Endoscopic Treatment of Ileal Pouch Sinus

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Background and aims: Pouch sinus is a serious complication in patients undergoing ileal pouch-anal anastomosis. The aim of this study was to verify the efficacy and safety of endoscopic needle knife sinusotomy (NKSi) in the management of pouch sinus.

Methods: All consecutive patients with a pouch sinus treated with NKSi from 2008 to 2016 were identified. The primary outcomes were complete healing of the sinus and pouch survival.

Results: A total of 109 patients were included. During a median follow-up of 2.1 years (interquartile range: 0.7–4.4), 54 (49.5%) patients achieved complete healing and 20 (18.3%) patients had partial healing, Twenty-two (20.2%) patients developed sinus-related pouch failure. In multivariable analysis for the sinus healing, Crohn's disease of the pouch was a risk factor [odds ratio (OR): 0.3, 95% confidence interval (CI): 0.1–0.8), whereas a longer interval between NKSi (OR: 1.1, 95%CI: 1.0–1.1) and high body mass index (OR: 1.2, 95%CI: 1.0–1.3) were protective factors. In the multivariable analysis for surgery-free survival, previously documented acute anastomotic leak (OR:3.5, 95%CI: 1.2–10.4), toxic megacolon (OR: 7.4, 95%CI: 1.9–29.1), an increased length of sinus (OR: 1.4, 95%CI: 1.0–2.0), and increased duration from sinus diagnosis to NKSi (OR: 2.6, 95%CI: 1.1–6.2) were risk factors; and a longer interval between NKSis (OR: 0.9, 95%CI: 0.9–0.99), and concurrent use of dextrose 50% (OR: 0.2, 95%CI: 0.04–0.6) and doxycycline during the NKSi procedure (OR: 0.2, 95%CI: 0.04–0.7) were protective factors. NKSi-associated complications were reported in 6 (1.8% per procedure) cases.

Conclusions: NKSi is an effective and safe procedure for treating pouch sinus.

Key Words: anastomotic leak, electroincision, endoscopy, inflammatory bowel disease, ileal pouch, needle knife, sinus, sinusotomy, ulcerative colitis

INTRODUCTION

Ileal pouch-anal anastomosis (IPAA) after proctocolectomy has become the surgery of choice for patients with medically refractory ulcerative colitis or indeterminate colitis, colitis-associated neoplasia, familial adenomatous polyposis, or a highly selected subset of patients with refractory Crohn's colitis. On the other hand, short- and long-term adverse events were seen in as high as 60% of patients who underwent IPAA[1–3] leading to pouch excision or permanent diversion in 4%–10 % of cases.[4–7] Pouch sinus is defined as a blind tract resulting from chronic pouch-anal anastomotic leak or suture/staple line leak.[8] It occurs in 2.8% to 8% of IPAA patients.[9–11] Anastomotic sinus not only can delay ileostomy closure, but also is one of the common causes for pouch failure in the long term.[9, 12, 13] Although acute leaks could treated with observation, chronic leak, ie, pouch sinus would eventually require surgical intervention in current clinical practice with incision and drainage, debridement, unroofing, occlusive treatment with fibrin glue, pouch diversion, or redo pouch.[9–11, 13–15] The results from these interventions varied. Therefore, endoscopic approaches have been explored.

Alternatively endoscopic treatment such as stapled marsupialization and local vacuum sponge treatment have been shown to be effective in treating acute anastomotic leak.[16–18] We developed endoscopic needle knife sinusotomy (NKSi) for chronic pouch sinus, with a promising success rate.[19–21] In our previous series of 65 patients treated with NKSi, 43.1% had complete healing of the sinus during a median follow-up of 1.1 years. The current study is a natural extension of our previous investigation with a larger patient population and a longer follow-up. The aim of this study were to verify the efficacy and safety of NKSi in the treatment of the pouch sinus and to assess risk factors associated with delayed healing or nonhealing and subsequent pouch failure.

PATIENTS AND METHODS

Data Sources

All consecutive patients with an ileal pouch that were treated with NKSi for their sinus in our Interventional Inflammatory Bowel Disease (*i*-IBD) Unit from 2008 to 2016 were identified from our established *i*-IBD registry. This study

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Abbreviations. BMI, body mass index; CD, Crohn's disease; CI, confidence interval; EUA, examination under anesthesia; GI, gastrointestinal; IBD, inflammatory bowel disease; i-IBD Unit, the Interventional Inflammatory Bowel Disease Unit; IPAA, ileal pouch anal anastomosis; IQR, interquartile range; IRB, the Institutional Review Boards; MRI, magnetic resonance imaging; MV, multivariable analysis; NSAID, non-steroidal anti-inflammatory drugs; NKSi, needle knife sinusotomy; OR, odds ratio; RBC, red blood cells.

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was approved by the Cleveland Clinic Institutional Review Board . Written informed consent was obtained from patients for the procedure.

Inclusion and Exclusion Criteria

The inclusion criteria were as follow: (1) patients with the primary diagnosis of IBD who underwent IPAA; (2) the presence of pouch presacral sinus; and (3) the sinus was treated with NKSi.

Patients who did not carry a primary diagnosis of IBD were excluded from this study.

Diagnostic Criteria

The diagnosis of sinus was obtained by pouchoscopy with or without the evaluation with magnetic resonance imaging (MRI) or gastrografin enemas (Fig. 1). A pouch sinus was defined as a blind-ending tract at the presacral space of the pouch arising from anastomosis/distal pouch, the tip of the "J" pouch, and pouch body. The diagnosis of sinus was made at least 6 months apart from the latest surgery. Complex sinus was defined as multiple sinus (≥2) or branched sinus. The length of the sinus was measured by an endoscopic soft-tip guide wire during the pouchoscopy with or without concurrent measurement with MRI or gastrografin enema.

