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REZUMATUL TEZEI DE DOCTORAT

SCORING IN ACUTE APPENDICITIS IN CHILDREN

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KEY WORDS: Acute appendicitis, Diagnosis, Alvarado score, Samuel score

The PhD thesis includes:

The general part consists of three chapters totaling 48 pages

The personal part consists of four chapters totaling 82 pages

170 bibliographic references

26 figures

78 tables

Note: The tables and figures inserted in the summary of the thesis retain the original numbering in the thesis. The content of the abstract is the one found in the doctoral thesis.

Introduction

Although it is the most common surgical condition of the child, early diagnosis of acute appendicitis, in general and in children, in particular, often remains difficult.

Diagnostic delay or diagnostic errors favor progress towards complications involving increased hospitalization costs, a negative impact on the patient and caregivers, and increased risk of forensic litigation.

On the other hand, early intervention, even before the diagnosis is completed, leads to an increase in the rate of negative appendectomy with unjustified material costs and the exposure of patients to anesthetic and surgical risks that are not negligible.

Ideally, the therapeutic decision should be taken quickly enough to prevent the development of complications, but at the same time be sufficiently argued to limit as much as possible the rate of negative appendectomy.

Considering the polymorphic symptomatology of acute appendicitis in the 1980s, different scoring systems have been imagined to try to improve the diagnosis rate.

Improving imaging means in the 1990s has led to a temporary decrease in interest in scoring systems.

The limits of imaging in the diagnosis of acute appendicitis, both in terms of US (operator dependence, poor performance in the diagnosis of complicated forms and non-inflammatory appendix) and CT (high costs, exposure to ionizing radiation) led to a return interest for scoring systems in the last two decades .

The scores include anamnestic data, symptoms, clinical signs and paraclinical data, to which different diagnostic values are assigned. Depending on the value obtained, a stratification of the patients is made regarding both the risk of acute appendicitis and the therapeutic indications (discharge, clinical follow-up, complementary investigations, immediate surgical treatment).

Scoring systems are fast, simple, non-invasive, repeatable, and do not involve extra costs. They are very useful for doctors in emergency services, for training surgeons, for resource-poor hospitals. Scoring systems seek to minimize subjective physician factors such as professional experience, recent negative experiences in similar cases, fear of litigation, stress.

Chapter I. In the first chapter I made a brief overview of the current knowledge about acute appendicitis in terms of anatomy, physiology, embryology, normal appendix as well as epidemiology, pathophysiology, pathological anatomy and bacteriology of acute appendicitis.

Chapter II. In the second chapter I briefly outlined the current knowledge regarding clinical diagnosis (symptomatology, objective examination, clinical forms) and paraclinic (laboratory examinations, imaging) as well as trends in treatment.

Chapter III. In the third chapter I briefly read Alvarado, Samuel scores, other scores, scores comparisons

Chapter IV. Purpose and objectives

The main goal of the study is the validation of the Alvarado and Samuels scores at the Emergency County Hospital Piatra Neamţ, a hospital with a multivalent emergency service where the child's surgical emergencies are resolved both by general surgery surgeons and pediatric surgeons.

The specific objectives of the paper were as follows:

· Assessing the overall performance of PAS and Alvarado in the diagnosis of acute appendicitis in a number of pediatric patients.

· Accuracy at the optimum CUT POINT defined by Samuel and Alvarado

· Define a CUT POINT that maximizes the performance of scores in the series studied

· Comparing the performance of the two scores by age group

- Potential impact on results (negative appendectomy rate, undiagnosed acute appendicate rate), reduction of imaging exploration needs by applying scores.

Chapter V. Material and Method

The study was conducted on two series of pediatric patients admitted following the diagnosis of acute appendicitis in the General Surgery and Surgery and Pediatric Orthopedics Departments of Neamţ County Emergency Hospital, a hospital that employs a population of approximately 500,000 inhabitants.

-The first series includes patients admitted during the period 01.01.2009 - 31.12.2011, their data being obtained retrospectively

-The second series consists of patients admitted during the period 01.01.2012 - 31.12.2014, their data being obtained prospectively.

