, in "symptomatic controls," and in the different groups

	Overall population ($n = 1453$)	"Symptomatic controls" ($n = 345$)	FD alone ($n = 465$)	FD-IBS ($n = 187$)	FD-BPS ($n = 133$)	FD-IBS-BPS ($n = 107$)	p-value
Mean age, years	47.4 (±15.7)	49.3 (±16.1)	48.1 (±15.5)	44.8 (±15.7)*	48.8 (±15.4)	43.7 (±13.9)*	0.0016
Mean BMI[a], $kg.m^{-2}$	24.7 (±5.3)	25.4 (±4.9)	24.6 (±5.5)*	24.7 (±5.5)	23.8 (±4.4)*	24.3 (±5.4)	0.011
Sex ratio male/female (% males)	0.35 (26.2)	0.55 (35.4)	0.35 (26.0)*	0.25 (19.8)*	0.25 (20.3)*	0.19 (15.9)*†	<0.0001
Episode of gastroenteritis before the onset of dyspeptic symptoms, n (%)	59 (4.06)	8 (2.3)	18 (3.9)	10 (5.3)	5 (3.8)	8 (7.5)*‡	0.10
GIQLI	83.7 (±22.4)	97.0 (±20.2)	84.1 (±20.8)*	74.8 (±20.7)*†	76.5 (±20.7)*†	64.4 (±18.2)*†‡□	<0.0001
HADS	15.5 (±7.2)	13.3 (±7.1)	15.2 (±6.8)*	16.1 (±6.5)*	16.7 (±7.1)*	19.9 (±7.5)*†‡□	<0.0001
HADS-A	9.50 (±4.3)	8.29 (±4.2)	9.4 (±4.2)*	9.6 (±3.9)*	10.4 (±4.1)*	11.7 (±4.3)*†‡	<0.0001
HADS-D	6.00 (±4.0)	5.01 (±3.9)	5.78 (±3.8)*	6.51 (±3.8)*	6.36 (±4.1)*	8.17 (±4.4)*†□	<0.0001
PSQI	7.87 (±3.9)	6.81 (±3.7)	7.87 (±3.7)*	8.18 (±3.8)*	8.69 (±4.2)*	9.73 (±3.9)*†‡	<0.0001
ISI	11.0 (±6.5)	9.01 (±6.1)	10.8 (±6.3)*	11.9 (±6.4)*	12.3 (±6.7)*	14.1 (±6.0)*†	<0.0001

Note: Continuous variables are expressed as mean score ± SD. The last column indicates p-values of the global ANOVA. The symbols *, †, ‡, and □ indicate p-values <0.05 vs. "symptomatic controls," FD alone patients, FD-IBS patients, or FD-BPS patients, respectively.

Abbreviations: BMI, Body Mass Index; BPS, Bladder Pain Syndrome; GIQLI, GastroIntestinal Quality of Life Index; HADS, Hospital Anxiety Depression Scale; HADS-A and HADS-D, HADS Anxiety and Depression subscales, respectively; IBS, Irritable Bowel Syndrome; ISI, Insomnia Severity Index; n, number; PSQI, Pittsburgh Sleep Quality Index; SD, Standard Deviation.

[a]There are 11 missing values for BMI.

practice. Indeed, the prevalence of unspecified diseases of the urinary tract was around 2–3% among FD patients based on ICD10 diagnoses in the UK[37].

We found that the five groups differed overall on sex ratio, QoL, dyspeptic symptoms severity, anxiety-depression, and sleep. Globally, the presence of overlap with BPS or IBS in FD is associated with younger age, increased female predominance, reduced QoL, increased symptoms severity, higher anxiety and depression levels, and altered sleep. Even if an increased severity of psychopathological features and a lower QoL were already reported in the literature for FD-IBS overlap[38,39], it has never been reported for the overlap with BPS to our knowledge. The presence of overlaps in FD patients identifies a subgroup of dyspeptic patients with more severe disease and which deserves likely broader management. Interestingly, assessing IBS comorbidity in BPS patients has been reported to be clinically relevant since IBS comorbidity predicted poor outcome to bladder hydrodistension, a treatment frequently used in this urinary disorder[40]. Impact on treatment outcomes of BPS overlap in FD patients with or without IBS remains, however, unknown. Female predominance in BPS overlapping syndromes was expected since it is commonly reported for both IBS[41] and FD[42], and since women report more frequently lower urinary tract symptoms compared with men[43].

