

Endoscopic retrograde appendicography: an effective diagnostic method for acute appendicitis

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Abstract

Background and Aim: Appendicography had been used in the diagnosis of chronic appendicitis. To our knowledge, the role of endoscopic retrograde appendicography for the diagnosis of acute appendicitis remains unknown. The aim of this study was to evaluate the role of endoscopic retrograde appendicography for the diagnosis of acute appendicitis.

Patients and Method: Patients with suspected acute appendicitis between December 2013 and November 2015 at Second Affiliated Hospital of Harbin Medical University underwent endoscopic retrograde appendicography. The findings and complication were analyzed retrospectively.

Results: Thirty-three patients (20 men and 13 women, average age 44 ± 18 years) with suspected acute appendicitis were studied. Acute appendicitis was ruled out by normal endoscopic retrograde appendicography in 24% and confirmed in 69.6% (23). In 2 patients (8%) appendiceal orifice cannulation failed. Colonoscopic findings in acute appendicitis were mucosal hyperemia and edema of appendiceal orifice (83%), outpouring of pus from the appendiceal orifice (74%), and swollen cecal mucosa (61%). Appendicographic findings were either normal or in acute disease showed diffuse luminal dilation (diameter: 0.8 ± 0.4 mm), partial stenosis (43%), stiffness or inflexibility (87%) and filling defects (22%). There were no complications during or after follow-up for a median of 13 months (IQR: 9-24 months).

Conclusions: Endoscopic retrograde appendicography appears to be a reliable and safe method to confirm or exclude the diagnosis of acute appendicitis and prevent unnecessary appendectomy.

Introduction

The preoperative diagnosis of acute appendicitis (AA) is primarily based on clinical evaluations that is often only resolved by appendectomy. The rate of false positive diagnoses of acute appendicitis has remained unchanged following the introduction of new imaging techniques such as multidetector enhanced computed tomography (CT) or ultrasonography (US) [1, 2]. While false positive tests to negative appendectomy, false negative diagnoses may result in delayed management and complications of the disease. A more accurate diagnostic method is needed especially when the initial diagnostic approach is not definitive.

Colonoscopic appendicography has been reported as a useful technique in differentiate indistinct abdominal symptoms [3]. Endoscopic retrograde appendicitis therapy (ERAT) was first reported in 2012 as a new procedure for management of acute appendicitis [4]. The first step in ERAT is endoscopic retrograde appendicography (ERA) performed to confirm the diagnosis of acute appendicitis. The aim of this study was to systematically evaluate the efficacy of endoscopic retrograde appendicography in the diagnosis of acute appendicitis.

Patients And Methods

Consecutive patients with suspected acute uncomplicated appendicitis were offered endoscopic retrograde appendicography and ERAT at the Second Affiliated Hospital of Harbin Medical University (a tertiary care center in China) between December 2013 and November 2015. Inclusion criteria included: patients clinically suspected to have acute appendicitis (i.e., Alvarado scores ≥ 5) [5], and who were reluctant to undergo operative appendectomy but consented to receive ERAT. Exclusion criteria included those with perforated appendicitis or periappendiceal abscess confirmed by non-enhanced CT (16-detector-row) or US. In preparation for endoscopic retrograde appendicography, bowel preparation was done using either 2L polyethylene glycol electrolyte solution or low-pressure cleansing enemas (300-500 mL per enema) given five times. For patients with mild and moderate symptoms the oral prep was given 4-6 hour before the procedure. For clinically severe cases or patients with anorexic or nauseous/vomiting low-pressure cleansing enemas (300-500 mL per enema) were recommended approximately 30 minutes prior to endoscopy so as not to delay treatment of appendicitis.

The study was performed according to the principles of the Declaration of Helsinki, and was approved by the Institutional Review Board of the Second Affiliated Hospital of the Harbin Medical University. The written informed consent was obtained from the patients before the study.

