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RESEARCH ARTICLE

Anal Fissure Patients: Before Treatment, First Consider Irritable Bowel Syndrome, Defecation Disorder and Psychopathology

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ABSTRACT

Aim: The exact etiology of anal fissure (AF) remains unclear but it appears that constipation and stress may instigate AF. Little is known about the role of functional bowel disorder and psychopathology in AF. The aim of this study was to investigate the comorbidity of irritable bowel syndrome (IBS) in AF and its effect on quality of life (QoL).

Method: This was a cross-sectional observational study. Ninety-six AF patients (76 female; 79.2%) with a mean age of 36.54±14.98 years were recruited. The Rome 3 Criteria were applied to diagnose IBS, functional constipation (FC) and no functional gastrointestinal disorder (NoGIS). Depression, anxiety, stress level, stressful life events and QoL were evaluated.

Results: Of the AF patients, 42.7% had IBS, 36.4% had FC, and 20.8% had noGIS. Furthermore, 59% had defecation disorder, characterized by obstructive defecation symptoms. Patients with IBS tended to have more anteriorly located AF (IBS: 40.5%, FC: 24.1%, NoGIS: 7.1%; p=0.053). IBS patients had a significantly higher anxiety score (p=0.021). More severe depression predicted IBS (p=0.009) and IBS predicted more severe depression score (p=0.027). Depression, pain symptom severity and IBS were the most important negative factors affecting QoL (p<0.05).

Conclusion: IBS, FC and defecation disorder are frequent comorbidities in patients with AF. IBS especially and defecation disorder caused a more anxious emotional state, resulting in a decreased QoL. Depression and pain symptom severity appeared to have a greater negative effect on QoL than the other symptoms of AF itself.

Keywords: Anal fissure, irritable bowel syndrome, defecation disorder, psychopathology, quality of life

Introduction

Anal fissure (AF) is a benign anorectal problem even though it can cause significant pain and a negative quality of life (QoL).[1-3] Approximately 40% of patients who present with acute AFs progress to chronic AFs resulting in frequent hospital visits and a high economic cost.[4] However, the exact etiology and natural history is still not well understood and the optimal therapy algorithm for AF is still controversial.

Fissure can be either primary or secondary to predisposing factors, including inflammatory bowel disease, tuberculosis, human ımmunodeficiency virus (HIV), anal cancer, and/or prior anal surgery.[5] The majority of primary acute AFs is thought to be due to the passage of hard stools or diarrhea. Impaired bowel function and defecation disorder might be common among these patients.[6] However, data are limited concerning the risk factors and associated comorbidities of this disorder, although these additional illnesses can further affect the care of this patient population.[7]

Irritable bowel syndrome (IBS) is a common gastrointestinal disorder characterized by abdominal pain and symptoms of constipation, diarrhea or both. Rome classification divides IBS into subtypes based on the predominant stool pattern. IBS-constipation (IBS-C), a subtype of IBS and functional constipation (FC) are described as two major functional diseases according to the Rome III consensus conference.[8]

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However, the pathophysiology of IBS and constipation is broad and includes abnormalities involving motility, visceral sensation, brain-gut interaction, and psychosocial distress.[9] Psychosocial factors, such as depression and anxiety, have been shown to be associated with functional gastrointestinal disorders, such as IBS and constipation but, little is known about the impact of functional bowel disease in the complex etiology of AF.[10] The aim of this study was to investigate the comorbidity of IBS and defecation disorder in AF and what impact, if any, these coexisting disorders have on AF.

Materials and Methods

Patient Recruitment

Patients with AF were recruited from the department of surgery. The study protocol was approved by the Bolu Abant İzzet Baysal University Faculty of Medicine Institutional Ethics Committee (approval number: 2014/06-57, date: 25.02.14). Informed consent was obtained from all patients.

