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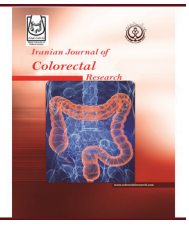

Endoscopic Retrograde Appendicitis Therapy – A Review of an Innovative Appendix Preserving Treatment Modality

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Abstract

Acute appendicitis (AA) is one of the most frequent surgical emergencies and typically results from obstruction of the appendiceal orifice. Currently, laparoscopic appendectomy is the gold standard treatment for appendicitis. However, recent research has demonstrated the importance of the vermiform appendix in maintaining gut flora and immunological function, and it is no longer considered vestigial. Consequently, there is a growing need to develop appendix-preserving treatment modalities for AA. Antibiotic therapy was the first attempt in this direction, and endoscopic retrograde appendicitis therapy (ERAT) represents a recent advancement. The objective of this article is to provide an overview of this novel treatment modality and raise awareness among healthcare professionals. A search of PubMed Gateway, Google Scholar search engine, Web of Science platform, and ResearchGate social networking site was conducted to obtain relevant scientific articles published in English. Since its introduction in China in 2012, several case series have confirmed the use of ERAT in both uncomplicated and complicated appendicitis. ERAT is a promising treatment option for AA that preserves the appendix; however, it has potential limitations and complications, just like other therapeutic approaches.

Keywords: Acute appendicitis; Endoscopic retrograde appendicitis therapy; Appendectomy; Fecalith

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Introduction

Acute appendicitis (AA) is one of the most frequent surgical emergencies and typically results from obstruction of the appendiceal orifice. Fecaliths (hard, crushable concretions) are the most frequent obstructing agents; less common causes include appendiceal calculi (hard, non-crushable calcified stones), tumors, parasites, vegetable matter, foreign bodies, infections, and lymphoid hyperplasia (1-4). Due to its limited luminal capacity, obstruction causes the appendix to rapidly distend, with intraluminal pressures rising to 50 to 65 mm Hg. This increase in pressure gradually leads to arteriolar thrombosis, resulting in ischemia, gangrene, and perforation(2, 5, 6).

Currently, appendectomy (laparoscopic or open) is considered a safe and effective treatment for the management of AA (7). However, recent research indicates that the appendix serves as a "safe house" for beneficial gut flora and contributes to immunological function. This has prompted exploration of non-

operative management (NOM) strategies that preserve the appendix while treating AA (8). In this context, NOM with antibiotics has been tried as an alternative treatment for patients presenting with uncomplicated AA; however, this approach is associated with a longer hospital stay and a higher recurrence rate of approximately 30% within a year, making it less favorable than appendectomy (9-11).

Endoscopic retrograde appendicitis therapy (ERAT) is a novel and minimally invasive technique recently introduced for the management of acute and chronic appendicitis. This approach targets the etiopathogenesis by effectively eliminating appendiceal obstructions, leading to patient recovery (12, 13). The objective of this article is to provide an overview of ERAT's historical background, procedural steps, indications, contraindications, treatment efficacy, adverse effects, and limitations.

Search Strategy

The author conducted a search using the PubMed gateway, Google Scholar search engine, the Web of Science platform, and the ResearchGate social networking site to identify relevant scientific articles. The search employed combinations of the keywords 'appendicitis,' 'endoscopic,' 'retrograde,' and 'therapy.' The reference lists of the retrieved articles were also reviewed to find additional relevant articles related to ERAT. No date restrictions were applied to the literature search. Only the articles published in English were included; those non-English languages were excluded. A total of 13 articles related to ERAT were found. Additionaly, 15 other articles related to AA but unrelated to ERAT were used to support the manuscript.

Historical Background

Liu B. et al., from the Second Affiliated Hospital of Harbin Medical University, Harbin, People's Republic of China, in 2009 were the first to perform ERAT in 2009, drawing inspiration from endoscopic retrograde cholangiopancreatography for the treatment of acute obstructive suppurative cholangitis (14). They subsequently presented this innovation at the American Digestive Diseases Week conference in 2011, and it was published in 2012.