Technique procedures

Endoscopic retrograde appendicography and ERAT were performed as described previously. Briefly, endoscopic retrograde appendicography involves an colonoscope (CF-H260 or GIF-Q260J, Olympus, Japan) with an attached transparent cap introduced. After finding Gerlach's valve in the cecum, the colonoscope was positioned close to the appendiceal orifice. Gerlach's valve was pushed aside using the transparent cap so that the tip of a catheter (OE-104-2225DL, EndoFlex, Germany) could be wedged into the appendiceal orifice. A 0.035 inch guide wire (Boston Scientific, US) was then inserted into the appendiceal lumen over the catheter and placed deep into the lumen under fluoroscopic guidance. Decompression of the appendiceal lumen was achieved by suction using a syringe (5 mL) attached to the catheter. A soluble contrast agent was then infused to fill the appendix while being monitored by fluoroscopy to check the location, length, shape, content and flexibility of the appendix. Successful ERAT was defined as resolution of abdominal pain and normalization of the leukocyte count after treatment. If abdominal pain was not relieved within 48 hours after ERAT, emergency appendectomy was performed.

The reference standard for confirming acute appendicitis was defined as symptoms resolution after successful ERAT with subjects remaining recurrence-free during follow-up. In the cases of failure ERAT, or recurrence after ERAT, subsequent appendectomy and histological findings were consistent with acute appendicitis. Patients without appendicitis included those for whom another disease was diagnosed or who uneventfully recovered after corresponding treatment based on the current guidelines .

The primary outcome measures were the performance characteristics (sensitivity, specificity, positive and negative predict values) of endoscopic retrograde appendicography in the patients with suspected acute appendicitis. The diagnostic features of endoscopic retrograde appendicography are shown in **Table 1**.

The diagnosis of acute appendicitis was made when the endoscopic retrograde appendicography features of the patient matched (1) or (2) (3) as shown in Table 1.

The secondary outcome measures included complications, appendiceal cannulation rate, colonoscopy and endoscopic retrograde appendicography findings and the accuracy of CT and US.

Telephone follow-up was conducted to assess for recurrent symptoms and long-term complications until the end of the study period. If any symptoms were present, such as abdominal pain, fever or other digestive symptoms, the patient was recommended to return for further examination, laboratory tests and US or CT, as necessary.

Statistical analyses

Results were expressed as mean \pm standard deviation (SD) or median (inter-quartile range, IQR). Quantitative variables were compared between the two groups using the t-test or the Mann–Whitney U test, as appropriate. Categorical variables were compared between the two groups using the Fisher's exact test. A two-tailed P value <0.05 was considered to be statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 17.0 for Windows.

Results

The 33 consecutive patients (20 men and 13 women, average age 44 ± 18 years) were enrolled. The patient characteristics of patients are shown in **Table-2**. In patients with clinically suspected acute appendicitis, the median of Alvarado scores was 7 (IQR: 5.5-8); 25 of the 33 patients (75.7%) were diagnosed as definite acute appendicitis. In 8 patients (24.2%) acute appendicitis was excluded on the basis of reference standards.

Thirty-one patients (93%) successfully underwent endoscopic retrograde appendicography, including 23 patients with acute appendicitis, 2 (8%) had failed cannulation of the appendiceal orifice due to blockage by fecaliths and 8 patients did not have acute appendicitis. The colonoscopic and radiological findings are shown in **Table-3**. In the 23 patients with acute appendicitis, colonoscopic findings showed mucosal hyperemia and edema of appendiceal orifice (83%) (**Figure 1A, B**), swollen mucosa of cecum (61%) and discharge of pus from appendiceal orifice (74%) (**Figure 1C**). Appendicography showed intraluminal filling defect sign (22%) (**Figure 1D**), lumen distension (median 0.7 cm, IQR=0.4-1.0cm), partial stenosis (43%) (**Figure 1E**), and inflexibility or stiffness (87%). The median luminal diameter of the appendix in patients without acute appendicitis was significantly less than the patients with acute appendicitis (0.3 cm vs. 0.7 cm, $p=0.004$) although the luminal length was not significant difference (6.7 ± 2.3 cm vs. 6.5 ± 1.6 cm, $p=0.802$). **Figure 1F** shows a normal appendix.

All the patients with confirmed acute appendicitis by endoscopic and endoscopic retrograde appendicography recovered uneventfully. The diagnosis of acute appendicitis in the 2 patients in whom the appendiceal orifice could not be cannulated were confirmed on the basis of appendectomy and

histology. We included these 2 failure cases in the equivocal ERA results. During follow-up (median: 13 months; IQR: 9-24 months), 2 (8%) of the patients with acute appendicitis subsequently underwent appendectomy for recurrent abdominal pain and were histologically diagnosed with acute appendicitis.