Surgical Assessment

Diagnosis of AF, physical examination and clinical evaluation of all patients was performed by an expert colorectal surgeon. AF was categorized as primary and secondary and those deemed to be suffering from secondary AF (coexisting IBD, tuberculosis, HIV, anal malignancy, active cancer treatment, anal incontinence) were excluded from the study. Chronic AF was diagnosed when non-healing symptoms were present for more than six weeks and there were signs of chronicity on examination (hypertrophied anal papillae, keratinous edges, sentinel pile and/or visible sphincter fibres at the base). Visual analog scale (VAS) for pain and bleeding was used for the assessment of the severity of symptoms of AF.

A Turkish validated, self-administered, 27-item symptom questionnaire, which was based on the Rome III criteria, was used to identify IBS, FC and no functional gastrointestinal disorder (NoGIS).[11] IBS was defined as recurrent abdominal pain of at least three days per month in the last three months, associated with two or more of the following criteria: related to defecation; associated with a change in frequency of stool; and associated with a change in the form (appearance) of stool. Patients who did not meet any of these criteria were accepted as NoGIS patients.

In addition, according to the same questionnaire, defecation disorder was recorded according to the presence of two or more of the following: (i) straining; (ii) sensation of incomplete evacuation; (iii) sensation of anorectal obstruction/blockage; and (iv) manual manoeuvres to facilitate in more than 25% of defecations.

Psychiatric and Quality of Life Assessment

Patients underwent psychological testing at the time of their first clinic visit. Depression and anxiety severity was evaluated with the self-rated Hospital Depression and Anxiety Scale (HAD). The validated Turkish version was used in this study.[12] Stress level was evaluated by two different questionnaires. The first was the Turkish validated form of the self-rated Perceived Stress scale measuring the stress level in the previous month by asking 10 questions, with higher scores indicating higher perceived stress level.[13] Stressful life events were also evaluated by the Sorias Life Events Questionnaire which assesses for 107 stressful life events, including those causing economic, health, relationship, and emotional stress, that occurred in the last one year.[14] Finally, QoL was measured with the Turkish validated form of self-rated SF-36 questionnaire.[15]

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) for Windows, version 22.0, was used for all statistical analyses (SPSS Inc., Chicago, IL, USA). Patients with and without IBS were accepted as constituting internal control and no healthy controls were included. The primary outcome measures were functional gastrointestinal disorder frequency, depression, anxiety, stress level and QOL. Chi-square test, Student's t-test or Mann-Whitney U test were used according to the normality of distribution of data assessed by Kolmogorov-Smirnov test. Pearson's correlation analysis was used to assess the correlations. Binary logistic regression analysis was done to analyze which independent variables (age, sex, fissure type, pain VAS, HAD score) predicted IBS presence. General linear models were created to predict HAD score and subscales of SF-36 QoL scores. Statistical significance was accepted at a p-value of <0.05.

Results

Patient's demographic, symptom severity, fissure type and location data are shown in Table 1. Mean age for the whole cohort was 36.5±14.9 years with a sex distribution of 20 men (20.8%) and 76 women (79.2%). Mean disease duration was 32 months and the most common symptoms were pain (98%), with a mean VAS of 7.5 and bleeding (86%) with a mean VAS of 3.8. Patients with acute fissure tended to have a higher pain VAS score than chronic fissure patients (6.93±2.60 vs. 5.55±2.49, p=0.053). All patients had a primary fissure with no previous surgery for AF. The most common fissure location was posterior (48.8%). The proportions of anterior, anterior + posterior and lateral fissure locations were 28.7%, 20% and 2.5% respectively. More than half (51%) had an additional colorectal disease (20 hemoroid and 29 pruritis ani).

In total, 42.7% of AF patients had IBS, 36.5% had FC and 20.8% had NoGIS. None of these patients were screened for functional gastrointestinal disease (FGID) before, so their

Table 1. Comparison of demographic variables of anal fissure patients with IBS, FC and with no functional gastrointestinal disorder symptom

