Changes in perspective and practice in the diagnosis and treatment of appendicitis in childhood: five decades of experience

PhD thesis

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Abbreviations

CAA	Complicated Acute Appendicitis
CI	Confidence Intervals
COVID	COronaVIrus Disease
CRP	C-Reactive Protein
CT	Computed Tomography
ERAS	Enhanced Recovery After Surgery
IBD	Inflammatory Bowel Disease
IQR	Interquartile Range
LA	Laparoscopic Appendectomy
LOS	Length Of Hospital Stay
MIS-C	Multisystem Inflammatory Syndrome in Children
MRI	Magnetic Resonance Imaging
OA	Open Appendectomy
PCR	Polymerase Chain Reaction
PCT	Procalcitonin
PIMS	Paediatric Multisystem Inflammatory Syndrome
PIRS	Percutaneous Inguinal Ring Suture
SARS-CoV-2	Severe Acute Respiratory Syndrome CoronaVirus-2
UCAA	UnComplicated Acute Appendicitis
UTI	Urinary Tract Infection

Introduction

Acute Appendicitis in Childhood

Incidence

In childhood, the incidence of acute appendicitis increases with age after birth, reaching its peak around puberty (approximately 16–18 years). However, appendicitis may occur at any age, most commonly between 5 and 45 years. Statistically, the highest incidence occurs at 28 years of age. The incidence rate is 8.6% in males and 6.7% in females *(Téoule, 2020)*.

Pathophysiology

Obstruction of the appendiceal lumen results in increased intraluminal and mural pressure. This leads to local venous and lymphatic congestion, followed by impaired arterial blood flow. Due to the obstruction, the luminal contents (mucus) accumulate progressively. The resulting tension causes ischemia of the tissue layers, leading to necrosis. This process is further aggravated by the local bacterial flora. Once the appendiceal wall becomes permeable or perforates, bacteria can enter the peritoneal cavity, resulting in abscess formation and peritonitis *(Schumpelick, 2000; Barlow, 2013)*.

Clinical and Histopathological Diagnosis of Acute Appendicitis

The appendix can be regarded as a diverticulum of the colon, containing all typical tissue layers: mucosa, submucosa, longitudinal and circular muscular layers, and serosa. The main histological distinction lies in the lamina propria of the mucosa, which is rich in lymphoid follicles containing B- and T-lymphocytes. Clinically, it is important to note that the muscular layer of the appendix is thin, making it prone to early perforation and dissemination of the inflammatory process into the peritoneal cavity *(Barlow, 2013; Kooij, 2016)*. The severity of appendicitis can be histologically classified into different groups: simple, catarrhal, phlegmonous, gangrenous, and perforated. Clinically, acute appendicitis is nowadays categorized into complicated (CAA) and uncomplicated (UCAA) forms. While gangrenous and perforated appendicitis were previously both classified as complicated, gangrenous appendicitis without perforation is now considered uncomplicated *(Nordin, 2019)*.

In childhood, the classical symptoms include pain initially located around the umbilicus that later migrates to the right lower quadrant, accompanied by nausea, vomiting, and anorexia. The inflammatory process is associated with a low-grade fever, later often progressing to a moderate fever *(Snyder, 2018)*. Physical examination remains the most sensitive diagnostic tool, particularly the assessment of direct tenderness at McBurney's point *(McBurney, 1894)*. Several indirect signs (Rovsing's, Blumberg's, Dunphy's, psoas signs) can assist in the differential diagnosis *(Aerts, 2018)*. These indirect signs indicate peritoneal irritation and localized inflammation. Laboratory investigations typically show leucocytosis, neutrophilia, and elevated C-reactive protein (CRP) and procalcitonin (PCT) levels. On abdominal ultrasound, an appendix with a diameter of 7 mm or greater is considered pathological *(Hwang, 2018)*.

In Hungary, routine imaging does not include CT (computed tomography) or MRI (magnetic resonance imaging), but these modalities are indicated in obese children, advanced inflammatory processes, or unclear cases.

History and Evolution of Appendectomy

Traditional (Open) Appendectomy

The first appendectomy performed on a patient preoperatively diagnosed with appendicitis was carried out by Tait in 1880. The term "appendicitis" for the disease and "appendectomy" for the surgical removal of the appendix were introduced by Fitz *(Switzer, 2012)*. However, when thinking about the history of appendectomy, McBurney's name most often comes to mind. Although McArthur was the first surgeon who performed the appendectomy using the right-lower quadrant incision, McBurney was the first who described the procedure in the *Annals of*

Surgery in 1894 *(Burney, 1894; Hamill, 2016)*. Subsequently, Elliot and Lanz modified the original skin incision technique.

