Very Early Pouchitis is Associated with an Increased Likelihood of Chronic Inflammatory Conditions of the Pouch

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Background

Chronic inflammatory conditions of the pouch are common after colectomy with ileal pouch-anal anastomosis (IPAA) for ulcerative colitis (UC).

After IPAA for UC approximately 17% of patients will develop chronic antibiotic dependent pouchitis (CADP) while 10% will develop Crohn's-like disease of the pouch (CLDP).

Despite the high prevalence of these inflammatory complications after IPAA surgery, there remains a lack of knowledge regarding the risk factors for the future development of these complications.

Aim

To investigate the relationship between very early pouchitis, defined as pouchitis within the first 180 days of the final stage of IPAA surgery, and the future development of CADP and CLDP.

Methods

Design: Retrospective cohort study

Population: Adults who underwent proctocolectomy with IPAA for UC at UNC between 1/1/2004 and 12/31/2016.

Primary Outcome: The development of CADP in patients with very early pouchitis.

Secondary outcomes: The development of CLDP in patients with very early pouchitis.

Analysis: Multivariable logistic regression was used to evaluate the relationship between very early pouchitis and the development of CADP and CLDP.

Results

Table 1. Univariate comparison of demographic and clinical characteristics of patients with and without pouchitis in the two years following an IPAA.

	Patients without early pouchitis (n=489)		Patients with early pouchitis (n=137)		p-value
	median	IQR	median	IQR	
Age at surgery, in years	40.3	28.8-52.4	43.1	33.7-54.5	0.094
Disease duration prior to surgery	5.9	2.2-14.2	6.3	1.96-13.6	0.854
	n	%	n	%	
Male Sex	249	50.9	75	54.7	0.429
Race					0.923
White	424	89.3	121	89.0	
Non-White	51	10.7	15	11.0	
Hispanic	6	1.4	7	5.6	0.006
Family history of CD or UC	83	16.2	14	20.0	0.421
Indication for surgery					0.059
Medically-refractory colitis	376	76.9	118	86.1	
Dysplasia or cancer	72	14.7	11	8.0	
Other indication/multiple indications	41	8.4	8	5.8	
Disease extent prior to surgery					0.405
Proctitis	23	5.0	3	2.3	
Left-sided colitis	133	29.1	40	30.8	
Extensive colitis	301	65.9	87	66.9	
Stages involved in IPAA Surgery					0.977
1	92	18.9	24	17.5	
2	173	35.5	51	37.2	
Modified 2	183	37.5	11	37.2	
3	40	8.2	51	8.0	
Abscess or pelvic sepsis after IPAA surgery	94	19.2	23	16.8	0.518
Evidence of an IPAA leak immediately after surgery	38	7.8	8	5.8	0.444
Primary Sclerosing Cholangitis	13	2.7	6	4.4	0.299
Medications Prior to Colectomy					
Systemic aminosalicylate	380	77.7	115	83.9	0.113
Topical aminosalicylate	230	47.0	72	52.6	0.253
Thiopurine	299	61.2	91	66.4	0.256
Methotrexate	58	11.9	9	6.6	0.077
Anti-TNF	252	51.5	69	50.4	0.809
Vedolizumab	11	2.3	6	4.4	0.175
Cyclosporine	13	2.7	13	9.5	<0.001
Prednisone use at the time of last stage of surgery	192	39.3	58	42.7	0.487

Anti-tumor necrosis factor alpha (anti-TNF); Crohn's disease (CD); ileal pouch-anal anastomosis (IPAA); interquartile range (IQR); ulcerative colitis (UC)

Among 626 patients undergoing IPAA for UC, 137 (22%) developed very early pouchitis, 75 (12%) developed CADP, and 59 (9%) developed CLDP

The median duration of follow up was 5.18 years (IQR 0.94 – 10.8 years).

Table 2. Odds of developing chronic antibiotic dependent pouchitis after ileal pouch-anal anastomosis for ulcerative colitis

	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Very Early Pouchitis (acute pouchitis within 180 days of IPAA)	3.61 (2.18 – 5.96)	3.65 (2.19 – 6.10)
Duration of ulcerative colitis prior to colectomy		
≤2 years	0.75 (0.33 – 1.74)	0.78 (0.34 – 1.79)
3-5 years	Reference	Reference
6-10 years	1.28 (0.58 – 2.82)	1.19 (0.53 – 2.66)
>10 years	1.68 (0.85 – 3.31)	1.53 (0.76 – 3.07)
Primary sclerosing cholangitis	4.78 (1.81 – 12.5)	3.97 (1.44 – 11.0)

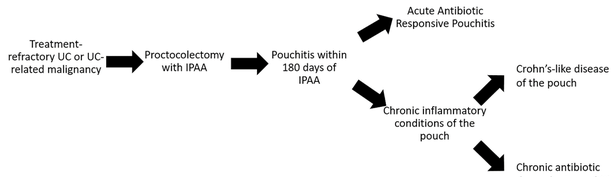
Note: All factors included in the multivariable model are shown above.

Table 3. Odds of devloping Crohn's like disease of the pouch after an ileal pouch-anal anastomosis for ulcerative colitis

	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Very Early Pouchitis (acute pouchitis within 180 days of IPAA)	2.78 (1.58 – 4.82)	2.77 (1.54 – 4.98)
Delayed Pouch Creation	1.21 (0.70 – 2.08)	1.27 (0.72 – 2.24)
Family history of CD or UC	2.20 (1.18 – 4.11)	2.14 (1.13 – 4.05)

Note: All factors included in the multivariable model are shown above.

Figure 1. Disease progression in chronic inflammatory pouch diseases.



Conclusions

Very early pouchitis is associated with an increased risk developing CADP and CLDP.

The identification of very early pouchitis has the potential to serve as a unique risk factor for future chronic inflammatory conditions of the pouch.

Future studies should focus on treating very early pouchitis as an individual phenotype to prevent future chronic pouch related disorders.

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