Demographics	IBS + (group 1) (n=41)	FC + (group 2) (n=35)	NOGIS (group 3) (n=20)	X^2/t/z	p	Post-hoc
Age (years)	35.73 ±14.99	32.69±12.45	45.37±16.37	7,591	**0.022**	1=2<3
Sex						
Male	8 (19.5%)	8 (22.9%)	4 (20/0%)	0.139	0.933	1=2=3
Female	33 (80.5%)	27 (77.1%)	16 (80/0%)			
Disease duration (months)	29.70±62.96	25.91±39.61	47.68±68.45	2,390	0.303	1=2=3
Fissure type						
Acute	3 (7.3%)	10 (28.6%)	3 (15.0%)	6,192	**0.045**	1>2
Chronic	38 (92.7%)	25 (71.4%)	17 (85.0%)			
Fissure location						
Anterior	15 (40.5%)	7 (24.1%)	1 (7.1%)	12,457	**0.053**	1>3
Posterior	17 (45.9%)	15 (51.7%)	7 (50.0%)			
Anterior + posterior	5 (13.5%)	5 (17.2%)	6 (42.9%)			
Lateral	0 (0.0%)	2 (6.9%)	0 (0.0%)			
Symptoms						
Pain VAS	5.18±2.29	6.85±2.47	5.15±2.68	9,231	**0.009**	2>1=3
Bleeding VAS	3.61±2.74	4.21±2.50	3.41±2.18	1,262	0.532	1=2=3
Additional anorectal disease	18 (43.9%)	18 (51/4%)	12 (65/0%)	2,398	0.302	1=2=3
Defecation disorder	27 (69.2 %)	26 (78.8%)	1 (5.0%)	-	<0.001	1=2<3

Mean ± standard deviation and t or z values are given according to the normality of distribution of continuous variables. n (%) and X^2 value are given for categoric variables and p<0.05 is accepted for statistical significance. IBS: Irritable bowel syndrome, FC: Functional constipation, NoGIS: No functional gastrointestinal disorder, VAS: Visual analog scale

diagnosis was made for the first time with this study. FC was associated with acute (28.6%) and IBS was associated with chronic (92.7%) fissure development (p=0.045). Pain VAS was significantly higher in the FC patients (FC: 6.85, IBS: 5.18, NoGIS 5.15, p=0.009). Patients with IBS tended to have a more anteriorly located AF (IBS: 40.5%, FC: 24.1%, NoGIS: 7.1%, p=0.053).

Psychiatric data are given in Table 2. Forty-eight patients (50%) were found to have either an anxiety disorder or a depressive disorder. Among these 48 patients, 42 (87.5%) had a depressive disorder, while six (12.5%) had an axiety disorder. It is notable that only 12 (25%) were on antidepressant medication at the time of inclusion in the study. IBS patients had a higher anxiety score (p=0.021) and their QoL was significantly worse on four out of eight of the SF-36 subscales (p<0.05).

Defecation disorder was defined according symptom questionnaire. According to these questions, 59% were found to have a defecation disorder with no gender difference (61.6% in females, 47.4% in males, p=0.260) (Table 1). Defecation disorder was characterized by obstructive defecation symptoms. Digitation symptom severity was found to be associated with a higher VAS bleeding score (r=0.238, p=0.027). The FC ratio was much higher (79.4% vs 46.6%, p=0.002) in patients with a defecation disorder while IBS ratio did not differ (68.4% vs. 51.9%, p=0.112). Patients with a defecation disorder were significantly more anxious (p=0.010) with a higher number of stressful life events (p=0.042), a higher distress score (p=0.004) and a higher adaptation score (p=0.048). Half of their QoL scores (physical and emotional role limitations, vitality, mental health scores) were also significantly lower than non-defecaton disorder patients (all; p<0.05).

The binary logistic regression model was significant (Omnibus test=0.006, Hosmer-Lemeshow test=0.668) and explained 23.9% of the variance (Nagelkerke R^2=0.239). Only HADD score predicted being in the IBS group (p=0.009, B=-0.162).