Laparoscopic Appendectomy

Dominic Frimberger performed the first laparoscopic appendectomy in 1983 *(Nano, 2012)*, while the first laparoscopic appendectomy in a child was reported in 1992 *(Gilchrist, 1992)*. It is now well established that laparoscopic appendectomy offers advantages over open surgery in children, including shorter hospital stays and fewer postoperative complications *(Jen, 2010; Markar, 2012; Svenson, 2016; Fadgyas, 2021)*.

Elective Appendectomy and Conservative Management Options

In selected cases, elective (*à froid*) appendectomy can be performed. In Sweden in 2015, conservative antibiotic treatment was introduced as an option for managing uncomplicated pediatric appendicitis *(Svensson, 2015)*. Thus, it was not surprising that during the COVID-19 pandemic (COronaVIrus Disease), antibiotic therapy was increasingly adopted to treat uncomplicated appendicitis across Europe *(Bethell, 2020)*. In cases of periappendicular mass, conservative management is recommended due to the expected lower complication rates *(Simillis, 2010)*. Following conservative treatment, elective (*à froid*) appendectomy may be performed according to local protocols. In the presence of periappendicular mass, complication rates are reduced compared to early surgery, although the total length of hospital stay is longer *(van Amstel, 2020)*.

SARS-CoV-2 Infection and Appendicitis in Childhood

During the first wave of the COVID-19 pandemic, SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) infection affected children relatively mildly *(Ludvigsson, 2020; Parri, 2020)*. Most infected children were likely asymptomatic. In the mildest cases, symptoms resembled those of a common cold *(Molteni, 2021; Karászi, 2021)*. Severe lower respiratory tract involvement requiring invasive ventilation was rarely observed *(Howard-Jones, 2022)*. In

April 2020, a new syndrome resembling Kawasaki-syndrome emerged, later termed MIS-C (Multisystem Inflammatory Syndrome in Children) or PIMS (Paediatric Inflammatory Multisystem Syndrome). This syndrome, characterized by fever, gastrointestinal symptoms, and myocarditis, was caused by a post-viral vasculopathy following SARS-CoV-2 infection, affecting the brain, heart, lungs, gastrointestinal tract, and kidneys *(Becker, 2020; Viner, 2020)*. In clinical practice, MIS-C presented a major diagnostic challenge for pediatric surgeons in the differential diagnosis of acute abdominal conditions *(Valitutti, 2021).*

Impact of the COVID-19 Pandemic on the Management of Appendicitis

Most pediatric surgical departments adapted new protocols for the management of appendicitis during the pandemic, favouring non-operative treatment *(Bethell, 2020).* In many centers, traditional (open) surgery replaced the previously standard laparoscopic approach *(English, 2020)*.

Aims

The main objectives of the research were as follows:

1. To investigate the management of pediatric appendicitis over the past three decades, with particular focus on the evolution of surgical techniques, the rate of complications, and the length of hospital stay.
2. To perform a clinical comparison between laparoscopic appendectomy and traditional (open) appendectomy.
3. To examine the learning curve of laparoscopic appendectomy.
4. To assess the changes in the incidence of perforated appendicitis during the COVID-19 pandemic.
5. To evaluate the concordance between the intraoperative surgical assessment and the subsequent histopathological findings regarding the severity of acute appendicitis.

Theses

1. The use of modern surgical techniques has resulted in fewer complications and shorter hospital stays in the treatment of pediatric appendicitis today.
2. The laparoscopic approach is superior to the traditional open procedure in children.
3. The learning curve of laparoscopic appendectomy is short and successful.
4. During the COVID-19 pandemic, the incidence of perforated appendicitis in children increased in Hungary compared to the pre-pandemic period.
5. The intraoperative surgical assessment correlates with the subsequent histopathological findings regarding the severity of acute appendicitis.

Samples and Methods

A retrospective, observational cohort study was conducted regarding appendectomies performed at Heim Pál National Pediatric Institute (with different time intervals analyzed in the individual sub-studies). The study was approved by the Institutional Research Ethics Committee (Approval No.: 10470/2017). Inclusion criteria were age under 18 years and a preoperative diagnosis of acute appendicitis. Exclusion criteria included patients with underlying malignant diseases (leukaemia, lymphoma, appendix carcinoid), patients older than 18 years, and planned appendectomies (e.g., for chronic appendicitis or post-conservative appendicitis treatment). The presence of concomitant infectious diseases (e.g., pneumonia, SARS-CoV-2 infection, MISC) was not an exclusion criteria. Patients were divided into two groups based on surgical technique: open appendectomy (OA) – which included converted laparoscopic surgeries – and laparoscopic appendectomy (LA). Based on the final histological findings, cases were further classified into uncomplicated acute appendicitis (UCAA – non-inflamed, simple, catarrhal, phlegmonous, gangrenous) and complicated acute appendicitis (CAA – perforated) subgroups. Appendectomy was performed as soon as possible after establishing the diagnosis. All patients received a single-shot dose of amoxicillin-clavulanate preoperatively, according to institutional protocol. In cases of UCAA where pus was observed intraoperatively, amoxicillin-clavulanate therapy was prolonged for 24–48 hours. In cases of complicated appendicitis, broad-spectrum antibiotics were initiated intraoperatively (combinations included cefotaxime-metronidazole, ceftriaxone-metronidazole, or amoxicillin-clavulanate-metronidazole, or meropenem). Broad-spectrum antibiotic therapy generally lasted 3–5 days, with the duration determined based on laboratory results and clinical status, often in consultation with an infectologist. If culture results were available, targeted antibiotic therapy was pursued. In cases of postoperative intra-abdominal abscess or primary periappendicular mass, meropenem was the first-line antibiotic. In cases of periappendicular mass, interval (*à froid*) appendectomy was performed 3–6 months later *(Zavras, 2020).*

