

Obesity and Appendicitis In Childhood

Philosophy Doctor (Ph.D) Thesis of

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Abbreviation

AUC – Area Under ROC Curve

FN – False negative

FP – False positive

BMI – Body Mass Index

CRP – C-reactive protein

CT – Computer tomography

WBC – White blood count

IL-1 β - Interleukin 1 β

IL1R – Soluble receptor of Interleukin 1

IL-6 – Interleukin 6

iv. – via intra vein

mg/kg – Milligramm/body kilogram

MRI – Magnetic Resonance Imaging

Neu - Percentage of Neutrophil in the blood

NOTES – Natural Orifice Transluminal Endoscopic Surgery

NPV – Negative predictive value

po. – via per os

POT – Primary omental torsion

PPV – Positive predictive value

ROC curve – Receiver operating characteristic curve

SD – standard deviation

STEP port – laparoscopic port (radially expanding system)

HNA: Histologically negative appendectomy

TNF α - Tumor necrosis factor α

TNF R – Soluble receptor of tumor necrosis factor α

US – Ultrasound

VAS – Visual analog scale

TN – True negative

TP – True positive

WHO – World Health Organization

Introduction

Obesity in childhood

During the past two decades, the incidence of childhood obesity has increased and alarming rates throughout the world. The medical community has started to see the consequences of childhood obesity. Half of new diagnosis of type 2 diabetes are made in children younger than 18. Increased rates of asthma, hypertension and obstructive sleep apnea have also been linked to this trend, among multiple illnesses. The incidence of childhood obesity is now 23% in Hungary, 27% in Ireland and 32% in USA, however it was twenty years ago only 4% in USA and 6-6% in Hungary and Ireland.

The reason of childhood obesity is still a question and many of studies have been carried out this topic. They speculate that the increased food intake (especially chunk food) and decreased physical activity are the main reasons.

The definition of obesity is currently based on the body mass index (BMI- weight in kilograms divided by height in meters squared) in adults. For children, BMI varies considerably with age, so generally the BMI of a child is compared with the BMI of a reference population of children of the same sex and age. In adults, the cutoffs to define obesity or overweight are based on fixed BMI values related to health risk. In children, there are no risk-based fixed values of BMI used to determine overweight, because it is unclear what risk-related criteria to use. Consequently, a statistical definition of overweight based on the 85th and 95th percentiles of BMI-for-age in a specified reference population is used in childhood.

Obesity is associated with a variety of physiological changes that may impair a patient's response to surgery, including impairment of cardiac, pulmonary and immune functions. Not surprisingly, then, within adult surgical population, obesity has been shown to be associated with increased risks of complications and technical difficulties during and after operative procedures. However, these concerns have not been addressed in the pediatric surgical literature. With the rising rates of childhood obesity, pediatric surgeons must appreciate differences in the management and outcomes of these patients.

Appendicitis in childhood

Appendicitis is the most common surgical emergency in childhood and it occurs approximately 1-4 per 1000 children per year. About one third of patients with abdominal pain have appendicitis.

Many terms have been used to describe the varying stages of appendicitis, including acute appendicitis, suppurative appendicitis, gangrenous appendicitis and perforated appendicitis. These distinctions are vague, and only the clinically relevant distinction of simple and complicated appendicitis can be made. Because gangrenous appendicitis represents dead intestine that functionally acts as a perforation.

The diagnosis of acute appendicitis sometimes can be difficult. Initially the patient may describe mild gastrointestinal symptoms before the onset of pain, such as decreased appetite, indigestion or subtle changes in bowel habits. Typical early visceral pain is nonspecific in the periumbilic region. The continued distention of the appendiceal wall elicits nausea and vomiting, which typically follows the onset of right lower abdominal pain within a few hours.

The clinical presentation of appendicitis can be understood in terms of its pathophysiology. Appendicitis results from luminal obstruction followed by infection. Although it is clear that luminal obstruction causes appendicitis, the cause of the obstruction is not always clear. Fecaliths often play a role and fecaliths can be surgically found in approximately 20% of children with acute appendicitis and are reported in 30-40% of children with perforated appendicitis. The presence of fecaliths can often be documented radiographically. Parasitic infections, foreign bodies and carcinoid tumors also can lead to luminal obstruction of the appendix.