Data Collection

Demographic clinical data, including age, gender, ethnicity, weight, and body mass index (BMI) were documented. Current smoker was defined as consumption of more than 7 cigarettes per week for at least 6 months and ex-smoker was defined as cessation of smoking at least 6 months before data entry. Family histories recorded were those of the first-degree relatives to the patient. Chronic antibiotic-refractory pouchitis was defined as a modified Pouchitis Disease Activity Index[22] ≥ 5 points and symptoms lasting 4-week course of single antibiotic therapy (ciprofloxacin, metronidazole, or tinidazole). Crohn's disease (CD) of the pouch was diagnosed based on the previously published criteria.[23] Concurrent stricture, fistula, and cuffitis were diagnosed via pouchoscopy and the closest abdominal and pelvic imaging testing if available.

Indication and Technique of NKSi

The decision on whether to perform NKSi was at the discretion of the treating endoscopist (B.S.) based on a combined assessment of clinical, endoscopic, and imaging presentation and weighing of risks and benefits.

All NKSi procedures were performed by the experienced treating endoscopist (B.S.). Pouchoscopy was performed under conscious sedation in an outpatient setting without the need for fluoroscopy. Patient was put on left later decubitus position to help the orientation of scope and sinus. Therefore, the posterior wall, presacral sinus is normally located at 10- to 11-o'clock position. The length of sinus was measured by a soft-tip guide wire, in addition to preprocedural abdominal and pelvic imaging. The principle of our technique was advanced from the traditional surgical procedure of unroofing of acute anastomotic leak. The goals were to open the sinus orifice by cutting the common wall between the pouch body and the sinus and to lay open the sinus tract merging the sinus cavity to become part of the pouch wall. The sinus was treated with a triple-lumen needle knife (Boston Scientific, Marlborough, MA) or isolation tip knife (Olympus, Tokyo, Japan) in the setting of endoscopic retrograde

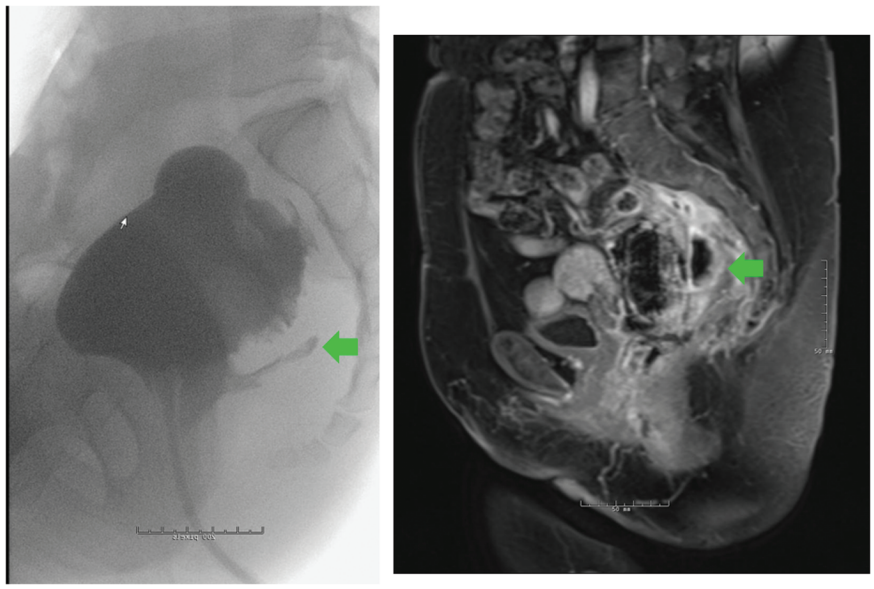

FIGURE 1. Distal pouch, presacral sinus (green arrow) on (A) gastrograffin enema and (B) MRI .

cholangiopancreatography (ERCP) "Endocut" on ERBE (USA Incorporated Surgical Systems, Marietta, GA). The key point for the endoscopic sinusotomy is to deploy Endoclips (Cook Medical, Bloomington, IN) along both excised edges of sinus to prevent reclosure of sinus orifice and to reduce the risk of bleeding. (Fig. 2) The sinus cavity was sprayed with 50% dextrose and doxycycline, or mix, to promote the formation of fibrosis, at the discretion of the endoscopist.[24, 25] All patients were periodically followed-up at least once annually. However, the interval between clinic and pouchoscopy visits varies because of logical reasons such as flares of symptoms. Whether a patient required multiple therapy depended mostly on follow-up pouchoscopy presentation.

Outcome Measurements

The primary outcome was partial or complete healing of the sinus. Complete healing was defined as the resolution of the sinus tract on endoscopy identified with the soft-tip guide wire and/or water contrasted pouchogram or MRI. Partial healing was defined as at least 50% of reduction in the length of sinus.

The secondary outcome was pouch failure, defined as pouch excision, pouch revision surgery, or permanent pouch diversion. Follow-up time was defined as the time from the inception of endoscopic therapy to the latest clinical/telephone follow-up or disease-related surgery, whichever came first. Disease- or NKSi- related emergency department visits or hospitalizations also were evaluated. Preplanned admission for purely surgical purposes was not included for the analysis. Recurrence of sinus after surgery was diagnosed and confirmed by follow-up pouchoscopy or abdominal imaging.