A general linear model was created to predict HADD score where IBS presence, age, sex, disease duration, pain VAS and stress score were entered as independent variables. The model explained 48.9% of the variance (R^2=0.489) and

Table 2. Comparison of psychiatric variables of anal fissure patients with IBS, FC and with no functional GIS symptom (NOGIS)

Psychiatric variable	IBS + (group 1) (n=41)	FC + (group 2) (n=35)	NOGIS (group 3) (n=20)	X^2/t/z	p	Post-hoc
HADA	8.97±4.67	7.61±4.86	5.31±4.11	4,109	**0.021**	1>3
Anxiety present	18 (45.0%)	10 (29.4%)	3 (15.8%)	5,137	0.070	1=2=3
HADD	7.42±4.32	5.47±4.02	5.25±4.05	2,557	0.084	1=2=3
Depression present	21 (55.3%)	15 (44.1%)	6 (37.5%)	1,173	0.425	1=2=3
PSS-14	20.48±6.97	18.70±6.24	17.63±5.79	1,388	0.255	1=2=3
Number of stressful life events	5.43±5.10	3.93±3.39	2.79±2.75	3,543	0.170	1=2=3
Distress score	284.05±273.66	203.76±187.87	151.14±158.05	2,956	0.228	1=2=3
Adaptation score	254.05±245.46	183.38±168.14	132.93±139.44	3,193	0.203	1=2=3
GH	15.38±4.23	15.17±3.21	15.36±3.25	0.556	0.757	1=2=3
PF	24.71±4.74	25.40±4.97	25.77±4.69	0.844	0.656	1=2=3
RLP	6.20±1.54	6.80±1.47	7.26±1.32	7,636	**0.022**	1<3
RLE	4.33±1.22	5.02±1.12	5.40±0.82	11,622	**0.003**	1<2=3
SF	7.24±2.22	7.34±2.37	8.52±1.61	4,309	0.116	1=2=3
P	7.00±1.98	6.92±2.18	8.22±1.64	6,611	**0.037**	1=2<3
V	13.55±4.45	14.74±3.88	15.72±3.28	2,992	0.224	1=2=3
MH	18.94±5.55	19.97±5.10	22.73±2.97	3,738	**0.028**	1<3

Mean ± standard deviation and t- or z-values are given according to the normality of distribution of continuous variables. n (%) and X^2 value are given for categoric variables and p<0.05 is accepted for statistical significance. HADA: Hospital Anxiety and Depression Scale-anxiety score, HADD: Hospital Anxiety and Depression Scale-depression score, PSS-14: Perceived Stress Scale score, GH: General health, PF: Physical function, RLP: Role limitations physical, RLE: Role limitations emotional, SF: Social function, P: Pain, V: Vitality, MH: Mental health

HADD was signicantly predicted by the presence of IBS (p=0.027, B=1.684) and stress score (p<0.001, B=0.398).

In other general linear models, QoL subscales scores were entered as dependent variables and age, sex, HAD score, pain VAS, fissure type and IBS presence were entered as independent variables. Physical function was predicted by age (p=0.009) and HADD score (p=0.007); physical role limitation was predicted by HADD (p<0.001) and pain VAS (p=0.022); emotional role limitation was predicted by HADD (p<0.001), pain VAS (p=0.023) and IBS presence (p=0.001); social function was predicted by HADD (p<0.001) and pain VAS (p=0.058); pain was predicted by HADD (p=0.001) and pain VAS (p<0.001); vitality was predicted by HADD (p<0.001); mental health was predicted by HADD (p<0.001).

Discussion

The present study showed that almost half of the patients with AF also had IBS and approximately two-thirds had a defecation disorder, characterized by obstructive defecation symptoms. The presence of IBS presence was associated with chronic fissure development while FC seemed to be associated with acute fissure development. AF patients with IBS were more anxious, with poorer QoL compared to patients with no IBS. All subscales of the SF-36 QoL tool were negatively predicted by depression severity and some subscales were negatively predicted by pain severity, rather than other clinical aspects of AF, such as fissure type and location. To the best of our knowledge, this is the first study invesigating the prevalance and effect of IBS and defecation disorder in AF patients.

