Endoscopic retrograde appendicitis therapy

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***Abstract*:** Endoscopic retrograde appendicitis therapy (ERAT) is a novel and minimally invasive technological alternative for the management of acute or chronic appendicitis. Through endoscopic appendiceal intubation, obstructions such as appendiceal feces and parasites within the appendiceal lumen can be effectively eliminated, leading to patient recovery. Additionally, in cases where the orifices are swollen or complicated appendicitis is present, a stent may be inserted following appendiceal flushing. Due to the utilization of endoscopy for accessing the orifices of the appendix in order to alleviate appendiceal obstruction, patients were able to avoid undergoing appendectomy and experienced a reduced likelihood of recurrence when compared to antibiotic therapy. Additionally, the ERAT provided alternative options for individuals with appendicitis and comorbidities. Recent advancements in techniques, such as the "mother–baby" endoscopic system and the use of microbubble contrast agents, have expanded the range of indications and the eligible patient populations. The objective of this review is to present a comprehensive overview of the development, procedural aspects, therapeutic principles, treatment efficacy, therapeutic applications, and potential complications associated with ERAT.

Plain language summary

Endoscopic retrograde appendicitis therapy

The objective of this review is to present a comprehensive overview of the development, procedural aspects, therapeutic principles, treatment efficacy, therapeutic applications, and potential complications associated with endoscopic retrograde appendicitis therapy (ERAT).

Keywords: appendicitis, efficacy, endoscopic surgery, endoscopic retrograde appendicitis therapy

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Introduction

The endoscopic retrograde appendicitis therapy (ERAT) technique, developed by a Chinese scholar who drew inspiration from endoscopic retrograde cholangiopancreatography technology,[1] emerged as a supplementary alternative particularly well-suited for the treatment of appendicitis. While surgical intervention yields direct therapeutic outcomes and reduces complications, ERAT offers a non-invasive or less invasive approach without the need for appendectomy. The placement of a stent following endoscopic retrograde appendiceal flushing has proven highly effective in achieving therapeutic benefits through a natural orifice.[2] ERAT has demonstrated a significant decrease in the rate of appendectomy through the utilization of colonoscopic direct-vision imaging or fluoroscopic endoscopic retrograde appendicography imaging,[3] as well as endoscopic appendix debridement and drainage to restore the appendix's normal microenvironment, resulting in favorable therapeutic outcomes. Additionally, the selection of ERAT also encompasses the confirmation of previous diagnoses to prevent unnecessary surgical procedures or appendectomies, as well as the qualitative

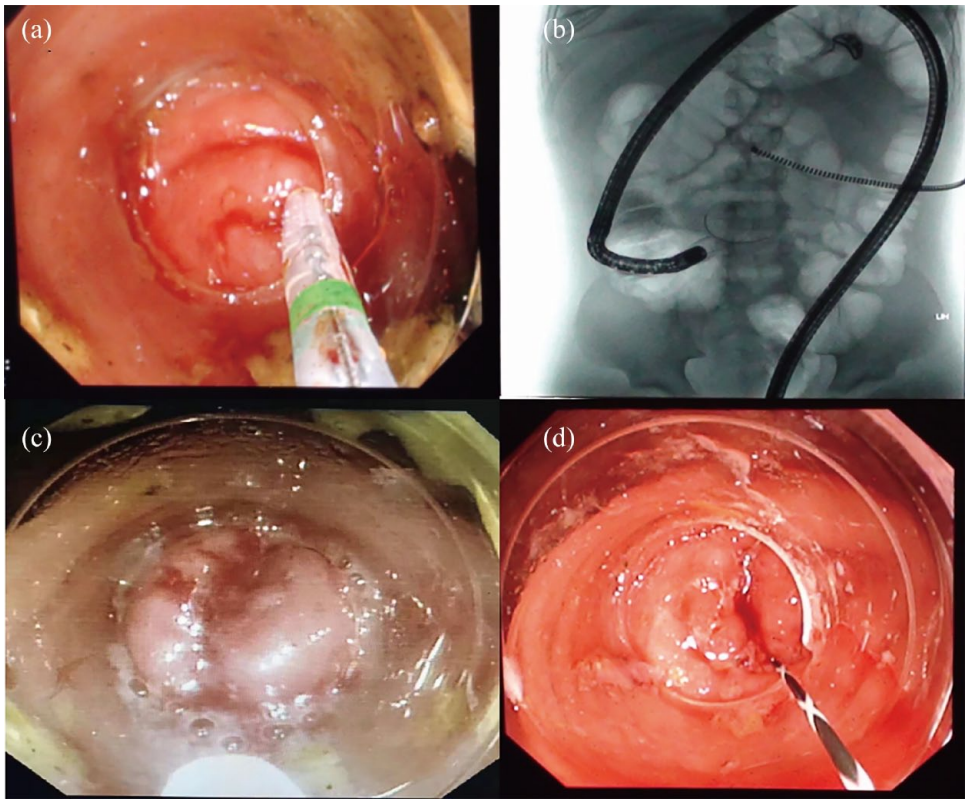

Figure 1. The procedure of classical ERAT. (a) Intubation. (b) X-ray guided. (c) Flushing. (d) Stent implantation by zebra wire.
ERAT, endoscopic retrograde appendicitis therapy.

diagnosis of appendicitis, aiding in the determination of the underlying cause of appendiceal infection and the extent of appendiceal injury. The objective of this review is to present a comprehensive overview of the development, procedural aspects, therapeutic principles, treatment efficacy, therapeutic applications, and potential complications associated with ERAT.