In our study, QoL was further altered in FD patients with overlap and dyspeptic symptoms severity was increased among FD patients if an overlap with BPS and/or IBS was present, with the more comorbidities the more severe symptoms globally. It has already been shown that FD and FD-IBS overlap impairs QoL compared with the general population and FD patients without overlap, respectively[4,44]. In patients with BPS, the presence of IBS is also known to be associated with worse QoL[45]. Likewise, patients with FD-IBS overlap experience more severe symptoms compared with patients with FD or IBS alone[6]. More generally, overlaps between DGBI are associated with increased disease severity and poorer quality of life[46]. Severity of the symptoms is also known to be associated with anxiety/depression comorbidity[47]. We have shown in our study that overlaps with IBS and/or BPS further strengthen the association between FD and anxiety-depression. This association has already been reported in the literature concerning FD patients[48], especially in the PDS subgroup[49]. Patients with FD-IBS overlap have also higher depression scores[7,47]. Concomitant psychiatric disorders have also been associated with lower QoL[50]. Furthermore, although not studied in depth in our report, life stress events have been shown to be associated with IBS and FD and may participate to higher depression scores in patients with FD-BPS overlap[51].

Mechanisms of overlap between DGBI and BPS are poorly understood. Visceral hypersensitivity is common in DGBI, particularly IBS[52] and FD[53], and functional bladder disorders, OAB and BPS being hypothesized to represent a continuum of a bladder hypersensitivity syndrome[54]. However, even if cross-organ visceral sensitization is well described between bladder and colon[55], the presence of cross-organ visceral sensitization between the upper GI tract and bladder has never been investigated to the best of our knowledge. On the other hand, common psychological comorbidities are found in both patients with DGBI and BPS, which is confirmed by our study, but knowing if they are a cause or a

