Endoscopic retrograde appendicitis therapy vs. Laparoscopic appendectomy for uncomplicated acute appendicitis

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Abstract:

Background and study aims: To assess the efficacy and clinical outcomes of endoscopic retrograde appendicitis therapy (ERAT) versus laparoscopic appendectomy (LA) for patients with uncomplicated acute appendicitis (AA).

Patients and methods: We adopted propensity score matching (1:1) to compare ERAT and LA patients with uncomplicated AA from April 2017 to March 2020. We reviewed a total of 2880 patients with suspected acute appendicitis, of whom 422 patients with uncomplicated AA met the matching criteria (ERAT, 79; LA, 343), yielding 78 pairs of patients.

Results: The rate of curative treatment within one year after ERAT was 92.1%; 95% CI, [83.8% - 96.3%]. The percentage of Visual Analog Scale (VAS) ≤ 3 at six hours after treatment was 94.7%; 95% CI [87.2% - 97.9%] in the ERAT group, and significantly higher than that in the LA group 83.3%; 95% CI [73.5% - 90.0%]. Median operative/procedure time and median hospital length of stay in the ERAT group were significantly lower compared to the LA group. At one year, the median recurrence time was 50 days (IQRs, 25-127) in the ERAT group. The overall adverse event rate was 24.3%; 95% CI [14.8% - 33.9%] in the LA group and 18.4%; 95% CI [9.7% - 27.1%] in the ERAT group, with no significant difference between the two groups.

Conclusions: ERAT is a technically feasible method to treat uncomplicated AA compared to LA.

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Conclusions: ERAT is a technically feasible method to treat uncomplicated AA compared to LA.

Introduction

Appendicitis is a common abdominal surgical emergency condition that occurs most often between the ages of 10 and 20 years, with a male-female ratio of 1.4:1 [1]. Abraham Groves performed the first recorded appendectomy in 1883 [2]. A century later, Semm first introduced laparoscopic appendectomy (LA) in 1983 [3]. While appendectomy remains the most effective treatment in cases of uncomplicated appendicitis, it causes complications and carries the risk of negative appendectomy [4].

Endoscopic retrograde appendicitis treatment (ERAT) is a new and minimally invasive alternative method for the diagnosis and treatment of acute appendicitis. Liu first introduced and implemented it in 2012 [5]. ERAT is inspired by Endoscopic Retrograde
Cholangio-Pancreatography (ERCP) technology. The basic principle is using an endoscope with a transparent cap at its distal end intubating the appendix and thereby decompressing the lumen, the appendix cavity is fully drained using a Seldinger technique. The novel technique requires direct endoscopic imaging or fluoroscopic endoscopic retrograde appendicography (ERA) to separate suspected acute appendicitis from actual acute appendicitis. For patients with uncomplicated AA, we performed ERAT to relieve the appendiceal lumen obstruction. Studies have shown that up to 93.8 to 95% of uncomplicated AA did not have a recurrence following ERAT [6,7].

To date, there is no report to compare ERAT and LA for uncomplicated AA. Therefore, we conducted this non-inferior retrospective study to assess the feasibility of ERAT compared with LA in patients who were hospitalized with acute appendicitis.

**Methods**

**Patient selection**

Following approval by the institutional review board, we retrospectively reviewed data on patients admitted to the First Affiliated Hospital of Zhengzhou University between April 2017 and March 2020, requiring treatment for appendix disease. The inclusion criteria for this study were patients aged 18 - 60 years with uncomplicated AA (Appendix >6 mm in diameter with wall thickening, along with periappendiceal edema and/or a small collection of fluid, without appendiceal stones, perforation, abscess, or suspected tumor) confirmed by computed tomography (CT), opting for LA or ERAT. We excluded those who had any of the stated findings: (i) younger than 18 years of age; (ii) older than 60 years of age; (iii) with complicated acute appendicitis found on preoperative examination or intraoperatively (For appendix tumor: a CT scan showing an appendix larger than 15 mm with thickened or irregular walls is suspected of neoplasia. During the ERAT procedure, if the colonoscopy shows an involuted, mass-like protrusion, mucus or polyp-like tissue at the opening of the appendix, appendiceal tumors are suspected; when the following three criteria are met, mucosal malignancies are suspected during ERA: 1. a filling defect is observed in the appendiceal lumen; 2. the defect remains after repeated flushing; 3. a fecal stone is excluded); (iv) could not be contacted during follow-up. The ERAT and LA procedures were carried out independently by experienced doctors or by beginners under the supervision of an experienced doctor. We gathered the following clinical data: age, gender, temperature, white blood cell count, C-reactive protein (CRP), and level of abdominal pain (presentation to hospital); duration of procedure/operative time, hospital length of stay, comorbidities, and adverse events. The Visual Analog Scale
(VAS) was applied to assess the level of abdominal pain (0 - 10 cm line; 0: no pain; 0.1 - 3.0: mild pain; 3.1 - 7.0: moderate pain; 7.1 - 9.9: severe pain; 10: unbearable pain). We followed up all enrolled patients by telephone and/or medical records.