The development of ERAT

Classical ERAT

In 2012, Liu et al.[4] initially documented the utilization of endoscopic treatment of suppurative cholangitis technology as a reference for performing endoscopic procedures on patients diagnosed with acute uncomplicated appendicitis (AUA). This approach involved the guidance of X-rays to facilitate the endoscopic treatment, distinguishing it from antibiotic and surgical interventions. Notably, ERAT considered the prompt resolution of appendectomy and the non-invasive attributes of non-operative management (NOM) treatment (Figure 1).

Ultrasound-assisted ERAT

The conventional ERAT procedure was conducted with the aid of fluoroscopy which was found to have detrimental effects on the growth and development in pediatric patients.[5,6] Consequently, its application in the treatment of appendicitis in children was limited. In response to this issue, Kang et al.[7] proposed an innovative modification to the ERAT technique, replacing X-rays with ultrasound for real-time monitoring of the appendix from the body surface. Additionally, the introduction of the ultrasound contrast agent, sulfur hexafluoride, through the catheter allowed for observation of luminal stenosis and content within the appendix cavity (Figure 2).

The ultrasound-assisted ERAT demonstrated ease of manipulation, resulting in cost savings,

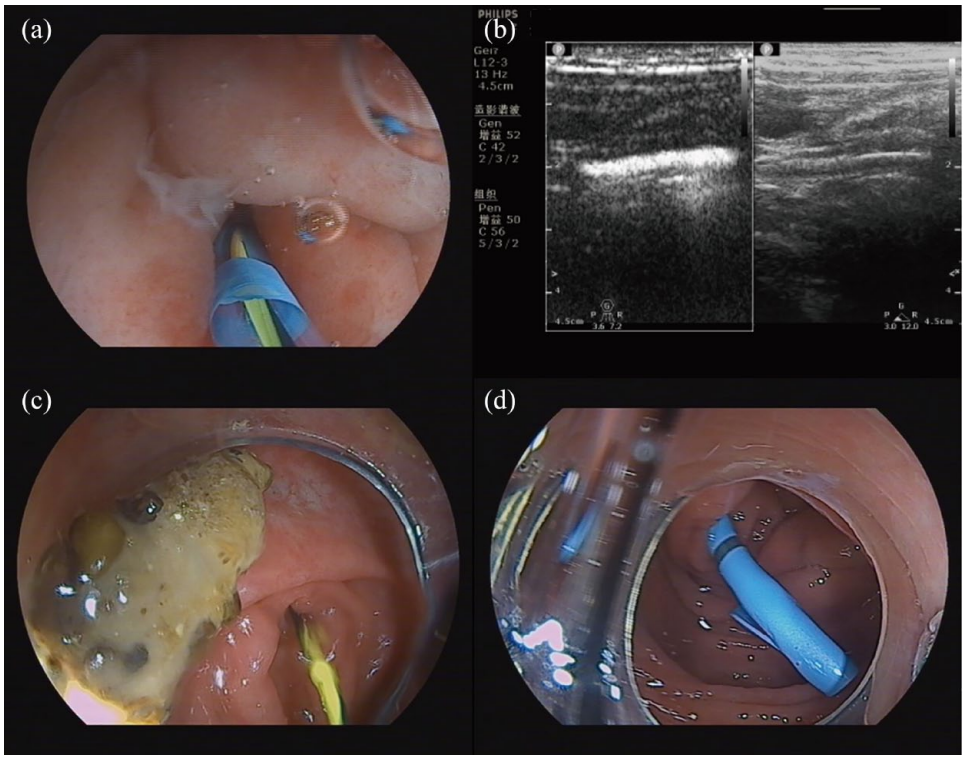

Figure 2. The procedure of ultrasound-assisted ERAT. (a) Intubation. (b) Ultrasound guided. (c) Flushing the appendicolith. (d) Stent implantation.
ERAT, endoscopic retrograde appendicitis therapy.

avoidance of anesthesia, and surgical trauma,[8] and thus holds significant potential for application in appendicitis cases among vulnerable populations such as children, pregnant women, and elderly patients with underlying health conditions.