Statistical Analysis

Categorical variables were summarized as percentages. Quantitative variables with normal distribution were summarized as mean ± standard deviation. Quantitative variables with paranormal distribution were summarized in median and interquartile range (IQR). Comparisons between 2 groups were made by using the 2-tail t test (or Wilcoxon rank sum test if indicated) for continuous variables and chi-square test (or Fisher exact test if indicated) for categorical variables. Multivariable (MV) logistic regression analysis and Cox multivariate analysis were constructed to evaluate the factors associated with sinus healing and pouch survival, respectively. MV models were constructed using the variables significant from univariable analysis. All statistical analyses were performed with SPSS software, version 20.0 (SPSS, Chicago, IL). $P < 0.05$ was considered statistically significant.

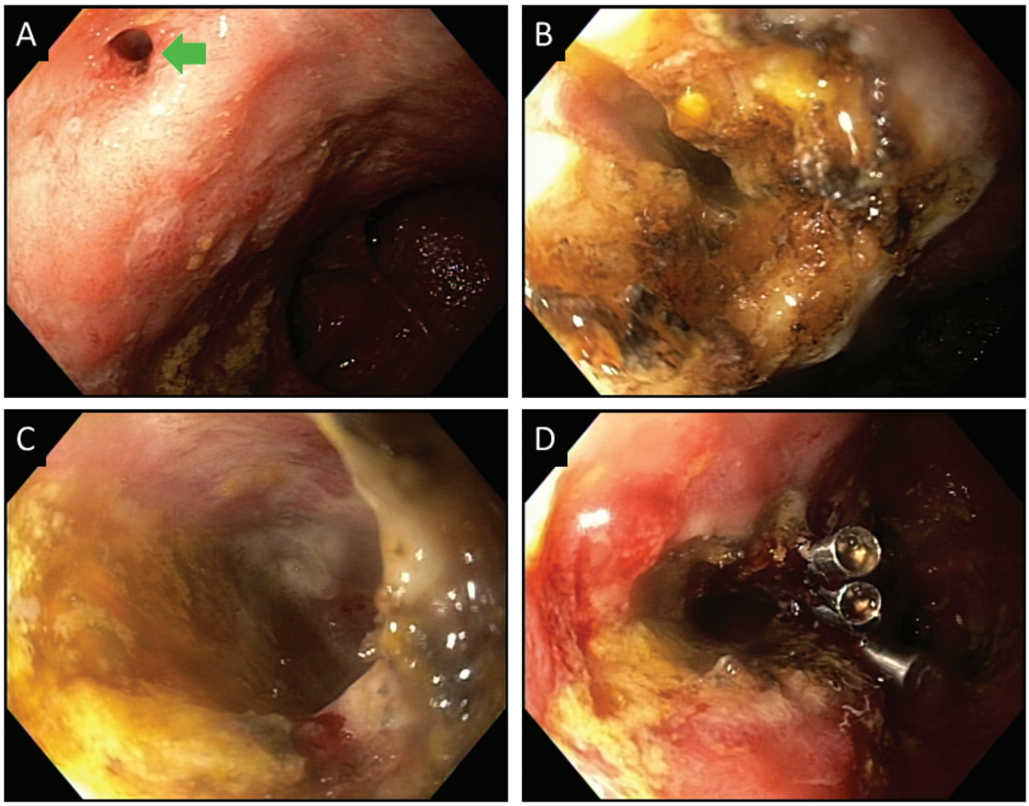

FIGURE 2. Endoscopic sinusotomy. A,. The opening of the deep presacral sinus (green arrow); (B) Needle- knife electroincision of the wall between the sinus and pouch body; (C) The opened sinus cavity; (D) Deployment of endoclips along the incised edges of the sinus.

RESULTS

A total of 109 patients with pouch sinus treated at our *i*-IBD Unit were included in this study. A flow chart of patient's enrollment, treatment, and follow-up is attached (Fig. 3).

Demographics and Characteristics of Sinus

Demographic information was listed in Table 1. Patients were mostly white (N = 102, 94.4%) and male (N = 85, 78.0%). Nine patients had fecal diversion at the diagnosis of pouch sinus. A total of 102 patients (93.6%) had preprocedural documentation of symptomatology and 84 (82.4%) of patients were symptomatic at the time of sinus diagnosis. (Table 2) Sinus was located in the presacral area of the pouch-anal anastomosis in 101 (92.7%) patients. The length of pouch was recorded in 100 patients, with a median of 4.8 (IQR: 3.0–6.0) cm. Complex sinus was documented in 38 patients (34.9%).

Treatment and Outcomes

Patients underwent a median of 2.0 sessions of NKSi (IQR: 1.0–3.0). Symptomatic improvement was documented in 79/102 (77.5%) patients after the initial procedure (Table 3). At the latest endoscopy, complete healing of the sinus was documented in 54 (49.5%) patients and partial healing in 20 (18.3%). Symptomatic improvements was seen in 44/54 (81.5%) patients with complete healing and 15/20 (75.0%) patients with partial healing.

Recurrent sinus occurred in 14 (25.9%) patients who had had complete healing of the sinus after a median interval of 10.4 (IQR: 6.0–15.5) months. One patient was treated with loop ileostomy and later had surgical pouch redo. The other 13 patients were treated with additional sessions of NKSi and 6 of the 13 patients reported complete healing after a single session.

