Efficacy and Safety of Small-Caliber Disposable Digital Cholangioscope-Assisted Endoscopic Retrograde Appendicitis Therapy in Acute Uncomplicated Appendicitis

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AIM: To compare perioperative outcomes and short-term safety of endoscopic retrograde appendicitis therapy (ERAT) assisted by a single-use small-caliber digital cholangioscope (digital cholangioscope) and laparoscopic appendectomy (LA) in patients with acute uncomplicated appendicitis. This study utilized a direct-vision technique in which a digital cholangioscope was advanced over a guidewire through the colonoscope working channel into the appendiceal lumen, enabling intraluminal evaluation and intervention under direct visualization.

METHODS: A total of 60 patients with acute uncomplicated appendicitis treated at Hangzhou Ninth Hospital between January 2023 and December 2024 were retrospectively included and allocated, based on the actual treatment received, to an ERAT group (n = 32) or an LA group (n = 28). In the ERAT group, a digital cholangioscope was advanced over a guidewire through the colonoscope working channel into the appendiceal lumen, and intraluminal evaluation and treatment were performed under direct vision. Perioperative outcomes, inflammatory and pain-related parameters within 48 h postoperatively, and in-hospital complications were compared between the groups. Continuous perioperative outcomes were analyzed using multivariable linear regression, adjusted for prespecified covariates, whereas in-hospital complications were compared using a two-sided Fisher's exact test.

RESULTS: Compared with the LA group, the ERAT group demonstrated shorter operative time, reduced intraoperative blood loss, shorter postoperative bed rest, and a shorter length of hospital stay (all $p < 0.001$). Total in-hospital costs were significantly higher in the ERAT group than in the LA group ($p < 0.001$). At 48 hours postoperatively, levels of inflammatory markers (interleukin-6 [IL-6], tumor necrosis factor-α [TNF-α], C-reactive protein [CRP], and procalcitonin [PCT]) and pain-related mediators (dopamine [DA], substance P [SP], 5-hydroxytryptamine [5-HT], and prostaglandin E2 [PGE_2]) were significantly lower in the ERAT group than in the LA group (all $p < 0.05$). A lower crude in-hospital complication rate was observed in the ERAT group than in the LA group (two-sided Fisher's exact $p < 0.05$).

CONCLUSIONS: In this single-center retrospective cohort study of patients with acute uncomplicated appendicitis, digital cholangioscope-assisted ERAT was associated with improved perioperative recovery and reduced short-term inflammatory and pain responses compared with LA, without evidence of an increased in-hospital complication rate. These findings suggest that ERAT may represent a feasible appendiceal-preserving minimally invasive treatment option. However, given the retrospective, non-randomized design, the results should be interpreted cautiously as associative rather than causal.

Keywords: small-caliber digital cholangioscope; endoscopic retrograde appendicitis therapy; acute appendicitis; laparoscopic appendectomy

Introduction

Acute appendicitis is one of the most common acute abdominal emergencies. Based on imaging findings and intraoperative or pathological features, it is typically classified as uncomplicated or complicated, with uncomplicated appendicitis accounting for the majority of cases. Laparoscopic appendectomy (LA) provides definitive removal of the diseased appendix and effective source control, and has long been considered the standard treatment. However, as a resectional procedure, LA may still impose perioperative burdens, including postoperative pain, incision-related complications, and the risk of adhesions or bowel obstruction. Meanwhile, the appendix is rich in lymphoid tissue and may contribute to mucosal immunity and maintenance of gut microbial homeostasis. With the increasing emphasis on minimally invasive care and organ preservation, "preserving the appendix whenever safe" has increasingly become an important clinical consideration for some patients [1].

For imaging-confirmed acute, uncomplicated appendicitis, an antibiotics-first strategy may represent an alternative to

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surgery in selected patients. Nonetheless, some patients experience early treatment failure, subsequent recurrence, and additional healthcare utilization or rehospitalization. These risks may be higher in specific subgroups, such as those with an appendicolith, underscoring an unmet clinical need for appendix-preserving approaches that are less invasive while maintaining reliable infection control [2–7].

Endoscopic retrograde appendicitis therapy (ERAT) involves identification of the appendiceal orifice during colonoscopy and retrograde cannulation of the appendiceal lumen, allowing interventions such as irrigation, stone extraction, drainage, and placement of a catheter or stent. The therapeutic goal is to relieve luminal obstruction and control infection while preserving appendiceal integrity. Available evidence suggests that ERAT may offer advantages in selected perioperative recovery outcomes and complication profiles. However, the current evidence base remains limited by small sample sizes, heterogeneity in study design and procedural protocols, and variability in outcome definitions. Key questions, including recurrence risk, delineation of benefit across clinically relevant subgroups, and long-term outcomes, require further investigation [8–11]. In addition, a practical limitation of conventional ERAT is the difficulty in direct visualization of intraluminal pathology. Identification and management of causative factors, including appendicoliths, strictures, and purulent secretions, rely largely on indirect findings, which may constrain precise assessment and targeted intervention.

In recent years, single-use small-caliber digital cholangioscope (digital cholangioscope) also referred to as disposable small-caliber digital scopes, repurposed from digital single-operator cholangioscopy platforms as ultra-slim direct-vision endoscopes, have been introduced for use in ERAT. Advanced over a guidewire through the colonoscope working channel into the appendiceal lumen, these devices allow intraluminal assessment and intervention under direct visualization. This approach may address a key limitation of conventional ERAT, namely its largely non-direct-vision nature, and enhance identification and management of intraluminal etiologies [12]. However, real-world comparative evidence between digital cholangioscope-assisted ERAT and LA remains limited. Existing studies also vary in procedural standardization and outcome definitions, and comparative data on "biological recovery" indicators, such as postoperative inflammatory responses, remain scarce.

Against this background, we retrospectively included patients with acute uncomplicated appendicitis treated at our institution to compare digital cholangioscope-assisted ERAT and LA with respect to perioperative recovery-related outcomes, inflammatory and pain-related parameters within 48 h after surgery, and in-hospital complications. The aim was to generate clinically interpretable real-world evidence to support minimally invasive, appendix-preserving interventional strategies. We hypothesized that, compared with LA, digital cholangioscope-assisted ERAT would be associated with more rapid perioperative recovery and a reduced short-term inflammatory and pain response, while maintaining an acceptable in-hospital safety profile.

Methods

General Data

This was a single-center, retrospective observational study. A total of 60 consecutive patients with acute, uncomplicated appendicitis who presented to Hangzhou Ninth Hospital between January 2023 and December 2024 and underwent surgical or endoscopic intervention were included. Upon admission, all patients received standardized clinical assessment and imaging, and the diagnosis was established based on clinical signs and symptoms, in combination with laboratory findings. Treatment decisions were made following comprehensive informed discussion, and patients were assigned to groups according to the treatment actually received during hospitalization. The cohort comprised an ERAT group (n = 32; digital cholangioscope-assisted ERAT) and an LA group (n = 28). It may introduce potential confounding due to the non-randomized design.