"Mother–baby" assisted ERAT

In addition, despite the potential for ERAT to be performed with imaging-guided techniques such as X-ray or ultrasound, there is a notable failure rate of 1%–2% for intubation.[9] The utilization of "baby" endoscopy allows for direct visualization and control of the entry into the lumen of the appendix. However, this procedure necessitates the expertise of two operators during the insertion of the "baby" endoscopy. Consequently, the concept of "mother–baby" assisted ERAT has recently been proposed as a treatment option for acute appendicitis. The "baby" endoscopy technique was utilized to visually examine the inner wall, shape, and contents of the appendix, such as appendicolith, pus, or moss, within the cavity. Presently, there are two commercially accessible "mother–baby" endoscopic systems. The first system is the SpyGlass DS system (Boston Scientific, USA),[10] which consists of four channels, including a clamping channel, an optical fiber channel, and two flushing channels. Originally designed for imaging purposes in the biliary pancreatic duct, this system is a disposable digital imaging system.[11] The outer sheath of this system has a diameter of 3.3 mm. The adjustability of the head end of the outer sheath in four directions facilitated the direct entry of SpyGlass DS into the appendiceal lumen for precise endoscopic treatment, thereby enhancing the accuracy of both diagnosis and treatment compared to the other two ERAT technologies (Figure 3). Additionally, the eyeMax insight, a recently developed alternative, offers superior cost-effectiveness, improved imaging capabilities, enhanced visualization of the appendix cavity, and a narrower diameter for seamless operation within the constricted confines of the appendix cavity.[12,13]

Simultaneously, the modified ERAT, utilizing ultrasound or "baby" endoscopy instead of fluoroscopy, enables observation of the appendix

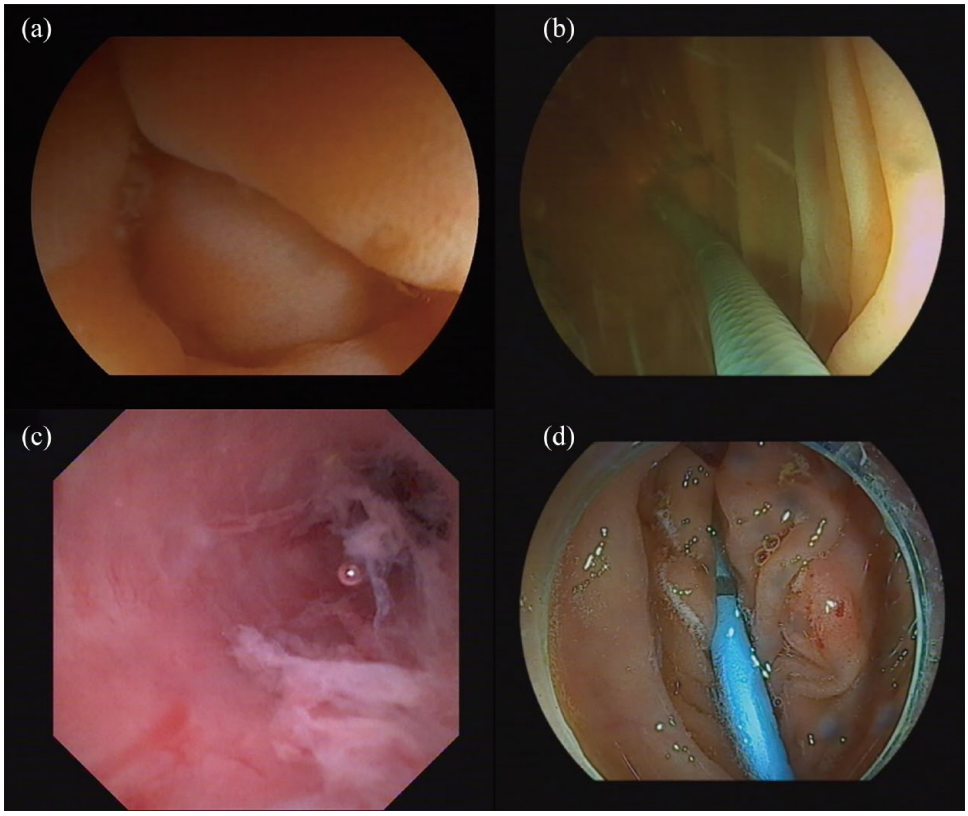

Figure 3. The procedure of "mother–baby" assisted ERAT. (a) Appendiceal orifice. (b) Intubation by baby endoscopy. (c) Flushing under direct visualization. (d) Stent implantation.
ERAT, endoscopic retrograde appendicitis therapy.

without subjecting patients to radiation, thereby expanding its suitability for use in special populations, particularly children, pregnant women, and the elderly.