Since then, ERAT has been implemented in various parts of the world and has evolved into a potentially effective minimally invasive treatment option for AA, with benefits such as reduced trauma, accelerated recovery, and preservation of appendiceal function (15).

Procedure: In the original version, as demonstrated by Liu BR. et al.(14) and validated by subsequent researchers, ERAT consists of the following primary steps (Figures 1 and 2).

1. *Bowel Preparation:* The ERAT procedure requires proper bowel preparation, similar to that of a colonoscopy. A rectal enema can be used as a supplement to oral bowel preparation. Additionally, if available, an intracolonic cleansing device can be used for rapid stool preparation in emergency situations (15).

2. *Endoscopic Appendiceal Intubation:* The classical method involves identifying the appendiceal orifice and using the guidewire-catheter technique to intubate the appendiceal lumen under X-ray guidance. Ultrasound is increasingly being used instead of X-rays, particularly in pregnant women and children, to monitor the appendix in real time from the body surface to avoid the harmful effects of radiation. In both modalities, the appendiceal morphology is observed by injecting a diluted water-soluble contrast agent through the catheter (13, 15, 16).

3. *Appendiceal Decompression:* Following successful intubation, purulent fluid is released from the appendiceal cavity, relieving pressure in the appendiceal lumen and reducing the symptoms associated with appendicitis. The appendiceal cavity is thoroughly irrigated to remove the debris and fecaliths, and the color of the flushing fluid is monitored to ensure the lumen is cleared (15-18).

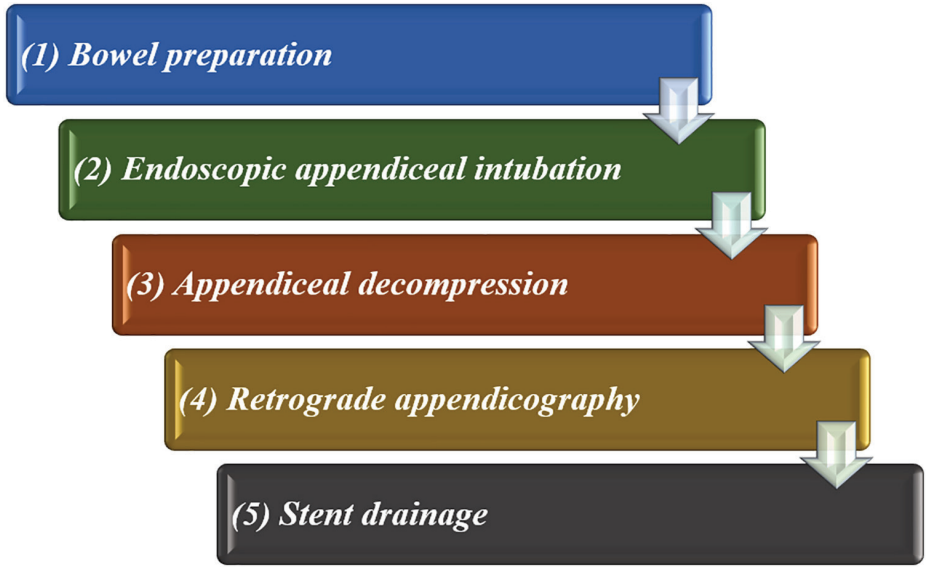

Figure 1: Steps in endoscopic retrograde appendicitis therapy. (Image credit: Sajad Ahmad Salati – Author)