The study protocol was reviewed and approved by the institutional ethics committee of Hangzhou Ninth Hospital (Approval No. 2024-048) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

Inclusion criteria: (1) fulfillment of established imaging and clinical diagnostic criteria, with abdominal ultrasonography or computed tomography indicating acute appendicitis without perforation, abscess, or diffuse peritonitis, and a final diagnosis of acute uncomplicated appendicitis; (2) time from admission to surgical or endoscopic intervention $\leq$48 h; (3) absence of absolute contraindications to general anesthesia, laparoscopy, or endoscopic intervention, allowing safe completion of the procedure; and (4) clear consciousness and adequate treatment compliance.

Exclusion criteria: (1) imaging or intraoperative findings confirming complicated appendicitis, including appendiceal perforation, periappendiceal abscess, or diffuse peritonitis; (2) severe cardiac, hepatic, or renal dysfunction and/or coagulopathy precluding the procedure; (3) history of major abdominal surgery with severe adhesions rendering endoscopic or laparoscopic intervention unsafe; and (4) active malignancy at another site requiring ongoing or imminent systemic therapy.

Grouping and Control of Confounding

Patients were grouped as ERAT versus LA based on the treatment actually received during hospitalization. Because treatment allocation was non-randomized, selection bias and confounding could not be excluded. To mitigate potential confounding, baseline characteristics were systematically collected and compared between groups (Table 1), including age, sex, body mass index (BMI), symptom-related time indices (time from onset to procedure and symptom

duration), history of prior appendicitis episodes, prior abdominal surgery, temperature, heart rate, imaging findings (appendicolith: yes/no), and American Society of Anesthesiologists (ASA) class. Symptom onset was defined as the time of the first reported symptom documented in the medical history. Admission time was defined as the registration timestamp in the electronic medical record (EMR). The time of surgery or endoscopic intervention was obtained from the anesthesia record or the timestamp in the endoscopy report. Time from symptom onset to admission was calculated in days (d), and time from admission to surgery or intervention was calculated in hours (h).

For outcome analyses, multivariable linear regression models were constructed for primary continuous endpoints with prespecified covariates for adjustment. Because complication events were infrequent, complications were compared using unadjusted between-group analyses (Fisher's exact test), and unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported (see Section "Statistical Analysis").

Data Sources, Extraction Procedures, and Quality Control

Study data were obtained from the hospital's EMR, including admission notes, progress notes, and discharge summaries, as well as anesthesia records, operative records, endoscopy center procedure reports, the imaging reporting system, and the laboratory information system (LIS). To minimize information bias inherent in retrospective studies, a standardized case report form (CRF) and a variable dictionary were developed prior to data extraction, specifying operational definitions and data sources for each variable, such as operative time, intraoperative blood loss, time to ambulation, and definitions and time windows for complications.

The data extraction and quality control workflow were as follows: Two uniformly trained investigators, neither involved in the surgical or endoscopic procedures, independently extracted all cases and performed cross-checking. Any discrepancies were resolved by a third investigator after review of the original medical records. Data entry followed a double-entry approach, with logic checks for value ranges, missing data, and outliers; when necessary, source documents were re-examined for verification and correction. For key variables that could not be verified or were missing, values were recorded as missing according to prespecified rules and handled in the statistical analyses based on available data.

Sample Size Estimation

This single-center retrospective observational study included all patients during the study period who met the inclusion and exclusion criteria and had complete data; therefore, the sample size was primarily determined by data availability. To assess feasibility and statistical power for the primary endpoint, operative time was prespecified as the main continuous outcome, and a power-based sample size calculation was performed using a two-sample test for the difference in means (two-sided $\alpha = 0.05$; power $1–\beta = 0.80$), according to the following formula:

$$n = \left(Z_{\alpha/2} + Z_{\beta}\right)^2 \left(\sigma_1^2 + \sigma_2^2\right) / \delta^2$$

where δ represents the minimum clinically meaningful difference to be detected, and σ_1 and σ_2 denote the standard deviations in the two groups. Based on previous literature and our center's pilot data, a common standard deviation of approximately 10 minutes for operative time was assumed, with a clinically meaningful between-group difference of 8 min. Under these assumptions, approximately 25 patients per group would provide about 80% power to detect this difference. Given the potential for missing or unusable data inherent in retrospective research, the final cohort comprised 32 patients in the ERAT group and 28 in the LA group, which was considered sufficient for the primary analysis and feasibility assessment.

Furthermore, given that multivariable linear regression analyses were planned, only a limited number of covariates were prespecified to minimize the risk of overfitting. For binary outcomes such as complications, the expected number of events was limited; thus, analysis relied primarily on descriptive statistics and Fisher's exact test for between-group comparisons. Unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported, and multivariable logistic regression was not performed to avoid model instability due to sparse events.

Surgical/Endoscopic Procedures

Appendectomy Group: Laparoscopic Appendectomy

Patients underwent routine preoperative fasting and received prophylactic antibiotics according to institutional perioperative infection-prevention protocols. Under general anesthesia, patients were positioned supine. A CO_2 pneumoperitoneum was established via an umbilical port (insufflation pressure approximately 12 mmHg), and a standard three-port laparoscopic technique was employed. The abdominal cavity was inspected; any exudate was evacuated, and adhesiolysis was performed as necessary. After identifying the appendix and managing the mesoappendiceal vessels, the appendiceal base was securely ligated with titanium clips (double clips on the cecal side and a single clip distally). The appendix was transected approximately 3–5 mm distal to the proximal (cecal-side) clip, and the appendix was retrieved. The appendiceal stump was re-examined to ensure secure closure and absence of leakage or bleeding. Depending on the degree of intraoperative contamination, peritoneal irrigation and drainage placement were performed as indicated. At the conclusion of the procedure, pneumoperitoneum was released, and incisions were closed in layers.

ERAT Group: Digital Cholangioscope–Assisted ERAT

The digital cholangioscope used in this study was a disposable digital direct-visualization platform originally designed for intraductal inspection and therapy of the biliary and pancreatic ducts. In the present study, it was repurposed as a small-caliber direct-vision digital cholangioscopy system. Under guidewire assistance, the scope was advanced through the colonoscope working channel into the appendiceal lumen, enabling direct visualization and therapeutic intervention through a non-papilla-based route. This access method was consistent with prior technical reports describing digital single-operator cholangioscopy (DSOC) for ERAT. As use of this device within the appendiceal lumen constitutes an off-label application, the protocol was approved by the institutional ethics committee, and written informed consent was obtained from all patients before the procedure.

