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Effects of Emergency Department Analgesia on the Management Timeline and Clinical Outcomes of Acute Appendicitis

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ABSTRACT

Objectives: This study aimed to evaluate the association between the administration of analgesics (Opioids or Nonsteroidal Anti-Inflammatory Drugs [NSAID]) after the initial examination in the emergency department and the diagnostic process of acute appendicitis, the timing of surgery, and postoperative complications in patients presenting with abdominal pain and suspected acute appendicitis.

Methods: A total of 925 patients aged 18–65 years who underwent surgery for acute appendicitis between January 2020 and May 2025 were retrospectively reviewed. Two age- and sex-matched groups were formed: 98 patients who experienced a delay in surgical treatment (case group) and 98 patients who underwent surgery within 24 hours following diagnosis (control group). Delay in surgical treatment was defined as an interval exceeding 24 hours from the initial examination to surgery. Early analgesia was defined as the administration of parenteral analgesics after the initial examination. Group comparisons used Fisher's exact test for categorical variables and t-test or Mann–Whitney U test as appropriate for continuous variables, with two-sided α=0.05.

Results: The groups were similar with respect to demographic and clinical characteristics. The rates of early opioid use were 24.5% in the case group and 26.5% in the control group, with no significant difference between them (P=0.742). In contrast, early NSAID use was significantly higher in the case group (32.7% vs. 18.4%, P=0.021). The delayed-treatment group had markedly higher rates of perforation (28.6% vs. 12.2%, P=0.004) and postoperative abscess (14.3% vs. 4.1%, P=0.013).

Conclusions: Early opioid analgesia was not associated with diagnostic delay or complications, suggesting it may be used safely in patients with acute appendicitis. In contrast, NSAID administration was associated with diagnostic delays, leading to postponed surgical intervention and higher complication rates. It is therefore advisable to avoid NSAID use, particularly in patients presenting with atypical abdominal pain.

Keywords: Acute Appendicitis, Analgesia, Opioids, Nonsteroidal Anti-Inflammatory Drugs

Acute appendicitis is one of the most common surgical causes of acute abdominal pain in patients presenting to the emergency department [1]. The optimal treatment for patients diagnosed with acute appendicitis is early appendectomy, which helps prevent complications [2]. However, the diagnostic

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process can sometimes be challenging, and delays in diagnosis and treatment may result in undesirable outcomes such as perforation, intra-abdominal abscess, and increased morbidity [3]. Pain control is a fundamental component of patient care in the emergency department. However, the traditional surgical perspective has opposed the use of analgesics before a definitive diagnosis, due to concerns that analgesia might obscure clinical findings [4]. More recent studies, however, have demonstrated that early administration of opioid analgesics does not negatively affect diagnostic accuracy [5, 6]. International guidelines likewise recommend adequate management of pain [7]. Nonetheless, the majority of studies in the literature have primarily focused on opioid analgesics. The role of nonsteroidal anti-inflammatory drugs (NSAIDs) in acute appendicitis has been less extensively investigated [8]. By suppressing inflammation and peritoneal irritation, NSAIDs may mask the clinical presentation, potentially increase the risk of misdiagnosis and adversely affect the timing of treatment [9, 10]. Evidence supporting the suppressive effect of NSAIDs on peritoneal inflammation has been reported in animal experiments and case series [11, 12]. This study aimed to evaluate the impact of early administration of opioid and NSAID analgesia on the diagnostic process and surgical management in patients presenting with suspected acute appendicitis.

METHODS

Our study included patients who presented with abdominal pain to the Emergency Department of Amasya University Şerefeddin Sabuncuoğlu Training and Research Hospital between January 2020 and May 2025 and were diagnosed with acute appendicitis. The study protocol was approved by the Amasya University Non-Interventional Research Ethics Committee (Protocol No: 2025/145).

The case group comprised patients with a treatment delay, defined a priori as >24 hours from the first ED assessment to the start of surgery. Controls were drawn from the same source population and time window and underwent surgery within 24 hours. For each case, one control was randomly selected from all eligible candidates matched on age (±5 years) and sex to minimize confounding by these strong determinants of presentation and outcomes. Importantly, analgesic exposure (opioid or NSAID) was not used as a matching factor to avoid over-matching. This design reduces the risk of selection bias because cases and controls arise from the same underlying population under identical ascertainment procedures.

For each patient in the case group, a control patient was randomly selected from the control group matched for age (±5 years) and sex. In total, 98 matched controls were identified for 98 cases. Data were obtained from the hospital information management system (HBYS) and patient medical records.

Age, sex, and body mass index (BMI); The time interval from symptom onset to emergency department presentation. vital signs including temperature, heart rate, and blood pressure, Leukocyte counts and C reactive protein (CRP) level, Diagnostic imaging modalities (Ultrasonography, Computed Tomography) and radiology reports; Type of analgesics administered (opioids: morphine, pethidine, fentanyl; NSAIDs: ketorolac, diclofenac), along with dosage and timing of administration; Time of surgery, surgical approach (open or laparoscopic); Complications documented in the operative notes (perforation, intra-abdominal abscess) and length of hospital stay was evaluated.