During the follow-up period of 2.1 years (IQR: 0.7–4.4), 22 (20.2%) had pouch failure resulting from recurrent sinus, sinus refractory to the endoscopic therapy, or the subsequent development of nonprocedure-related abscess. Of the 22 cases, 8 had pouch excision; 6 had permanent diversion; and 8 had diverting ileostomy followed by pouch excision. Seven patients (31.8%) developed recurrent sinuses after surgery.

Factors Associated with Healing of Pouch Sinus

Factors that contributed to the healing of sinus were listed in Table 1. In MV analysis, complete healing of the sinus was seen in patients with a higher BMI [odds ratio (OR): 1.2, 95% confidence interval (CI): 1.0–1.3], suggesting an improvement in nutritional status (Table 4). Patients with an eventual healed sinus had a longer median interval in between the sessions [10.1 months (IQR: 6.7–22.1) vs 5.4 months (IQR: 1.9–13.8),

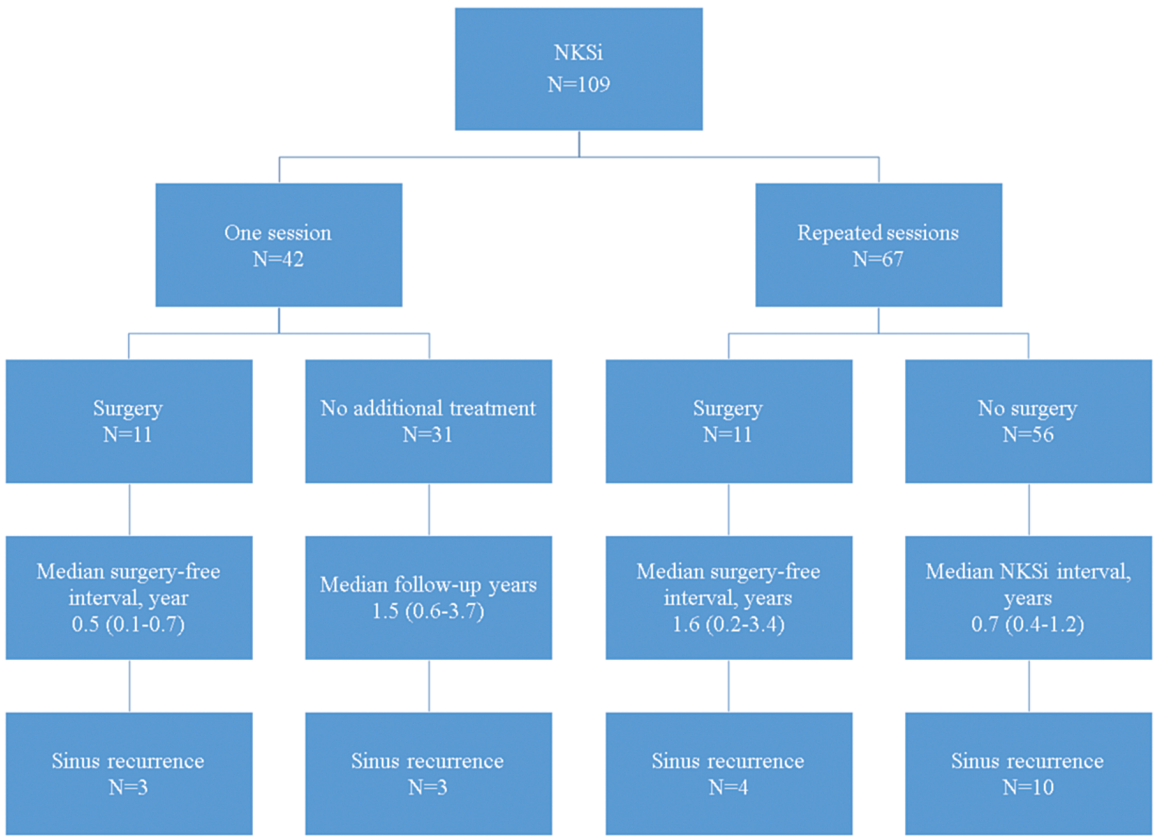

FIGURE 3. Flow chart of patient enrollment and follow-up.