**Description of ERAT technique**

Preparation for ERAT included bowel cleansing using either 2 L polyethylene glycol electrolyte solution or low-pressure cleansing enemas (300-500 ml per enema) given five times. For patients with mild/moderate symptoms, the oral prep was given 4–6 hours before the procedure. For clinically severe cases or patients with anorexia or nausea/vomiting, low-pressure cleansing enemas were given about 30 minutes prior to endoscopy [8]. We performed the ERAT procedure as described previously [5]: (I) An endoscope with a transparent cap attached on the tips inserted into the cecum to the level of Gerlach’s valve; (II) Gerlach’s valve is then pushed aside using the transparent cap, and the appendix is intubated using the guide wire-catheter technique; (III) Under radiographic surveillance, pus is aspirated from the appendiceal lumen through the catheter. The lumen of the appendix is then imaged with a water-soluble contrast agent to observe the morphology and internal diameter of the appendiceal lumen, and evaluate the wall smoothness, filling defects, leakage of the contrast agent, and whether the position and peristalsis of the appendiceal lumen are normal; (IV) The appendix lumen is then repeatedly flushed with 50~100 ml of saline; (V) For patients with a large amount of pus or narrowing of the appendiceal lumen, a 7-8.5 Fr plastic stent (5-7cm length; Cook Medical, USA) is placed over the guidewire under X-ray surveillance to drain the pus and support the luminal stenosis to continuously reduce the pressure in the appendiceal lumen. After 2-4 weeks, patients undergo abdominal radiography to determine if the stent should be removed. In some patients, the stent may dislodge on its own. **Figure 3a-3f** shows endoscopic images of the ERAT procedure.

**Primary and secondary outcomes**

The primary outcome was curative treatment: in the ERAT group, we defined curative treatment as successful appendiceal intubation and non-recurrence of appendicitis during the one-year follow-up period; in the LA group, we identified curative treatment as a successful appendectomy without converting to open appendectomy. Secondary measured outcomes included duration of treatment, rate of post-operative pain relief from moderate/severe to mild/no pain within 6 hours of treatment, hospital length of stay, short-term (within 30 days) adverse events, and long-term adverse events (occurred >30 days). Overall adverse events included both short-term and long-term adverse events. In the ERAT group, short-term adverse events included recurrent appen-
Dicitis, gastrointestinal perforation, fever, bleeding and blood transfusion, abdominal abscess, contrast allergy, and systemic adverse events (pulmonary embolism, stroke, cardiac events, acute renal failure, and sepsis). Long-term adverse events included recurrent appendicitis, abdominal pain, diarrhea, constipation and appendiceal tumors. In the LA group, short-term adverse events included incisional infection, incisional pain, anastomotic leak, abdominal abscess, anesthesia-related, and systemic adverse events. Long-term adverse events included bowel obstruction, abdominal pain, incisional hernia, diarrhea, and constipation. The definitions of adverse events are shown in Supplementary Table 1.

Sample size calculation
In this study, we assumed a 99% success rate for uncomplicated AA in the LA group relative to a 95% success rate in the ERAT group. A non-inferiority margin of 11% was used to calculate the sample size, meaning that the lower pass limit for ERAT would be 88%. We estimated that a sample size of 74 patients per group would give an 80% power to establish whether ERAT was not inferior to LA regarding the treatment success using a one-sided significance level $\alpha$ level of 0.05. The calculation was performed using Proc Power version 9.4 (SAS Institute Inc) [9].