The obstructed appendix is a perfect breeding ground for the trapped bacteria. As intraluminal pressure increases, lymphatic drainage is inhibited, leading to further edema and swelling. Finally, the increase in pressure causes venous obstruction, which leads to tissue ischemia, infarction and gangrena. Bacterial invasion of the wall of the appendix then occurs. Fever, tachycardia and leukocytosis develop as a consequence of mediators released by ischemic tissues, white blood cells and bacteria. When the inflammatory exudate from the appendiceal wall contacts the parietal peritoneum, somatic pain fibers are triggered and the pain localizes

near the appendiceal site, most typically at McBurney's point. With a retrocecal or pelvic appendix, this somatic pain is often delayed because the inflammatory exudate does not contact the parietal peritoneum until rupture occurs and infection spreads. Further breakdown of the appendiceal wall leads to perforation with spillage of infected intraluminal contents with localized abscess formation or generalized peritonitis.

The routine use of rectal examination in the diagnosis of appendicitis has been questioned. Pain during this examination is nonspecific for appendicitis. It is rather unpleasant for children and there is a wide range of laboratory and imaging modalities available to contribute to the decision making in case a surgical intervention is necessary.

If appendicitis is allowed to progress, either diffuse peritonitis and shock or shock will occur or the infection will become isolated and an abscess will be created. Diffuse peritonitis is more common in infants, probably because of the absence of omental fat. Older children and teenagers are more likely to have an organized abscess.

Many hospitals place particular emphasis on a careful and unhurried physical examination in patients with suspected appendicitis. If doubt and concern still exist then the child is sedated and re-examined some hours later by same surgeon. This management has been termed active observation. It was found that this approach is safe and efficient. A recent report demonstrated that this type of management decreased the negative appendectomy rate, the duration of hospitalization and associated cost without causing extra complications.

There is no specific laboratory test for acute appendicitis. Every studies, which we are using, are non-specific and were made for the detection of inflammation.

Total leukocyte and neutrophil counts have been extensively investigated. The sensitivity of an elevated leukocyte count ranges from 52% to 96% and that of a left-shifted neutrophil count from 39% to 96%. The latter is of better diagnostic value. However, normal leukocyte count occurs in 5% of patients with appendicitis.

Positive values for C-reactive protein (CRP), Interleukin-6 (IL6) and the erythrocyte sedimentation rate are useful, but negative values do not necessarily rule out the disorder. However, combination of all these tests may be the most helpful.

During the past three decades, the diagnostic accuracy of the radiographic and radiopharmaceutical studies have increased.

Plain radiography can be helpful. Fecaliths are present in 10-20% of patients and are indicative for surgery even when symptoms are mild. A chest radiograph to rule out pneumonia may be indicated.

In skilled hands, ultrasonography (US) has proved to be an effective diagnostic aid. Most studies demonstrate a sensitivity greater than 85% and a specificity greater than 90%. Demonstration of a noncompressible appendix that is 7mm or larger in anteroposterior diameter is the primary criterion for the diagnosis. The presence of an appendicolith is helpful. In progressed cases, localized periappendicular infiltratum or abscess also can be seen and can be monitored the progress of conservative treatment.

In the past decade, computed tomography (CT) has become more widely used in the diagnosis of appendicitis. The sensitivity of CT scan is over 90% and its specificity is over 80%. However, the use of CT as a routine diagnostic method in paediatric population with suspected appendicitis has to be carefully considered because of exposure to ionising radiation.

Magnetic Resonance Imaging (MRI) is also a useful method in the diagnosis of appendicitis. The advantages of MRI are the same as CT without ionizing radiation. However, MRI investigation is more expensive and much less machine is available in use.

The use of antibiotics for the treatment of appendicitis is clearly beneficial. Therefore, there has recently been an increase in the use of antibiotic therapy as primary treatment for acute appendicitis. Although a nonsurgical approach in appendicitis can reduce the complications rate, the lower efficacy prevents antibiotic treatment from being a viable alternative to surgery.

Early appendectomy has been the treatment of choice for acute appendicitis. There is a trend away from performing immediate operation, including procedures done in the middle of the night.

Both open and laparoscopic appendectomy has an advantage and disadvantage. Advantages of laparoscopic appendectomy claimed include shorter hospitalizations, decreased postoperative pain, decreased wound complications, increased ability to diagnose uncertain cases, surgical ease

in an obese patient, and faster recovery. Disadvantages of these are a higher cost because of equipments needs, increased training and experience required for surgeons and ancillary support staff. Although the conclusions regarding the advantages of minimal invasive technique over the open technique vary widely, especially in children, laparoscopic appendectomy seems to be a safe and effective means of performing an appendectomy.

Every surgical procedure can develop with complication. Complications of appendectomies include wound infection, intra-abdominal abscess formation, postoperative intestinal obstruction, prolonged ileus, and rarely enterocutaneous fistula. Wound infection is the most common complication, but the rate has fallen from 50% to less than 5%, even in complicated appendicitis using antibiotics. Sepsis and multisystem organ failure can occur in children who had prolonged illness before diagnosis.