TABLE 1: Patient and Pouch Sinus-Related Characteristics

Characteristics		Total Case No. = 109	Patients with Healed Sinus No. = 54	Patients with Nonhealed Sinus No. = 55	*P* value
Male patients		85 (78.0%)	41 (75.9%)	44 (80.0%)	0.61
White patients		102 (94.4%)	67 (87.0%)	55 (100.0%)	0.006
Baseline BMI , kg/m^2		24.1 ± 4.1	25.1 ± 4.1	23.2 ± 4.2	0.02
History of smoking	Current	8 (7.3%)	2 (3.7%)	6 (10.9%)	0.21
	Former	23 (21.1%)	14 (25.9%)	9 (10.9%)	
Family history of IBD		21 (19.3%)	9 (16.7%)	12 (21.8%)	0.50
Age at the diagnosis of IBD, years		25.5 ± 12.2	26.2 ± 13.5	25.6 ± 11.3	0.79
Precolectomy diagnosis	Ulcerative colitis	103 (94.5%)	52 (96.3%)	51 (92.7%)	0.37
	Indeterminate colitis	4 (3.7%)	2 (3.7%)	2 (3.6%)	
	Crohn's colitis	2 (1.8%)	0 (0.0%)	2 (3.6%)	
Extent of disease	Extensive colitis	104 (95.4%)	52 (96.3%)	52 (94.5%)	1.00
	Left-sided colitis/proctitis	5 (4.6%)	2 (3.7%)	3 (5.5%)	
Toxic megacolon		8 (7.3%)	2 (3.7%)	6 (10.9%)	0.28
Extraintestinal manifestation		32 (29.4%)	15 (27.8%)	17 (30.9%)	0.72
Preoperative use of biologics		45 (41.3%)	22 (40.7%)	23 (41.8%)	1.00
Age at colectomy, years		33.9 ± 13.7	34.7 ± 14.6	32.8 ± 13.1	0.47
Indication for colectomy	Neoplasia	16 (14.7%)	9 (16.7%)	7 (12.7%)	0.56
	Refractory disease	93 (84.5%)	45 (83.3%)	48 (87.3%)	
Stage of pouch construction	1	7 (6.4%)	3 (5.6%)	4 (7.3%)	0.95
	2	64 (58.7%)	33 (61.1%)	31 (56.4%)	
	3	23 (21.1%)	11 (20.4%)	12 (21.8%)	
	Redo pouch	15 (13.8%)	7 (13.0%)	8 (14.5%)	
Configuration of the pouch	J pouch	105 (96.3%)	52 (96.3%)	53 (96.4%)	1.00
	S pouch	4 (3.7%)	2 (3.7%)	2 (3.6%)	
Post IPAA leak		41 (37.6%)	18 (33.3%)	23 (41.8%)	0.36
Concurrent stricture		27 (24.8%)	12 (22.2%)	15 (27.3%)	0.54
Concurrent cuffitis		29 (26.6%)	11 (20.4%)	18 (32.7%)	0.14
Concurrent refractory pouchitis		18 (16.5%)	9 (16.7%)	9 (16.4%)	0.97
Concurrent CD of pouch		28 (25.7%)	9 (16.7%)	19 (34.5%)	0.03
Age at the diagnosis of sinus, years		40.5 ± 13.8	41.3 ± 14.8	39.7 ± 13.0	0.56
Duration from pouch completion to diagnosis of pouch sinus, years		2.7 (1.2–7.9)	2.8 (1.1–8.5)	2.4 (1.1–7.6)	0.97
Location of sinus orifice	Pouch anastomosis	101 (92.7%)	49 (90.7%)	52 (94.5%)	0.49
	The tip of the "J"	4 (3.7%)	3 (5.6%)	1 (1.8%)	
	Pouch body	4 (3.7%)	1 (3.7%)	2 (1.8%)	
Depth of pouch sinus (No. = 100), cm		4.8 (3.0–6.0)	4.5 (3.0–6.0)	4.8 (3.0–5.0)	0.86
Complex pouch sinus		38 (34.9%)	18 (33.3%)	20 (36.4%)	0.74
Symptomatic patients (No. = 102)		84 (82.4%)	43 (79.6%)	41 (74.5%)	0.52
Preprocedural medications	Aminosalicylates	29 (26.6%)	14 (25.9%)	15 (27.3%)	0.87
	Antibiotics	48 (44.0%)	25 (46.3%)	23 (41.8%)	0.64
	Corticosteroids	30 (27.5%)	12 (22.3%)	18 (32.7%)	0.22
	Immunomodulators	6 (5.5%)	2 (3.7%)	4 (7.3%)	0.41
	Biologics	9 (8.3%)	3 (5.6%)	6 (10.9%)	0.31
Age at NKSi, years		40.7 ± 13.9	41.5 ± 14.8	39.9 ± 13.0	0.56
Concurrent use of doxycycline		38 (34.9%)	21 (38.9%)	17 (30.9%)	0.38
Concurrent use of 50% dextrose		42 (38.5%)	24 (44.4%)	18 (32.7%)	0.21
Multiple NKSi therapy		67 (61.5%)	34 (63.0%)	33 (60.0%)	0.75
Total sessions of NKSi		2.0 (1.0–3.0)	2.0 (1.0–3.3)	2.0 (1.0–3.0)	0.53
Interval between NKSi therapy, months		8.1 (4.0–17.6)	10.1 (6.7–22.1)	5.4 (1.9–13.8)	<0.0001
Number of pouch clinic visits		3.0 (2.0–5.0)	3.5 (2.0–5.3)	3.0 (2.0–5.0)	0.33
Interval of clinic visits, months		6.5 (2.5–11.2)	7.0 (4.2–12.2)	4.1 (0.9–8.9)	0.001

TABLE 2: Comparison of Symptoms and Weight Before and After Endoscopic NKSi Therapy

	Before Treatment	After Treatment	
Symptoms	No. = 102	No. = 94	*P* value
Symptomatic	84 (82.4%)	63 (67.0%)	0.03
Urgency	57 (55.9%)	40 (36.7%)	0.02
Diarrhea	53 (48.6%)	37 (33.9%)	0.05
Abdominal pain	48 (44.0%)	32 (29.4%)	0.03
Weight loss	8 (7.3%)	0 (0.0%)	0.005
Perianal discomfort/pain	13 (11.9%)	13 (11.9%)	1.00
Dyschezia	11 (10.1%)	2 (2.2%)	0.02
Fever	5 (4.9%)	1 (1.1%)	0.10
Weight, kg	75.2 ± 15.7	75.3 ± 16.2	0.92
BMI index, kg/m^2	24.2 ± 4.3	24.3 ± 4.4	0.55

$P < 0.0001$], making an increase interval between sessions a protective factor for healing (OR: 1.1, 95% CI: 1.0–1.1). CD of the pouch, on the other hand, was a risk factor for sinus healing (OR: 0.3, 95% CI: 0.1–0.8).