Routine bowel preparation and perioperative anti-infective management were performed. Bowel cleansing was achieved using oral polyethylene glycol electrolyte powder (Shutaishen, Beijing Biopharmaceutical Co., Ltd.; H20040034), and prophylactic intravenous ceftriaxone (2.0 g; China National Pharmaceutical Group Weiqida Pharmaceutical Co., Ltd.; H14023501) was administered preoperatively. Under general anesthesia, patients were positioned in the left lateral decubitus or supine position. A colonoscope with a transparent distal cap was inserted per anus to reach the ileocecal region, exposing the appendiceal orifice (Gerlach's valve).

Under colonoscopic guidance, a 0.025-inch hydrophilic guidewire was advanced through the working channel into the appendiceal lumen. Intraluminal positioning was confirmed before advancing the single-use small-caliber digital cholangioscopy system using one or more of the following criteria: (1) direct colonoscopic visualization of the appendiceal orifice with successful cannulation; (2) fluoroscopic confirmation of the guidewire trajectory consistent with appendiceal anatomy; (3) limited contrast appendicography demonstrating opacification of the appendiceal lumen without extravasation; and (4) fluoroscopic imaging confirming the guidewire course and target insertion depth, with the insertion length recorded. Only after these confirmations was the digital cholangioscopy system advanced over the guidewire into the appendiceal lumen for direct-vision assessment and intervention. Therefore, appendiceal-lumen access was verified using colonoscopic, fluoroscopic, and contrast criteria rather than intraluminal visualization alone.

The following procedures were then performed under direct visualization:

(1) Direct-vision assessment: the appendiceal mucosa was examined for hyperemia, edema, erosions, and adherent purulent secretions. Inflammatory severity was assessed, and the lumen was evaluated for appendicolith or strictures.

(2) Direct stone extraction: fecaliths were grasped and removed using retrieval devices under direct visualization.

(3) Irrigation and suction: repeated lavage and suction were performed until effluent clarity was achieved.

(4) Selective contrast study and stent drainage: after decompression and lavage, contrast was injected via catheter under fluoroscopic guidance to assess appendiceal morphology. In cases of stenosis, impaired drainage, or substantial purulent burden, a plastic stent was placed over the guidewire under combined endoscopic and fluoroscopic guidance to maintain drainage.

Postoperative anti-infective therapy was individualized according to clinical needs. For uncomplicated cases, routine antibiotic continuation was not performed. Antibiotics were administered only in the presence of a high purulent burden, stent or drain placement, fever, or persistently elevated inflammatory markers, with a 7-day course. Regimens followed the institutional perioperative pathway and were adjusted according to clinical response. Follow-up at 1–2 weeks included endoscopic stent removal and repeat irrigation when indicated.

Operator Qualifications and Procedural Consistency Control

To minimize performance bias arising from inter-operator variability, all procedures in both groups were performed by a fixed, senior team. LA was conducted by attending-level or higher gastrointestinal surgeons credentialed to independently perform LA, with an annual case volume of $\geq$30 procedures. ERAT was performed by attending-level or higher gastroenterologists or endoscopists credentialed for colonoscopy and biliopancreatic endoscopic interventions, experienced in ERAT or related intraluminal procedures, and with an annual procedural volume of $\geq$15 cases. Both groups adhered to institutional standardized perioperative pathways for antibiotic prophylaxis, analgesia, and discharge criteria, and key procedural steps and intraoperative findings were documented in standardized operative records. To mitigate potential learning-curve effects during the initial adoption of ERAT, all included cases were performed after workflow stabilization, either by senior operators or under direct supervision throughout the procedure.

Outcomes and Definitions (Definitions and Data Sources)

Study measures were categorized as perioperative outcomes, inflammatory biomarkers, pain-related mediators, and in-hospital complications. Data on perioperative outcomes, complications, and routine laboratory tests were extracted from the EMR, anesthesia records, operative and endoscopy procedure notes, nursing documentation, and the laboratory information system (LIS). Non-routine indices, including interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and pain-related mediators, were obtained by centralized batch testing of stored serum samples (see Section "Blood Sample Sources and Laboratory Testing Methods").

Perioperative Outcomes (During Hospitalization)

(1) Procedure time (min)

Definition: For LA, time from skin incision to skin closure; for ERAT, time from colonoscope insertion to complete withdrawal. Source: Anesthesia records and operative/endoscopic procedure notes. Note: ERAT procedure time encompassed guidewire cannulation, advancement of the single-use digital cholangioscopy system, intraluminal maneuvers, and catheter/stent placement when required.

(2) Intraoperative blood loss (mL)

Definition/Source: Estimated blood loss (EBL) recorded in the anesthesia chart. Note: Blood loss in ERAT was typically negligible; irrigation fluid volume was excluded from calculations. Quantification may therefore be less precise than in LA. Missing values were not imputed and analyzed based on available data.

(3) Time to first ambulation (d)

Definition: Interval from the end of surgery/endoscopic intervention to the first out-of-bed activity (standing or walking). Source: Nursing records; recorded in hours and converted to days (h/24), reported to two decimal places.

(4) Length of hospital stay (d)

Definition: Duration from admission registration to execution of the discharge order, converted from hours to days. Source: EMR admission and discharge timestamps.

Inflammatory Biomarkers

Measured biomarkers included IL-6, TNF-α, C-reactive protein (CRP), and procalcitonin (PCT). Sampling windows were within 1 h preoperatively and at 48 h postoperatively ($\pm$6 h permitted). CRP and PCT were obtained from routine LIS testing, whereas IL-6 and TNF-α were assessed through batch testing of stored serum (see Section "Blood Sample Sources and Laboratory Testing Methods").

Value selection rule: When multiple measurements were available within a given window, the value closest to the preoperative 1 h or postoperative 48 h target was selected. Measurements outside the defined windows were considered missing.

Pain-Related Mediators

Pain-related mediators included dopamine (DA), substance P (SP), 5-hydroxytryptamine (5-HT), and prostaglandin E2 (PGE_2). Sampling windows were within 1 h preoperatively and at 48 h postoperatively ($\pm$6 h permitted). Data were obtained through centralized batch testing of stored serum samples (see Section "Blood Sample Sources and Laboratory Testing Methods").

Value selection rule: When multiple measurements were available within the same time window, the value closest to the target time point was selected; when no measurement met the time-window criteria, the value was recorded as missing. All indices were reported in standardized units.

In-Hospital Complications

Observation window: From completion of ERAT or surgery to hospital discharge (index hospitalization).