Length of hospital stay (LOS, in days), early (within 1 month postoperatively; wound healing disorders, intra-abdominal abscess, paralytic ileus), and late (after 1 month postoperatively; wound healing disorders, bowel obstruction, reoperation) complications were analyzed. Data were extracted from the electronic medical database and paper-based patient records. Extracted data were compiled in Microsoft Excel spreadsheets. During the different sub-studies, various statistical methods were employed, detailed below. Statistical analyses were performed using SPSS 26.0.0.0 and GraphPad Prism 9 software. For normally distributed variables, mean and standard deviation were reported; for non-normally distributed variables, median and interquartile range (IQR) were presented. Differences were considered significant if the p-value was <0.05.

I. Pediatric Appendicitis: What Has Changed Over the Past Three Decades?

Patients aged 0–14 years who underwent surgery for suspected acute appendicitis were examined during two periods: 1976–1985 (Group A) and 2011–2020 (Group B). Patients older than 15 years and those with missing data were excluded (note: in the earlier period, patient care at Heim Pál Hospital extended to age 14, whereas at its successor institution, Heim Pál National Pediatric Institute, care extends to age 18). Patients were further subdivided by age: younger group (Y) for 0–6 years, and older group (O) for 7–14 years. Categorical variables were analyzed using Fisher's exact test (if group size <5) or chi-square test (if group size ≥ 5), depending on group size *(Fadgyas, 2024).*

II. Comparison of Laparoscopic and Open Appendectomy

A retrospective, observational cohort study was performed on appendectomies conducted at Heim Pál National Institute of Pediatrics between 2011 and 2020. Patients were divided into two groups: open and laparoscopic appendectomy. Surgeries initiated laparoscopically but converted to open were classified under open surgeries. Categorical variables were analyzed using Fisher's exact test or chi-square test, depending on group size. Distribution of variables was tested with the Shapiro–Wilk test. Since variables were not normally distributed, the Mann–Whitney U test was used to compare continuous variables *(Fadgyas, 2024)*.

III. Learning Curve for Laparoscopic Appendectomy

Acute appendectomies performed at the Department of Surgery and Traumatology of Heim Pál National Pediatric Institute between January 1. 2016 and December 31. 2017 were analyzed. Patients were divided into two groups based on whether they underwent OA or LA; conversions were included in the OA group. Operative time was measured from skin incision to wound closure based on anaesthesiology records. Operative time, hospital length of stay (LOS), and postoperative complications were analyzed according to the Clavien–Dindo classification *(Clavien, 2009)*. Chi-square tests were used for categorical variables (as all group sizes were ≥5). Shapiro–Wilk normality tests showed non-normal distribution; thus, the Mann–Whitney U test was used for continuous variables *(Fadgyas, 2022)*.

IV. Impact of the COVID-19 Pandemic on Pediatric Acute Appendicitis

Children who underwent acute appendectomy at the Department of Surgery and Traumatology of our institute between January 1. 2012, and December 31. 2020 were analyzed. Monthly breakdowns were performed for patients operated on in 2020, and SARS-CoV-2 infection status was also recorded. Categorical variables were analyzed with Fisher's exact test or chi-square test, depending on group size *(Fadgyas, 2021)*.

V. Severity of Pediatric Appendicitis: Correlation Between Surgical and Histopathological Findings

The intraoperative clinical diagnosis and the histopathological findings were compared regarding the severity of appendicitis. Intraoperative diagnosis was determined by the operating surgeon based on visual findings; histopathological evaluation was performed by the pathologist. Demographic data were presented with sample sizes (n) and percentages (%), as needed. Since the data deviated from normal distribution, non-parametric tests were used for age and LOS, reporting median and interquartile range (IQR). Spearman's correlation was used to measure associations ($r=0$–0.10 negligible, $r=0.10$–0.39 weak, $r=0.40$–0.69 moderate, $r=0.70$–0.89 strong, $r\geq0.90$ very strong correlation) *(Schober, 2018)*. Concordance between the two groups was assessed with Cohen's kappa (κ) coefficient, with 95% confidence intervals; weighted kappa values were also calculated when appropriate to adjust for varying degrees of disagreement, which is useful for ordinal data *(Bakeman, 1997)*. Kappa interpretations were: $\kappa=0$–0.20 slight, $\kappa=0.21$–0.40 fair, $\kappa=0.41$–0.60 moderate, $\kappa=0.61$–0.80 substantial, and $\kappa=0.81$–1.00 almost perfect agreement *(Landis, 1977)*. Continuous variables were compared using the Mann–Whitney U test; categorical variables were compared using the chi-square test *(Fadgyas, 2024)*.