Factors associated with Sinus-related Pouch Failure

A total of 22 patients had a pouch failure due to sinus or the subsequent development of abscess during a median follow-up time of 2.1 years (IQR: 0.7–4.4). Cox regression identified following risk factors regarding pouch survival (Table 5): history of acute anastomotic leak (OR: 3.5, 95% CI: 1.2–10.4), history of toxic megacolon (OR: 7.4, 95% CI: 1.9–29.1), an increased length of sinus (OR: 1.4, 95% CI: 1.0–2.0), and an increased duration from the sinus diagnosis to the NKSi procedure (OR: 2.6, 95% CI: 1.1–6.2). Conversely, protective factors for pouch survival included concurrent administration of 50% dextrose (OR: 0.2, 95% CI: 0.04–0.6) and doxycycline (OR: 0.2, 95% CI: 0.04–0.7) and a longer interval between NKSi sessions (OR: 0.9, 95% CI: 0.9–0.99). The median interval between NKSi sessions for pouch failure was 5.5 (1.8–10.1) months, whereas it was 9.0 (5.2–18.2) months for the nonpouch-failure patients. The median sinus length was 5.0 cm (IQR: 3.0–6.0) in patients with pouch failure whereas for functional pouch it was 4.0 cm (IQR: 3.0–5.0).

Safety

A total of 334 NKSi procedures were performed. The majority of patients tolerated the procedure well and procedure-associated complications were encountered in 6 (1.8% per procedure) occasions. One patient (0.3% per procedure) with sinus at the tip of the "J", who responded to the first NKSi, developed perforation at the second NKSi and required urgent single-port diverting loop ileostomy and perforation repair. Three years after the incident, she still carried diverting ileostomy and had an improved quality of life as compared to that before NKSi inception. One patient (0.3%) aspirated during the procedure following CT enterography and that patient was hospitalized and recovered. This male patient later on underwent diverting ileostomy for pouch failure from a long, persistent sinus. Four patients (1.2% per procedure) experienced a postprocedural bleeding in whom one required an emergency department visit without blood transfusion and 3 required hospitalizations with 1 requiring embolization of branches of ileocolic artery, 1 requiring 1 unit of red blood cells (RBC) transfusion, and 1 requiring 4 unit of RBC transfusion. There was no procedure-related mortality.

DISCUSSION

In this historic cohort, we evaluated 109 IBD patients with pouch sinus who were treated with NKSi and the results confirmed our earlier reported findings. The current study provides additional findings due to the expanded sample size and longer duration follow-up with more powerful MV analyses. Approximately half of the patients achieved complete healing of the pouch and 18.3% of them had partial healing. During a median follow-up of 2 years, 22 (20.2%) patients had sinus-related pouch failure. Risk factors for sinus healing include concurrent diagnosis of CD of the pouch and frequent NKSi (the median interval of 5 months vs 9 months). Risk factors for pouch survival include a longer sinus, frequent NKSi, longer sinus duration, and previous anastomotic leak. The overall complication rate of NKSi was 1.8% per procedure.

Sinus is a serious complication for patients undergoing IPAA and is typically a sequela and a later presentation of a previous acute anastomotic leak.[8] The diagnosis is often achieved by careful pouchoscopy, contrasted pouchogram, and pelvic MRI. Persistent sinus could cause various consequences ranging from delayed ileostomy closure, impaired pouch function, permanent ileostomy, or even pouch excision.[9–12, 18] In addition, coccyx osteomyelitis and malignant changes have been reported.[26–30] The natural history and optimal management of pouch sinus are not well defined. Although patients with acute, asymptomatic leaks may heal spontaneously with a reported healing rate of 53%–95%, surgery has been the mainstay of treatment for persistent sinus.[9–13, 31] Various surgical options have been described, including mucosal advancement flaps, pouch advancement, neoileoanal anastomosis, and pouch excision with an end ileostomy.[13] Other treatment modalities include debridement of the sinus in combination with unroofing of the cavity or the use of fibrin glue.[9, 10, 15] The reported overall healing rate of surgery as shown in Table 6 ranged from 60%–100%.[9, 10, 15, 31] A previous study from our center included 45 patients with chronic sinus who were treated with the following treatment options (healing rate%): observation (65%), drainage (66%), unroofing (50%), sinus closure (67%), fibrin glue (67%), diversion (50%), or redo pouch (66%).[12] The overall healing rate in this study was approximately 60% (27/45) and

TABLE 3: Outcomes of NKSi Therapy for Pouch Sinus

Outcomes		No. (%)
Follow-up time, years		2.1 (IQR: 0.7–4.4).
Endoscopic response	None	35 (32.9%)
	Partial (decrease in size)	20 (18.3%)
	Complete (disappearance of the sinus track)	54 (49.5%)
Symptoms improvement (No. = 102)		79 (77.6%)
Sinus recurrence (No. = 54 with complete healing)		14 (25.9%)
Interval of sinus recurrence, months		10.7 (IQR:6.8–15.5)
Procedure adverse events (No. = 334)		6 (1.8% per procedure)
	Bleeding	4 (1.2%)
	Perforation	1 (0.3%)
	Aspiration	1 (0.3%)
Disease-related hospitalization (No. = 71)		40 (36.7% per patient)
	Sinus/abscess	20 (28.2%)
	Fistula	13 (18.3%)
	Abdominal pain	14 (19.7%)
	Pouchitis	6 (8.5%)
	Incisional hernia	4 (5.6%)
	Examination under anesthesia	3 (4.2%)
	Malnutrition	2 (2.8%)
	Bloody diarrhea	1 (1.4%)
	IBD-associated arthropathy	1 (1.4%)
	Colon cancer	1 (1.4%)
	NKSi- related hospitalization	6 (8.5%)
Stricture -related emergency department visit (No. = 30)		15 (13.8% per patient)
	Abdominal pain	10 (33.3%)
	Sinus	5 (16.7%)
	Pouchitis	4 (13.3%)
	Dehydration	4 (13.3%)
	Arthropathy	2 (6.7%)
	Bloody diarrhea	1 (3.3%)
	Peritonitis	1 (3.3%)
	NKSi related	3 (10.0%)
Pouch failure (causes)		32 (29.1%)
	Sinus/abscess/leak	22 (20.2%)
	Bowel obstruction	5 (4.6%)
	Chronic antibiotic-refractory pouchitis	5 (4.6%)