Data sources: Progress notes, vital signs, repeat laboratory testing, imaging reports, and records of clinical interventions, including antibiotics, hemostatic therapy, and drainage procedures.

Prespecified complication types:

(1) Gastrointestinal bleeding: Overt hematochezia, melena, or hematemesis requiring additional hemostatic therapy, blood transfusion, or endoscopic or interventional hemostasis.

(2) Incisional infection (surgery group only): Erythema, swelling, warmth, and pain at the incision site with purulent discharge, or requiring antibiotic therapy and/or wound care.

(3) Intra-abdominal abscess or infected fluid collection: Imaging-confirmed and requiring escalation of antibiotics and/or percutaneous aspiration or catheter drainage.

(4) Bowel obstruction: Clinical symptoms with imaging evidence of obstruction requiring fasting, gastrointestinal decompression, or further intervention.

(5) ERAT-specific complications: Guidewire or cannulation-related appendiceal or colonic perforation; significant mucosal injury or bleeding requiring intervention; stent-related complications (if placed), including migration or occlusion; and in-hospital intra-abdominal infection or abscess, with management and outcomes recorded.

Adjudication: Complications were independently adjudicated by two investigators according to the prespecified definitions; disagreements were resolved by a third investigator.

Blood Sample Sources and Laboratory Testing Methods

CRP and PCT are routine perioperative tests for acute appendicitis, and results were obtained directly from the laboratory information system (LIS). IL-6, TNF-α, and pain-related mediators (DA, SP, 5-HT, and PGE_2) are non-routine indices and were measured retrospectively using centralized batch testing of stored serum samples.

Sample Collection, Processing, and Storage

Venous blood samples were collected according to the institutional perioperative phlebotomy protocol within 1 h preoperatively and at 48 h postoperatively ($\pm$6 h permitted). After centrifugation, serum was separated, aliquoted using de-identified codes, and stored at –80 °C, with no more than one freeze-thaw cycle. All assays were conducted in a single batch after case enrollment was completed to minimize inter-batch variability.

Assay Methods and Replicate Wells

DA, SP, 5-HT, and PGE_2 were measured using enzyme-linked immunosorbent assays (ELISAs). IL-6 and TNF-α were also quantified by ELISA. All procedures were

Table 1. Baseline characteristics of patients in the ERAT and LA groups.

Variable	ERAT group (n = 32)	LA group (n = 28)	Statistic ($\chi^2/t/Z$)	p-value
Age (years), mean ± SD	42.25 ± 5.60	41.35 ± 5.76	0.617	0.540
Gender (male/female), n	19/13	16/12	0.031	0.861
BMI (kg/m^2), mean ± SD	22.65 ± 0.76	22.54 ± 0.92	0.507	0.614
Time from admission to surgery/endoscopic intervention (h), mean ± SD	28.10 ± 7.36	28.32 ± 7.16	0.114	0.909
Time from symptom onset to admission (d), mean ± SD	2.57 ± 0.45	2.63 ± 0.50	0.489	0.627
History of prior appendicitis (yes/no), n	7/25	5/23	0.151	0.698
History of prior abdominal surgery (yes/no), n	6/26	6/22	0.067	0.796
Body temperature (°C), mean ± SD	37.78 ± 0.50	37.83 ± 0.47	0.397	0.693
Heart rate (beat/min), median (Q_1, Q_3)	87.00 (82.75, 104.50)	95.50 (82.50, 102.25)	–0.415	0.678
ASA physical status classification (I/II), n	25/7	21/7	0.082	0.775
Appendicolith (yes/no), n	10/22	9/19	0.006	0.941

ERAT, endoscopic retrograde appendicitis therapy; LA, laparoscopic appendectomy; BMI, body mass index; SD, standard deviation; ASA, American Society of Anesthesiologists.

performed in accordance with the manufacturer's instructions, including standard curves and quality-control samples. Each sample was analyzed in duplicate wells, and the mean value was used for statistical analyses. Details of assay kits, including manufacturer, catalogue number, analytical range, sensitivity, and intra- and inter-assay coefficients of variation, are provided in the **Supplementary Materials** (IL-6: **Supplementary Table 1**; TNF-α: **Supplementary Table 2**).

Blinding and Quality Control

During laboratory testing, personnel and plate readers were blinded to treatment allocation. After export from laboratory records, assay results were linked to clinical data using coded identifiers. Samples exhibiting hemolysis, lipemia, or other conditions that could compromise assay validity were retested according to prespecified quality-control procedures; samples that remained unsuitable were recorded as missing. For values outside the detection range, retesting was conducted as recommended by the kit instructions, including repeat measurement with appropriate dilution when required. Results that could not be reliably obtained were recorded as missing.

Handling of Missing Data

Data were considered missing if no sample met the prespecified time window or if quality control procedures failed and reliable retesting was not feasible. No imputation methods were applied; all analyses were conducted using available-case data.

Statistical Analysis

All statistical analyses were performed using SPSS version 26.0 (IBM, Armonk, NY, USA). The distribution of continuous variables was evaluated using the Shapiro-Wilk test supplemented by visual inspection of Quantile-Quantile (Q–Q) plots. A summary of normality testing results for key continuous outcomes is presented in **Supplementary Table 3**, and representative Q–Q plots are shown in **Supplementary Figs. 1–54** to illustrate distributional characteristics and their consistency with formal test results.

Normally distributed continuous variables were presented as mean ± standard deviation and compared between groups using the independent-samples t-test. When the assumption of homogeneity of variance was violated (Levene's test $p < 0.05$), Welch's t-test was applied. Non-normally distributed variables are presented as median (interquartile range [IQR]) and were compared using the Mann–Whitney U test. Categorical variables are expressed as counts (%) and were compared using the chi-square (χ^2) test or Fisher's exact test, as appropriate. All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant.

For normally distributed continuous variables, effect sizes are reported as mean differences (MDs) with 95% confidence intervals (CIs). For Mann–Whitney U tests, the Hodges–Lehmann estimator of the location shift (ERAT minus control) and its corresponding 95% CI were reported.

Given the retrospective design and non-randomized treatment selection, multivariable linear regression models were constructed for key continuous outcomes, including procedure time, intraoperative blood loss, time to first ambulation, and length of hospital stay, to mitigate potential confounding. The models included the treatment group (ERAT = 1; LA = 0) and prespecified covariates, including age, sex, BMI, time from symptom onset to surgery, ASA class, and presence of an appendicolith. Results are presented as unstandardized regression coefficients (adjusted B) with 95% CIs.