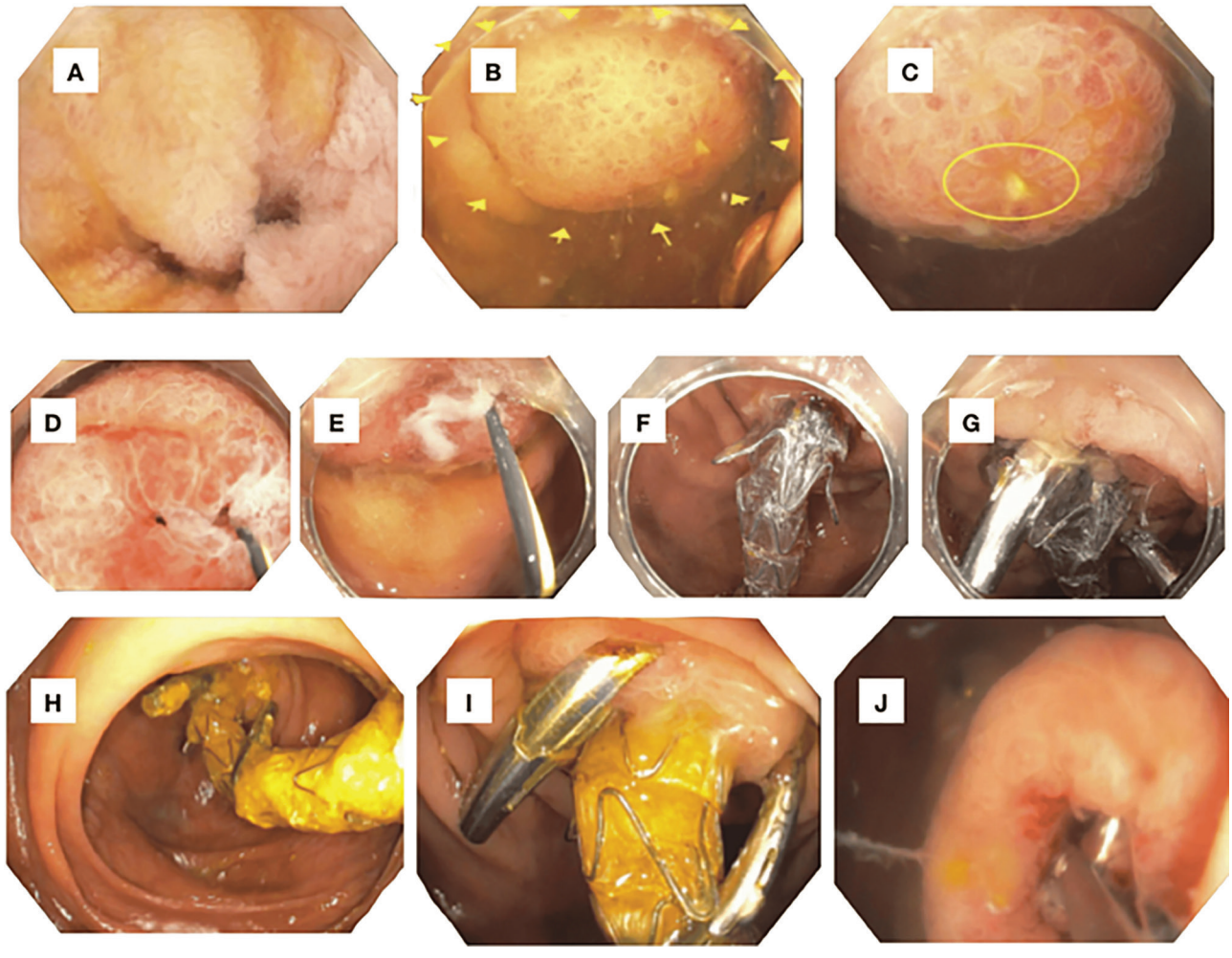

Figure 2: Endoscopic retrograde appendicitis therapy. A: Ileocecal valve. B: Cecum with partially prolapsed appendix. C: Appendiceal orifice with pus. D: Appendiceal orifice with inserted. E: Appendiceal orifice with guidewire inserted and spontaneous pus drainage. F: Appendiceal orifice with placement of a fully covered Viabil stent. G: Appendiceal orifice with three Instinct clips anchoring the Viabil stent. H: Appendiceal orifice showing the previously placed Viabil stent protruding. I: Appendiceal orifice showing the previously placed Viabil stent protruding. J: Appendiceal orifice after removal of the Viabil stent.
Image source: Raxwal B, Payappagoudar J, Patel S. Endoscopic retrograde appendicitis therapy in subacute appendicitis with abscess: a comprehensive case study and innovative insights. Cureus 16(2): e54087. doi:10.7759/cureus.54087. Reused under the terms of the Creative Commons Attribution License CC-BY 4.0. https://creativecommons.org/version4/

Retrieval baskets or balloons may be used if irrigation is unable to expel the fecalith. Additionally, laser lithotripsy and the peroral cholangioscopy equipment can be used in tandem to perform lithotripsy and remove the obstructive fecalith (17).

4. *Retrograde Appendicography:* After thorough irrigation, the morphology of the appendix is re-evaluated by injecting contrast under imaging guidance(15).

5. *Stent Drainage:* When suppurative appendicitis is diagnosed with luminal stenosis, a stent is inserted to drain the remaining pus and reduce luminal pressure. The stent may either discharge spontaneously from the appendiceal cavity or be retrieved approximately four weeks after confirming its position with abdominal radiography or computed tomography scan (CT Scan) (15).

Pre-Procedure Assessment

Accurate preoperative evaluation of the anatomy and pathology of the appendix is critical to the success of ERAT. By assessing factors such as the thickness of the intestinal wall at the appendiceal orifice, the diameter and texture of fecaliths, and the distance between the appendiceal orifice and the ileocecal valve, high-frequency ultrasound (HFUS) has been demonstrated to increase the feasibility of ERAT (19).

Indications

ERAT is primarily indicated for uncomplicated AA. Its effectiveness in more complex scenarios remains undetermined; however, cases have been reported as follows:

***Acute Complicated Appendicitis*:** Appendicitis with peri-appendiceal abscess, perforation, or gangrene, that traditionally requires urgent appendectomy, are referred to as complicated appendicitis.

Song et al.(20) reported a case of a 73-year-old woman who presented with severe abdominal

pain, fever, tachycardia, and leucocytosis. CT Scan revealed periappendiceal and subhepatic abscesses. ERAT was performed because, due to her poor general condition, she was not considered a candidate for surgery. Massive amounts of pus was drained through the appendiceal orifice and the stent. The patient experienced immediate relief from abdominal pain following ERAT, and was discharged from the hospital after five days. A CT scan taken 12 days later showed disappearance of the periappendiceal and subhepatic abdominal abscesses, and at two months, imaging demonstrated a normal periappendiceal bowel wall with no evidence of periappendiceal or subhepatic abscesses or periappendiceal fat stranding. There was no recurrence during the six-year follow-up, highlighting the potential of ERAT in managing periappendiceal abscesses (20).

Stump Appendicitis: Stump appendicitis (SA) is a rare complication that occurs after a primary appendectomy when a longer stump (remaining appendix tissue) forms fecaliths and becomes inflamed (21). Haller and Gasche have reported the safe and effective management of SA with ERAT using the removal of obstructing fecaliths (22).

ERAT in Special Clinical Situations

Pregnancy: ERAT can potentially be performed during pregnancy by avoiding X-ray imaging and using peroral cholangioscopy system or abdominal ultrasound guidance. Kong et al. successfully performed ERAT on a 33-year-old woman in the first trimester of pregnancy. She had experienced migratory right lower quadrant pain twice, once before and once after gestation, respectively and ultrasonography indicated AA. She subsequently had an uneventful delivery at term (23).

Paediatrics: Appendix preservation has a greater significance in children due to its role in the immune system and maintaining intestinal flora balance. Numerous reports of successful ERAT procedures have been published, and it is strongly recommended to use abdominal ultrasound or cholangioscope for guidance to avoid radiological adverse effects (24, 25).