The study thus has both a retrospective and a prospective component, being a cohort observational study.

Inclusion criteria:

· All pediatric patients aged between 4 and 18 years admitted consecutively to suspected acute appendicitis

Exclusion criteria:

· Patients under 4 years of age

· Patients with appendicular plastron

- Patients with incomplete or lost tracking data

For data collection we used observation sheets, the operative book and anatomopathological bulletins.

The information used was entered in digital format using an application for tabular calculations. The primary data used in the study are: initials of the name and surname, sex, age, date of admission, date of surgery, date of discharge, admission diagnosis, discharge diagnosis, results of possible imaging experiments, Alvarado and Samuels scores, macroscopic postoperative diagnosis, histopathological diagnosis.

For calculating the scores I used the formulas described by Alvarado in 1986 and Samuel in 2002.

The positive diagnosis of acute appendicitis was based on the result of the positive histopathological examination of acute appendicitis. Where this was not possible due to the logistical difficulties of the Pathological Anatomy Laboratory, we used the anatomopathological description and postoperative diagnosis of the operative book to confirm the diagnosis of acute appendicitis. Acute catarrhal appendicitis is often a

euphemism for negative appendectomy, which is why we considered unconfirmed cases with macroscopic diagnosis of acute catarrhal appendicitis, histopathologically unconfirmed.

Management of admitted patients Depending on the initial examination of the patients, we proceeded to:

-Surgical emergency surgery

-Recovery and surgery within the first 24 hours

-Discharge or transfer to the pediatric department

Surgery was performed strictly on clinical criteria for patients in the first series, and for the second series , scores were considered, except in equivocal cases when predominantly clinical impression was considered.

Statistical analysis Collected data was processed using Microsoft Excel and IBM SPSS version 14 and Medcalc version 14. The threshold used to consider the result of a statistically significant test was $p \leq 0.05$.

Chapter VI Outcomes

General characteristics of the studied lots

Lots studied The study is based on two groups of patients.

- The first batch is represented by the patients whose evaluation was retrospective, being patients admitted during 2009-2011-700 patients

The second batch is the batch of patients prospectively investigated, between 2012 and 2014 - 627 patients.

Distribution by patient gender, male patients are 40.7% while female patients account for 59.3% of the total of cases included in this study.

Seasonal distribution Most of the patients in this study were hospitalized in March (11.8%) and October (10.5%) respectively. The fewest cases were admitted during the summer months (June, July and August) with a percentage of less than 7% for each of these months.

Confirmation of gender diagnosis from the point of view of confirming the diagnosis of acute appendicitis, in the case of male sex, it was confirmed at 74.3%, whereas for female patients, the confirmation of the diagnosis of acute appendicitis Achieved in a proportion of 65.9%.

Distribution by Age The mean age of patients enrolled in this study is 11.79 years, with a standard deviation of 3.7 years. The maximum age is 18 years, while the minimum age

is 4 years. The median is 12 years old, and the age with the highest frequency of admissions is 10 years.

Number of days of hospitalisation The average number of days of hospitalisation is 5.74, with a standard deviation of 2,838 days. The median is 6 days, and the most common is also 6 days of hospitalization. Although the average number of admission days does not differ statistically significantly, we noticed the existence of a significantly higher number of admission days during the retrospective study period.

Age of patients based on confirmation of diagnosis The mean age of patients whose diagnosis of acute appendicitis was confirmed is 12.23 years with a standard deviation of 3.57 years. For patients whose diagnosis was not confirmed, the mean age was 10.79 years with a standard deviation of 3.79.

Diagnostic value of the component elements of the scores: As regards the diagnostic value of the signs, symptoms and laboratory tests that compose the Alvarado and Samuel scores on the given series, we obtained the following data:

-**Migration of pain** in patients with acute appendicitis, this sign was present in more than half of the cases (50.4%), while in patients whose diagnosis of appendicitis was denied, the pain migration occurred in 28% Of cases. Thus, it is observed that the frequency of cases of pain migration is almost twice as high in patients diagnosed with acute appendicitis.