Statistical analysis
Propensity score matching (PSM) was used to minimize selection bias. The propensity score was estimated by logistic regression, with treatment as the dependent variable and independent variables, including sex and age. We matched patients 1:1 using the nearest-neighbor matching algorithm without replacement, with the caliper value fixed at 0.1 for the propensity matching scores [10]. Continuous variables (procedure/operative time, length of hospital stay, age, recurrent time, and hospitalization cost) were expressed as medians with 95% CIs and interquartile ranges (IQRs), categorical variables were expressed as frequency and percentages with 95% CIs. The Mann-Whitney U test was applied for continuous variables. The Pearson $x^2$ test or Fisher’s exact test were used for categorical variables. We computed the cumulative incidence of recurrent appendicitis in the ERAT group using the Kaplan-Meier approach. We performed PSM and all calculations using Stata/SE 15.0 (Stata Corp, College Station, TX). All tests were two-sided. P-values < 0.05 were considered statistically significant.

Results

Patient characteristics
We extracted the data of 2880 patients with suspected acute appendicitis from the in-patient database of the First Affiliated Hospital of Zhengzhou University from April 2017 to March 2020. Of these patients, we excluded 356 patients younger than 18 years of age, 297 patients older than 60 years of age, 103 patients with perforation on CT, and 176 patients with periappendiceal abscess on CT. A total of 1948 patients with uncomplicated acute appendicitis were confirmed by CT and opted for treatment. Then we excluded: 918 patients treated with antibiotics, 3 patients with periappendiceal abscess diagnosed during LA, 5 patients with perforation diagnosed during LA, 2 patients with carcinoid tumors confirmed by postoperative pathology, 543 patients with chronic appendicitis confirmed by postoperative pathology, and 55 patients who could not be contacted (lost to follow-up). We identified 422 eligible patients for matching (ERAT, 79; LA, 343). Propensity score matching yielded 78 patient pairs (Figure 1). Supplemental Figure 1 presents the distribution of the propensity scores in the LA and ERAT group. Table 1 shows the characteristics of the matched patients.

**Primary outcome**

In the ERAT group, a total of three endoscopists performed ERAT for patients with uncomplicated AA. There were 76 (97.4%; 95% CI [91.1% - 99.3%]) patients who had successful appendiceal intubation, and two (2.6%; 95% CI [0.7% - 8.9%]) patients were referred to surgery because of failed intubation during the ERAT process. In total, 70 (92.1%; 95% CI [83.8% - 96.3%]) patients with uncomplicated AA did not require surgical intervention during the one-year follow-up period after ERAT. With a predetermined 11% non-inferiority margin for this study, we were able to demonstrate that ERAT is non-inferior to LA. There were 28 (36.8%; 95% CI [26.9% - 48.1%]) patients who underwent saline flushing of the appendiceal lumen and placement of a stent, and 48 (63.2%; 95% CI [51.9% - 73.1%]) patients had only saline flushing of the appendiceal lumen. In the LA group, all patients received laparoscopic surgical resection successfully. Intra-operative abdominal tubes were placed in 3 patients and removed after 24 hours of observation. Postoperative pathology confirmed uncomplicated AA in all 78 patients, including 58 (74.4%; 95% CI [63.7% - 82.8%]) with acute simple appendicitis and 20 (25.6%; 95% CI [17.3% - 36.3%]) with acute suppurative appendicitis.

**Intraoperative and postoperative outcomes**

The median operative time was 50 minutes (95% CI, 50 - 55) in the LA group, which was significantly longer than that of the ERAT group 40 minutes (95% CI, 35 - 45), (p < 0.001; difference, 10 minutes [95% CI, 6 - 15]). A total of 72 (94.7%; 95% CI [87.2% - 97.9%]) patients had VAS ≤ 3 six hours after treatment in the ERAT group, while 65
(83.3%; 95% CI [73.5% - 90.0%]) patients had VAS ≤ 3 six hours after surgery in the LA group, with a statistical difference between the two groups (p = 0.023; difference, 11.4 percentage points [95% CI, 1.7 - 21.1]). The median hospital length of stay was 4 days (95% CI, 3 - 4) in the LA group, which were significantly longer than those in the ERAT group 2 days (95% CI, 2 - 2), (p < 0.001; difference, 2 days [95% CI, 1 - 2]).