Most surgeons and published expert opinions describe AF as "common", but there is scarce published epidemiologic data and the causative factors for AF are poorly understood.[6] By understanding the associated risk factors or coexisting disorders, prevention and treatment could be improved. It is well known that associated constipation is the most common factor causing chronic AF. However, constipation is a very broad spectrum and it can be classified as obstructed defecation disorder, slow-transit constipation, constipation-predominant IBS and FC.[16] These classifications are not mutually exclusive and significant overlap exists, but IBS is the most common of these disorders. Although worldwide prevalence of IBS is 10-15%, there is no epidemiologic data about the prevalance of IBS in AF.[17] Surprisingly few data exist on the interplay between AF and IBS, and what impact this comorbidity has on the presentation and course of AF.

Interestingly, none of our patients had been questioned about IBS prior to this study, had not been diagnosed with IBS, and had not received any specific treatment for it, despite the proportion of AF patients with IBS being 43% in this cohort.

The most common location of primary AF is posterior midline (90%). However, we found that the presence of IBS was associated with a more frequent anterior fissure location in this study. The posterior region receives less than half of perfusion in comparison to the rest of the anal canal and reduced anodermal blood flow associated with hypertonicity of the internal anal sphincter is the most common accompanying physiology in AF.[18] However, manometric studies have shown that up to 50% of patients with AF do not have increased anal pressures.[19] Anterior midline location is rare and accounts for up to about 25% of primary fissures in women (particularly postpartum women) and about 8% of primary fissures in men. Up to 3% of patients present with both primary anterior and posterior fissures simultaneously.[20] The cause of these other locations is not well known. These patients are typically women with anterior midline AF, which, in small studies, has been associated with vaginal delivery, external sphincter injury/dysfunction, rectocele, and rectoanal intussusception.[21] In this study, although we had a female preponderence in the cohort, no gender difference was found in terms of fissure location. So, IBS seemed to be associated with anterior fissure development in this cohort.

Approximately 40% of patients who present with acute AF progress to chronic AF.[5] Over the years, the pathophysiological mechanisms of the persistance and chronicity of AF have not been identified. According to the present study, the presence of IBS seemed to be associated with chronic fissure development while fuctional constipation seemed to be associated with acute fissure development. Apart from that, in IBS patients, no significant difference in pain symptom severity was reported but pain intensity was found to be significantly higher in FC patients compared to IBS patients, probably due to acute fissure.

Defecation disorder may also play a role in patients with AF or hemorrhoids.[6] Whether these disorders are secondary to defecation disorder or are responsible for the abnormal defecatory act remains conjectural. In the present study, more than half of the AF patients had a defecation disorder characterized by obstructed defecation symptoms. However, we do not know whether these findings are related to dyssynergic defecation or anatomical abnormality, such as rectocele, intussusception, or AF per se, since we did not perform manometric or radiological evaluations.

Furthermore, there was no difference in terms of fissure location or severity of fissure-related symptoms between patients with and without a defecation disorder, except for the higher ratio of FC in defecation disorders patients. Although there was no difference in terms of IBS prevalance in patients with and without defecation disorder, defecation disorder patients were much more anxious and stressed with a lower QOL. Thus, stress and related anxiety seems to be asociated with defecation disorder and FC seems to be associated with the development of AF. However, it could it be that AF and the associated painful defecation and bleeding may also result in defecation disorders and FC, which may produce stress and anxiety as well. Prospective cohort studies may be needed to evaluate this cause-effect relationship.

As mentioned, in this study, it was found that AF patients had a higher frequency of FGID-like FC, obstructed defecation disorder and IBS. Although many studies have focused on the intensity of psychological parameters in FGID subtypes and have shown significant associations between FGID symptoms and psychological factors, frequently no difference was found in terms of psychiatric comorbidity between subjects with different FGID subtypes.[22] However, we found that IBS patients had statistically significant higher anxiety levels than FC patients, although depression has been shown to be associated with constipation. Defecation disorder patients were also more anxious and stressed compared to non-defecation disorder patients.