Results

I. Acute appendicitis in childhood: What has changed over the past three decades?

During the study period, a total of 2475 appendectomies were performed: 1293 in Group A (1976–1985) and 1182 in Group B (2011–2020). In Group A, 264 patients (20.4%) were younger (aged 0–6 years) and 1029 (79.6%) were older (aged 7–14 years). In Group B, 166 patients (14%) were younger and 1016 (86%) were older. In both groups, the majority of patients were over 6 years of age.

The proportion of surgeries performed in the 0–6 years age group was significantly higher in Group A (20.4%) compared to Group B (14.0%) ($p<0.0001$).

More uncomplicated appendicitis (UCAA) cases were operated on in Group B than in Group A, especially among the older patients (aged 7–14 years) ($p<0.0001$). Removal of non-inflamed or simplex inflamed appendices was more frequent in Group A compared to Group B, a difference observed across all subgroups ($p<0.0001$).

Among older patients, complicated appendicitis (CAA) was significantly more common in Group A compared to Group B ($p<0.0001$). Complicated cases were more frequent among younger patients than older ones, both in Group A (29.5% vs. 18.3%) and Group B (28.3% vs. 11.2%).

No significant difference was found between Group A and Group B regarding the occurrence of early postoperative complications ($p=0.2472$). However, late complications ($p<0.0001$) and the overall complication rate ($p=0.0105$) were significantly higher in Group B.

When analyzing only the open appendectomy (OA) cases within Group B - thus excluding laparoscopic appendectomies (LA) - the rate of late complications was significantly higher in both UCAA and CAA subgroups compared to Group A (Table 1.).

	complication	A group (1976-85)	B group (2011-20)	p
All appendectomies A group: OA B group: OA and LA	**Early**	5.4% (70/1293)	6.5% (77/1182)	0.2472
	Late	0.6% (8/1293)	3.9% (46/1182)	**<0.0001**
	All	6.0% (78/1293)	8.7% (103/1182)	**0.0105**
OA	**Early**	5.4% (70/1293)	6.9% (49/714)	0.1882
	Late	0.6% (8/1293)	4.9% (35/714)	**<0.0001**
	All	6.0% (78/1293)	9.8% (70/714)	**0.002**
OA, UCAA	**Early**	2.5% (26/1027)	3.7% (22/598)	0.1877
	Late	0.1% (1/1027)	3.9% (23/598)	**<0.0001**
	All	2.6% (27/1027)	6.4% (38/598)	**0.0002**
OA, CAA	**Early**	16.5% (44/222)	23.27% (27/116)	0.1197
	Late	2.6% (7/266)	10.3% (12/116)	**0.0033**
	All	19.2% (51/266)	38.6% (32/116)	0.0667

Table 1.: Complication rates stratified by the chosen surgical technique and the severity of appendiceal inflammation (OA – open appendectomy, LA – laparoscopic appendectomy, CAA – complicated acute appendicitis, UCAA – uncomplicated acute appendicitis).

II. Comparison of Laparoscopic Versus Open Appendectomy

During the study period, a total of 1,444 appendectomies were performed (open appendectomy [OA]: 842 cases; laparoscopic appendectomy [LA]: 602 cases). The majority of patients were male (boys: 883, girls: 561), with a mean age of 10.93 years. No significant difference was observed in the incidence of postoperative complications between the two surgical techniques, either in uncomplicated or complicated cases (p>0.05). The length of hospital stay was shorter following laparoscopic surgery compared to open surgery (3 (2;3) vs. 4 (3;5) days). Over the study period, the number of open procedures gradually decreased, whereas the number of laparoscopic appendectomies steadily increased. The rate of conversions remained consistently low.