Aims of the study

In adults, the relations between obesity and appendicitis has been investigated, however there have been no previous studies analyzing the special characteristics of appendicitis in very obese children. The purpose of this study was to determine the relationship between obesity and appendicitis:

- Are the age and gender a risk factors associated with histologically normal appendix in children undergoing emergency appendectomy for suspected appendicitis?
- Is there any difference in the incidence of histologically normal appendix in obese and non-obese children undergoing emergency appendectomy for the clinical diagnosis of acute appendicitis?
- Is there any special disease in obese patient, which can mimic acute appendicitis?
- Is there any different in the inflammatory markers between very obese and non-obese children presenting with acute appendicitis?
- Which operative techniques (open or laparoscopic) are associated with better surgical outcomes in very obese children? Which one is recommended for obese children?

Methods

The hospital and histological records of 1,228 consecutive patients, who underwent appendectomy for acute appendicitis, were retrospectively analyzed from January 2000 to December 2008 at The National Children's Hospital, Dublin. Appendectomy was performed when there was a high clinical suspicion of acute appendicitis, based on clinical symptoms and signs. Those patients, who had diagnostic laparoscopy with appendectomy, were excluded from this study. US and CT was performed only when the clinical findings were equivocal. The following parameters were studied: incidence of acute suppurative appendicitis, perforation rate and the rate of negative appendectomies, and incidence of other pathologies both in very obese and non-obese children.

The deviation of the standardized mean weight for age was calculated retrospectively in each child. Very obese was defined as greater than 2 standard deviations above the standardized

mean weight for age. Those patients who were obese or overweight (greater than 1.5 and less than 2 standard deviation above the standardized mean weight for age) were excluded from this study.

Appendix histology was divided into three groups: histologically negative, suppurative and perforated appendicitis. Acute appendicitis was defined as the presence of transmural inflammation of appendix. Negative appendectomy was defined as the state in which appendectomy was performed on a clinical diagnosis of acute appendicitis but the appendix was found to be normal on histopathological examination. Perforated appendectomy was based on the operating surgeon's macroscopic evaluation and verified by the histological findings.

All ultrasounds were done by experienced pediatric radiologist. The sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) of ultrasound were calculated using the histology results as a gold standard.

CT was performed only in few, selected cases. Therefore the results of CT in obese and non-obese children were not included in this study.

CRP, white blood count (WBC) and neutrophil count (Neu) levels and histological reports of appendices both in very obese and non-obese children were recorded. CRP levels were measured using the immunoturbidimetry method with a normal level of 0.9 mg/dL or less. The WBC and Neu were measured by an automated hematology analyser. The upper limits of the reference interval for WBC count and Neu percentage were $10.5 \times 10^9 /L$ and 75% respectively.

The length of hospital stay (LOS), operation time (OT), complication rate and frequency of taking postoperative pain reliefs were compared between open and laparoscopic appendectomy in very obese children and between appendectomy in obese and non-obese children.

The postoperative care was the same in every operation. A normal diet was given soon after surgery and patient can be discharged 1 day after surgery. The hospital stay was only depended on the patient condition. Iv morfin pump was used in every child in the first 24 hour postoperatively, and then, when children complained for pain, non-steroid painkillers were

given. Therefore the frequency of taking postoperative pain relief was only depended on the child's pain.

The operation time was defined as the time between starting to the finishing of anaesthesia. The LOS was measured in days postoperatively, including complications. The postoperative pain was measured by recording the frequency of taking postoperative pain relief when there was no difference in the pain management between the two groups.

Statistical analysis was performed using MedCalc statistical software (Version 9.6.4.0). Differences in patient characteristics and outcomes between laparoscopic and open groups were analyzed using 2-sample *t* test. For categorical data, differences were obtained by 2-sample *Z* tests. For postoperative LOS, operating time and postoperative analgesia required, the Mann–Whitney *U* test was used to assess differences by incision type. The results of US were analyzed using a Chi-square test. A calculated *P* value of less than 0.05 was considered as significant.

The sensitivity, specificity, positive and negative predictive value of CRP, WBC and Neu were calculated both in very obese and non-obese children group using the histology results as a gold standard. Receiver operating characteristic (ROC) curve was constructed for CRP, WBC and Neu. The ROC curve, which is defined as a plot of test sensitivity as the y coordinate versus its 1-specificity or false positive rate (FPR) as the x coordinate, is an effective method of evaluating the performance of diagnostic tests. The ROC curve is also helpful when we want to compare the diagnostic accuracy of two or more tests. It helps in deciding which of the tests is better for the purpose for which they are being used. The optimal ROC curve is the one connecting the points highest and farthest to the left. The rationale for the optimal ROC curve is that one wants the highest true-positive rate (sensitivity) for the lowest false-positive rate. Area under curve (AUC) is a measure of the overall performance of a diagnostic test and is interpreted as the average value of sensitivity for all possible values of specificity. The overall diagnostic performance of different tests can be compared by their AUCs with Wilcoxon-rank sum test. The bigger its AUC is the better the overall performance of the diagnostic test.