The diagnoses of the 8 patients without acute appendicitis are shown in **Table 4**. All 8 patients uneventfully recovered after corresponding treatment and no recurrences occurred during follow-up. One attempted endoscopic retrograde appendicography had failed because the appendiceal orifice was blocked by a malignant tumor. We also included the patient with carcinoma in the equivocal negative results. Overall, in 8 patients (24%) acute appendicitis was definitely ruled out through endoscopic retrograde appendicography.

Overall, endoscopic retrograde appendicography correctly diagnosed 23 patients with acute appendicitis and ruled it out in 8 cases; 2 cases had equivocal results due to failure appendix cannulation. If the equivocal results were included, the sensitivity and specificity of ERA were 92% and 83%, respectively. The positive predict value and negative predict value of ERA were 92% and 83% respectively. Furthermore, there were no complications during a median follow-up period of 13 months (IQR:9-24 months) .

Comparison with CT and ultrasound

In the study, CT scans were performed in 24 patients and US in 17 before endoscopic retrograde appedicography; both CT scan and US were performed in 7 patients. With US, 6 patients (35%) were incorrectly diagnosed and 2 other patients (12%) had equivocal results. Four patients (17%) were misdiagnosed and 8 patients (33%) had equivocal results using CT scans. Even if the equivocal results of CT and US were excluded from the calculations, the sensitivity and specificity of CT was 88% and 71% respectively. The sensitivity and specificity of US was 73% and 50% , respectively. The sensitivity and specificity of the endoscopic retrograde appendicography results were 100% and 100%, respectively (when equivocal results were included , 92% and 89% respectively) (**Table 5, 6**). Overall, 8 patients (24%) were prevented from having unnecessary surgery.

Discussion

Acute appendicitis is one of the common causes of acute abdominal pain. Although the classical symptoms of acute appedicitis is periumbilical pain migrating to the right lower quadrant, the presentation is rarely typical and diagnostic errors are common resulting in both negative appendectomies or appendical perforations. This study systematically investigated the value of endoscopic retrograde appendicography in the diagnosis of acute appendicitis and showed a high diagnostic yield in patients with acute abdominal pain. Possibly more importantly was the ability to prevent unnecessary operations and preserve the normal appendix.

Previous studies have reported colonoscopy as a useful diagnostic method of acute appendicitis in the patients with atypical presentation of abdominal pain or with non-diagnostic imaging studies [6, 7]. Chang et al. [7] described the colonoscopic features of acute appendicitis, including hyperemia and

bulging at the appendiceal orifice area with surrounding mucosal edema and drainage of pus from the appendiceal orifice. Our study confirms the value of these features. However, some patients with acute appendicitis did not have any of these colonoscopic features. In our study, although there were 17 patients (74%) with pus discharge from the appendiceal orifice, only 4 (23%) had spontaneous pus discharge. In 13 (77%) pus discharge only occurred after successful cannulation of appendiceal orifice. Moreover, one patient presented with normal mucosa around the area of appendiceal orifice which is consistent with the fact that in some patients the inflammatory changes may affect only the distal appendix [8]. Thus, colonoscopy alone is unable to reliably predict which patients have an abnormal appendiceal lumen. In contrast, appendicography combined with colonoscopy allowed acquisition of clear images both of appendiceal orifice and lumen for providing more accurate diagnosis.

The advantage of endoscopic retrograde appendicography over traditional barium enema lies in higher success rate of filling appendix. The diagnosis of acute appendicitis by barium enema is mainly based on non-filling of the full appendix [9]. However, 15–23% of normal appendices fail to fill [10, 11] such that failed filling of the appendix is not a reliable sign for acute appendicitis [12]. On the contrary, with a remarkable success (91%) of filled appendix, endoscopic retrograde appendicography easily identified the presence of lumen dilatation, partial stenosis, lack of flexibility and intraluminal filling-defects and thus can reliably confirm the diagnosis of acute appendicitis.