Table 2 displays the main outcomes of the two matched groups.

**Short and long-term adverse events**

The median follow-up time was 1 year. The overall short-term adverse event rate was 7.7%; 95% CI [3.6% - 15.8%] in the LA group and 6.6%; 95% CI [1.0% - 12.2%] in the ERAT group, with no significant difference between the two groups. In the ERAT group, we found one patient with a fecal stone in the distal appendiceal cavity during ERA. The contrast agent diffused into the abdominal cavity, thus confirming the appendiceal perforation. With the patient’s consent, we placed two abdominal drains and administered peritoneal flushing for him. The patient recovered with no intra-abdominal abscesses or other adverse events and was discharged after 7 days of conservative antibiotic treatment. A month later, we successfully performed ERAT once again using ultra-fine choledochoscopy (SpyGlass™, Boston Scientific Corp, Marlboro, MA, USA) to break the fecal stone and then removed it. The patient had no recurrence during the follow-up period. There were two (2.6%; 95% CI [0.7% - 9.1%]) patients in the ERAT group who developed fever after treatment and recovered following conservative antibiotic treatment. During the one-year follow-up period, there were no deaths in both groups, no bowel obstruction and hernia in the LA group, and no appendiceal tumors in the ERAT group. The overall long-term adverse event rate was 16.6%; 95% CI [10.0% - 26.5%] in the LA group and 11.8%; 95% CI [4.6% - 19.1%] in the ERAT group (p = 0.491; difference, 4.8 percentage points [95% CI, -6.2 - 15.8%]). Five (6.6%; 95% CI [2.8% - 14.5%]) patients in the ERAT group had varying degrees of abdominal pain two months after treatment, 3 had spontaneous resolution of symptoms, and 2 went to the hospital for examination. One patient was diagnosed with enteritis and the other with pelvic infection, both of them recovered after conservative treatment. In the LA group, a total of 3 (3.9%; 95% CI [1.3% - 10.7%]) patients had Grade 1 diarrhea (<4 stools/day) and 6 (7.7%; 95% CI [3.6% - 15.8%]) patients had Grade 2 diarrhea (4-6 stools/day), all of whom recovered after symptomatic treatment.

**Recurrence in the ERAT group**

There was no recurrence of appendicitis in patients who had stents placed, while 6 (7.9%; 95% CI [3.7% - 16.2%]) patients recurred in those without stents. Among the
patients with recurrent appendicitis, two of them recurred within 30 days, with a median recurrence time of 50 days (IQRs, 25 - 127). One patient underwent laparoscopic surgery 4 months after ERAT and recovered well after surgery. A post-operative pathology confirmed chronic appendicitis. The other five patients had recurrence of uncomplicated appendicitis. We performed ERAT again for one of them and placed a stent for adequate drainage; four other patients received antibiotic therapy, then all five patients experienced no recurrence during the follow-up period. Figure 2 shows the cumulative incidence of recurrent acute appendicitis in the ERAT group.

Discussion

The appendix is a lymphoid organ whose lymphoid tissue begins to appear at birth and reaches its peak between 12 and 20 years; it has immune functions, as evidenced by the fact that it can be a good host for biofilms that are essential for beneficial microorganisms [11]. In addition, a comprehensive study found that appendectomy was associated with a higher risk of Crohn’s disease [12]. In 2009, a study from China demonstrated that the appendix may have a protective effect against colon cancer and that appendectomy may be a risk factor for the development of colorectal cancer [13]. Furthermore, the appendix is closely associated with intestinal microecology. In 2014, Japanese researchers compared rats with and without appendectomy and found that the appendix provides immune cells to the intestine and plays a role in maintaining intestinal bacterial homeostasis [14].