Results

Of the 1,228 children, 207 (16.9%) were very obese and 1,021 (83.1%) were non-obese. Among the non-obese children, 612 (59.9%) children were male and 409 (40.1%) were female. The mean age at presentation in non-obese children was 10.6 years. Among the very obese children, 113 (54.6%) children were male and 94 (45.4%) were female. The mean age in very obese children at presentation was 10.5 years. One hundred and two (9.9%) of the 1,021 non-obese children were found to have a histologically normal appendix compared to 51 (24.6%) of the 207 very obese children who had histologically normal appendix ($P < 0.001$). The negative appendectomy rate was significantly higher in female children (17.2 and 34.6%) than in males (6.4 and 17.4%), both in non-obese and obese children, respectively ($P < 0.001$).

Perforation of appendix was seen in 256 (25.1%) of the 1,021 non-obese patients and 32 (15.5%) of the 207 very obese patients. The perforation rate was significantly higher ($P < 0.0001$) in the non-obese (25.1%) children group compared with the very obese (15.5%) patients. Faecolith was detected in 41 of the 256 non-obese perforated appendixes and in 2 of the 32 obese appendixes. The difference in the rate of luminal faecolith was found to be significantly higher in non-obese (16%) patients than in very obese (6.26%) patients ($P < 0.001$).

The incidence of negative appendectomy was significantly higher in school age children compared to preschool age children (9.1% and 9.9% vs 5.1%, $p < 0.05$). Multi- and univariate analysis revealed that age ($p < 0.0001$) and gender ($p = 0.0003$) were the significant independent risk factors associated with histologically normal appendix in children.

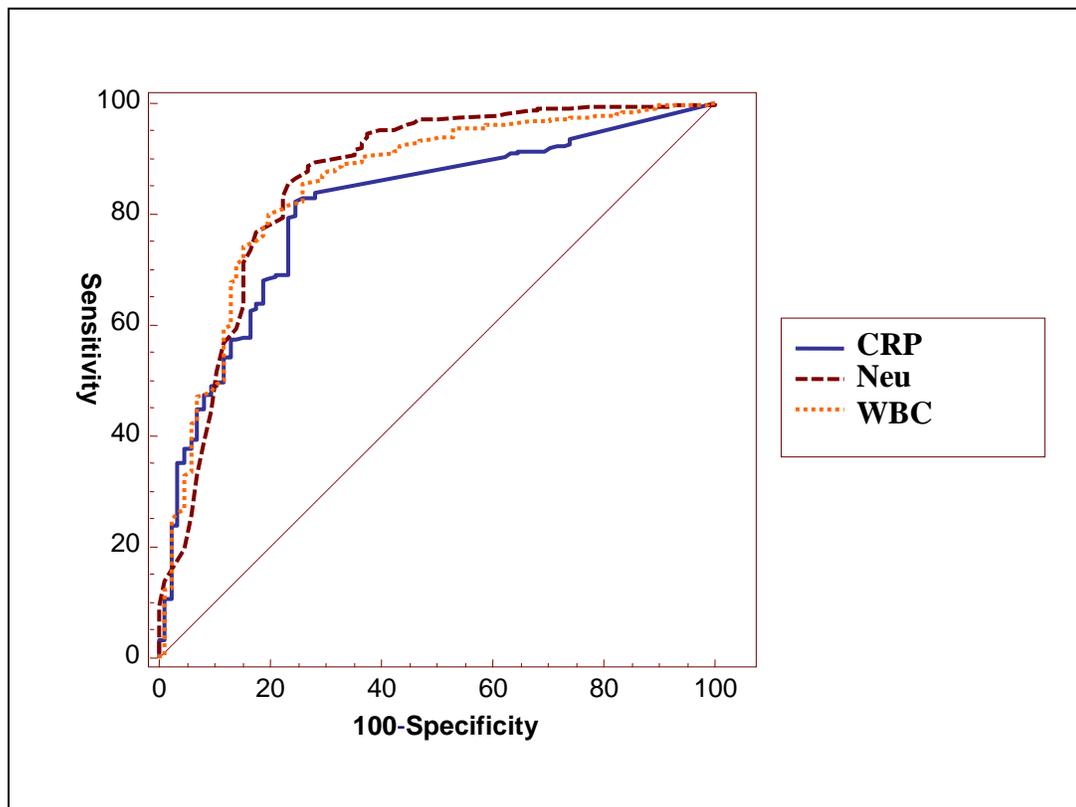
Carcinoid tumor was present in 4 patients (0.32%). Appendiceal diverticulitis was seen in 3 patients (0.24%). Two children (0.2%) had primer omental torsion and one child (0.1%) showed Crohn's disease on appendiceal history.