Another advantage of endoscopic retrograde appendicography over CT or US is that it provides radiological imaging of appendix with more objectivity, irrespective of shape and position of appendix within abdominal cavity. Although some studies have reported high sensitivity and specificity of CT and US [13–15], Wilson et al. described the equivocal rates of CT (28%) and US (75%) [16], which is consistent with the result of CT (33%) in the present study. However, the equivocal rate of US (12%) was lower than the previous study, maybe due to the small sample size. US is more operator dependent, relying both on the US technician and the interpretation by the radiologist. Even though CT is more objective, the diagnostic accuracy is also limited by technical and interpretative pitfalls due to the shape and position of appendix inside the abdomen [17]. Actually, clinicians have reported potential negative appendectomy rates of 22% due to CT [18]. Another reason for relative lower accuracy of CT and US in our study is that many cases underwent endoscopic retrograde appendicography because of equivocal results of CT scan or US. Moreover, CT exposes the patient to more ionizing radiation than radiography and is associated with a risk of radiation-induced cancer.

Another advantage of endoscopic retrograde appendicography compared to CT or US lies in differential diagnosis of abdominal pain mimicking acute appendicitis. During the procedures, the endoscopist can visualize the entire colon or appendix and make histological diagnosis by biopsy. In the present study, endoscopic retrograde appendicography identified 4 patients with ileocecal lipoma, ulcerative colitis, colon and appendix carcinoma and typhlitis. However, further study is necessary to obtain a full comparison of the diagnostic accuracy of endoscopic retrograde appendicography, CT and US.

Previous studies have also reported that the patients with an atypical presentation were diagnosed as acute appendicitis using colonoscopy [19]. However, colonoscopy was not widely used for diagnosis of acute appendicitis, because the conventional wisdom is that colonoscopy may aggravate abdominal pain and induce complications. However, there were no complications in this study. In contrast, the results showed that endoscopic retrograde appendicography can be safely performed on the patients with suspected acute uncomplicated appendicitis.

Endoscopic retrograde appendicography procedure can be performed in the outpatient department. Initially, we admitted patients after undergoing ERAT as this was a preliminary study. Now, in China more than 3000 cases of ERAT (using ERA as a diagnostic tool) have been performed and it is recognized that it is not necessary to admit the patients to hospital. The procedure can also be performed in outpatient settings which is currently widely practiced in China.

This is a preliminary study with a limited sample size, a prospective controlled randomized trial is necessary to provide more valuable information for clinical implication of endoscopic retrograde appendicography. However, with the development of colonoscopic technology, we believe this method will become the most reliable method of diagnosis for acute appendicitis in the future.

Conclusion

Our study suggests that endoscopic retrograde appendicography can accurately diagnosis and exclude acute appendicitis. Endoscopic retrograde appendicography provides the physicians with clear images of both appendiceal orifice and lumen which other methods cannot do. However, further study is needed to compare the efficacy of ERA with other radiological examinations.

Abbreviations

Endoscopic retrograde appendicography (ERA); Endoscopic retrograde appendicitis therapy (ERAT); Acute appendicitis(AA); Computed tomography (CT); Ultrasonography (US); Barium enema (BE)

Declarations

Ethics approval and consent to participate

The present study was undertaken under the guidance of the ethics committee of The First Affiliated Hospital of Zhengzhou University. The authors have declared that no ethical conflicts. The written informed consent for participation in the study was obtained where participants are children (under 16 years old) from their parent or guardian.

Consent for publication

Written informed consent of publication of their images and other information was obtained from the patient.

Availability of data and materials

All data generated or analyzed during this study are included in this articles.

Competing interest

The authors declared that they have no competing interests.

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Author's contribution

Study concept and design: BL

Acquisition of data: SU, CP

Manuscript writing: SU, XM

Administrative, technical or material support: LD, JS, KJ

Critical revision of manuscript : BR

all authors have read and approved the manuscript, and ensure that this is the case.

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Conflicts of Interests:

None to disclose.

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Tables

Table 1: The positive findings of ERA for the diagnosis of acute appendicitis.