Contraindications

Patients who are unable to undergo a standard colonoscopy, such as those with significant cardiac malfunction, impaired lung function, or insufficient intestinal preparation, are contraindications for ERAT(15). Similarly, patients allergic to contrast agents or presenting with pneumoperitoneum or frank peritonitis are not candidates for ERAT (13).

Potential Complications

Appendiceal Perforation: ERAT carries a risk of perforation because infection or inflammation weakens the Ao wall. Cai et al.(26) reported a case of a six-year-old girl whose CT scan confirmed AA without any signs of perforation. ERAT was performed and the cholangioscope entered the appendiceal lumen smoothly, revealing purulent secretions and a perforation. The procedure was aborted, and laparoscopic appendectomy (LA) was subsequently performed without complications.

Recurrence: ERAT may result in incomplete clearance of the appendiceal lumen, leaving behind residual debris and fecaliths, which can lead to recurrent symptoms and appendicitis. Ma et al.(27) retrospectively analyzed 60 patients who underwent ERAT for chronic fecalith appendicitis and found recurrent abdominal pain in 3 cases (5.0%) and recurrent appendicitis in 2 cases (3.3%) as chronic adverse effects.

Pata et al., in their meta-analysis, did not identify any statistically significant differences between ERAT and appendectomy or antibiotics regarding clinical success during the index admission and recurrence at one-year follow-up (28).

Limitations

Technical: The inaccessibility of the appendiceal lumen presents a major technical challenge to ERAT. The success rate of guidewire insertion is significantly affected by the unique anatomical characteristics of the appendix, including its tortuosity, narrow orifice, and adhesions to surrounding tissues. Additionally, fecaliths or parasites can restrict the appendiceal opening, further complicating intubation, and reducing the likelihood of success (19).

Logistics: There is a need for significant investment in specialized equipment, such as loop-head guidewires, funnel-hood assistants, and cholangioscopes (15). ERAT requires advanced endoscopic skills and a thorough understanding of appendiceal anatomy, making it a highly operator-dependent procedure. Research highlights the importance of education and expertise in resolving technical issues and minimizing complications (15).

Comparison of ERAT with Other Treatment Modalities for Appendicitis

Although its relevance compared to traditional treatments remains under discussion, ERAT has been suggested as an alternative approach for treating appendicitis.

Pata et al. (28) conducted a systematic review in which six studies met the authors' eligibility criteria. Four of these studies compared appendectomy (n=339) with ERAT (n=236 patients) and found no statistically significant differences in technical success during the index admission, although ERAT was associated with a higher likelihood of recurrence at one-year follow-up. ERAT demonstrated a shorter procedure time, reduced overall hospital stay, and less post-procedure pain. Two additional studies compared ERAT (n=269) and antibiotic treatment (n=280). Technical success at admission and recurrence of appendicitis at one year did not differ significantly; however, the overall length of hospital stay was shorter for patients receiving ERAT.

Basukala et al. compared the outcomes of ERAT and LA in a systematic review and meta-analysis (29). They found that ERAT had a procedural time that was 10.93 minutes shorter and lower cost of care, but it had 5.46 times lower odds of achieving technical success and 14.25 times more odds of recurrence. There was no significant difference between the two groups in terms of overall length of hospital stay and complications.

Conclusion

ERAT is a minimally invasive therapeutic option for appendicitis that is emerging as an alternative to appendectomy. Studies have demonstrated that its clinical and technical success rates are comparable to those of appendectomy and antibiotic therapy, although recurrence rates remain relatively high. The advantages of preserving the appendix, reduced invasiveness, and shorter hospital stays make this approach appealing despite its limitations, and it is anticipated to become more widely accepted in the coming years.

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Data Availability Statement

This study did not generate any new data; however, the references that were utilized may be provided upon appropriate request.

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