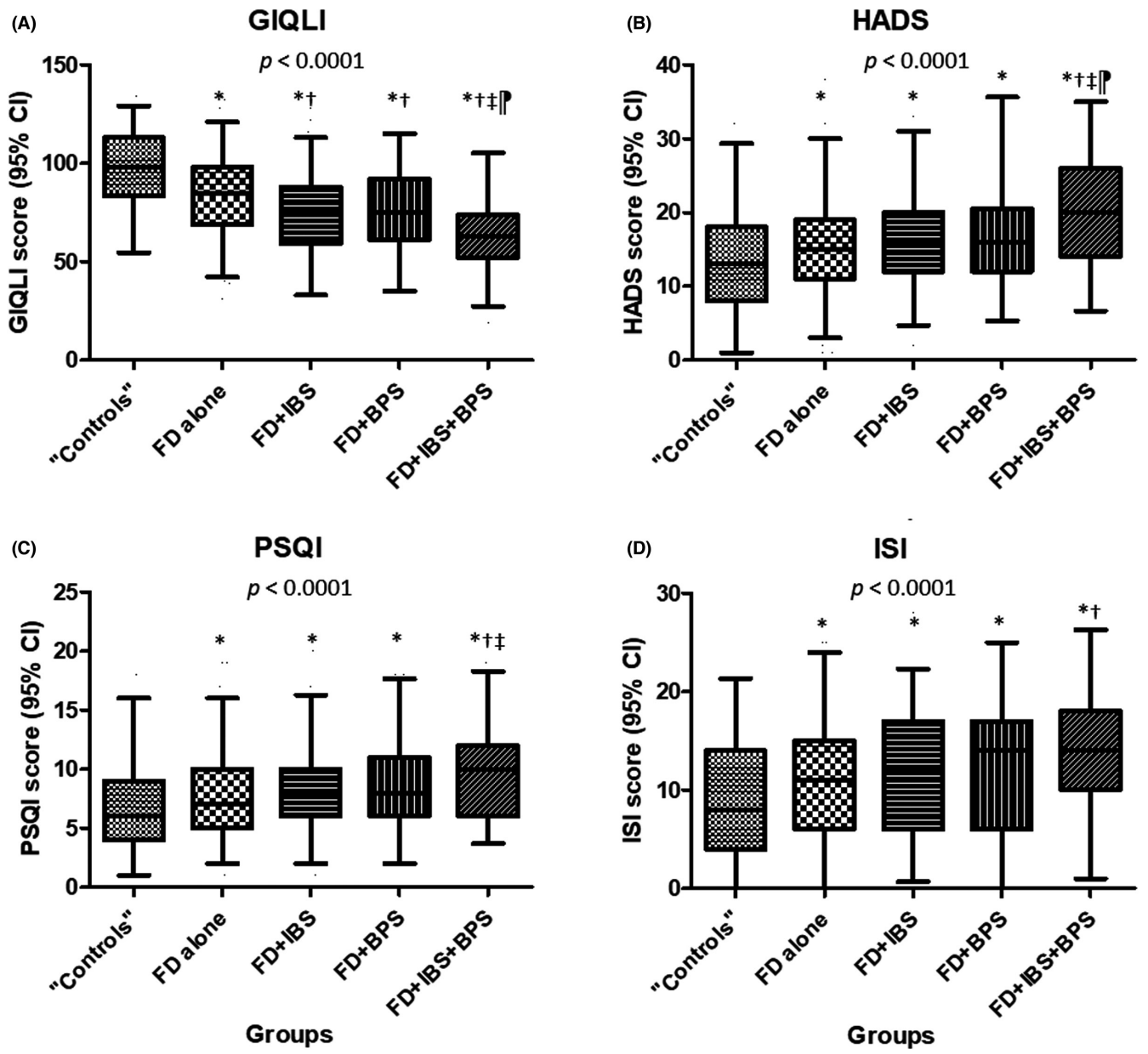
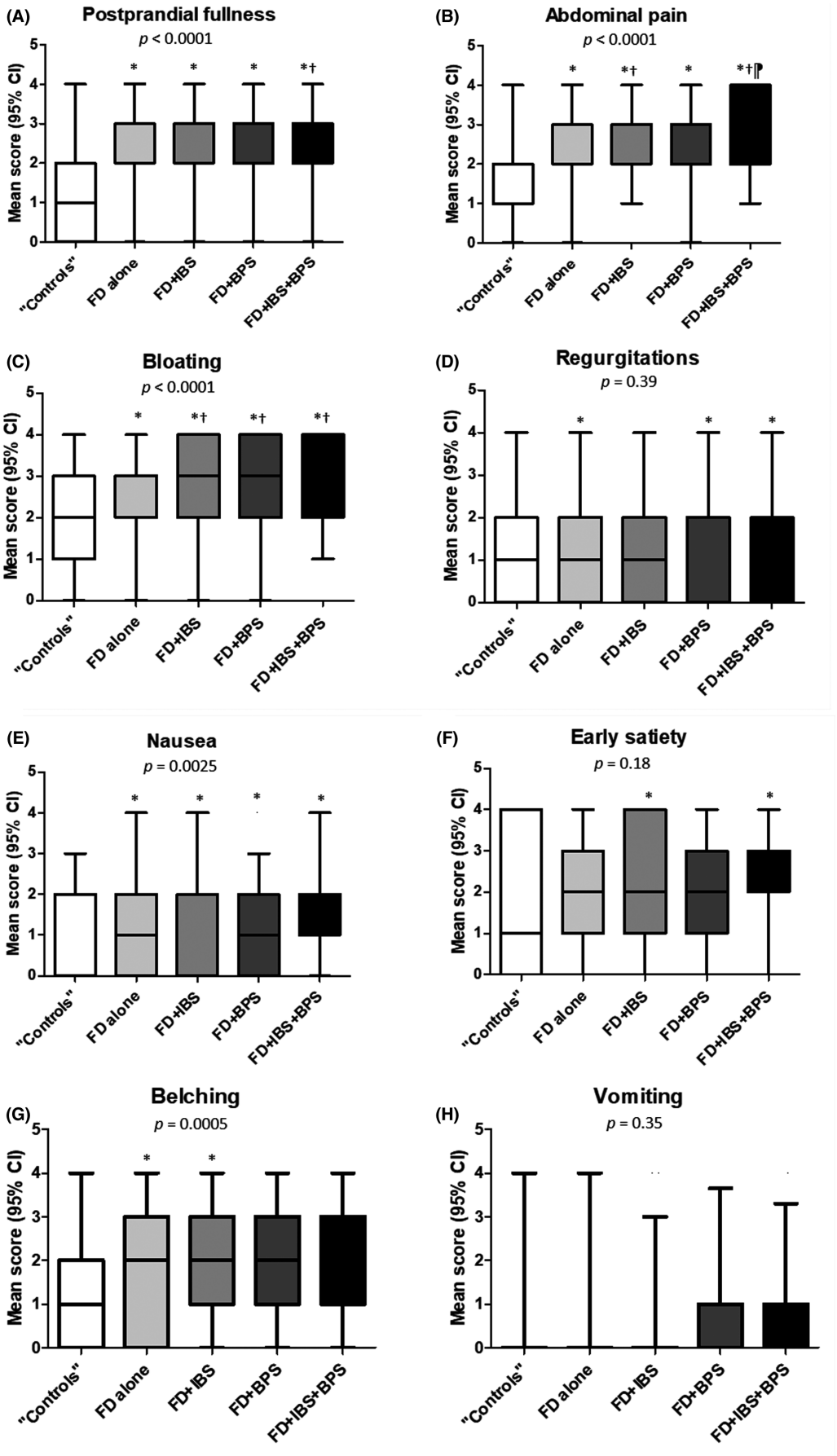