Although there are many studies showing significant associations between IBS symptoms, psychological factors and psychiatric comorbidity, our study is the first to investigate this association in AF patients. Previous studies have shown that mood disorders, anxiety and somatization were the most common psychiatric comorbidities in IBS patients.[23] These psychosocial factors were shown to be associated with increased IBS symptom severity, impaired QOL, and visceral hypersensitivity.[24] In our patient group, patients with IBS were more anxious with a lower QoL compared to patients with no IBS. All subscales of the SF-36 were predicted negatively by depression severity and some subscales were negatively predicted by pain severity rather than the other clinical aspects of the disease, such as fissure type and location. The presence of IBS and stress level predicted depression severity in this patient group to a greter degree than the other clinical variables, while depression severity also predicted having IBS. Thus, there seems to be a mutual interaction between stress, depression, presence of IBS and QOL. Of course this result does not explain the old dilemma of whether depression causes IBS or IBS causes depression; it only indicates a bi-directional relationship between the two.

The link between psychosocial factors and gastrointestinal function (motility, sensation, inflammation) is through the brain-gut axis, implying bidirectional communication between the gastrointestinal tract and the brain, through neural, neuroimmune and neuroendocrine pathways. Stress has an impact on important physiological functions of gut through sympathetic overactivation causing abnormalities in gut motility, secretion, visceral sensitivity, mucosal blood flow and intestinal microbiota, leading to the development of a broad array of FGID's.[25] So, surgically correctable anorectal disease and disorders of the brain-gut axis, such as IBS, may be two clinically distinct entities that are mutually exclusive. Given this observation, we argue that patients referred for management of AF should be screened and treated for FGID's, such as IBS, FC and defecation disorder, before considering surgical treatment.

Study Limitations

Our study is limited by a relatively small cohort size and there was no follow-up in this cohort study so, no cause-effect relationships can be drawn. The small number of cases may also be insufficient to make a robust association between IBS with constipation and the occurrence of chronic AF through its association with increased anxiety. In addition, FGID subtypes were defined according to a self-rated questionnarie. The Rome III criteria for FGID separates IBS with constipation and FC into separate entities and excludes a diagnosis of FC in patients satisfying the criteria for IBS. Recent studies, however, suggest that there is a lack of symptom profile specificity and much diagnostic overlap exists between these groups, and that they might be part of the same condition, with patients located along a spectrum of pain/discomfort severity.[26,27] We have also found an overlap between these FGID subtypes, although no manometric or radiologic study was done to show objective evidence for defecation disorders. Furthermore, our data reflected a subset of treatment-seeking individuals and, therefore, our findings may not be generalized to primary care settings or community populations. Lastly, some of our patients were on antidepressant medication at the time of inclusion in the study, which might cause a change in bowel movements, but this was a small percent (25%) and most of the patients were free of medication at time of inclusion.

Conclusion

Our findings suggest that assessment of IBS symptoms and obstructed defecation symptoms may be an important part of the evaluation of AF. Recognition of IBS/subtypes and obstructed defecation disorder that may be more amenable to conservative treatments may be necessary before proceeding with more invasive treatment modalities in AF, since psychological symptoms like anxiety are frequent features in IBS. Also, psychological factors including cognitive (anxiety sensitivity) and emotional (depression) elements seem to be as important as somatic symptoms (severity of AF) in predicting QoL in these patients. Thus, a concept of the biopsychosocial model of illness may integrate all possible accountable factors for the pathogenesis and clinical expression of AF. These findings further solidify the recommendation of non-operative management for AF. However, additional evidence is needed to support this approach in clinical care. Thus, future prospective studies which focus on the effect of surgical or non-surgical treatment to show if the findings persisted or resolved upon healing of the so-called resultant fissure would help to resolve this question.

Ethics

Ethics Committee Approval: The study protocol was approved by the Bolu Abant İzzet Baysal University Faculty of Medicine Institutional Ethics Committee (approval number: 2014/06-57, date 25.02.14).

Informed Consent: Informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.Ş., Ö.A., D.Y., U.A., Concept: N.Ş., Ö.A., Design: N.Ş., Ö.A., Data Collection or Processing: N.Ş., Ö.A., D.Y., U.A., Analysis or Interpretation: N.Ş., Ö.A., Literature Search: N.Ş., Ö.A., Writing: N.Ş., Ö.A.

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