Furthermore, the advancement from classical ERAT to modified ERAT has resulted in a more refined and developed technology (Table 1). This significant progression has revolutionized the observation of the treatment process. It is worth noting that acute appendicitis commonly manifests in individuals aged 10–20 years.[14] However, the surgical complications associated with appendectomy and the uncertain efficacy of antibiotic treatment fail to meet the specific needs of this age group. Additionally, appendectomy is linked to higher rates of digestive system diseases.[15–17] Consequently, prioritizing the preservation of the appendix and minimizing the recurrence rate were crucial in the management of acute appendicitis in children and adolescents, and the employment of modified ERAT offered a distinct advantage in achieving these objectives. By implementing modified ERAT in pediatric patients, the preservation of the appendix was emphasized, thereby circumventing the unfavorable outcomes associated with surgical intervention resulting from the failure of NOM and substantially mitigating the distress experienced by children.

The procedure of ERAT

All patients in the ERAT cohort underwent bowel preparation by orally consuming polyethylene glycol electrolyte powder the day prior to surgery. Enemas were administered concurrently to patients with poor adherence or severe clinical presentations. The specific protocols for ERAT have been outlined in previous studies.[1,7,10,12] The workflow of ERAT encompassed five primary stages.

Sedation

Prior to undergoing the routine ERAT procedure, patients received sedation through the

Table 1. The development of ERAT.

Variable	Classical ERAT	Modified ERAT	
		Ultrasound-assisted ERAT	**"Mother–baby" assisted ERAT**
Year of first publication	2012	2018	2020
Population of application	Adult (major), children (minor)	Children	Adult, children
Imaging-guide tool	X-ray	Ultrasound	Direct visualization
Application	(a) AUA diagnosis and treatment. (b) Periappendiceal abscess	(a) AUA diagnosis and treatment. (b) Chronic appendicitis	(a) AUA diagnosis and treatment. (b) Chronic appendicitis diagnosis

AUA, acute uncomplicated appendicitis; ERAT, endoscopic retrograde appendicitis therapy.

administration of dexmedetomidine hydrochloride injection 30 min in advance.

Intubation

The distal end of the colonoscope, equipped with a transparent cap, was advanced to the ileocecal junction to assess the state of the appendiceal orifice. A transparent cap could help endoscopists undergo appendiceal intubation easily. As a rule, transparent cap could be classified as ordinary or subulate. The latter is easier to intubate. Subsequently, a zebra guide wire would be introduced into the appendiceal cavity, aided by abdominal ultrasound or X-ray, while displacing Gerlach's valve with the transparent cap. Ultimately, the appendiceal incubation was accomplished by employing a sphincterotome along the guide wire. It is worth noting that the procedure for "mother–baby" endoscopy differs slightly in its execution. The infant endoscopy procedure involved the direct insertion of a device into the lumen of the appendix, allowing for visual examination of the inner wall, shape, and contents such as appendicolith, pus, or moss.

Imaging-guided

A contrast medium was introduced into the appendix through a sphincterotome, enabling the observation of appendix formation, inner diameter, filling defects, contrast extravasation, and characteristics of appendicolith (including location, number, size, and density) using real-time X-ray or sonographic guidance. Importantly, the procedure did not require the use of an image guide for "mother–baby" assisted ERAT.

Flushing

The appendiceal cavity was repeatedly irrigated with 50–60 ml of saline solution until the flushing liquid became clear.

Stent implantation

In cases where patients exhibited a swollen appendiceal orifice, luminal stenosis, or a greater amount of pus in the appendiceal cavity, a stent was inserted.

Re-examination

Patients who received a stent were readmitted for stent removal via colonoscopy within 1–2 weeks after discharge.

Therapeutic principle of ERAT

The etiology of acute appendicitis remains uncertain at present, but established factors include infection of the appendiceal flora, obstruction of the appendiceal lumen, and neurogenic influences.[18] Of these, lumen obstruction is widely regarded as a primary contributor to appendicitis. Consequently, the primary objectives of appendicitis treatment, whether through antibiotic therapy or surgery, are to alleviate obstruction and prevent the dissemination of infection. Furthermore, perforated appendicitis, a form of

Table 2. The indication of three treatments for appendicitis.

Variable	Appendectomy	Antibiotics	ERAT
Disability time	7–14 days (open appendectomy) 4–7 days (laparoscopic appendectomy)	4–5 days (if effective)	1–3 days
Indication	(a) AUA (b) Chronic appendicitis (c) Acute complicated appendicitis	(a) AUA without appendicolith	(a) AUA (b) Chronic appendicitis (c) Appendiceal abscess (d) Atypical appendicitis diagnostics

AUA, acute uncomplicated appendicitis; ERAT, endoscopic retrograde appendicitis therapy.

complicated appendicitis, results in the propagation of inflammation and the development of severe complications. As a result, ERAT demonstrated its reliability as a viable option based on the aforementioned etiological presumptions.