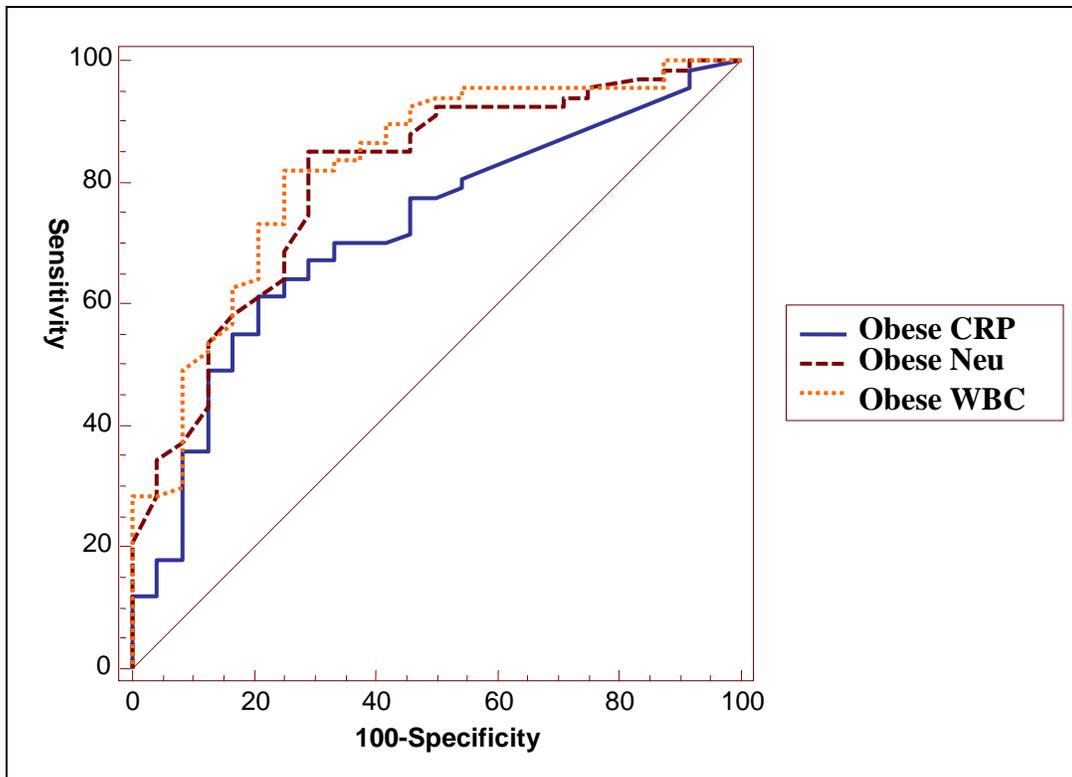
Three hundred and ninety-eight (39%) of the 1,021 non-obese and 77 (37%) of 207 very obese children had ultrasound preoperatively. The false positive rate of US (6 vs. 26%) was significantly higher ($P < 0.05$) in very obese children group. The specificity, sensitivity, PPV and NPV of ultrasound were also significantly lower in the very obese children group than in the non-obese group.

The mean CRP levels were significantly higher in very obese children with histologically normal appendix compared to non-obese children with normal appendix (15.1 vs. 3.6, $P < 0.001$). There were not any differences in the mean WCC levels and leukocyte count between very obese and non-obese children group.

The specificity and the positive predictive value of CRP were significantly lower in the very obese children group than in the non-obese group (50 vs. 69.66%; 84.14 vs. 95.2%, $P < 0.001$). There were not any differences in the predictive value of WCC and Leukocyte count between very obese and non-obese children group.

Receiver operating characteristic (ROC) curve was constructed for CRP, WBC and Neu. Among the non-obese children, the diagnostic accuracy of CRP, WCC and Leukocyte count were similar. In the very obese children group, the diagnostic accuracy of CRP was lower compare to the diagnostic accuracy of WCC and Leukocyte count.