Anorexia In patients diagnosed with acute appendicitis, anorexia was present in 85.4% of the patients, while in the control group, anorexia was present at 78.4%. These high values are explained by the fact that anorexia is a common symptom of many gastrointestinal disorders. We then calculated, using the ratio of odds, the risk of patients with anorexia of acute appendicitis. This is 1.6 (95% CI 1.2 - 2.18), indicating a significantly increased risk

-**Nauseea and / or vomiting** The percentage of patients with nausea and / or vomiting in the entire batch of investigated patients is 62.5%. For patients without a diagnosis of acute appendicitis it is 57.7%, and for patients with acute appendicitis the proportion of those with nausea and / or vomiting is 64.7%. The observed difference is statistically significant. The risk for patients with nausea and / or vomiting to be diagnosed with acute appendicitis is 1.34 (95% CI 1.05 - 1.7).

- **Tenderness in the right lower quadrant** The results of this study indicate that this sign is extremely common, being encountered in all patients diagnosed with acute appendicitis and in over 97% of patients diagnosed with other conditions. The risk expressed in the Quota Report is difficult to interpret because of the way cases are distributed. The

calculated confidence interval is very broad, and it does not allow a realistic risk estimate of Odds Ratio = 53.47 (95% CI 3.33 - 956.14).

- **Rebound pain** (Bloomberg sign), specific for the identification of peritoneal irritation, was present in 69% of patients diagnosed with acute appendicitis. In the case of those without acute appendicitis, the Bloomberg sign was present at 18.2%.

There is a statistically significant association (p <0.001) of the Bloomberg sign with the presence of acute appendicitis. The risk that a patient with Bloomberg positive sign showing acute appendicitis is approximately ten times higher Odds Ratio = 10.02 (95% CI 7.51 - 13.37)

-**Fever** was present in over half of patients with acute appendicitis -54.2%, respectively. In the case of patients who were not diagnosed with acute appendicitis, the proportion of those with fever was 39.6%. The risk of patients with fever to develop acute appendicitis in terms of odds ratio is 1.81 (95% CI 1.43 - 2.29).

- **Leucocytosis** was present in more than two-thirds of patients with acute appendicitis (69.7%). In this case, a similar proportion was also found in patients in whom the diagnosis of acute appendicitis was not confirmed (68.1%). Following the similar proportions observed in both groups, there was no statistically significant association between the presence Leukocytosis and diagnosis of acute appendicitis (p = 0.698).

-**Neutrophilia** was identified in about 4 out of 5 patients diagnosed with acute appendicitis (82.6%), while in the case of patients without acute appendicitis, about half of them had neutrophilia (53.3%). The difference is statistically significant (p <0.001), indicating a statistically significant association between the presence of neutrophilia and the diagnosis of acute appendicitis.

ANALYSIS OF SCORES on given series

Alvarado score

In terms of the Alvarado score, it is noted that most patients had a score of 6, representing about 31% of all cases. There follows in descending order of frequency the score of 7 with 24%, 8 with 19%, 9 with 13% and 5 with 9%. (Figure 24). The comparative descriptive statistical analysis of the Alvarado score based on the diagnosis of acute appendicitis indicates that for patients with confirmed diagnosis the median value is 7.44 with a median of 7, whereas in patients where the diagnosis of acute appendicitis was not Confirmed, the average score is 6.05 with the median of 6.

In the following we grouped the patients according to the Alvarado score into three categories: ≤ 6, 7-8 and 9-10.

The result provides a clearer picture of how patients are distributed, with a clear prediction of scores of less than or equal to 6 in patients whose diagnosis of acute appendicitis has not been confirmed (75.7%), and the high proportion of Patients with a 7-8 score for patients diagnosed with acute appendicitis. The association between the score group and the diagnosis of acute appendicitis is highly statistically significant,

p <0.001, patients with confirmed diagnosis having a statistically significantly higher score.