III. Learning Curve of Laparoscopic Appendectomy

During the study period, 309 appendectomies were performed. A total of 182 boys and 127 girls underwent surgery, with a mean age of 11.4 years. Open appendectomy (OA) was performed in 161 cases, while laparoscopic appendectomy (LA) was performed in 148 cases. Among OA cases, conversion to open surgery was necessary in 12 patients. Appendectomy for uncomplicated acute appendicitis (UCAA) was performed in 251 cases (OA: 121, LA: 130), and for complicated acute appendicitis (CAA) in 58 cases (OA: 40, LA: 18). Among UCAA cases, the number of open and laparoscopic procedures was similar during the study period. In CAA cases, open appendectomy was initially more common; however, by the end of the learning curve (2017), the number of laparoscopic procedures surpassed that of open surgeries even in this subgroup. The median operative time was 50 (40;63) minutes for OA - including a significantly longer duration for converted surgeries (102.5 (78;125) minutes) - and 40 (30;50) minutes for LA. At the beginning of the study (2016), the operative time did not differ significantly between OA and LA ($p=0.2872$), but by 2017, laparoscopic appendectomy had become significantly faster than the open technique ($p=0.0004$). The median length of hospital stay was significantly shorter following laparoscopic surgery (2 (2;3) days) compared to open surgery (4 (3;5) days) ($p<0.0001$). Postoperative complications were rare in both groups, mostly classified as Clavien-Dindo Grade I events (OA: 5.4%, LA: 4.0%). Reoperation was necessary in one case in each group, both due to mechanical bowel obstruction, classified as Clavien-Dindo Grade III.B.

IV. Impact of the COVID-19 Pandemic on Pediatric Appendicitis

During the study period, 1343 appendectomies were performed for suspected acute appendicitis. Most of the patients were treated for uncomplicated appendicitis (1,166/1,343). Starting from 2015, a significant increase was observed in the proportion of complicated (perforated) cases ($p=0.0002$). In a month-by-month analysis of 2020, higher rates of perforated appendicitis were recorded in January, May, and December relative to all cases of appendicitis. Among patients operated on for acute appendicitis, the SARS-CoV-2 PCR positivity rate was low. (PCR testing became available in March and was routinely implemented before surgery from May onward.) The first SARS-CoV-2 positive appendicitis case was detected in October, with the highest number observed in December. Patients with unknown SARS-CoV-2 status had not undergone PCR testing. In 2020, the proportion of SARS-CoV-2 positive patients among those operated on for complicated acute appendicitis was notably high in October and December (33.3% and 50%, respectively). Among confirmed SARS-CoV-2 positive patients, the rate of complicated appendicitis was significantly higher (5/8, 62.5%) compared to SARS-CoV-2 negative patients (15/92, 16.3%) (p=0.0075).

V. Correlation Between Surgical and Histopathological Severity Assessment in Pediatric Appendicitis

A total of 1444 patients were included in the analysis, with a mean age of 10.93 years. The correlation between the intraoperative surgical diagnosis and the histopathological findings is summarized in Table 2.

		Surgical diagnoses					
		Negative	Simplex/ catarrhal	Phleg	Gangr	Perf	**Total**
Histological diagnoses	Negative/incipient	29	84	64	1	1	**179**
	Simplex/catarrhal	0	2	5	0	0	**7**
	Phlegmonous (Phleg)	2	29	856	57	21	**965**
	Gangrenous (Gangr)	0	1	35	44	26	**106**
	Perforated (Perf)	0	0	9	39	139	**187**
	Total	**31**	**116**	**969**	**141**	**187**	**1444**

Table 2.: Comparison between Surgical Assessment and Histopathological Diagnosis.

In most cases, a phlegmonously inflamed appendix was removed. In cases where the appendix was found to be non-inflamed, other findings were sometimes identified (such as enteritis, Meckel's diverticulum, bowel adhesions, ovarian abnormalities, UTI, IBD, helminthiasis, renal ectopia, intussusception, or omental torsion), which explained the patients' symptoms. The two strongest correlations between surgical and histopathological findings were observed in phlegmonous appendicitis (856/965 cases, 88.7%) and perforated appendicitis (139/187 cases, 74.3%). A statistically significant, strong correlation (r=0.775) was identified, along with moderate to substantial agreement between the surgical and histopathological findings for all types of appendectomies (both LA and OA) (see Table 3.).

	Number of cases	Spearman's rho correlation coefficient	p	Cohen's kappa with 95% CI	Weighted kappa	p
Open Appendectomy	842	0.774	<0.0001	0.505 (0.460-0.551)	0.633	<0.0001
Laparoscopic Appendectomy	602	0.773	<0.0001	0.506 (0.449-0.563)	0.639	<0.0001
Total sample	1444	0.775	<0.0001	0.506 (0.471-0.542)	0.637	<0.0001

Table 3: Cohen's κ-values and the Degree of Agreement Between Surgical Assessment and Histopathological Findings (CI: Confidence Interval)

The length of hospital stay (LOS) was significantly longer in the complicated appendicitis (CAA) group compared to the non-complicated appendicitis (UCAA) group ($p<0.0001$). When the surgeon intraoperatively underestimated the severity of appendicitis compared to the subsequent pathological diagnosis, the median hospital stay was 4 (3;7) days. In contrast, when the surgical diagnosis accurately matched the histopathological findings, the hospital stay was only 3 (3;5) days ($p<0.0001$). In cases where the severity of appendicitis was underestimated during surgery, a higher postoperative complication rate (18.9%) was observed compared to cases where the surgical severity assessment was accurate (7.9%) ($p<0.0001$). Underestimation of the severity of appendicitis during surgery was associated with a significantly increased risk of postoperative complications (OR=2.693, 95% CI (1.641–4.420)).