Area under curve (AUC) is a measure of the overall performance of a diagnostic test and is interpreted as the average value of sensitivity for all possible values of specificity. The overall diagnostic performance of different tests can be compared by their AUCs. Among the non-obese children the AUC of CRP, WCC and Leukocyte count were similar. In very obese children, WCC and Neutrophil count had significantly better diagnostic value than CRP. Between non-obese and very obese patients, there were significant differences in CRP diagnostic value.

With ROC curves in 95% likelihood ratio, we can determine the optimal cut-off point in each test. The cut-off point of CRP was significantly higher in very obese children group, than in non-obese.

Fifty-two of 207 (25.1%) very obese patients had open appendectomy and 155 (74.8%) underwent laparoscopic appendectomy. Among the open appendectomy group, 27 (51.9%) children were male and the mean age at presentation was 10 years. Among the laparoscopic

appendectomy group, 81 (52.2%) children were male and the mean age at presentation was 10.6 years.

The perforation of appendix was seen in 8 of the 52 (15.38%) open appendectomy group and 23 of the 155 (14.8%) in laparoscopic appendectomy group. The incidence of histologically normal appendix was similar both in open appendectomy (23%) and laparoscopic appendectomy (24.5%) group.

The length of hospital stay was 2.82 days after open and 2.75 days after laparoscopic appendectomies. Compared to open appendectomy, we have found that the operating time was significantly shorter in the laparoscopic appendectomy group (46.8 min) than in open appendectomy group (59.87 min, $P < 0.05$).

The required postoperative analgesia was 6.97 occasions in the open appendectomy group and 4.73 in the laparoscopic appendectomy group. Laparoscopic appendectomy is associated with significantly lesser postoperative analgesia requirement ($P < 0.05$).

In laparoscopic appendectomy, the overall complication rate was 4.5%. Four of 155 (2.5%) children developed wound infections and 3 of 155 (2%) had postoperative intraabdominal collections which was treated conservatively. Among those who underwent open appendectomy, 4 of 52 (7.7%) patients had postoperative complications: wound infections in 3 (5.8%) and intraabdominal collections in 1 (1.9%). The overall postoperative complication and especially the wound infection rate were significantly lower in the laparoscopic appendectomy group than in the open appendectomy group ($P < 0.05$).

Between non-obese and very obese children there was no difference in the surgical outcomes of negative and suppurative appendectomy cases. The low number ($n=9$) of the open appendectomy in the very obese children group prevented us to make statistical analysis, however, the open appendectomy seems to be associated with worsen surgical outcomes in very obese children group compare to non-obese children.

In the laparoscopic complicated appendectomy group, obesity was associated with significantly longer length of hospital stay (7.1 days vs 10.2 days, $P < 0.05$). Among the non-obese children the mean operation time was 45.8 minutes and it was 50.1 minutes in the very

obese children group. The mean operation time was significantly higher in the very obese children group than in non-obese ($P < 0.05$).

The required postoperative analgesia was 6.5 occasions in the non-obese group and 7.8 in the very obese group. Obesity is associated with significantly more postoperative analgesia requirement ($P < 0.05$).

In the non-obese children group, the overall complication rate was 6.1%. Six of 164 (3.6%) children developed wound infections and 4 of 164 (2.5%) had postoperative intraabdominal collections which was treated conservatively. Among those who were very obese, 4 of 23 (17.3%) patients had postoperative complications: wound infections in 2 (8%) and intraabdominal collections in 2 (8%). The overall postoperative complication, the wound infection and the postoperative intraabdominal abscess rate were significantly higher in the very obese children group than in the non-obese children group ($P < 0.05$).

Discussion

During the past two decades, the incidence of childhood obesity has increased at alarming rates throughout the world. Obesity as a risk factor affecting the perioperative and operative outcomes of surgery has been well documented in adults. However, there is a little information on the outcome of surgical procedures in obese children.

The incidence of histologically normal appendixes in patients presenting clinically with suspected appendicitis ranges from 7.7% to 54%. In the present study, we investigated the incidence of histologically normal appendectomy in very obese children. There have been no previous studies analyzing the incidence of normal appendectomy in very obese children undergoing appendectomy for clinically suspected appendicitis. The findings of our study clearly indicate that the incidence of normal appendectomy is significantly higher in very obese children compared to non-obese children.

The relation between age and normal appendectomy has not been investigated to date. It is well known that the perforation rate in preschool children is higher than in school age children. Delayed presentation and misdiagnosis are frequent occurrences in this age group, and have resulted in perforation rates excess of 90%. Anatomic immaturity, in particular the lack of an adequate omental barrier, may contribute to the rapid progression to perforation and peritonitis in these patients. Our data show that school age female children are more likely to have negative appendectomy when operated for suspected appendicitis. This observation deserves special attention during decision making in clinical diagnosis and treatment in school age girls with suspected appendicitis.