Because the length of hospital stay exhibited a skewed distribution in unadjusted analyses, model inference in the regression model was based on Huber–White robust standard errors. Additionally, a log-transformed model using the natural logarithm (ln) was constructed as a sensitivity analysis to assess the robustness of the findings, defined as consistency in the direction and statistical significance of the

Table 2. Comparison of perioperative outcomes between the ERAT and LA groups.

Outcome	ERAT group (n = 32)	LA group (n = 28)	Effect estimate (MD or HL; ERAT–LA)	95% CI	*p*-value
Operative time (min), mean ± SD	44.20 ± 9.35	63.10 ± 10.13	MD –18.90	–23.97 – –13.83	<0.001
Intraoperative blood loss (mL), mean ± SD	11.83 ± 1.65	22.63 ± 3.45	MD –10.80	–12.25 – –9.35	<0.001
Time to first ambulation (d), mean ± SD	1.54 ± 0.50	3.20 ± 0.65	MD –1.66	–1.96 – –1.36	<0.001
Length of hospital stay (d), median (Q_1, Q_3)	3.20 (2.90, 3.40)	5.40 (4.83, 5.85)	HL –2.20	–2.50 – –1.90	<0.001

Note: Data are presented as mean ± standard deviation (SD) for normally distributed variables and as median (Q_1, Q_3) for non-normally distributed variables. Between-group comparisons were performed using the independent-samples *t*-test or the Mann-Whitney U test, as appropriate. Effect estimates are reported as mean difference (MD) for *t*-test outcomes and as the Hodges-Lehmann (HL) estimator for Mann-Whitney outcomes, calculated as ERAT minus LA, with corresponding 95% confidence intervals (CIs).

Table 3. Multivariable linear regression analysis of perioperative outcomes: association between treatment modality and surgical outcomes.

Outcome	Adjusted B (ERAT vs. LA)	95% CI	*p*-value
Operative time (min)	–18.429	–23.505 – –13.353	<0.001
Intraoperative blood loss (mL)	–10.813	–12.225 – –9.400	<0.001
Time to first ambulation (d)	–1.624	–1.914 – –1.335	<0.001
Length of hospital stay (d)	–2.305	–2.659 – –1.950	<0.001

Note: Adjusted B represents the unstandardized regression coefficient (in the same unit as the outcome), representing the between-group difference (ERAT vs. LA) after adjustment of covariates. Models included age, sex, BMI, time from symptom onset to surgery, ASA class, appendicolith status, and other prespecified variables; treatment was coded as ERAT = 1 and LA = 0. For the length of hospital stay, Huber–White robust standard errors were applied, and a log-transformed model was additionally fitted as a sensitivity analysis, yielding consistent effect direction and statistical significance.

estimated effects. Model assumptions were evaluated using residual diagnostics.

Binary outcomes (complications: yes/no) are presented as counts and percentages (n [%]). Given the limited number of events, between-group comparisons were performed using two-sided Fisher's exact test, and unadjusted odds ratios (ORs) with 95% CIs were reported. Multivariable logistic regression was not conducted to avoid model instability associated with sparse outcome events.

Results

Baseline Characteristics

Baseline characteristics were generally well balanced between the two groups (Table 1). No statistically significant differences were observed in age, sex, BMI, time from admission to surgery or endoscopic intervention, time from symptom onset to admission, body temperature, heart rate, ASA classification, or the presence of appendicolith, among other baseline characteristics (all $p > 0.05$).

Perioperative Outcomes

In unadjusted analyses, compared with the LA group, the ERAT group demonstrated a significantly shorter operative time (mean difference [MD], –18.90 min; 95% CI: –23.97 – –13.83), reduced intraoperative blood loss (MD, –10.80 mL; 95% CI: –12.25 – –9.35), and a shorter time to first ambulation (MD, –1.66 d; 95% CI: –1.96 – –1.36), all $p < 0.001$ (Table 2). Length of hospital stay was also significantly shorter in the ERAT group (Hodges-Lehmann estimate, –2.20 d; 95% CI: –2.50 – –1.90; $p < 0.001$).

After adjustment for prespecified covariates in multivariable linear regression models, ERAT remained independently associated with shorter operative time (adjusted B, –18.429; 95% CI: –23.505 – –13.353), lower intraoperative blood loss (adjusted B, –10.813; 95% CI: –12.225 – –9.400), shorter time to first ambulation (adjusted B, –1.624; 95% CI: –1.914 – –1.335), and reduced length of hospital stay (adjusted B, –2.305; 95% CI: –2.659 – –1.950), all $p < 0.001$ (Table 3).

In-Hospital Costs

Total in-hospital costs were significantly higher in the ERAT group than in the LA group (mean difference [MD], 2500.00 CNY (1 USD ≈ 6.83 CNY); 95% CI: 1522.13 – 3477.87; $p < 0.001$) (Table 4).

Inflammatory Markers (Within 48 h)

At 1 h preoperatively, no statistically significant between-group differences were observed in IL-6, TNF-α, CRP, or PCT (all $p > 0.05$) (Table 5).

At 48 h postoperatively, IL-6 levels were significantly lower in the ERAT group (MD, –7.33; 95% CI: –10.53 – –4.13; $p < 0.001$), as were TNF-α (MD, –3.78; 95% CI:

Table 4. Comparison of in-hospital costs between the ERAT and LA groups (CNY).

Outcome	ERAT group (n = 32)	LA group (n = 28)	MD (ERAT–LA)	95% CI	*p*-value
In-hospital costs (CNY), mean ± SD	13,999.50 ± 2000.50	11,499.50 ± 1749.50	2500.00	1522.13 – 3477.87	<0.001

Note: Costs are presented as mean ± standard deviation and were compared using a two-sided independent-samples *t*-test; Welch's *t*-test was applied when variances were unequal. Effect size is expressed as the mean differences (MD; ERAT–LA) with 95% CIs. This table presents unadjusted comparisons. Test statistic: $t = 5.118$. 1 USD ≈ 6.83 CNY.

Table 5. Comparison of inflammatory markers between the ERAT and LA groups.