The primary principle of ERAT in the management of acute appendicitis involves the establishment of an appendix drainage channel. This procedure aimed to either remove the obstructive substances initially present or open the closed appendix opening, thereby facilitating complete drainage of the infected lumen and preventing the progression of inflammation. Consequently, when compared to antibiotic or surgical interventions, ERAT exhibited a more focused approach toward addressing the underlying causes of appendicitis and mitigating the severity of the infection.

Indication for ERAT

Currently, there are no formal indications for the ERAT. However, the present studies revealed that the ERAT is an alternative treatment method compared with appendectomy for uncomplicated appendicitis with appendicolith, appendiceal abscess, and early appendicular perforation (Table 2). Additionally, with the recent development of modified ERAT, they could be more widely used in younger and elder patients, even the pregnancy without being guided by an X-ray.

Overall, indications of ERAT were mainly AUA with or without appendicolith. It also is a new choice for patients with complicated appendicitis (appendiceal abscess), or chronic appendicitis. Additionally, patients with perforated appendix who require extensive drainage due to its potential benefits, chose ERAT may be a method that needs further study.[19] Alternatively, the ERAT is suitable for clinical atypical appendicitis diagnostics. Detailed criteria for choosing ERAT over other treatments in our department were as follows:

(1) Patients aged 6 months and older or weighing at least 8 kg who are able to tolerate a colonoscopy examination.
(2) Diagnosis of appendicitis based on comprehensive assessment of clinical symptoms, physical signs, laboratory, and imaging tests.
(3) For patients with complicated appendicitis such as perforation or intra-abdominal abscesses, in whom emergency surgery is not advisable or requires extensive abdominal drainage, consultation with a surgeon suggests the consideration of ERAT for appendicitis due to its potential benefits.
(4) Chronic abdominal pain lasting for more than 3 months and imaging evidence suggesting the presence of fecaliths in the appendix.
(5) Exclusion of acute conditions such as cholecystitis, pancreatitis, and urinary tract stones.

Patients with those conditions may need to exclude ERAT.

(1) Patients who cannot tolerate colonoscopy; (2) patients under 6 months old or weighing less than 8 kg, or other factors that prevent them from tolerating colonoscopy; (3) ERAT cannot benefit the children compared with surgical removal of the appendix; (4) patients with free gas in the

peritoneal cavity on abdominal X-ray and with acute abdomen caused by urinary, gynecological, etc.; (5) patients with severe heart and lung function impairment who have contraindications for colonoscopy or are allergic to contrast agents; and (6) patients do not wish to undergo ERAT.

Treatment efficacy of ERAT

The current therapeutic approach for treating appendicitis typically involves the use of antibiotics and appendectomy. Historically, antibiotics were commonly used as an important supplementary therapy both before and after the surgical procedure. However, there have been several clinical trials exploring the use of antibiotics as a NOM method for treating AUA.[20–22] Additionally, appendectomy, including both open appendectomy and laparoscopic appendectomy (LA),[23,24] has been considered the standard treatment for appendicitis. Therefore, in this study, we will compare the efficacy of the ERAT with these two established treatment methods.

ERAT versus antibiotics

Antibiotic therapy has demonstrated a notable success rate within a 30-day timeframe, yielding short-term advantages such as expedited recuperation and enhanced quality of life scores in contrast to surgical intervention.[20] Furthermore, all patients undergoing this therapy were able to promptly return home. Consequently, prognostic markers such as quality of life scores and disability duration were lower in comparison to appendectomy. However, it is important to note that the recurrence rate of NOM was higher during the subsequent observation period. Studies have reported a success rate ranging from 60% to 70% after 1 year of follow-up,[25,26] thus indicating the uncertain effectiveness of antibiotic treatment.

There are two primary factors to consider when evaluating the effectiveness of ERAT treatment in comparison to antibiotic therapy. The first aspect pertains to the initial success rate, which has been reported to be nearly 99% in ERAT.[27] However, it should be noted that intubation failure is the primary reason for the failure of ERAT. Conversely, the initial success rate in patients treated with antibiotics is not as certain, ranging from 85% to 95%.[28–30] The presence of appendicolith is identified as the primary cause for the failure of antibiotic treatment.[23] Additionally, ERAT has demonstrated efficacy in managing complicated appendicitis, such as abscess of the appendix and appendicular perforation, resulting in favorable therapeutic outcomes. The second factor to consider is the recurrence rate. Previous studies have demonstrated that the recurrence rate for acute appendicitis treated with antibiotics varies between 30% and 40% within a period of 1–2 years,[25,31] which contradicts patients' expectations. Our analysis, presented in Table 3, reveals a lower recurrence rate within the follow-up (6%–15%). In accordance with the 2020 World Society of Emergency Surgery (WSES) guidelines for acute appendicitis, nonsurgical treatment should be prioritized for uncomplicated cases.[32] Consequently, ERAT represents a novel therapeutic option for acute appendicitis.

