Journal of Inflammatory Bowel Diseases & Disorders

Wheeler et al., J Inflam Bowel Dis & Disord 2016, 1:2

Research Article OMICS International

Initial Site of Crohn's Disease is not an Independent Predictor of Outcome of Short Bowel Syndrome

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Received date: October 17, 2016; **Accepted date:** October 27, 2016; **Published date:** November 01, 2016

Abstract

Objective: Patients with Crohn's disease (CD) are at risk for Short Bowel Syndrome (SBS). Our aim was to determine the effect of initial site of disease on outcome in patients with CD developing SBS.

Methods: We reviewed the outcome of 87 adult CD patients with SBS. Thirty-eight (44%) had initial ileocolonic disease, 27(31%) had colonic disease and 22(25%) had small intestinal disease.

Results: Compared to patients with small intestinal and ileocolonic disease, patients with initial colonic disease were more likely to have a total colectomy (85% *vs* 32% and 37%, p<.05) and have an ostomy (89% *vs* 37% and 34%, p<.05). Intestinal remnant length was similar. Intestinal remnant length was the only predictor of need for long-term(>1year) Parenteral Nutrition (PN) (p<0.0001). CD site at presentation was not significant on multivariate analysis (p=0.40).

Conclusion: Patients with CD with colon as the initial site of disease who develop SBS have different anatomic characteristics. However, initial site of disease is not an independent predictor of need for long-term PN.

Keywords: Crohn's disease; Short bowel syndrome; Intestinal resection; Intestinal failure; Crohn's colitis

Introduction

Patients with Crohn's disease (CD) are at risk for development of Short Bowel Syndrome (SBS). Up to 80% of patients with Crohn's disease will require at least one intestinal resection during the course of the disease. They frequently require multiple surgical interventions for recurrence or complications of surgical therapy. Outcome of CD is related to several factors, including age at onset, nature of disease, and initial site of disease [1-5]. In a previous study of SBS and CD, we found that initial site of disease influenced intestinal remnant length and frequency of ostomy formation [6]. The aim of the present study was to determine the effect of initial site of disease on outcome in a larger cohort of patients with CD developing SBS.

Methods

We reviewed the records of 530 patients with SBS evaluated at the University of Nebraska Medical Center between 1982 and 2014. Eighty-seven patients (16%) had CD. There were 48 women and 39 men ranging in age from 23 to 76 years. SBS was defined as an intestinal remnant less than 180 cm with associated malabsorption requiring specialized enteral or parenteral nutrition. Intestinal length was determined by operative reports when documented or radiologic studies at initial presentation. CD was diagnosed by standard clinical, radiographic, endoscopic and pathologic criteria.

Intestinal anatomy as described by Messing [7]: Type 1 (end jejunostomy), Type 2 (Jejunocolic anastomosis) and Type 3 (Jejunoileocolic anastomosis). Records were reviewed to determine the time and site of initial presentation, time to development of SBS, treatment of SBS and outcome. Patients were followed for a minimum of 12 months.

Descriptive statistics included counts and percentages for categorical data and means, standard deviations (SDs), medians, minimums and maximums for continuous data. Fisher's exact test was used to look at associations between categorical variables. Analysis of variance (ANOVA) was used to compare continuous data between the three groups. The Cochran Armitage test for trend was used to evaluate a linear trend between remnant and PN >1 year. Multiple logistic regression was used to assess predictors of PN>1. A p-value < 0.05 was considered statistically significant.

Results

The three groups were similar with respect to gender (Table 1). Age at diagnosis of Crohn's disease, time interval to SBS and age at SBS were also similar. There were no significant differences in number of previous resections, history of stricturoplasty or use of biologic therapy. Only 9% of all patients had undergone stricturoplasty for management of Crohn's disease. Intestinal remnant length was similar in the three groups (p=0.14) (Table 2). Patients with colonic disease were more likely to have a total colectomy, have an ostomy, and have Type 1 anatomy compared to patients with ileocolonic and small intestinal disease (p<0.05).

	Ileocolonic	Colonic	Small Intestine	Total
Number	38	27	22	87
Gender				
Female	22 (58%)	15 (56%)	11 (50%)	48 (55%)
Male	16 (42%)	12 (44%)	11 (50%)	39 (45%)
Age at Crohn's (years)	26.4 (14-75)	26.3 (8-69)	23.6 (8-45)	25.6 (8-75)
Interval Crohn's to SBS (years)	16.5 (1-45)	17.6 (2-36)	20.1 (2-36)	17.7 (1-45)
Age at SBS (years) mean (range)	43.1 (24-76)	44.3 (23-71)	43.8 (23-57)	43.6 (23-76)
Previous resections Mean	4.6+2.8	4.0+1.3	4.2+2.3	4.3+2.3
<4	28 (74%)	19 (70%)	13 (59%)	60 (69%)
>4	10 (26%)	8 (30%)	9 (41%)	27 (31%)
Stricturoplasty				
Yes	3 (8%)	1 (4%)	4 (18%)	8 (9%)
No	35 (92%)	26 (96%)	18 (82%)	79 (91%)
Biologic therapy				
Yes	22 (58%)	9 (33%)	7 (32%)	38 (44%)
No	16 (42%)	18 (67%)	15 (68%)	49 (56%)

Table 1: Patient Demographics. SBS: Short Bowel Syndrome.