Group	n	IL-6 (pg/mL)		MD (ERAT–LA)	95% CI
		1 hour preoperatively	48 hours postoperatively		
ERAT group	32	10.35 ± 2.16	14.30 ± 4.50	–7.33	–10.53 – –4.13
LA group	28	10.43 ± 2.25	21.63 ± 7.26		
t	-	0.143	4.622		
p-value	-	0.887	<0.001		
Group	n	TNF-α (pg/mL)		MD (ERAT–LA)	95% CI
		1 hour preoperatively	48 hours postoperatively		
ERAT group	32	14.90 (11.85, 19.52)	18.65 ± 4.75	–3.78	–6.34 – –1.22
LA group	28	14.15 (12.43, 19.75)	22.43 ± 5.10		
Statistic (*Z* or *t*)	-	Z = –0.541	*t* = 2.964		
p-value	-	0.589	0.004		
Group	n	CRP (mg/L)		MD (ERAT–LA)	95% CI
		1 hour preoperatively	48 hours postoperatively		
ERAT group	32	23.56 ± 4.86	28.36 ± 5.75	–6.49	–10.58 – –2.40
LA group	28	23.32 ± 4.95	34.85 ± 9.30		
t	-	0.188	3.200		
p-value	-	0.852	0.003		
Group	n	PCT (ng/mL)		HL (ERAT–LA)	95% CI
		1 hour preoperatively	48 hours postoperatively		
ERAT group	32	0.63 ± 0.25	0.90 (0.80, 1.32)	–0.30	–0.60 – –0.10
LA group	28	0.64 ± 0.22	1.40 (1.08, 1.60)		
Statistic (*Z* or *t*)	-	*t* = 0.165	*Z* = 2.828		
p-value	-	0.869	0.005		

Note: Table 5 presents unadjusted between-group comparisons. Effect estimates (MD or HL) and 95% CI correspond to the between-group differences at 48 hours postoperatively (ERAT–LA), not baseline values or change scores.
HL represents the Hodges–Lehmann estimator based on all pairwise between-group differences, rather than the simple difference between the two group medians.
IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; CRP, C-reactive protein; PCT, procalcitonin.

–6.34 – –1.22; $p = 0.004$), and CRP (MD, –6.49; 95% CI: –10.58 – –2.40; $p = 0.003$). Postoperative PCT levels were also lower in the ERAT group (Hodges-Lehmann estimate, –0.30 ng/mL; 95% CI: –0.60 – –0.10; $p = 0.005$).

After adjustment for baseline (preoperative) levels and prespecified covariates, ERAT remained independently associated with lower IL-6 (adjusted B, –7.339; 95% CI: –10.546 – –4.131; $p < 0.001$), TNF-α (adjusted B, –3.811; 95% CI: –6.481 – –1.142; $p = 0.006$), CRP (adjusted B, –7.128; 95% CI: –10.935 – –3.321; $p < 0.001$), and PCT (adjusted B, –0.341; 95% CI: –0.562 – –0.121; $p = 0.003$ (Table 6)).

Pain-Related Mediators (Within 48 h)

At 1 h preoperatively, no statistically significant between-group differences were observed in any pain-related mediator (all $p > 0.05$) (Table 7).

At 48 h postoperatively, DA levels were significantly lower in the ERAT group (mean difference [MD], –41.17; 95% CI: –49.23 – –33.11; $p < 0.001$), and PGE_2 levels were also lower (MD, –98.54; 95% CI: –107.66 – –89.42; $p < 0.001$). Postoperative SP (Hodges-Lehmann estimate, –74.15 pg/mL; 95% CI: –87.20 – –62.20; $p < 0.001$) and 5-HT (Hodges-Lehmann, –91.35 ng/mL; 95% CI: –103.10 – –71.70; $p < 0.001$) were likewise significantly lower in the ERAT group.

After adjustment for baseline levels and prespecified covariates, ERAT remained independently associated with lower DA (adjusted B, –42.264; 95% CI: –49.836 – –34.691), lower SP (adjusted B, –77.730; 95% CI: –88.741 – –66.720), lower 5-HT (adjusted B, –88.679; 95% CI: –103.355 – –74.003), and lower PGE_2 (adjusted B, –98.949; 95% CI: –107.711 – –90.188), all $p < 0.001$ (Table 8).

Table 6. Multivariable linear regression analysis: association between treatment modality and inflammatory markers.

Outcome	Adjusted B (ERAT vs. LA)	95% CI	*p*-value
IL-6 (pg/mL)	–7.339	–10.546 – –4.131	<0.001
TNF-α (pg/mL)	–3.811	–6.481 – –1.142	0.006
CRP (mg/L)	–7.128	–10.935 – –3.321	<0.001
PCT (ng/mL)	–0.341	–0.562 – –0.121	0.003

Note: Adjusted B denotes the covariate-adjusted between-group mean difference (ERAT–LA). Models included the corresponding preoperative (1 hour) biomarker, age, sex, BMI, time from symptom onset to procedure, ASA classification, and appendicolith status. Treatment was coded as ERAT = 1 and LA = 0.

Table 7. Comparison of pain-related mediators between the ERAT and LA groups.

Group	n	DA (pg/mL)		MD (ERAT–LA)	95% CI
		1 hour preoperatively	48 hours postoperatively		
ERAT group	32	43.05 (39.10, 49.27)	51.54 ± 7.81	–41.17	–49.23 – –33.11
LA group	28	45.95 (41.25, 51.17)	92.71 ± 19.69		
Statistic (*Z* or *t*)	-	*Z* = –0.904	*t* = 10.373		
p-value	-	0.366	<0.001		
Group	n	SP (pg/mL)		HL (ERAT–LA)	95% CI
		1 hour preoperatively	48 hours postoperatively		
ERAT group	32	68.35 (55.05, 75.35)	54.45 (49.65, 66.80)	–74.15	–87.20 – –62.20
LA group	28	64.20 (58.75, 75.30)	131.15 (112.55, 168.95)		
Z	-	0.096	–6.631		
p-value	-	0.923	<0.001		
Group	n	5-HT (ng/mL)		HL (ERAT–LA)	95% CI
		1 hour preoperatively	48 hours postoperatively		
ERAT group	32	139.43 ± 33.52	134.75 (105.05, 151.35)	–91.35	–103.10 – –71.70
LA group	28	142.40 ± 32.78	210.40 (200.22, 239.25)		
Statistic (*Z* or *t*)	-	*t* = 0.345	*Z* = –6.453		
p-value	-	0.731	<0.001		
Group	n	PGE_2 (pg/mL)		MD (ERAT–LA)	95% CI
		1 hour preoperatively	48 hours postoperatively		
ERAT group	32	74.74 ± 13.28	66.39 ± 12.93	–98.54	–107.66 – –89.42
LA group	28	76.81 ± 16.81	164.93 ± 20.67		
t	-	0.532	21.771		
p-value	-	0.597	<0.001		

DA, dopamine; SP, substance P; 5-HT, 5-hydroxytryptamine; PGE_2, prostaglandin E2.

HL represents the Hodges–Lehmann estimator based on all pairwise between-group differences, rather than the simple difference between the two group medians.

In-Hospital Complications

The incidence of at least one in-hospital complication, defined as the primary complication outcome, was 1/32 (3.13%) in the ERAT group and 8/28 (28.57%) in the LA group, with a statistically significant between-group difference (two-sided Fisher's exact test $p = 0.009$; OR = 0.08, 95% CI: 0.01 – 0.69) (Table 9). Specifically, gastrointestinal bleeding occurred in one patient in each group. In the LA group, additional complications included two cases of surgical site infection, two cases of intra-abdominal abscess or infected fluid collection, and three cases of bowel obstruction, whereas none of these events was observed in the ERAT group.