Furthermore, it has been observed that patients experience enhanced mobilization and faster recovery following ERAT treatment. A comprehensive analysis of multiple studies indicated that the duration of spontaneous pain and clinical symptoms in the ERAT group were significantly lower compared to the appendectomy group.[33]

ERAT versus appendectomy

Appendectomy is widely recognized as the preferred and definitive approach for treating appendicitis.[32] The advent of laparoscopic and robotic technologies has progressively reduced complications associated with appendectomy, particularly intestinal obstruction and wound infection. Nevertheless, as our understanding of the appendix deepens, it is no longer regarded as a vestigial organ.[34] There was a significant presence of lymphoid tissues in the appendix.[35] Additionally, the appendix served as a sanctuary[36] for the microbiota and played a role in restoring intestinal flora in cases of dysbiosis or antibiotic-induced disruption. Furthermore, appendectomy was associated with an increased number of days of disability following the procedure[37] and a higher incidence of colorectal cancer[38] and inflammatory bowel diseases.[22] Several studies have reported a normal appendectomy rate of 10%–18% in postoperative pathology.[39–41] Consequently, the decision to retain or remove the appendix is a matter worthy of consideration.

There exists a substantial body of research that examines the role of ERAT. Thus far, the therapeutic effectiveness of ERAT appears to be comparable to that of appendectomy.[4] The majority

Table 3. The therapeutic effect of ERAT.

Author, year	Sample size	Patients	Study design	ERAT method	Intubation success rate (%)	Initial success rate (%)	Recurrence rate (%)	Follow-up
Liu et al., 2012[1]	4	AUA	Retrospective single-arm study	Classical ERAT	4/4 (100%)	4/4 (100%)	0/4 (0%)	4–19 months
Liu et al., 2015[2]	34	AUA	Retrospective single-arm study	Classical ERAT	33/34 (97%)	32/33 (97%)	2/33 (6%)	12 months
Li et al., 2016[3]	20	AUA	Retrospective single-arm study	Classical ERAT	20/20 (100%)	20/20 (100%)	1/20 (5%)	12 months
Yang et al., 2022[4]	78	AA	RCS	Classical ERAT	76/78 (97%)	76/76 (100%)	6/76 (8%)	12 months
Kang et al., 2021[7]	36	AUA	RCT	Untrasound-assisted ERAT	36/36 (100%)	36/36 (100%)	2/36 (5%)	9
Tao et al., 2020[10]	11	AUA	Retrospective single-arm study	"Mother–baby"-assisted ERAT	11/11 (100%)	11/11 (100%)	–	–
Ge et al., 2023[12]	11	AA	Retrospective single-arm study	"Mother-baby"-assisted ERAT	11/11 (100%)	11/11 (100%)	0/11 (0%)	1–4 months
Kong et al., 2021[13]	14	AUA	Reteospective single-arm study	"Mother-baby"-assisted ERAT	14/14 (100%)	14/14 (100%)	0/14 (0%)	2–24 months
Ding et al., 2021[43]	70	AA	RCS	Classical ERAT	70/70 (100%)	70/70 (100%)	2/70 (3%)	6 months
Shen et al., 2022[44]	33	AA	RCT	Classical ERAT	29/33 (88%)	29/29 (100%)	3/29 (10%)	22 months
Kang et al., 2022[50]	30	CA	Retrospective single-arm study	Untrasound-assisted ERAT	30/30 (100%)	29/30 (97%)	1/28[a] (3%)	11 months
Jia et al., 2022[52]	30	AUA	RCS	Classical ERAT "Mother-baby"-assisted ERAT	30/30 (100%)	30/30 (100%)	2/30 (7%)	7–20 months
Ye et al., 2018[59]	22	AA	Retrospective single-arm study	Classical ERAT	22/22 (100%)	22/22 (100%)	2/22 (9%)	33 months
Zheng et al., 2021[60]	81	AA	RCT	Classical ERAT	81/81 (100%)	81/81 (100%)	1/81 (1%)	6 months
Cui et al., 2021[61]	9	PA	single-arm study	Classical ERAT	9/9 (100%)	9/9 (100%)	0/9 (0%)	2-12 months
Liu et al., 2022[62]	55	AUA	RCT	Classical ERAT	52/55 (94%)	52/52 (100%)	8/52 (15%)	36 months
Guo et al., 2022[63]	36	AA	RCS	Untrasound-assisted ERAT	131/136 (96%)	131/131 (100%)	7/131 (5%)	6 months
Xu et al., 2022[64]	64	AA	Retrospective single-arm study	Classical ERAT and Untrasound-assisted ERAT	62/64 (97%)	59/62 (95%)	5/62 (8%)	NA
Zhang et al., 2023[65]	228	AUA	Retrospective single-arm study	Untrasound-assisted ERAT	221/228 (97%)	221/221 (100%)	14/204[b] (7%)	12 months