Early and late postoperative complications occurred more frequently in complicated (CAA) than in non-complicated (UCAA) appendicitis cases ($p<0.0001$).

No significant difference was found between the open (OA) and laparoscopic (LA) groups regarding agreement between surgical and histopathological assessments, as the 95% confidence intervals (CIs) of the Cohen's κ-values overlapped between the two groups.

Discussion

I. Pediatric Appendicitis: What Has Changed Over the Last Three Decades?

The authors conducted a retrospective observational study analyzing the records of 2475 patients treated between 1976–1985 and 2011–2020. They examined the proportions of younger (0–6 years) and older (7–15 years) children and the postoperative complication rates in relation to the severity of appendicitis. Based on their findings, the use of modern diagnostic tools has led to a decrease in the number of surgeries performed for non-inflamed and simple inflamed appendices compared to previous decades. Similar results were previously published by Boenigk *(Boenigk H et al., 2012)*, who compared three periods (1974–1985, 1986–1996, 1997–2000) and found a continuous decline in surgeries for non-inflamed appendices. A large Swedish study analyzing 56774 patients between 1987 and 2009 also showed a decrease in surgeries performed for both non-inflamed and perforated appendicitis *(Almström, 2018).* In the present study, the occurrence of complicated appendicitis (CAA) appeared slightly lower today than in the past; however, this difference was not statistically significant. Anderson et. al similarly reported a decreasing trend in the incidence of perforated appendicitis between 1995 and 2009 *(Anderson, 2012)*. In contrast, Ricci et al. observed increasing perforation rates: 0% in 1944, 13.6% in 1964, and 31.5% in 1984 *(Ricci, 1988).* The current study highlights that CAA occurs more frequently in younger children, a well-known phenomenon in the preschool age group *(Bonadio, 2015).* The limitation of the study is the short follow-up period. Previously, postoperative complications were typically registered at the initial treating institution (Group A, 1976–1985). Today, postoperative complications occurring within the first month must be treated at the original hospital due to the "warranty rule", but later complications may be managed. Thus, some late complications in Group B (2011–2020) might not have been recorded. Furthermore, late bowel obstruction developing even decades after appendectomy could not be assessed in either group. Additionally, evolving microbial patterns and the increasing severity of infections caused by multidrug-resistant bacteria could also influence current postoperative complication rates. Our hypothesis - that the management of pediatric appendicitis has improved over the decades - was only partially confirmed. Today, fewer appendectomies are performed for non-inflamed appendices, and fewer surgeries are required in younger, more challenging age groups, suggesting better diagnostic capabilities. However, early complication rates remained unchanged, and the reasons for the increased incidence of late complications require further investigation. It would be worthwhile to compare the microbiological and antibiotic resistance profiles of CAA cases between the two periods to explore possible links with long-term complications.

II. Comparison of Laparoscopic and Open Appendectomy

Initially introduced in gynaecology, then in general surgery, laparoscopy eventually became part of daily practice in pediatric surgery as well. In the Heim Pál National Pediatric Institute, early attempts at laparoscopic appendectomy started in the early 2000s but were limited to daytime hours, due to surgeon inexperience, limited equipment, and sterilization constraints. A major advancement occurred around 2016–2017 following infrastructure development and comprehensive staff training, leading to the routine use of laparoscopic appendectomy *(Fadgyas, 2022)*. In adult general surgery, laparoscopic appendectomy quickly proved advantageous over the open technique, with shorter hospital stays and lower complication rates *(Kingler, 1998; Golub, 1998; Sauerland, 1998; Chung, 1999; Garbutt, 1999)*. Pediatric studies soon echoed these findings *(Jen, 2010; Markar, 2012; Svensson, 2016; Fadgyas, 2021)*. Similarly, our study observed shorter hospital stays but no significant differences in complication rates, fully aligning with international literature. Initially, laparoscopic procedures were performed mainly for uncomplicated appendicitis (UCAA) cases, with trainees sometimes converting to open surgery. As experience grew, laparoscopic management expanded to complicated appendicitis (CAA) cases, and conversion rates decreased dramatically by 2020. Interestingly, during the COVID-19 pandemic, international recommendations led to a temporary preference for open surgery due to the risk of aerosolizing SARS-CoV-2 during laparoscopic desufflation. Our hypothesis - that laparoscopic appendectomy offers advantages over open surgery - was confirmed: hospital stays were shorter with no difference in complication rates, indicating that both techniques are equally safe. However, the trend toward shorter hospitalizations likely also reflects broader perioperative improvements, such as the implementation of ERAS (enhanced recovery after surgery) protocols.