Discussion

Using a single-center, retrospective real-world cohort, this study compared in-hospital outcomes between digital cholangioscope–assisted ERAT and LA in patients with acute uncomplicated appendicitis. Overall, the ERAT group appeared to exhibit a more favorable perioperative recovery profile across multiple recovery-related endpoints, including operative time, intraoperative blood loss, time to first ambulation, and length of hospital stay. At 48 h postoperatively, inflammatory markers and pain-related mediators were consistently lower in the ERAT group. In addition, the proportion of patients experiencing at least one in-hospital complication was lower in unadjusted compar-

Table 8. Multivariable linear regression analysis: association between treatment methods and pain-related mediators.

Outcome	Adjusted B (ERAT vs. LA)	95% CI	*p*-value
DA (pg/mL)	–42.264	–49.836 – –34.691	<0.001
SP (pg/mL)	–77.730	–88.741 – –66.720	<0.001
5-HT (ng/mL)	–88.679	–103.355 – –74.003	<0.001
PGE_2 (pg/mL)	–98.949	–107.711 – –90.188	<0.001

Table 9. In-hospital surgery-related complications (n (%)).

Complication outcome	ERAT group (n = 32)	LA group (n = 28)	*p*-value[+]
Gastrointestinal bleeding	1 (3.13)	1 (3.57)	
Surgical-site infection (LA only)	0 (0.00)	2 (7.14)	
Intra-abdominal abscess/infected fluid collection	0 (0.00)	2 (7.14)	
Bowel obstruction	0 (0.00)	3 (10.71)	
Any complication (≥1 event per patient)	1 (3.13)	8 (28.57)	0.009

Note: Data are presented as counts (within-group percentage), n (%), with patients as the unit of analysis. Each complication category reflects the number of patients experiencing that specific event. Patients with multiple complications were counted once per category but only once in the composite endpoint (≥1 complication). No patients experienced overlapping complications in this cohort (≥2 complication types in the same patient). [+]Between-group comparisons were performed using the two-sided Fisher's exact test. The reported *p*-value, unadjusted odds ratio (OR), and 95% CI correspond to the composite outcome (≥1 complication). Given the limited number of events, multivariable logistic regression was not performed.

isons, whereas total in-hospital costs were higher in the ERAT group. However, because this study was retrospective, included a relatively small sample (n = 60), evaluated multiple outcomes, and recorded a limited number of complication events, the stability and inferential strength of these findings remain constrained.

Importantly, given the retrospective and non-randomized design, these findings should be interpreted as observational associations within the in-hospital setting rather than causal effects. Accordingly, they should not be construed as definitive evidence of superior efficacy or safety.

Faster Perioperative Recovery: Plausible Mechanisms Alongside Alternative Explanations

From a mechanistic perspective, digital cholangioscope–assisted ERAT accesses the appendiceal lumen via a natural orifice to decompress, irrigate, extract fecaliths, and drain the appendix. This approach may reduce the extent of tissue injury associated with abdominal wall incisions, pneumoperitoneum establishment, and mesoappendiceal manipulation, which is consistent with the observed reductions in time to ambulation and length of hospital stay [13]. Moreover, intraluminal evaluation and targeted intervention under direct visualization, including identification and management of fecaliths or strictures and confirmation of effective drainage, may mitigate ongoing inflammatory stimuli and thereby facilitate early postoperative recovery [14].

However, in non-randomized comparisons, alternative explanations and potential sources of bias warrant careful consideration. First, treatment selection may be associated with unmeasured or difficult-to-quantify indicators of disease severity, such as pain intensity, systemic inflammatory burden, volume of purulent intraluminal secretions, degree of luminal narrowing, and detailed imaging characteristics. These factors may influence both treatment allocation and recovery trajectories [15]. Second, length of hospital stay and discharge decisions may be influenced not only by clinical recovery but also by non-clinical factors, including patient preference, physician practice patterns, institutional bed management policies, and healthcare reimbursement structures. Such factors may introduce variability that is not directly attributable to the intervention itself [16].

Although multivariable regression models were applied to adjust for key covariates in continuous outcomes, residual confounding and selection cannot be fully excluded. Therefore, a more conservative interpretation is that, within a carefully selected cohort of patients with uncomplicated appendicitis treated by an experienced multidisciplinary team at this center, digital cholangioscope–assisted ERAT was associated with faster in-hospital recovery. Given the modest sample size, these associations should be viewed as hypothesis-generating rather than definitive. The magnitude, consistency, and external validity of these associations warrant confirmation in prospective, preferably randomized, studies.

Differences in Inflammatory and Pain-Related Mediators at 48 h Postoperatively: Interpretation as Biological Signals of Recovery

At 48 h postoperatively, IL-6, TNF-α, CRP, PCT, as well as DA, SP, 5-HT, and PGE_2 were all lower in the ERAT group. This pattern is consistent with the mechanistic hypothesis of a reduced trauma- and stress-related burden. However, the scope of interpretation should be defined cautiously [17].

First, only two time points (preoperative and 48 h postoperatively) were available, precluding characterization of peak

levels, time to peak, or rates of decline. Accordingly, these data do not permit inference regarding dynamic processes such as "accelerated resolution of inflammation" or "more rapid pain recovery". Second, pain-related mediators are exploratory biomarkers and do not directly correspond to clinical pain outcomes (e.g., pain scores, rescue analgesia requirements, opioid/Nonsteroidal Anti-Inflammatory Drug (NSAID) consumption, or functional recovery). Because patient-reported outcomes and analgesic utilization were not concurrently collected, extrapolation from "lower mediator levels" to "improved subjective pain" should be undertaken with caution [18]. Third, although perioperative analgesia followed a standardized institutional protocol, retrospective data may not fully capture individualized rescue analgesia or variation in sedation/analgesia intensity, which could influence both biomarker levels and recovery trajectories. Fourth, multiple inflammatory and pain-related parameters were evaluated, increasing the risk of type I error due to multiple comparisons; although effect directions were concordant and remained stable after adjustment, these findings are more appropriately interpreted as supportive signals rather than definitive evidence [19]. Accordingly, these biomarker analyses should be regarded as exploratory, and statistical significance should not be overinterpreted in isolation. Future studies should prespecify primary biomarker endpoints within a prospective framework, concurrently capture analgesic regimens and patient-reported pain outcomes, and incorporate denser longitudinal sampling to strengthen causal interpretability.