No.	Examination component	Findings
(1)	Appendiceal orifice	Pus discharge from appendiceal orifice
(2)	Appendiceal orifice and surrounding mucosa	Hyperemic and bulging mucosa
(3)	Appendiceal lumen	Distension, irregular stenosis, inflexibility, filling-defect

Table 2: Basic characteristics of patients

underwent ERA

Characteristics	ERAT (n=33)
Age (years)	44±18.5
>50 years or <15 years, n(%)	18 (53%)
Sex	
Male, n (%)	20 (60.41%)
Female, n (%)	13 (39.39%)
Co-morbid diseases, n (%)	9 (27%)
Cholelithiasis	1
Cerebral infarction	2
Liver cirrhosis	1
Coronary heart disease	1
Others	4
RLQ pain* (n)	33 (100%)
Lower-right quadrant tenderness (n)	32 (97%)
Rebound pain (n)	13 (40%)
Body temperature(°C)	37 (36.5-38)
White blood cells($\times 10^9/L$)	12.2±3.9
Alvarado scores	7 (5.5-8)

Data are mean ±deviation (SD), numbers (%) or median (inter-quartile range, IQR)

* right lower quadrant, RLQ

Table 3: Colonoscopic and radiological findings of ERA

Appendicitis (n=23)	
Appendiceal intubation	22 (96%)
Colonoscopic findings	
Mucosal hyperemia (<i>n</i>)	19 (83%)
Mucosal edema (<i>n</i>)	19 (83%)
Pus discharge* (<i>n</i>)	17 (74%)
Swollen surrounding mucosa (<i>n</i>)	14 (61%)
ERA findings	
Diameter (<i>mm</i>)	0.8±0.4
Length (<i>cm</i>)	6.6±2.3
Stenosis (<i>n</i>)	10 (43%)
Inflexibility (<i>n</i>)	20 (87%)
Filling-defect sign (<i>n</i>)	5 (22%)
CA leakage into abdominal cavity	0

Data are numbers (%) and mean ± deviation(SD). * Pus discharge includes spontaneously discharge in 4 patients and discharge after appendiceal intubation in 12 patients. CA, contrast agents

Table 4: Alternative diagnosis of patients without AA

Alternative diagnosis	No. of patients	Management	Outcomes
Non-specific abdominal pain	2	Clinical observation	Recovery
Pelvic infection	2	Antibiotics	Recovery
Typhlitis	1	Antibiotics	Recovery
Mucinous adenocarcinoma	1	Right hemicolectomy	Symptom relieved
Ileocecal lipoma	1	ESD	Recovery
Ulcerative colitis	1	Mesalazine (4g/d)	Symptom relieved

All of patients were uneventfully recovery after treatment and discharged. No recurrent symptoms in the patients during follow-up (median: 13 months, IQR: 9-24 months). ESD, endoscopic submucosal dissection.

Table 5: Imaging results and accuracy of CT, US and ERA

	Total No.	Patients with acute appendicitis	Patients without appendicitis
CT scan	24	17	7
AA	11	9 (53%)	2 (29%)
NA	5	2 (12%)	3 (42%)
Equivocal	8	6 (35%)	2 (29%)
US	17	11	6
AA	11	8 (73%)	3 (50%)
NA	4	3 (27%)	1 (17%)
Equivocal	2	0	2 (33%)
ERA	34	25	9
AA		23 (92%)	0
NA		0	8 (89%)
Equivocal	3	2 (8%)	1(11%)

Data are given as the number (percentage) of patients. The sensitivity and specificity of the computed tomography (CT) results were 88% and 71% respectively (when equivocal results were included , 53% and 42% respectively). The sensitivity and specificity of the ultrasonography (US) results were 73% and 50% , respectively (when equivocal results were included , 73% and 17% respectively). The sensitivity and specificity of the endoscopic retrograde appendicography (ERA) results were 100% and 100%, respectively (when equivocal results were included , 92% and 89% respectively)

Table-6: Comparison of ERA, CT and US

	ERA (n=33)	CT group (n=17)	US group (n=20)	P value
True-positive rate, % (n)	100% (23/23)	69% (9/13)	69% (9/13)	
True-negative rate, % (n)	100% (11/11)	75% (3/4)	43% (3/7)	
False-negative rate, % (n)		31% (4/13)	31% (4/13)	
False-positive rate, % (n)		25% (1/4)	57% (4/7)	
Accuracy, % (n)	100%(34/34) ^a	71% (12/17) ^c	60% (12/20) ^b	<0.001

ERA, endoscopic retrograde appendicography. Comparison between any 2 groups of the 3 groups were compared with *Chi-square test*. a, ERA vs CT (P=0.003); b, ERA vs US (P<0.001); c, CT vs US (P=0.731).