The utility of Alvarado score in the diagnosis of acute appendicitis

In order to estimate the utility of the Alvarado score in diagnosing acute appendicitis in suspected patients, we used criteria such as: sensitivity, specificity, positive probability (+ LR) ratio, negative probability ratio (LR), positive predictive value, negative predictive value.

These were applied and calculated for each score, the results being detailed below.

We calculated the area under the ROC curve. It has an area of 0.805 (confidence interval 95% 0.783-0.826), statistically significantly differing (p <0.0001) from a surface of 0.5 corresponding to a test that can not provide information about the lot to which a Patient with a certain score.

After applying this Youden test for the 6-point Alvarado threshold, the value obtained is 0.4991. For this value, the calculated sensitivity is 74.24 and the specificity is 75.68 (Table LIII). For this value, the positive probability ratio is 3.05, the negative probability ratio is 0.34, the positive predictive value is 87.3%, and the negative predictive value is 56.5%.

In Figure 27, I represented the ROC curve. It is noted that the points used in making the calculations are marked, and the threshold value which when used is the ideal balance between sensitivity and specificity.

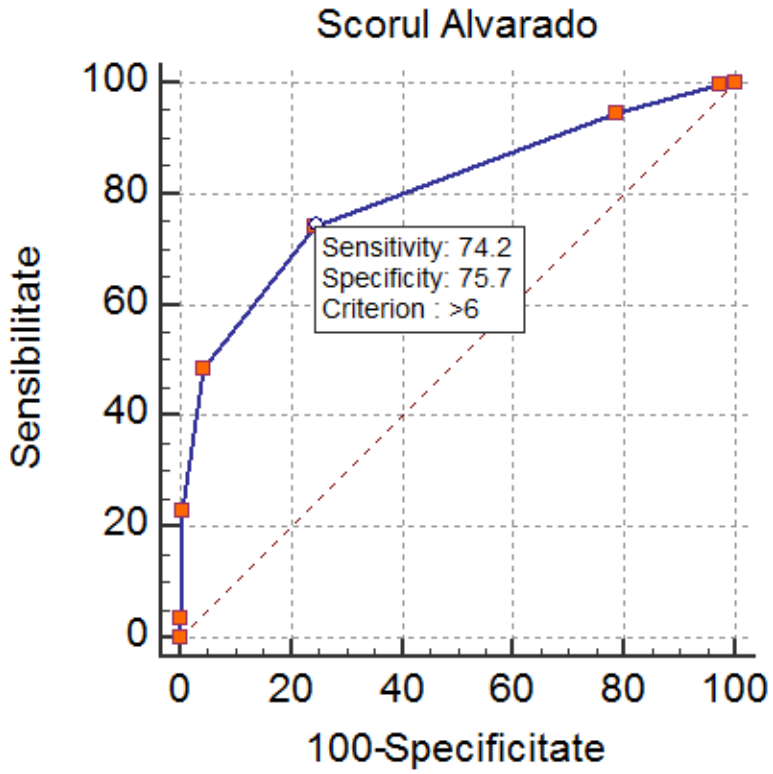


Figure 27.ROC curve for Alvorado score

For a complete picture of Alvarado's performance in the diagnosis of acute appendicitis, we calculated the indicators for each test value found in this study.