Statistical Analysis

The statistical evaluation was performed with IBM SPSS Statistics 27.0 (Windows). Normality of distribution for continuous data was assessed by the Shapiro–Wilk test. Variables showing normal distribution were summarized as mean±standard deviation; otherwise, medians were reported. Intergroup differences were analyzed using the Independent Samples t-test for normally distributed data and the Mann–Whitney U test for data without normal distribution. Categorical variables were expressed as frequency and percentage, and Fisher's exact test was applied for comparisons. Results with P-values below 0.05 were considered significant.

RESULTS

Between January 2020 and May 2025, a total of 925 patients underwent surgery for acute appendicitis.

TABLE 1. Baseline Demographic and Clinical Profiles of the Case and Control Groups

Variable	Case group (n=98)	Control group (n=98)	P-value
Age (years)	36.4±12.8	35.9±13.1	0.785
Sex (female/male)	53 / 45	54 / 44	0.886
Body mass index (kg/m²)	26.1±4.3	25.7±3.9	0.482
Symptom duration (hours)	28.5 (18.0–42.3)	26.0 (16.0–38.0)	0.224
Admission temperature (°C)	37.6±0.8	37.5±0.7	0.341
Admission heart rate (beats/min)	92±14	90±13	0.278
Leukocyte count (×10³/μL)	14.8±3.9	14.3±3.5	0.321
CRP (mg/L)	48.5 (22.0–95.8)	42.0 (18.3–88.0)	0.189

Data are shown as mean±standard deviation or frequency (n) or median (minimum-maximum). CRP, C-reactive protein

Among them, 98 (10.6%) patients met the criterion of-diagnostic delay exceeding 24 hours and were assigned to the case group. For each case, one control patient matched by age and sex was selected, resulting in a control group of 98 patients. The demographic and baseline clinical characteristics of both groups are compared in Table 1. No statistically significant differences were observed between the groups regarding body mass index, the interval from symptom onset to emergency department admission (hours), body temperature (°C), heart rate, leukocyte count, or C-reactive protein (CRP) level (P>0.05).

The distribution and types of analgesic use in the case and control groups are presented in Table 2. The proportion of patients who received early analgesia (opioid or NSAID) was higher in the case group (57.1%) compared to the control group (44.9%); although this difference did not achieve statistical significance, it was close to the borderline level (P=0.087). The frequency of opioid administration was comparable between the groups (24.5% in the case group vs. 26.5% in the control group; P=0.742). By contrast, NSAID use was significantly more frequent in the case group (32.7% vs. 18.4%; P=0.021). The significant association found between NSAID use and a delay in surgical treatment suggests that NSAIDs may represent a potential risk factor.

Postoperative complication rates for the case and control groups are detailed in Table 3. The incidence of perforation was 28.6% in the case group compared with 12.2% in the control group (P=0.004). The occurrence of postoperative abscess was also significantly higher among case group (14.3% vs. 4.1%; P=0.013). Although gangrenous appendicitis was more frequent in the case group (16.3% vs. 9.2%), this difference did not reach statistical significance (P=0.134). The total major complication rate (including perforation, abscess formation, and gangrene) was significantly higher in the case group (48.0%) compared to the control group (24.5%; P=0.001)

Table 4 summarizes the imaging modalities and surgical techniques employed in the case and control groups. No statistically significant difference was observed between the groups regarding the use of ultra-

TABLE 2. Early Analgesic Utilization Across Case and Control Groups

Type of analgesic	Case group (n=98)	Control group (n=98)	P-value
Any early analgesic	56 (57.1%)	44 (44.9%)	0.087
Opioid	24 (24.5%)	26 (26.5%)	0.742
NSAID	32 (32.7%)	18 (18.4%)	0.021

Data are shown as frequency (%). NSAID, nonsteroidal anti-inflammatory drugs

TABLE 3. Distribution of Postoperative Complications Across Case and Control Groups

Complication	Case group (n=98)	Control group (n=98)	P-value
Perforation	28 (28.6%)	12 (12.2%)	**0.004**
Gangrenous appendicitis	16 (16.3%)	9 (9.2%)	0.134
Postoperative abscess	14 (14.3%)	4 (4.1%)	**0.013**
Surgical site infection	10 (10.2%)	7 (7.1%)	0.445
Total major complications	47 (48.0%)	24 (24.5%)	**0.001**

Data are shown as frequency (%).
Values with P<0.05 are presented in bold.

sonography or computed tomography, and the diagnostic yield for appendicitis was comparable in both modalities. Similarly, the frequency of laparoscopic procedures did not differ significantly between the two groups. In contrast, the length of hospital stay was significantly prolonged in the case group compared to the controls (3 vs. 1 days; P<0.001). This outcome highlights the adverse impact of delayed surgical intervention on hospital resource utilization.

While our age- and sex-matched design with random control selection from the same source population reduces the risk of selection bias, unmeasured confounding cannot be excluded in this retrospective, single-center study. Therefore, our findings should be interpreted as associations rather than causal effects.