In recent years, appendectomy has been challenged as the “gold standard” in the handling of acute appendicitis because of postoperative complications and a high rate of resection of the normal appendix [15-18]. The most updated guidelines recommend antibiotic treatment as a good option for patients with uncomplicated appendicitis [19]. The APPAC study showed that 73% of the 256 patients with uncomplicated AA treated with antibiotics did not require surgical therapy for a one-year follow-up period [20]. In addition, a comprehensive review and meta-analysis showed that antibiotics could be a viable and effective treatment option for imaging-proven uncomplicated appendicitis [21]. Nevertheless, the use of antibiotics in treating uncomplicated AA faces unavoidable problems: patients with appendiceal fecaliths are at higher risk of acute peritonitis because of complications of appendiceal perforation and have a higher recurrence rate after antibiotics treatment [20]. ERAT is useful for patients with appendiceal faecoliths, as it can flush the faecoliths out and relieve the obstruction, thus relieving symptoms and considerably reducing the recurrence rate of appendicitis [22]. Another advantage of ERAT over antibiotics for uncomplicated AA is that ERAT
rapidly eliminates painful symptoms, whereas patients experience varying levels of pain during antibiotic treatment. In this study, the curative treatment rate was better than that of the antibiotic treatment for uncomplicated AA [23-27]. Further prospective studies are needed to compare ERAT and antibiotic treatment of uncomplicated AA.

Although appendectomy is a routine surgical procedure, there remains a risk of surgical adverse events and negative appendectomy. Common complications included incisional infection (6%), abdominal infection (1.6% to 3%), small bowel adhesion obstruction (0.4% to 1.3%), incisional hernia (0.4%), and other complications such as interstitial pneumonia (2.5%), urinary tract infection (1.1%), and cardiovascular accidents (1.1%) [28]. In our study, there were 9 cases of diarrhea occurred after LA surgery, which might be because of the imbalance of intestinal flora after appendectomy. Further exploration of changes in gut flora after ERAT and LA may clarify the cause of diarrhea and bowel dysfunction. The six patients with recurrence in the ERAT group were treated with appendix flushing without stent placement for drainage. Interestingly, one patient with recurrence chose ERAT again and did not recur after stent placement, suggesting that adequate drainage may be an effective means of reducing recurrence of appendicitis. Therefore, exploring and differentiating the population at high risk of recurrence after ERAT is a key direction for future research. The median hospital length of stay in the ERAT group was shorter than that in the LA group. In China, patients usually choose to be kept in hospital for an observation period of 2-4 days after laparoscopic or open surgery.

However, this study still has its limitations: (i) retrospective design; (ii) relatively small sample size; (iii) potential selection bias, in particular that healthier patients could have been selected for ERAT (unmeasured confounders). There are also issues that the study cannot address: ERAT may exacerbate perforation, cancer diagnosis may be missed, and some patients need to undergo multiple colon examinations.

In conclusion, ERAT could be an effective and minimally invasive alternative approach to treat uncomplicated AA with rapid postoperative abdominal pain relief and preservation of the appendix without compromising the character of life and work efficiency. To further evaluate the safety and efficacy of ERAT, a comprehensive international, multi-center, randomized controlled prospective study is urgently needed.

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Figure legends:

Figure 1: Flow diagram of the entire and matched cohorts.

Figure 2: Kaplan-Meier graph for time to recurrence after ERAT at 1-year follow-up.

Figure 3a: Appendiceal opening;

Figure 3b: Appendiceal lumen cannulation;

Figure 3c: Filling defect in the appendiceal lumen is visible on imaging (red arrow);

Figure 3d: Pus or appendiceal fecal stone is flushed out;

Figure 3e: Appendiceal stent is placed;

Figure 3f: Radiographs after ERAT (red arrow indicates the stent).

Supplemental Figure 1: the distribution of the propensity scores in the LA and ERAT group.

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### Supplementary Table 1. Definitions of adverse events in this study