The diagnosis of appendicitis in very obese patients can be difficult and challenging. This is primarily due to the fact that the physical examination in obese patients may be more difficult. Several authors have advocated the use of different imaging techniques such as ultrasonography (US), computer tomography (CT) and magnetic resonance imaging (MRI) in obese adults with clinically suspected appendicitis. Ultrasound has been shown to be less effective in diagnosing appendicitis in obese patients. The negative influence of obesity on the detection rate of the appendix on US in adults even for a skillful and experienced radiologist has been reported. Some

authors have recommended CT and MRI in obese patients with inconclusive clinical presentation and ultrasound findings. However, the use of CT as a diagnostic method in pediatric population with suspected appendicitis has to be carefully considered because of exposure to ionizing radiation

Our ultrasound results highlight the importance of considering obesity when interpreting the significance of ultrasound results in children with suspected diagnosis of appendicitis. The significantly higher false positive rate of ultrasound and the difficult physical examination in very obese children may cause the significantly higher incidence of normal appendectomy.

Many pediatric surgeons place particular emphasis on a careful, unhurried and repeated physical examination in patients with suspected appendicitis. If doubt and concern still exist then the child is sedated and re-examined some hours later by the same surgeon. This management has been termed active observation. A recent report demonstrated that this type of management decreased the negative appendectomy rate, the duration of hospitalization and associated cost without causing extra complications. We believe that active observation may reduce the incidence of negative appendectomies in very obese children without increasing the incidence of complicated appendicitis.

Obesity and conditions which can mimic acute appendicitis have been reported. Obesity causing irregularly distributed accumulations of excess omental fat has been cited as a predisposing of primary omental torsion. A recent report postulated that increased fat deposit in obese children outstrips the blood supply to the developing omentum, leading to either relative ischaemia as inciting event, increased omental weight leading to torsion, or traction to the most distal parts of the omentum. The heavily fat-laden omentum in these obese children predisposes the omentum to twist around its long axis, leading to vascular compromise, infarction, and gangrene.

In acute inflammation such as acute appendicitis, the acute phase response develops. These conditions cause release of interleukin-6 and other cytokines that trigger the synthesis of CRP and fibrinogen by the liver. During the acute phase response, levels of CRP rapidly increase within 2 hours of acute insult, reaching a peak at 48 hours. With resolution of the acute phase

response, CRP declines with a relatively short half-life of 18 hours. CRP binds to phosphocholine on microbes. It is thought to assist in complement binding to foreign and damaged cells and enhances phagocytosis by macrophages (opsonin mediated phagocytosis), which express a receptor for CRP. It is also believed to play another important role in innate immunity, as an early defense system against infections. The role of CRP levels in non-obese patients with appendicitis has been extensively studied and found to be useful for the diagnosis of appendicitis. To our knowledge, this is the first study analyzing the relationship between CRP levels and very obesity in children presenting with suspected appendicitis. We found that mean CRP levels were significantly higher in very obese children with histologically normal appendix compared to non-obese children with normal appendix.

Visceral fat is known to be an important endocrine organ that is involved in the complex interrelationship between obesity and systemic inflammation. It is a major contributor to the elevated levels of a number of inflammatory proteins. Increased IL-6 secretion from visceral fat into the portal circulation stimulates hepatic production of acute-phase proteins such as CRP, causing systemic low-grade inflammation in overweight children and adults. Elevated CRP concentration in histologically proven normal appendixes in obese patients is the result of higher false positive rate of CRP. Therefore, CRP has significantly lower specificity and positive predictive value in obese group than in non-obese group. These data suggest that CRP is not a reliable marker of inflammation in obese children presenting with suspected appendicitis. Our data highlight the importance of considering obesity when interpreting the significance of an elevated CRP level in children with suspected diagnosis of appendicitis.

The relation between obesity and WBC and Neu has been investigated in adults and found to be significantly elevated compare to normal body weights patients. This relation has not been investigated in children. Interestingly, we did not found difference in WBC and Neu count levels between non-obese and very obese children.

Obesity as a risk factor affecting the perioperative and operative outcomes of surgery has been well documented in adults. However, there is a little information on the outcome of surgical procedures in obese children. In the present study, we investigated to compare appendectomy in non-obese and very obese children and open versus laparoscopic appendectomy in very obese

children. The findings of our study has shown that laparoscopic appendectomy for acute appendicitis in very obese children is associated with significantly shorter operating time, lower overall complication rate and lesser postoperative analgesia requirement. We also shown that in very obesity in childhood, appendectomy performed for complicated appendicitis is associated with a longer length of hospital stay and higher morbidity.