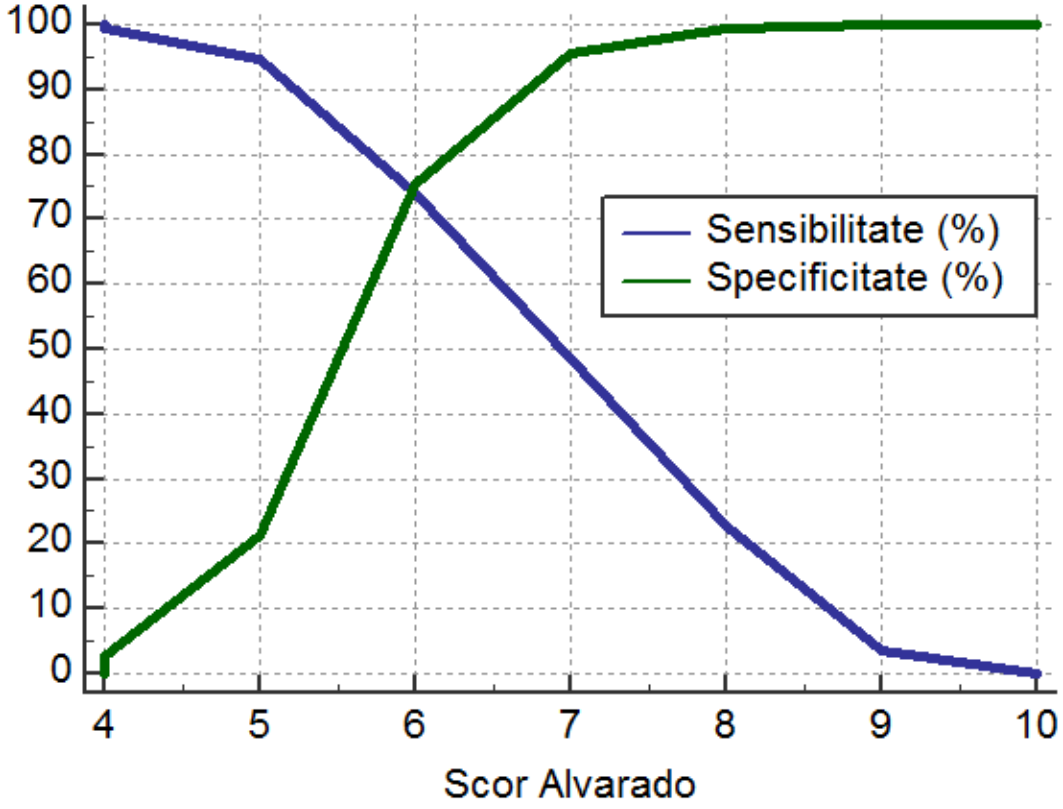
The result (Table LIV) provides information about estimated values for each score value. It is noted that if a score greater than 7 is taken as the threshold value, it gives a specificity of 95.82%, ie a correct recognition of the negative cases, with a positive predictive value of over 96%.

Tabel LIV Performance of Alvarado score

Criterion	≥4	>4	>5	>6	>7	>8	>9	>10
Sensitivity	100	99.67	94.78	74.24	48.59	22.93	3.8	0

95% CI	99.6 - 100.0	99.1 - 99.9	93.1 - 96.1	71.3 - 77.0	45.3 - 51.9	20.3 - 25.8	2.7 - 5.3	0.0 - 0.4
Specificity	0	2.7	21.38	75.68	95.82	99.51	100	100
95% CI	0.0 - 0.9	1.4 - 4.8	17.5 - 25.7	71.2 - 79.8	93.4 - 97.5	98.2 - 99.9	99.1 - 100.0	99.1 - 100.0
+LR	1	1.02	1.21	3.05	11.63	46.67		
95% CI	1.0 - 1.0	1.0 - 1.0	1.1 - 1.3	2.6 - 3.6	7.3 - 18.6	11.7 - 186.9		
-LR		0.12	0.24	0.34	0.54	0.77	0.96	1
95% CI		0.03 - 0.4	0.2 - 0.3	0.3 - 0.4	0.5 - 0.6	0.7 - 0.8	0.9 - 1.0	1.0 - 1.0
+PV	69.3	69.8	73.2	87.3	96.3	99.1	100	
95% CI	66.8 - 71.8	67.3 - 72.3	70.5 - 75.7	84.8 - 89.6	94.2 - 97.9	96.6 - 99.9	90.0 - 100.0	
-PV		78.6	64.4	56.5	45.2	36.4	31.5	30.7
95% CI		49.2 - 95.3	55.8 - 72.5	52.2 - 60.7	41.8 - 48.6	33.5 - 39.3	29.0 - 34.1	28.2 - 33.2

Regarding how sensitivity and specificity vary, these are plotted in Figure 28. This graph gives a good overall picture of Alvarado scores on children, confirming that a patient with a score of 5 or less has a very high probability of not having the disease, while a patient with a score of 7 or greater is highly likely to present the disease.