| Adverse events                  | Definition                                                                                                                                 |
|---------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| **Recurrent appendicitis**      | Presence of recurrent pain in the right lower abdomen after ERAT, with CT or ultrasound suggesting appendicitis.                           |
| **Gastrointestinal perforation**| Presence of progressive worsening of abdominal pain, combined with signs of peritonitis, with routine hematology and imaging suggesting perforation. |
| **Abdominal abscess**           | Presence of pus (cellular debris, enzymes and liquefied residue) or infected tissue in the abdominal cavity.                                |
| **Contrast allergy**            | Skin reactions (e.g., mild skin rash, hives) or cardiovascular, respiratory (e.g., dyspnea), or gastrointestinal (e.g., nausea, vomiting) symptoms several hours or days after contrast injection. |
| **Bowel obstruction**           | Presence of impaired passage of intestinal contents.                                                                                     |
| **Abdominal pain**              | The presence of pain between chest and groin. The Visual Analog Scale (VAS) was applied to assess the level of pain (0 - 10 cm line; 0: no pain; 0.1 - 3.0: mild pain; 3.1 - 7.0: moderate pain; 7.1 - 9.9: severe pain; 10: unbearable pain). |
| **Diarrhea**                    | Three or more loose or watery stools a day. Diarrhea was graded according to the National Institutes of Health criteria for adverse events. Grade 1 (<4 stools/day), Grade 2 (4-6 stools/day), Grade 3 (>=7 stools/day), Grade 4 (Life-threatening consequences). |
### Supplementary Table 1. Definitions of adverse events in this study

| Condition               | Definition                                                                                                                                 |
|-------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|
| **Constipation**        | Three or fewer bowel movements in a week. The stool can be hard and dry. Constipation was graded according to the National Institutes of Health criteria for adverse events. Grade 1 (Occasional or intermittent symptoms; occasional use of stool softeners), Grade 2 (Persistent symptoms with regular use of laxatives or enemas), Grade 3 (Obstipation with manual evacuation indicated), Grade 4 (Life-threatening consequences). |
| **Appendiceal tumors**  | A CT scan showing an appendix larger than 15 mm with thickened or irregular walls is suspected of neoplasia. During the ERAT procedure, if the colonoscopy shows an involuted, mass-like protrusion, mucus or polyp-like tissue at the opening of the appendix, appendiceal tumors are suspected; when the following three criteria are met, mucosal malignancies are suspected during ERA: 1. a filling defect is observed in the appendiceal lumen; 2. the defect remains after repeated flushing; 3. a fecal stone is excluded. |
| **Incisional hernia**   | Part of an internal organ or tissue bulges through near or along surgical scars in the abdomen.                                             |
| **Anastomotic leak**    | Presence of leak of luminal contents from a surgical join.                                                                                  |
| **Blood transfusion**   | The use of blood products during admission.                                                                                                   |
| **Delayed awakening**   | A state of unresponsiveness from which the patient cannot be aroused after general anesthesia.                                              |
Table 1. Baseline patient characteristics after PSM.

| Variable                      | ERAT group (n = 78) | LA group (n = 78) | P value |
|-------------------------------|---------------------|-------------------|---------|
| Sex, male, n (%)              | 40 (51.28%)         | 41 (52.5)         | 0.86    |
| Agea, years, (median with IQRs) | 30 (21 - 35.25)     | 30 (22.75 - 34.25) | 0.35    |
| Temperatureb, (> 37.2°C)      | 33 (42.31%)         | 31 (39.7)         | 0.74    |
| VAS                           |                     |                   |         |
| moderate (3.1 - 7.0)          | 29 (37.18%)         | 35 (44.8)         | 0.33    |
| severe (7.1 - 10.0)           | 49 (62.82%)         | 43 (55.1)         |         |
| CRPc, (> 5 mg/L)              | 63 (80.77%)         | 57 (73.0)         | 0.25    |
| Leukocytes countd, (> 10×10⁹/L) | 67 (85.90%)     | 61 (%)             | 0.21    |

Abbreviations: PSM, propensity score matching; VAS, Visual Analog Scale; Level of abdominal pain (0 - 10 cm line; 0: no pain; 0.1 - 3.0: mild pain; 3.1 - 7.0: moderate pain; 7.1 - 9.9: severe pain; 10: unbearable pain); CRP, C-reactive protein.

aAge is expressed as median, and data in parentheses are the interquartile ranges (IQRs).

bBaseline temperature, reference: 36.3°C - 37.2°C.

cBaseline CRP, reference: 0 - 5 mg/L.

dBaseline leukocytes count, reference: 0 - 10×10⁹/L.