III. Learning Curve of Laparoscopic Appendectomy

As mentioned previously, laparoscopic infrastructure improvements at the Institute enabled an increasing number of minimally invasive surgeries. The real breakthrough came in 2017 with significant investments in equipment and training. As a result, almost all appendectomies, including those performed during night shifts, became laparoscopic. Today, laparoscopic appendectomy and laparoscopic inguinal hernia repair (PIRS – Percutaneous Inguinal Ring Suturing) are among the standard training procedures for pediatric surgery residents in Hungary *(Ussia, 2021; Mán, 2016; Fadgyas, 2023).* Initially, there was resistance among support staff, who perceived laparoscopic surgery as longer. However, data showed that even in the early learning phase (2016), laparoscopy was sometimes faster than the open approach. From the outset, the goal was to achieve shorter hospital stays and no increase in complication rates, which was supported by numerous studies *(Jen, 2010; Markar, 2012; Svensson, 2016; Masoomi, 2012; Gosemann, 2016).* The study confirms that a surgical unit can easily and successfully transition to a new minimally invasive technique, especially when its efficacy has already been validated elsewhere and a sufficient surgical volume is available.

Interestingly, the learning curve was influenced by the age of the operating surgeon: older surgeons nearing retirement tended to prefer open surgery, whereas younger surgeons opted for laparoscopy even in unexpected situations (e.g., bleeding or unusual anatomy), sometimes by adding an extra port *(Garai, 2019)*. Thus, our hypothesis—that the learning curve for laparoscopic appendectomy is short and worthwhile—was confirmed, as an entire pediatric surgery department transitioned to minimally invasive appendectomy within about a year.

IV. Impact of the COVID-19 Pandemic on Pediatric Appendicitis

The study investigated acute appendicitis cases during the first two waves of the COVID-19 pandemic (2012–2020 period). While Hungary was more seriously affected during the second wave in autumn 2020, spring lockdowns already disrupted normal patient pathways and surgical care. Planned surgeries were suspended, and pediatric appendectomies initially reverted to the open approach to minimize the risk of SARS-CoV-2 aerosolization *(English, 2020)*.

In some countries, the incidence of pediatric appendicitis decreased *(Zvizdic, 2021; Tankel, 2020)*, but no such change was observed at the study center. However, the proportion of complicated (perforated) cases increased, consistent with international trends *(La Pergola, 2020; Orthopolus, 2020; Snapiri, 2020)*. Notably, this trend had already been observable since 2015, suggesting that it is unrelated to the pandemic.

No correlation was found between the monthly distribution of complicated cases and the domestic pandemic situation (high rates were seen both in January and December). The cause of the higher perforation rate among SARS-CoV-2-positive patients remains unclear, and the small sample size limits interpretation. However, it is likely not related to delays in patient pathways, as for other emergency conditions (e.g., testicular torsion), patients were operated on even earlier than before *(Fadgyas, 2023)*. An additional diagnostic challenge during the second wave was MIS-C (Multisystem Inflammatory Syndrome in Children), which may have delayed surgical decisions, contributing to a higher perforation rate *(Fadgyas, 2022)*.

Further research is necessary to fully understand the underlying causes of the increased incidence of perforated appendicitis during the pandemic.

In conclusion, a strong correlation was identified between the surgeon's intraoperative assessment and the pathologist's findings regarding the severity of pediatric acute appendicitis at one of Hungary's largest pediatric surgical centers. This enables the surgeon to adequately plan postoperative management directly at the operating table, immediately following the procedure. However, in cases where the surgeon underestimated the severity, a higher rate of complications and longer hospital stays were observed. Our hypothesis - that the intraoperative surgical evaluation would correlate with the later histopathological results concerning the severity of acute appendicitis - was confirmed.

The study analyzed acute appendicitis cases from Hungary's and Central Europe's largest pediatric center across two distinct decades and from multiple perspectives. One limitation of the study is its retrospective nature. Consequently, no power analysis could be performed, as parameters outside the chosen periods could not be influenced. To achieve stronger and more valid correlations, the aim was to select long but surgically homogeneous periods for analysis. Therefore, the fundamental questions of the thesis were examined over two ten-year intervals. Thanks to this approach, more than a thousand patients were included in each period, ensuring statistically robust results, even when broken down into subgroups. Another limitation is that data was collected from a single center. Additionally, a randomized prospective study would have provided stronger statistical conclusions when comparing different surgical techniques. However, by the time the center transitioned to routine laparoscopic surgery, relevant studies had already been published. Thus, randomizing patients to undergo the older, open surgical technique - with its known disadvantages - would have raised significant ethical concerns.

New Findings and Conclusions of the Thesis

1. Complicated acute appendicitis occurs more frequently in younger children (0–7 years) than in older age groups. Although not statistically significant, the occurrence of complicated cases was slightly lower in the more recent decade (2011–2020) compared to the earlier period (1976–1985).