The length of hospital stay is known to be shorter in laparoscopic appendectomy as compared to open appendectomy due to a quicker recovery. However, in our series, there was no significant difference in length of hospital stay in laparoscopic appendectomy as compared to open appendectomy. This is attributable to the fact that although children who undergo laparoscopic appendectomy mobilize a few hours earlier than those who undergo open appendectomy, this does not affect their length of hospital stay as they are kept in for administration of intravenous antibiotics for perforated appendicitis.

We have found that the operating time was significantly shorter in laparoscopic appendectomy group in very obese children then in open appendectomy group. It is reasonable to conclude that the time to gain access to the abdomen during open surgery is longer in overweight patients due to the greater amount of subcutaneous tissue. The skin incisions made for the open technique probably need to be longer to achieve the same view of the operating field as in patients of normal weight. The technique used to gain access to the abdomen during laparoscopic appendectomy is the same for both obese and non-obese patients.

There is no gold standard for the measurement of postoperative pain. In some studies, pain is measured by recording the required pain relief and in others it is monitored using visual analogue scale (VAS). We analyzed the amount of postoperative pain relief required and found that laparoscopic appendectomy is associated with lesser analgesia requirement in very obese children. Similar results in overweight adults with VAS have been reported. It is generally believed that the laparoscopic technique causes less pain due to the smaller skin incision.

Previous studies suggested that the postoperative complications of wound and intraabdominal infections are reduced in children undergoing laparoscopic appendectomy as compared with open appendectomy. A possible explanation is that in open appendectomies the

appendices are delivered directly through the wound, thereby risking contamination; whereas in laparoscopic surgery this is delivered wither via bag or into a laparoscopic port. In the present study, the complication rate following laparoscopic appendectomy in obese children was significantly lower as compared to open appendectomy. Similar results have been reported in morbidly obese adults.

Between non-obese and very obese children there was no difference in the surgical outcomes of negative and suppurative appendectomy cases. Interestingly very obesity in childhood is associated with a significantly longer length of hospital stay and higher morbidity only in complicated appendicitis cases. However in adults it has been demonstrated that all type of appendectomies is associated with higher morbidity in obese patients.

Limitations of this study include the use of retrospective data. Lack of consistent recording of heights in our patients prevented us from using the more commonly recognized measure of obesity, the body-mass index (BMI). Using ideal body weights is not as precise as using BMI, particularly in children where growth velocity is variable. However, ideal body weights have been a subject of a number of studies and generally well established. Moreover, the prevalence of obesity in our data was similar to a recently reported Irish study in which childhood obesity rates were calculated using BMI.

In conclusion, laparoscopic appendectomy for acute appendicitis in very obese children is associated with significantly shorter operation time, lower overall complication rate and less postoperative analgesia requirement. Laparoscopic appendectomy should be the procedure of choice for the treatment of acute appendicitis in very obese children.

Summary and conclusions

The incidence of normal appendectomy is significantly higher in very obese children compared to non-obese children.

The significantly higher false positive rate of ultrasound and the difficult physical examination in very obese children may cause the significantly higher incidence of normal appendectomy without histologically proven inflammation.

Elevated CRP concentration in histologically proven normal appendices in obese patients is the result of higher false positive rate of CRP. Therefore, CRP has significantly lower specificity and positive predictive value in obese group than in non-obese group. These data suggest that CRP is not a reliable marker of inflammation in obese children presenting with suspected appendicitis.

Compare to non-obese children, appendectomy performed for complicated appendicitis in very obese children is associated with a longer length of hospital stay and higher morbidity.

Compare to open appendectomy, laparoscopic appendectomy for acute appendicitis in very obese children is associated with significantly shorter operating time, lower overall complication rate and lesser postoperative analgesia requirement. Laparoscopic appendectomy should be the procedure of choice for the treatment of acute appendicitis in very obese children.

Publications and presentations

Publications in related with the Thesis:

1. **Kutasy B**, Hunziker M, Laxamanadass G, Puri P. Increased incidence of negative appendectomy in childhood obesity. *Pediatr Surg Int.* 2010 26:959-62
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2. **KutasyB**; LaxamanadassG, PuriP Is C-reactive protein a reliable test for suspected appendicitis in extremely obese children? *Pediatr Surg Int.* 2010 26:123-5.
(IF₂₀₁₀:1.002)
3. **Kutasy B**, Hunziker M, Laxamanadass G, Puri P.
Laparoscopic appendectomy is associated with lower morbidity in extremely obese children. *Pediatr Surg Int.* 2011 May;27(5):533-6.
(IF₂₀₁₀:1.002)
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