	Ileocolonic	Colonic	Small intestine	Total
Number	38	27	22	87
Small intestine remnant length (cm)				
<60 60-120 >120	8 (21%) 11 (29%) 19 (50%)	1 (4%) 6 (22%) 20 (74%)	5 (23%) 7 (32%) 10 (45%)	14 (16%) 24 (28%) 49 (56%)
Colon remnant				
Yes None	24 (63%) 14 (37%)	4 (15%) 23 (85%)*	15 (68%) 7 (32%)	43 (49%) 44 (51%)
Ostomy				
Yes No	13 (34%) 25 (66%)	24 (89%) 3 (11%)*	8 (37%) 14 (64%)	45 (52%) 42 (48%)
Anatomy type				
I II III	14 (37%) 19 (50%) 5 (13%)	22 (81%)* 5 (19%)* 0 (0%)	7 (32%) 13 (59%) 2 (9%)	43 (49%) 37 (43%) 7 (8%)

Table 2: Intestinal Anatomy. *p<0.05 vs ileocolonic and small intestine.

There were no differences in the use of operations to treat SBS (Table 3). Five patients underwent intestinal transplantation. Length of follow up and mortality rates were also similar.

	Ileocolonic	Colonic	Small intestine	Total	P- Value
Number	38	27	22	87	
Nutrition support					
No PN PN<1 year PN>1 year	15 (39%) 6 (16%) 17 (45%)	14 (52%) 6 (22%) 7 (26%)	7 (32%) 2 (9%) 13 (59%)	36 (41%) 14 (16%) 37 (43%)	0.22
Operation for SBS					
Stricturoplasty Close ostomy Reversed segment Intestinal lengthening Intestinal transplantation Total	1 2 2 1 2 8 (21%)	2 2 1 0 2 7 (26%)	2 1 0 1 1 5 (23%)	5 5 3 2 5 20 (23%)	0.95
Follow up (months)	70+74	46+54	41+43	55+62	0.14
Died					
Yes	8 (21%)	2 (7%)	4 (18%)	14 (16%)	0.36

Table 3: Nutritional outcome (PN: Parenteral Nutrition; SBS: Short Bowel Syndrome).

The only significant predictor of PN>1 year was remnant length (p<0.0001). Doing a test for trend it appears that as the remnant increases, the proportion of patients with PN>1 year decreases (p<0.0001). Site of CD at presentation trends towards significance (p=0.06). In multivariate logistic regression, site of CD at presentation was not a significant predictor of PN>1 year after adjusting for remnant length (p=0.40). Remnant length is a statistically significant predictor of PN>1 year after adjusting for site of CD at presentation (p=0.0001; odds ratio=0.14, 95%CI: 0.06-0.33). Increasing remnant length is associated with decreased odds of PN>1 year after adjusting for CD at presentation (Table 4).

	PN>1 year	PN<1 year or none	P value
Gender			
Female Male	22 (59%) 15 (41%)	26 (52%) 24 (48%)	0.52
Previous resections			
<4 >4	22 (59%) 15 (41%)	38 (76%) 12 (24%)	0.11
Small intestine remnant			
<60 60-120 >120	12 (32%) 17 (46%) 8 (22%)	2 (4%) 7 (14%) 41 (82%)	<0.0001
Ostomy			
Yes No	23 (62%) 14 (38%)	22 (44%) 28 (56%)	0.08
Colon remnant			
Yes No	18 (49%) 19 (51%)	25 (50%) 25 (50%)	1.00
Anatomy type			
I II III	21 (57%) 14 (38%) 2 (5%)	22 (44%) 23 (46%) 5 (10%)	0.48
Site of initial disease			
Small intestine Ileocolonic Colonic	13 (35%) 17 (46%) 7 (19%)	9 (18%) 21 (42%) 20 (40%)	0.06

Table 4: Risk of long-term PN (PN: Parenteral Nutrition).

There was no correlation between age at diagnosis of Crohn's disease (24+11 *vs* 27+14), age at diagnosis of SBS (42+9 *vs* 45+12), and interval between diagnosis of CD to SBS (18+9 *vs* 18+10) and need for long-term PN.