FIGURE 2 Different characteristics of the population according to the group Comparisons of (A) GastroIntestinal Quality of Life Index (GIQLI), (B) Hospital Anxiety and Depression Scale (HADS), (C) Pittsburgh Sleep Quality Index (PSQI), and (D) Insomnia Severity Index (ISI) between the five different diagnostic groups ("symptomatic controls," FD without overlap (FD alone), FD with IBS (FD-IBS), FD with BPS (FD-BPS), and FD with both IBS and BPS (FD-IBS-BPS)). Results are presented as whiskers with 95% confidence interval (CI). All global ANOVA *p*-values are <0.0001. The symbols *, †, ‡, and □ indicate *p*-values <0.05 vs. "symptomatic controls," FD alone patients, FD-IBS patients, or FD-BPS patients, respectively. "Controls" stands for "symptomatic controls" in the legend on *x* axis. BPS, Bladder Pain Syndrome; FD, Functional Dyspepsia; IBS, Irritable Bowel Syndrome

FIGURE 3 Comparison of dyspeptic complaints severity between groups Comparisons of the mean scores of each dyspeptic symptom in the past 15 days between the five different diagnostic groups ("symptomatic controls," FD without overlap syndrome (FD alone), FD with IBS (FD-IBS), FD with BPS (FD-BPS), and FD with both IBS and BPS (FD-IBS-BPS)): (A) postprandial fullness, (B) abdominal pain, (C) bloating, (D) regurgitations, (E) nausea, (F) early satiety, (G) belching, and (H) vomiting. Symptoms were graded from 0 to 4 using a 5-points Likert scale, with 0 corresponding to their absence and 4 to extremely severe symptoms. Results are presented as whiskers with 95% confidence interval (CI). Global ANOVA *p*-values are mentioned below titles. The symbols *, †, ‡, and □ indicate *p*-values <0.05 vs. "symptomatic controls," FD alone patients, FD-IBS patients, or FD-BPS patients, respectively. "Controls" stands for "symptomatic controls" in the legend on *x* axis. BPS, Bladder Pain Syndrome; FD, Functional Dyspepsia; IBS, Irritable Bowel Syndrome


(A)
Postprandial fullness
p < 0.0001
(B)
Abdominal pain
p < 0.0001
(C)
Bloating
p < 0.0001
(D)
Regurgitations
p = 0.39
(E)
Nausea
p = 0.0025
(F)
Early satiety
p = 0.18
(G)
Belching
p = 0.0005
(H)
Vomiting
p = 0.35
Mean score (95% CI)
"Controls"
FD alone
FD+IBS
FD+BPS
FD+IBS+BPS

consequence of both disorders is debated. Altered brain-gut interactions have been described in IBS[56] and FD[57], but neuroimaging studies are scarce in BPS, especially when overlapping with GI symptoms [58]. Interestingly, a history of "bladder and bowel dysfunction" in childhood has been suggested to predict an IBS-like phenotype in BPS patients[59]. However, a prospective evaluation of the onset of these disorders would be necessary to understand the natural history and risk factors of these overlaps[60]. Recently, IBS has been shown to increase the risk of developing BPS in a 12-year follow-up[61]. Sympathetic nervous system dysfunction, with sympathetic predominance, is also recognized in both IBS and BPS[62], suggesting a common underlying pathogenesis in both conditions[63]. Finally, somatization is a risk factor for multiple DGBI but was not assessed in our work.

One limitation of our study is that our population is composed of both Rome III and Rome IV cohorts. 971 (66.8%) patients were classified according to Rome III criteria, whereas 482 (33.2%) were categorized according to Rome IV criteria. However, BPS diagnoses were equally present in both cohorts. In addition, Rome III and Rome IV criteria for FD are quite similar with marginal changes. Another limitation of our study includes the retrospective analysis, although questionnaires, symptoms and QoL scores were acquired prospectively. In addition, our study was monocentric, from a tertiary center. Data acquired from our study may not be directly widespread to the general population.

In conclusion, an overlap between FD and BPS is found in 26.9% of FD patients in our cohort. A diagnosis of BPS is associated with decreased QoL, altered anxiety-depression scale, and altered sleep in FD patients. Overlap with IBS further impacts all dimensions in FD patients. The benefit on those dimensions of BPS treatment in FD patients should be assessed.

AUTHOR CONTRIBUTIONS

GG, MB, and FW designed the study. GG and MB were involved in acquisition of data. GG, MB and FW contributed to analysis and interpretation of data. GG and FW drafted the manuscript. GG, MB, CM, CD, JNC, AML, and FW were provided critical revision of the manuscript for important intellectual content. All authors approved the final version of the article, including the authorship list.

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DISCLOSURE

No competing interests were declared. CM has served as a consultant/advisory board member for Kyowa Kirin, Norgine, Biocodex, MayolySpindler, Tillots, and Ipsen. FW has served as a consultant for Menarini.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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