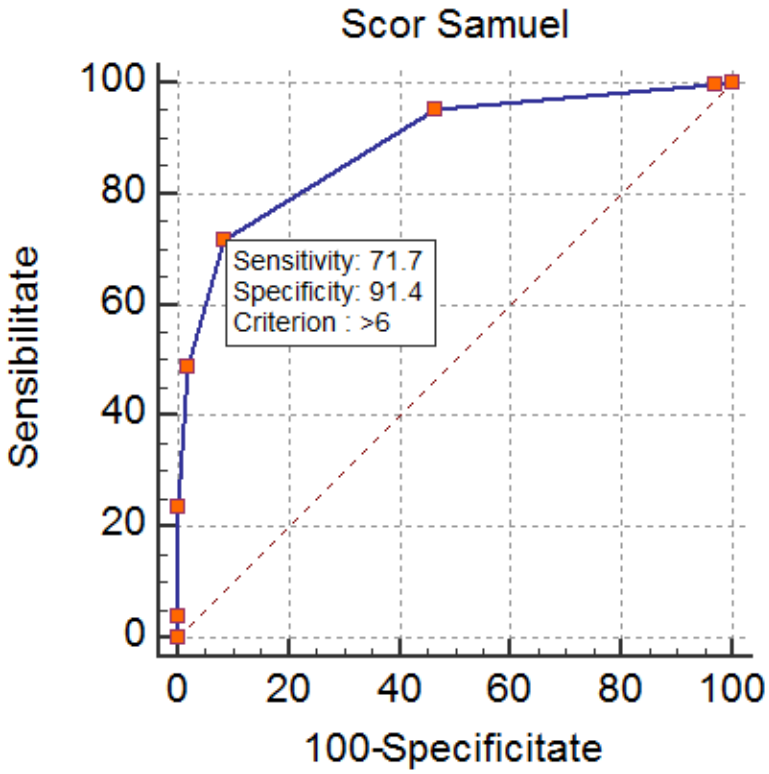


We have noticed that if a score greater than 7 is taken into account as a threshold value, we obtain 95.82% specificity, ie a correct recognition of negative cases, with a positive predictive value of over 96%.

Representing the ROC curves for Alvarado in children less than 10 years of age and those aged over 10 years of age, it is noted that the values for specificity and sensitivity are lower in children over 10 years of age compared to the values obtained For children less than 10 years of age.

Score Samuel

Samuel Performance Score Analysis: The area under the calculated ROC curve is 0.887 (95% confidence interval 0.869 - 0.903). The result obtained is statistically significantly different from a surface under the ROC curve of 0.5, $p < 0.0001$. The Youden index is 0.6314 for a 6-point threshold, in this case the sensitivity is 71.74% and the specificity is 91.4%.



R

OC curve for Samuel score

In Table LXIII are the calculated values for Samuel score performance indicators in the diagnosis of acute appendicitis in children.

Tabel LXIII Performanco of Samuel Score

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	95% CI	-LR	95% CI	+PV	95% CI	-PV	95% CI
≥4	100.00	99.6 - 100.0	0.00	0.0 - 0.9	1.00	1.0 - 1.0			69.3	66.8 - 71.8		
>4	99.89	99.4 - 100.0	2.95	1.5 - 5.1	1.03	1.0 - 1.0	0.037	0.005 - 0.3	69.9	67.4 - 72.4	92.3	64.0 - 99.8
>5	95.43	93.9 - 96.7	53.32	48.3 - 58.2	2.04	1.8 - 2.3	0.086	0.06 - 0.1	82.2	79.8 - 84.5	83.8	78.7 - 88.1
>6	71.74	68.7 - 74.6	91.40	88.2 - 93.9	8.34	6.1 - 11.5	0.31	0.3 - 0.3	95.0	93.1 - 96.5	58.9	54.9 - 62.7
>7	48.80	45.5 - 52.1	98.03	96.2 - 99.1	24.83	12.5 - 49.5	0.52	0.5 - 0.6	98.2	96.6 - 99.2	45.9	42.5 - 49.2
>8	23.70	21.0 - 26.6	100.00	99.1 - 100.0			0.76	0.7 - 0.8	100.0	98.3 - 100.0	36.7	33.9 - 39.6
>10	0.00	0.0 - 0.4	100.00	99.1 - 100.0			1.00	1.0 - 1.0			30.7	28.2 - 33.2

The way sensitivity and specificity vary according to the Samuel score are shown in Figure 34. Very good sensitivity results are obtained with a score of less than 5 and very good results for specificity are obtained with a higher score of 6.