sinus-associated pouch failure was 33% (15/45).[12] The surgical healing rate from our center is lower than that reported in other studies possibly due to the complexity of disease, larger sample size, and a shorter follow-up. However, when only asymptomatic patients were evaluated, our center's previous study showed a healing rate of 84%, which is comparable with reported findings from Swain (100%),[15] Akbari (95%), [9] and Zhou (86%) et al.[31] On the other hand, when only symptomatic patients were observed, the healing rate dropped to 30%.[12] Sinus recurrence rate was only reported in asymptomatic patients who underwent debridement in Akbari's study.[9] Recurrence of the sinus after ileostomy closure was seen in 1 out of 4 patients (25%) who had a negative pouchogram before ileostomy take down.[11] Study from our institution has briefly mentioned that 1 out of 3 (33.3%) patients did not benefit from redo pouch in the treatment for pouch sinus, and the new pouch was eventually excised.[12] Therefore, upfront nonsurgical approaches have been explored.

TABLE 4: Multivariate Analysis for Healing of Pouch Sinus

Factors	Odds Ratio (95% CI)	*P* value
Interval of NKSi therapies	1.1 (1.0–1.1)	0.02
Concurrent CD of the pouch	0.3 (0.1–0.8)	0.02
BMI index before procedure	1.2 (1.0–1.3)	0.008

Endoscopic approaches have recently emerged as a valid treatment option for anastomotic leaks in IPAA for a higher pouch survival rate, including endoscopic stapled marsupialization,[16] the placement of sponge, [17, 18] and needle knife therapy.[19–21] NKSi was first described by our team in 2010, although we have performed the procedure since 2008.[19] The principle of the technique is adapted from the surgical procedure of sinus unroofing and the goals are to promote fibrosis of the sinus cavity, to decompartmentalize the sinus and to convert the sinus cavity to epithelialized diverticulum. Needle knife or isolation tip knife was used to cut the pouch wall adjacent to the sinus to divide the common wall between the sinus and the pouch to lay open the sinus tract making multicompartments into 1 single cavity. This technique was shown to be effective in our previous study of 65 patients.[21] In the earlier study, complete healing of sinus was achieved in 28 patients (43.1%) and the pouch failure rate was 18.5%. The healing rate was similar between the symptomatic and asymptomatic patients (43.8% vs 42.9%). Due to the smaller sample size and the relatively shorter follow-up (median of 1.1 years), limited descriptive statistical analysis was performed. Our current study is a natural extension of our previous studies with a larger patient population and a longer follow-up.

In this cohort of 109 patients, we found similar male predominance (78.0%). Male gender has been found to be associated with a higher risk for multiple post IPAA complications, including chronic antibiotic-refractory pouchitis especially ischemic pouchitis, anastomotic leak, and pouch sinus.[32, 33] One of the explanations is that the narrower pelvis and/or a shorter length of the mesentery in male patients made the surgical procedure, particularly the creation of an anastomosis, technically more challenging.[34, 35] The complete healing rate in our current cohort was 49.5%, which may be considered lower than

TABLE 5: Multivariate Analysis for Surgery-Free Survival

Factors	Odds Ratio (95% CI)	*P* value
Previous anastomotic leak	3.5 (1.2–10.4)	0.02
Toxic megacolon	7.4 (1.9–29.1)	0.004
Length of sinus	1.4 (1.0–2.0)	0.04
Concurrent use of dextrose 50%	0.2 (0.04–0.6)	0.008
Concurrent use of doxycycline	0.2 (0.04–0.7)	0.01
Interval of NKSi therapies	0.9 (0.9–0.99)	0.02
Duration from sinus diagnosis to NKSi	2.6 (1.1–6.2)	0.03

that of surgical treatment.[12] This could be due to inadequate follow-up since 20 (18.3%) patients presenting with partial healing might achieve complete healing if the follow-up time is extended. However, when only symptomatic patients were observed, the healing rate of our current cohort was higher than that reported with surgical approach (51% vs 30%).[12] In our current study, patients who required more frequent NKSi therapies (5 months/per NKSi) appeared to have a lower chance for healing and a higher risk for subsequent pouch failure. Another factor associated with nonhealed sinus that showed in MV analysis was concurrent CD of the pouch. It has been a challenge to distinguish between surgery-associated sinus and CD-related sinus. It appears that patients without CD of the pouch are more likely to achieve complete healing by NKSi, whereas patients with CD required addition medical therapy to treat the underlying disease to promote complete healing. We feel that NKSi can be attempted for both CD and non-CD related sinuses and NKSi can serve as an adjunctive treatment to medical therapy for CD.