From an analytical perspective, archived serum samples were analyzed in batches under blinded conditions with predefined quality-control procedures to minimize inter-batch variability and observer bias; nevertheless, potential ELISA-related intra- and inter-assay variability and pre-analytical factors (e.g., freeze–thaw cycles, hemolysis, and lipemia) may still introduce measurement error [20]. Although assay performance characteristics and quality-control procedures were reported to enhance reproducibility, the inherent uncertainty associated with retrospective biospecimen-based analyses cannot be fully eliminated.

Higher Complication Rates in the LA Group: Consideration of Diagnostic Thresholds, Observation Windows, and Asymmetry of Complication Profiles

In this study, the proportion of patients experiencing ≥ 1 in-hospital complication was higher in the LA group, with bowel obstruction, surgical-site infection, and intra-abdominal abscess or infected fluid collection accounting for most events. Notably, this observed difference may be influenced by diagnostic criteria, the event observation window, and outcome-capture bias related to between-group differences in length of hospital stay.

First, bowel obstruction was defined using a prespecified operational definition: compatible clinical symptoms with imaging evidence of obstruction, accompanied by a requirement for interventions such as fasting, gastrointestinal decompression, or additional management. However, because outcome adjudication relied on retrospective medical records, even with standardized criteria, misclassification may occur due to incomplete documentation and variability in clinicians' diagnostic practices. Second, complications were ascertained only during the index hospitalization. Given that the length of hospital stay differed between groups, the LA group may have had a longer "at-risk" observation window, thereby increasing the likelihood of capturing in-hospital events (outcome-capture bias). Moreover, in-hospital outcomes may be affected by time-dependent biases and competing events such as discharge. Thus, the comparability of in-hospital event rates between groups should be interpreted cautiously [21]. Accordingly, the present safety comparison primarily reflects short-term in-hospital outcomes and should not be extrapolated to post-discharge complications, recurrence, readmission, or re-intervention.

Third, the complication profiles of these two strategies may be inherently asymmetric: Although LA has been associated with lower early post-appendectomy complication rates than open appendectomy, it remains an abdominal surgical approach and may still involve procedure-related adverse events, including incisional surgical-site infection, organ/space infection or intra-abdominal abscess, postoperative ileus, and rare adhesive intestinal obstruction [22]. In contrast, ERAT warrants particular attention to strategy-specific risks, including guidewire- or cannulation-related perforation, mucosal injury or bleeding requiring intervention, stent-related complications, and delayed intra-abdominal infection [23]. The absence of severe ERAT-related complications in this cohort does not imply a negligible risk profile; given the limited sample size and low expected event rates, the precision for estimating rare but clinically significant events remains constrained, and "zero events" should not be interpreted as "zero risk" [24]. Overall, ERAT did not demonstrate an increase in in-hospital complication signal in this study, and the crude overall complication rate was lower. However, given the restricted observation window and limited number of events, together with the exploratory nature of this small retrospective cohort, larger samples with standardized follow-up are required to more precisely delineate safety and define the boundaries of clinical applicability.

Higher Costs and Resource Utilization: Interpretation Should Avoid Over-Extrapolation

This study demonstrated higher in-hospital costs in the ERAT group, underscoring that "faster recovery" does not necessarily translate into "lower hospitalization costs". Potential contributors include the cost of the single-use digital cholangioscope and associated consumables, endoscopy-suite resource utilization, and stent placement with subsequent stent removal procedures. It should be emphasized

that cost outcomes are highly dependent on institutional charging structures, consumable procurement frameworks, and reimbursement policies, thereby limiting external generalizability [25]. Moreover, the present analysis was restricted to direct in-hospital costs and did not include formal cost-effectiveness or cost-utility analyses, nor did it capture downstream costs related to recurrence, readmission, or re-intervention. Given the sample size and multiple endpoints evaluated, these economic findings should also be interpreted cautiously. Future studies should prespecify health-economic endpoints and integrate longer-term clinical outcomes (recurrence, readmission, and re-intervention) into a comprehensive evaluation framework to more accurately characterize the overall cost-effectiveness and value of appendix-preserving strategies [26].

Limitations and Future Research Directions

The principal limitations of this study include: (1) a retrospective, non-randomized design, with inherent risks of selection bias and residual confounding; (2) a relatively small sample size and a low number of complication events, constraining the precision for rare severe events and rendering multivariable logistic regression inappropriate; (3) inflammatory and pain-related mediators measured at only two time points (preoperatively and 48 h postoperatively), without characterization of temporal trajectories, and the absence of patient-reported pain outcomes and detailed analgesic-consumption data; (4) complication surveillance restricted to the index hospitalization, introducing potential outcome-capture bias, particularly in the context of between-group differences in length of hospital stay; and (5) implementation within a single center by a fixed, experienced team, such that center-specific expertise and learning-curve effects may limit external generalizability. In addition, multiple clinical, biomarker, and cost-related outcomes were analyzed in a cohort of 60 patients, which may increase the probability of chance findings due to multiple comparisons; therefore, statistically significant results should be interpreted in an exploratory context, particularly where event numbers were small.

In light of these limitations, future investigations should prioritize multicenter prospective studies, preferably randomized controlled trials when feasible, or rigorously designed propensity score-based analyses, to enhance causal inference. Standardization of perioperative analgesic and antimicrobial strategies, along with systematic collection of patient-reported outcomes, structured complication grading, and extended follow-up (e.g., 30-day, 90-day, and 1-year endpoints for recurrence, readmission, and re-intervention), will be essential. In parallel, incorporation of formal health-economic evaluations will be critical to define the target population, quantify real-world benefits, and define the safety and applicability boundaries of digital cholangioscope–assisted ERAT.

Conclusions

In this single-center retrospective cohort, digital cholangioscope–assisted ERAT was associated with faster in-hospital perioperative recovery than LA in patients with acute uncomplicated appendicitis. However, given the non-randomized treatment allocation, limited in-hospital observation window, and low event rates, these findings should be interpreted as associative rather than causal. In addition, because this study included a relatively small sample (n = 60) and evaluated multiple outcomes, the possibility of unstable estimates and chance findings should be acknowledged, and statistically significant results should be interpreted cautiously within an exploratory context. Multicenter prospective studies with standardized methodologies and longitudinal follow-up are required to further clarify long-term clinical outcomes, cost-effectiveness, and the overall benefit–risk profile of appendix-preserving interventional strategies.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

WHT and MH designed and carried out the study; WHT, MH and QFY contributed to the data collection, data analysis and data interpretation; GQY and JCL contributed to data collection and assisted in data interpretation. All authors drafted the manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the institutional ethics committee of Hangzhou Ninth Hospital (Approval No. 2024-048) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.62713/aic.4481.

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