Figures

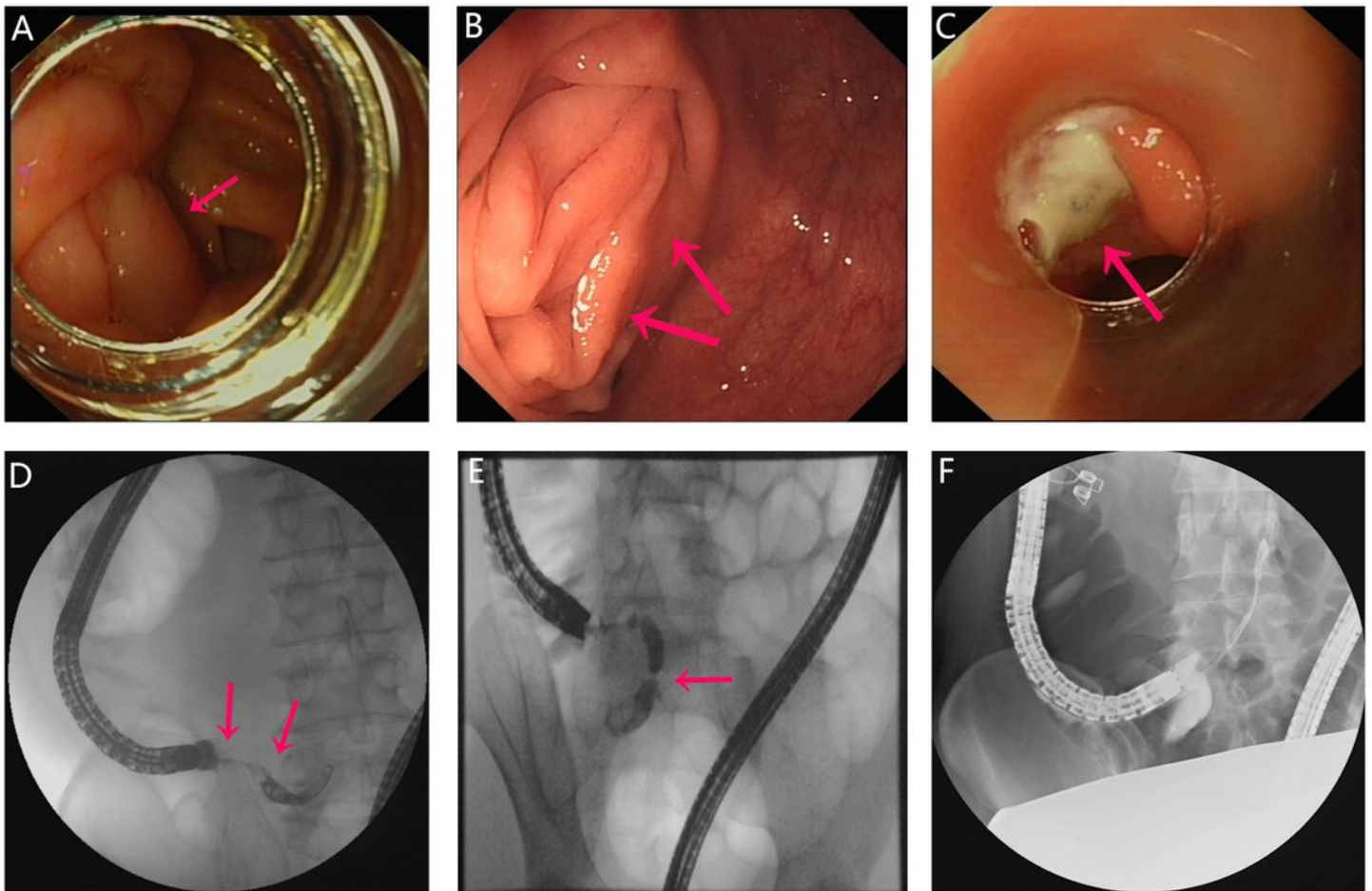


Figure 1

The colonoscopic and radiological findings during ERA. (A, B) Hyperemic and bulging mucosa around the appendiceal orifice. (C) Pus discharge from the appendiceal orifice. (D) Intraluminal filling-defect sign. (E) Luminal distension and stenosis. (F) Normal appendix.