Discussion

Despite the high rate of resection and recurrent disease, SBS remains uncommon in CD. The risk of developing SBS in patients with CD is approximately 1- 10% [3, 8-11]. Important risk factors for developing SBS that have been identified are penetrative type, intestinal remnant length, total colectomy, ostomy creation and severity of disease [9, 11]. Whether initial site of disease is also an important factor leading to SBS or affecting nutritional outcome has not been clearly established.

In the present study, initial site of disease was not an independent predictor of the need for long-term PN. Intestinal remnant length was the important factor. While there was a tendency found on univariate analysis, multivariate analysis accounting for intestinal remnant length found no significant association with initial site of CD. However, there were anatomic differences among the groups, particularly for patients with initial Crohn's colitis.

We do not know the total pool of patients with CD leading to SBS in our study since most patients are referred for SBS management. Thus, we cannot comment on whether site of initial CD affects the incidence of SBS. Forty-four percent of our SBS patients had initial ileocolonic disease, 31% colonic disease and 25% small intestinal disease. Uchino et al [9] reported that 24 (3%) of 721 patients undergoing resection for CD developed SBS. Twenty-two (92%) had initial ileocolonic disease and two (8%) had ileitis. Overall, 60% of patients undergoing resection for Crohn's had ileocolitis. While ileocolitis was a risk factor for SBS on univariate analysis, it was not an independent factor on multivariate analysis. Elriz et al. [11] reviewed 38 patients with SBS requiring PN related to CD. They found initial ileocolonic disease in 71%, small intestine in 18% and colonic disease in 11%. They suggested that initial small intestinal length and severity of disease were the main risk factors but site of initial disease was not evaluated. Sampietro et al. [10] reported only two (.5%) patients developing SBS among 393 patients undergoing conservative surgical therapy out of 502 patients with small intestinal Crohn's disease. Procedures were equally divided between minimal intestinal resection and Crohn's disease.

Site of initial disease might affect the development of SBS via several factors. Site of disease may influence risk of recurrent disease, need for surgical intervention, and resultant intestinal anatomy. Site of disease might also alter choice of medical and surgical therapy.

Location of initial disease was not found to be a risk factor for postoperative recurrence in a recent review [12]. In a Swedish population study, there appears to be rising cumulative risk of recurrence for small intestinal disease from approximately 30% at five years, 50% at 10 years and 60% at 15 years [13]. The cumulative risk of recurrence for ileocolonic disease was similar (30%, 50%, and 55% at 5, 10, and 15 years) [12]. The recurrence rate for colonic disease was 20% at five years and 35% at 10 years. A Mayo Clinic study found no difference for risk of recurrence based on site of disease [14]. An Italian referral center study found no difference in recurrence rates with intestinal (13%), ileocolonic (8%) or colonic disease (24%) [15]. However, Onali et al. [16] found a lower risk of symptomatic recurrence in patients with ileocolonic resection versus other resections (37% *vs* 100%).

We found that the mean time interval to development of SBS was 16 to 20 years and was similar regardless of initial site of disease. However, this interval ranged from one to 45 years. Elriz et al. [11] also found a median time from CD to SBS of 15 years. While the incidence of SBS remained stable over time, they found a shorter time to SBS over the period of their study. These findings suggest that the time courses of resections are similar. The proportion of patients undergoing more than four resections prior to SBS was also similar. Elriz et al. [11] found that the median number of resections leading to

SBS was three. Uchino et al. [9] reported that a history of more than three resections was a risk factor for PN.

We did confirm that initial site of disease influences intestinal anatomy. Our patients with initial colonic disease were more likely to have total colectomy, an ostomy, and type 1 anatomy. However, the number of resections leading to SBS and intestinal remnant length were similar in the three groups.

In the present study, the use of stricturoplasty and biologic therapy for management of CD prior to SBS was similar in the three sites of initial disease. While the use of biologics in the ileocolonic group approached statistical significance we do not have other information about disease severity. Thus we cannot make conclusions related to severity of disease in these patient populations. Uchino et al. [9] found that previous biologic therapy and use of stricturoplasty did not affect use of PN.

Elriz et al. [11] reported that one half of their SBS patients underwent rehabilitative surgical procedures. Only one fourth of our patients underwent these procedures, including 5% who underwent intestinal transplantation. Abu-Elmagd et al. [17] reported that 10% of intestinal transplants in adults were related to Crohn's disease. Crohn's disease recurrence had no impact on graft function. Initial site of disease is not a commonly recognized risk factor in the need for intestinal transplantation for Crohn's disease [18].

Conclusion

In summary, initial site of CD does influence certain anatomic characteristics of SBS patients. Patients with initial Crohn's colitis are more likely to have had a total colectomy, ostomy creation and type 1 anatomy. However, initial site of CD is not an independent predictor of the need for long-term PN.

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