The data are presented in the form n (%).
Table 2. Outcomes of the two matched groups.

|                               | ERAT group (n=76) | LA group (n=78) | Difference | P value |
|--------------------------------|-------------------|-----------------|------------|---------|
| Operative/procedure time, minutes | 40 (35 - 45)      | 50 (50 - 55)    | -10 (-15 - -6) | <0.001* |
| Hospital length of stay, days   | 2 (2 - 2)         | 4 (3 - 4)       | -2 (-2 - 1)  | <0.001* |
| Curative treatment rate         | 70 92.1 (83.8 - 96.3) | 78 100 (100 - 100) | -8 -7.9 (-14.0 - -1.8) | 0.013* |
| VAS ≤ 3 at six hours after treatment | 72 94.7 (87.2 - 97.9) | 65 83.3 (73.5 - 90.0) | 7 11.4 (1.7 - 21.1) | 0.023* |
| Overall adverse event rate      | 14 18.4 (9.7 - 27.1) | 19 24.3 (14.8 - 33.9) | -5 -5.9 (-18.9 - 7.0) | 0.368 |
| Recurrence of appendicitis      | 6a 7.9 (3.7 - 16.2) | 0 -- --         | 6           | 0.013* |
| Overall short-term adverse event rate | 5b 6.6 (1.0 - 12.2) | 6 7.7 (3.6 - 15.8) | -1 -1.1 (-9.2 - 7.0) | 0.791 |
| Incisional infection            | 0 -- --           | 2 2.6 (0.7 - 8.9) | -2          | 0.497 |
| Delayed awakening               | 0 -- --           | 1 1.3 (0.2 - 6.9) | -1          | >0.999 |
| Incisional pain                 | 0 -- --           | 3 3.8 (1.3 - 10.7)  | -3          | 0.245 |
| Feverc                         | 2 2.6 (0.7 - 9.1) | 0 -- --         | 2           | 0.241 |
| Appendiceal perforation         | 1 1.3 (0.2 - 7.1) | 0 -- --         | 1           | 0.494 |
| Overall long-term adverse event rate | 9d 11.8 (4.6 - 19.1) | 13 16.6 (10 - 26.5) | -4 -4.8 (-15.8 - 6.2) | 0.491 |
| Abdominal pain                  | 5 6.6 (2.8 - 14.5) | 4 5.1 (0.2 - 10.0) | 1 1.5 (-6.0 - 8.9) | 0.746 |
| Diarrhea                        | 0 -- --           | 9e 11.5 (6.2 - 20.5) | -9          | 0.003* |
| Outcomes of the two matched groups.  |
|------------------------------------|
| a Two patients experienced recurrence of appendicitis within 30 days after ERAT, and four patients had recurrence of appendicitis >30 days after ERAT. |
| b Including two patients with recurrent appendicitis within 30 days after ERAT. |
| c Baseline temperature, reference: 36.3°C - 37.2°C. Both patients had body temperatures less than 38°C. |
| d Including four patients with recurrent appendicitis >30 days after ERAT. |
| δ Three patients with Grade 1 diarrhea (<4 stools/day) and six patients with Grade 2 diarrhea (4-6 stools/day). |
| * Significant difference between the two groups. |
Patients with suspected acute appendicitis (n=2880) from April 2017 to March 2020

Excluded before treatment
- younger than 18 years of age (n=356)
- older than 60 years of age (n=297)
- combined perforation on CT (n=103)
- combined periappendiceal abscess on CT (n=176)

Acute appendicitis confirmed by CT (n=1948)

Excluded after treatment
- treated with antibiotics (n=918)
- combined perforation (n=5)
- combined periappendiceal abscess (n=3)
- confirmed chronic appendicitis (n=543)
- confirmed carcinoid tumors (n=2)
- could not be contacted (n=55)

Eligible patients (n=422)

Entire cohort
- ERAT group n=79
- LA group n=343

Matched cohort
- ERAT group n=78
- LA group n=78

PSM (1:1)
Endoscopic retrograde appendicitis therapy vs. Laparoscopic appendectomy for uncomplicated acute appendicitis

- **Retrospective study**
- **Propensity matching: 78 vs. 78**

### Curative Treatment Rate, %
- **ERAT:** 92.1%
- **LA:** 100.0%

### Overall Adverse Event Rate, %
- **ERAT:** 18.4%
- **LA:** 24.3%

### Hospital Length of Stay, days
- **ERAT:** 3
- **LA:** 4

### Median operative time, min
- **ERAT:** 40
- **LA:** 50

- **LA group: Off support**
- **LA group: On support**
- **ERAT group: On support**
- **ERAT group: Off support**