2. Today (2011–2020), fewer appendectomies are performed for non-inflamed appendices, and overall, fewer surgeries are carried out in younger children compared to earlier decades (1976–1985). However, a higher incidence of late complications is now observed.

3. The transition from open to laparoscopic appendectomy can be achieved rapidly. Even during the initial learning phase, the known advantages of laparoscopy (shorter hospital stay, comparable complication rates) were already evident.

4. During the first waves of the COVID-19 pandemic, the proportion of perforated appendicitis cases increased compared to previous years.

5. Based on the largest patient population and the longest observation period in the literature, a significant and strong correlation was found between intraoperative surgical and histopathological assessments, both for laparoscopic and open appendectomies. In cases where the severity was underestimated by the surgeon, higher complication rates and longer hospital stays were noted.

List of publications and other publications serving as the basis for the thesis, scientific indicators

Number of publications related to the topic of the dissertation: Total impact factor of the above publications: D1:-, Q1:-, Q2:1, Q3:-, Q4:3	5 (5 first author) **3,607**
Number of published scientific papers: Aggregated impact factor of the above publications: D1:-, Q1:2, Q2:2, Q3:-, Q4:6	34 (27 first author) **16,477**
Independent citations in MTMT: https://m2.mtmt.hu/frontend/#view/Citation/SmartQuery/1028/	**32**
Citations in Google scholar: https://scholar.google.com/citations?view_op=list_works&hl=hu&user=qMfaVJcAAAAJ Hirsch index: 4	**69**

Publication and papers accepted for congresses (IF: 3,607)

- Fadgyas B, Monostori G, Ori D, et al. Appendicitis in children: correlation between the surgical and histological diagnosis. Pediatr Surg Int. 2024; 40(1): 262. doi: 10.1007/s00383-024-05846-2. PMID: 39367226. **(IF:1,5 Q2)**
- Fadgyas B, Garai GI, Monostori G, et al. Appendicitis in Childhood: What has Been Changed in the Last Few Decades in Central-Europe? Surg Med Open Acc J. 2024; 5(5). SMOAJ.000624. 2024. DOI: 10.31031/SMOAJ.2024.05.000624
- Fadgyas B., Garai GI, Őri D, et al. Appendectomy in children: laparoscopic or open approach? [HUN] Orv Hetil. 2024; 165(19): 742–746. doi: 10.1556/650.2024.33056. **(IF: 0,8 Q4)**
- Fadgyas B, Garai GI, Ringwald Z, et. al. Laparoscopic appendectomy in children. Evaluation of the learning curve [HUN]. Orv Hetil. 2022; 163(25): 1001–1004. **(IF: 0,6 Q4)**
- Fadgyas B, Garai GI, Ringwald Z. How COVID-19 pandemic influences paediatric acute appendicitis cases? [HUN] Orv Hetil. 2021; 162(16): 608–610. **(IF: 0,707 Q4)**
- Fadgyas Balázs, Monostori Georgina, Őri Dorottya, Vajda Péter: Appendicitis in children: correlation between the surgical and histological diagnosis. HAP Young Surgeons' Forum, 2025, Budapest, Hungary (3. price)
- Fadgyas B, Őri D, Vajda P: Effect of the COVID-19 pandemic on the complicated acute appendicitis in children. WOFAPS congress 2022, Prague
- Fadgyas B, Gácsi LJ, Monostori G, et al. Appendicitis in children: correlation between surgical and histological findings WOFAPS congress 2022, Prague

- Fadgyas B, Garai GI, Monostori G, et al. Appendicitis in childhood: what has been changed in the last few decades? WOFAPS congress 2022, Prague
- Fadgyas B, Gácsi LJ, Monostori G, et al. Appendectomy in children. Is it still questionable whether laparoscopic or open? ESPES congress, Barcelona, 2022.
- Fadgyas B, Őri D, Vajda P. How COVID-19 pandemic influences paediatric acute appendicitis cases? MGYT, Kecskemét, 2022.
- Fadgyas B, Garai GI, Monostori G et al. Appendicitis in Childhood: What has Been Changed in the Last three Decades HAPS, Young Surgeons Forum, Szeged, 2021.
- Fadgyas B: How COVID-19 pandemic influences paediatric acute appendicitis cases? HAPS, Young Surgeons Forum, 2021.
- Fadgyas B, Monostori G, Gácsi LJ, et al. Appendectomya: is it better via laparoscopy? Visegrád, 2019.
- Fadgyas B, Sinkovits Gy, Garai GI: Laparoscopic appendectomy in children: experience of the first 2 years in a Central European National Institute, ESPES Brussels, 2018.
- Fadgyas B, Monostori G, Gácsi LJ, et al. Appendicitis in child: what has changed during the last 30 years? HAPS, Szeged, 2017.

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