DISCUSSION

This study demonstrated that the early administration of NSAIDs in patients with acute appendicitis was associated with a risk of delayed surgical treatment initiation compared to opioid use. Furthermore, the findings substantiated that this delay was correlated with more severe clinical outcomes, including higher rates of perforation and intra-abdominal abscess formation. Early use of opioids was not found to be associated with treatment delay or postoperative complications. Our findings are consistent with the existing literature regarding pain management. Several randomized controlled trials and meta-analyses have demonstrated that the administration of opioid analgesics does not significantly alter physical examination findings, does not increase the rate of misdiagnosis, and substantially improves patient comfort [5, 6, 13]. In a study conducted by Thomas *et al*. [14], the use of morphine was shown not to impair diagnostic accuracy and was even associated with improved patient satisfaction. Our study reinforces these findings, confirming that opioids can be used safely

TABLE 4. Distribution of Imaging Techniques and Operative Approaches in the Case and Control Groups

Variable	Case group (n=98)	Control group (n=98)	P-value
Ultrasonography performed	78 (79.6%)	82 (83.7%)	0.458
CT performed	65 (66.3%)	58 (59.2%)	0.295
Appendicitis detected on USG	45/78 (57.7%)	58/82 (70.7%)	0.082
Appendicitis detected on CT	52/65 (80.0%)	52/58 (89.7%)	0.138
Laparoscopic surgery	60 (61.2%)	68 (69.4%)	0.226
Length of hospital stay (days)	3.0 (2.0–6.0)	1.2 (1.0–1.8)	**<0.001**

Data are shown as frequency (%) or median (minimum-maximum). CT, computed tomography; USG, ultrasonography.
Values with P<0.05 are presented in bold.

by demonstrating this effect through a tangible clinical outcome, namely the absence of surgical treatment delay. Nevertheless, the most striking finding of our study was the indication of a potential risk associated with NSAID use. Our results support the retrospective study by Frei *et al*., which suggested that the administration of NSAIDs might be linked to delays in the surgical management of appendicitis [15]. The exact mechanism underlying this adverse effect of NSAIDs has not been fully elucidated; however, it is hypothesized that by inhibiting prostaglandin synthesis, these drugs may suppress peritoneal inflammation and thereby diminish rebound tenderness, guarding, and pain [9, 11]. Such an effect may mislead clinicians, particularly in patients who do not initially present with clear signs of peritonitis or who exhibit atypical symptoms, potentially resulting in premature discharge or postponement of diagnostic imaging [10, 16]. The observation that NSAID use is associated with diagnostic and surgical delays should be considered clinically relevant and taken into account when determining treatment strategies.

One of the most important findings of our study is that delayed surgical intervention was associated with higher complication rates. In the case group, the incidences of perforation and intra-abdominal abscess were significantly increased. These results are entirely consistent with the literature emphasizing the importance of early surgical management in appendicitis [2, 17, 18]. Consistent with the existing literature, a delay in surgical intervention was found to elevate the risk of complications by facilitating the progression of uncomplicated appendicitis to gangrenous or perforated appendicitis [19, 24].

Strengths and Limitations

This study has certain limitations. Its retrospective design necessitated reliance on previously recorded data, which may be influenced by incomplete documentation or inconsistencies in medical records. Furthermore, as the investigation was conducted in a single center, the generalizability of our findings to broader patient populations is limited. In addition, factors that could influence the choice of analgesics (such as clinician experience and variations in patients' perception of pain) could not be fully controlled. Although our results highlight a potentially important association between NSAID use and delays in surgical management, these observations alone are insufficient to establish a causal relationship.

CONCLUSION

In patients presenting to the emergency department with suspected acute appendicitis, the use of opioid analgesics was not associated with diagnostic errors, surgical delays, or an increased risk of complications, indicating that opioids can be administered safely. In contrast, early use of NSAIDs was found to be related to delays in both diagnosis and surgical intervention. Such delays were significantly associated with higher rates of perforation and intra-abdominal abscess. Emergency physicians should be aware of the potential risks of NSAID administration, particularly in patients with atypical clinical presentations, and should tailor their pain management strategies accordingly.

Ethics Approval and Consent to Participate

This study was approved by the Amasya University Non-Interventional Research Ethics Committee (Decision No: 2025/145; date: 02.10.2025) All procedures were conducted in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments. Informed consent was waived because of the retrospective nature of the study and the analysis used anonymous clinical data.

Data Availability

I confirm; the data supporting the findings of this study can be obtained from the corresponding author upon reasonable request.

Authors' Contribution

Study Conception: SE; Study Design: SE; Supervision: EA; Funding: N/A; Materials: EA; Data Collection and/or Processing: EA; Statistical Analysis and/or Data Interpretation: SE, EA; Literature Review: SE; Manuscript Preparation: SE; and Critical Review: SE.

Conflict of Interest

The author(s) disclosed no conflict of interest during the preparation or publication of this manuscript.

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Generative Artificial Intelligence Statement

No generative artificial intelligence tool or service was used in the preparation of this manuscript. All content was created, reviewed, and finalized by the authors in accordance with scientific research methods and academic ethical principles.

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