[a]One patient loss to follow-up.
[b]Seventeen patients lost to follow-up.
AA, acute appendicitis; AUA, acute uncomplicated appendicitis; CA, chronic appendicitis; ERAT, endoscopic retrograde appendicitis therapy; PA, periappendiceal abscess; RCS, retrospective cohort study; RCT, randomized controlled trial.

of patients undergoing ERAT experience pain relief, which is crucial in facilitating early mobilization and subsequently reducing the occurrence of postoperative ileus.[9,42] Furthermore, ERAT can be conducted without the need for general anesthesia, thereby mitigating the risk of anesthesia-related complications. Consequently, ERAT demonstrates shorter operation times and mean hospital stays compared to both open and LA procedures.[27,33] When estimating operation time, two studies have demonstrated that the costs of ERAT are either comparable to or lower than those of appendectomy therapy.[43,44] Additionally, the adverse events associated with the procedure differ from those of appendectomy. The concern regarding adverse events following ERAT primarily revolves around abdominal pain and recurrence (Table 4).

Therapeutic application of ERAT

Acute uncomplicated appendicitis

In general, the etiology of appendicitis is determined by the anatomic structure of the appendix. Numerous studies have shown that irrigation of the appendix lumen can alleviate inflammation and prevent disease progression. In cases of uncomplicated appendicitis, nonsurgical alternatives should be thoroughly evaluated. A study[45] investigating the effectiveness of classical ERAT in children with acute non-perforated appendicitis revealed that classical ERAT significantly reduced the average hospitalization time by nearly 48 h compared to LA, and also indicated the postoperative complications of classical ERAT and LA were no difference at the same time (9.52% vs 11.90%). Previous research has indicated that ERAT can effectively reduce the likelihood of recurrent appendicitis in patients with appendicolith. Furthermore, several studies have demonstrated that the treatment outcomes of ERAT are comparable between patients with appendicolith and those with uncomplicated appendicitis.[44,46] In a separate case report, Song et al.[47] successfully treated a particularly challenging case involving a large and hard appendicolith lodged in the appendiceal orifice using ERAT.

The present treatment approach for AUA primarily centers on ERAT. Findings from various meta-analyses suggest that ERAT may provide specific benefits in managing AUA. Notably, the incidence and recurrence rate of periprocedural complications significantly decreased, alongside a reduction in the likelihood of infection.

As ERAT technology advances, the accompanying imaging modalities also progress, enabling the assessment of safety and ease of manipulation through the "mother–son" endoscopic technique.

Acute complicated appendicitis

Currently, the utilization of ERAT has been implemented in cases of appendix abscess and perforated appendicitis. Ding et al.[43] documented the application of ERAT in 13 patients with periappendiceal abscess (PA). Subsequent to the procedure, abdominal color Doppler ultrasonography conducted on eight patients on the third day failed to detect a substantial increase in abscess size, while the appendicular abscesses in five patients exhibited a significant reduction compared to their preoperative measurements. Eleven patients diagnosed with PA achieved recovery after undergoing ERAT treatment, and none of them experienced recurrence during the follow-up period (mean follow-up time, 16.2 ± 9.3 months).[48] These findings suggest that ERAT is a suitable intervention for these patients; however, careful observation remains necessary. Further research is required to determine the specific indications for perforated appendicitis. Nevertheless, ERAT proves to be a viable approach for pediatric patients with acute complex appendicitis, emphasizing the importance of organ preservation. Our data indicate that early perforation and appendiceal abscess patients could undergo ERAT.

Chronic appendicitis

The effectiveness of ERAT for the treatment of chronic appendicitis is a topic of ongoing debate. Zhu[49] conducted a study that indicated that ERAT may not provide sufficient treatment for chronic appendicitis, as only 50% of patients achieved complete remission. One possible explanation for this outcome is the repeated activation of inflammatory cells in the mucous membrane of the appendix cavity, leading to the proliferation of fibroblasts and the excessive production of collagen, ultimately causing irreversible narrowing of the lumen due to scar formation. However, an alternative study yielded

Table 4. The short and long adverse events of ERAT.

Author, year	Sample size	Short adverse events (*n*)	Long adverse events (*n*)
Liu et al., 2012[1]	4	–	–
Liu et al., 2015[2]	34	Treatment failure (1)	Recurrence (2)
Li et al., 2016[3]	20	–	Abdominal pain (2); recurrence (1)
Yang et al., 2022[4]	78	Appendicular perforation (1); Fever (2)	Abdominal pain (5) Recurrence (4)
Kang et al., 2021[7]	36	–	Recurrence (2)
Tao et al., 2020[10]	11	–	–
Ge et al., 2023[12]	11	Abdominal pain (1)	–
Kong et al., 2021[13]	14	–	–
Ding et al., 2021[43]	70	Appendicular perforation (1)	Recurrence (2)
Shen et al., 2022[44]	33	–	Recurrence (3)
Kang et al., 2022[50]	30	Abdominal pain (1)	Recurrence (1)
Jia et al., 2022[52]	30	–	Recurrence (2)
Ye et al., 2018[59]	22	–	Recurrence (2)
Zheng et al., 2021[60]	81	Bleeding (2); stent shift (1)	Abdominal pain (3); recurrence (1)
Liu et al., 2022[62]	55	–	Recurrence (8)
Guo et al., 2022[63]	136	–	Recurrence (7)
Xu et al., 2022[64]	64	Bleeding (5); appendicular perforation (1); abdominal abscess (1); treatment failure (3)	–
Zhang et al., 2023[65]	228	Intestinal obstruction (1); treatment failure (3)	Recurrence (11)