The efficacy of NKSi in maintaining a functional pouch is evident in our current study, The pouch failure rate due to sinus occurred in 22 (20.2%) patients that is lower than reported with surgical treatment (33%).[12] Several factors were found to be associated with pouch survival. As our previous case series indicated, administering dextrose 50% and doxycycline can cause topic fibrosis and seemed to have a positive impact on pouch survival.[20] Another factor associated with pouch survival was previous acute anastomotic leak at pouch construction that concur with previous publications that reported a higher pouch failure rate (16.6%) in those with anastomotic leak than those of the general IPAA population (6–10%).[36–38] The length of the sinus also was found to be associated with pouch failure. From our cohort, we believe that the best efficacy of NKSi is achieved in those with shorter sinus tracts < 5 cm. The final factor associated with pouch failure in MV analysis was the duration from sinus diagnosis to NKSi. This can be explained as the longer the duration, more persistent the sinus, and the higher risk for surgical intervention.

The findings of this study have several clinical implications. The results justified NKSi as a feasible, effective, and safe procedure. It could be a valid option when the sinus failed to heal spontaneously and that invasive surgery is not preferred since NKSi is much less invasive with no hospitalization needed. To date, most published data focused only on the healing of the sinus and failed to mention the long-term outcome of the pouch and the recurrence of sinus. Compared with surgical interventions, NKSi did show a lower overall complete healing rate, but a higher healing rate in the symptomatic patients. Long-term pouch failure was observed in only 20% of patients, whereas the only reported pouch failure rate for an upfront surgical treatment of sinus was 33% (15/45).[12] However, the recurrence rate was similar between NKSi and debridement was (25.9% vs 25%).[9] Although postprocedural complication had not been described in patients treated with unroofing[10] and debridement with fibrin glue,[15] surgical treatment of pouch sinus posed risk for procedure-related complications such as evacuation disorder, pouch prolapse, and pouch fistula.[21] However, the actual adverse rate of surgery in the treatment of sinus had not been reported systemically in literature, especially the adverse outcome of persistent sinuses that required pouch reconstruction. Historically, early complication rate (<30 days) after pouch reconstruction for all causes was 24% (12/51) and late complication rate (>30 days) was 37%.[39] However, the complication rate of NKSi was only 1.8%. However, it is still extremely important that this procedure is conducted by an experienced endoscopist because 1 patient in our cohort had a severe complication of perforation that required surgery. Based on the result of our study, we recommend a trial of NKSi before undergoing surgery, even for patients with complex sinus or CD of the pouch. However, sinus that is longer than 5 cm might eventually need surgical intervention. It is also important to differentiate the patients with CD of the pouch, since the underlying disease should be treated to achieve complete healing of sinus. During the process of NKSi, attention should be paid to the intervals between therapies. If the patients required frequent NKSi therapies more often than every 5months-6 months, it is likely that the sinus would not be able to heal and it is at high risk for pouch failure. Lastly, the administration of 50% dextrose and doxycycline after NKSi may help to improve the outcome.

There are several limitations to this study. There might have been referral and selection bias as our Center for Ileal Pouch Disorders and *i*-IBD Unit are subspecialized in managing complex cases with trained endoscopist and supporting personnel. The specific treatment given was decided by individual physician and patient's preference. Now there is no established algorithm for the treatment of pouch sinus. A case-control study or prospective randomized control study is needed to directly compare the efficacy and adverse events between the endoscopic and surgical approaches.

CONCLUSIONS

In conclusion, we validate that endoscopic therapy is a feasible, effective, and safe procedure for ileal pouch patients

TABLE 6: Studies Describing the Outcome of Anastomotic Pouch Sinus Post IPAA

Study	No.	Diverted	Symptom	Acute vs Chronic (sinus) leak (%)	Treatment (healing rate %)	Overall Healing Rate No. (%)	Pouch Failure No. (%)	Median Follow-up Month	Ileostomy Closure	Recurrence
Whitlow 1996[10]	6	6	NA	NA	6: Unroofing (100)	6 (100)	NA	9	NA	0
Nyam 1996[11]	41	41	0	Acute (85) Chronic (15)	41: Observation (85)	35 (41)	NA	NA	41 (100)	2/41
Swain 2004[15]	7	5	0	Chronic (100)	7: Debrided + curettage + fibrin glue (100)	7 (100)	NA	11.2	5 (100)	0
Akbari 2009[9]	22	22	0	NA	19: Observation (53) 6: Debridement + curettage (80)	20 (95)	0	NA	21 (95.5)	1/4
Koperen 2008[18]	2	2	NA	Acute (100)	2: Endo-sponge (100)	2 (100)	0	1.5	NA	NA
Ahmed 2012[12]	45	23	25	Chronic (100)	23: Observation (65) 9: Drainage (56) 8: Unroofing (50) 3: Sinus closure (33) 2: Diversion (100)	27 (60)	15 (33)	7.5 (until sinus healed)	23 (100)	NA
Zhuo 2013[31]	20	20	13	Acute (100)	5: Observation (100) 7: Curettage (100) 4: Currettage + drainage (50) 3: Currettage + drainage + debridement (67) 1: Drain+ flap advancement (0)	16 (80)	NA	28	16 (80)	NA
Wu 2013[32]	65	0	49	Chronic (100)	65: NKSi therapy (43)	28 (43)	7 (10)	13.2	0	NA

with pouch sinus. The endoscopic approach should be a part of the algorithm for the treatment of this detrimental complication of IPAA surgery.

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