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contradictory findings.[50] Among the cohort of 30 pediatric patients experiencing chronic abdominal pain, a total of 27 individuals exhibited complete resolution of symptoms without any subsequent recurrence during a 1-year period of follow-up. This notable disparity can be attributed to significant advancements in technology.

Diagnosis of appendicitis

With the ongoing advancements in medical diagnostic technology, the diagnosis of appendicitis has become increasingly challenging due to its varied clinical manifestations. The rates of misdiagnosis and unnecessary surgical removal of the appendix in cases of acute appendicitis remain at 10%.[51] ERAT allows for direct visualization of appendix lesions, enabling the diagnosis of appendicitis and appendicular lump.[13,19] However, as ERAT relies on a meticulous endoscopic examination, it is considered a secondary option for differential diagnosis in cases of appendicitis. Nevertheless, ERAT demonstrates a high diagnostic and therapeutic value in identifying atypical cases of acute appendicitis. For patients with appendicitis, the endoscope may

show a red, swollen appendix orifice, accompanied or not by pus discharge, and accompanied or not by surrounding mucosal edema. The ERA findings were as follows: a fixed or twisted appendix trajectory, localized narrowing or dilation, an irregular inner wall, filling defects, and leakage of contrast agent out of the lumen (considered appendicitis perforation or appendiceal abscess).

Specifically, Jia et al.[52] effectively employed the SpyGlass DS technique to observe the successful elimination of appendicolith in the abdominal cavity for six young patients, thereby approximating the gold standard for diagnosing appendicitis due to its deterministic nature. Furthermore, the ERAT technology amalgamated the benefits of both diagnosis and treatment, enabling the accurate identification of appendicitis while simultaneously treating appendicitis.

Comorbidities

Extensive investigation has been conducted to explore the utilization of ERAT in various medical scenarios. These applications encompass a wide range of conditions, including uncomplicated and complicated appendicitis, acute and chronic appendicitis, as well as cases involving both adult and pediatric patients, and those with comorbidities or pregnancy-related complications.

In a study by Du et al.,[53] two patients with moderately severe acute pancreatitis were found to develop AUA during their hospitalization, which did not improve with antibiotic treatment. Remarkably, both individuals experienced rapid postoperative recovery and remained free from recurrence following ERAT. Zulqarnain et al. conducted a study on patients with inflammatory bowel disease who also had acute appendicitis. The patients underwent the ERAT procedure and showed successful recovery, as evidenced by the absence of further attacks in the right lower abdomen during the 1-year follow-up period.[54,55] Additionally, a pregnant patient with acute septic appendicitis underwent ERAT without anesthesia after coloclysis. One month after delivery, an endoscopy review revealed a completely normal appearance at the appendix opening and surrounding mucosa.[56]

In the aforementioned studies, the ERAT demonstrates its distinctive advantages. Individuals with comorbidities that necessitate immediate attention are unable to undergo appendectomy or receive the antibiotic treatment. Consequently, the utilization of ERAT presents itself as a favorable alternative.

Adverse event of ERAT

These adverse events can be categorized as either short-term or long-term, depending on whether they occur within or after 30 days following the procedure. Short-term adverse events primarily encompass appendicular perforation, bleeding, and fever, without any significant long-lasting consequences. Conversely, long-term adverse events commonly include abdominal pain and recurrence (Table 4). Overall, there are few studies on the long-term effects and follow-up studies. It is necessary for long-term follow-up studies to assess the durability of ERAT outcomes and any potential late-onset complications.[57]

Conclusion

The utilization of ERAT for the treatment of appendicitis has gained significant acceptance among Chinese medical practitioners. A comprehensive study conducted from November 2009 to September 2019 encompassed a total of 3196 appendicitis patients across 46 hospitals in China who underwent ERAT treatment.[58] The success rate and effectiveness of ERAT exceeded 90%, while the recurrence rate stood at 6.2%, comparable to that of surgical intervention. Moreover, the application of ERAT in cases of acute appendicitis, particularly AUA, has demonstrated favorable therapeutic outcomes. However, it is important to acknowledge the limited knowledge regarding the long-term effects of ERAT, signifying a novel area of investigation.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

We consent to the publication of this manuscript.

Author contributions

Anding Zhang: Conceptualization; Visualization; Writing – original draft; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

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