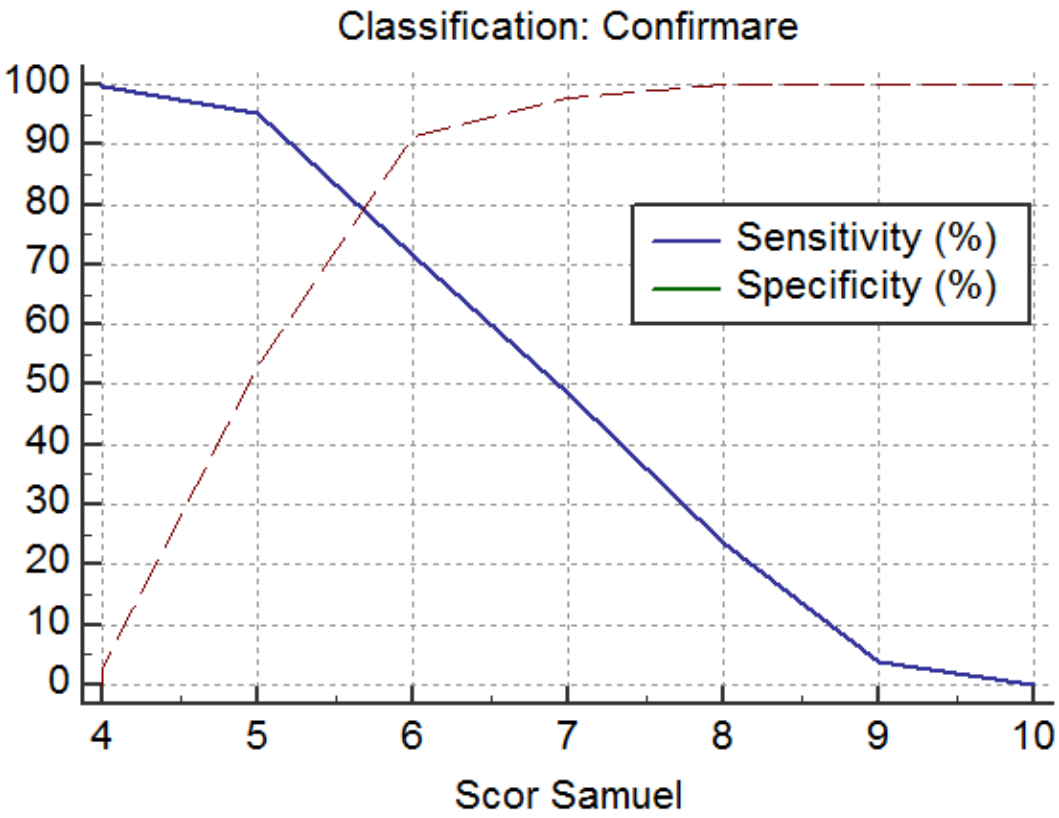


Figure 35 Representation of threshold value according to specificity and sensitivity for Samuel score

Analyzing the ROC curves for children under 10 years of age and over 10 years, we have a sensitivity of 78.4% and specificity of 90.5% for those under 10 years, and for those over 10 years we have a sensitivity of 68.4% and a specificity Of 92.2%.

Comparison between the accuracy of Alvarado and Samuel scores

The area under the ROC curve for the Alvarado score was 0.805 (confidence interval 95% 0.783-0.826), and for the Samuel score, it was 0.887 (confidence interval 95% 0.869-0.903).

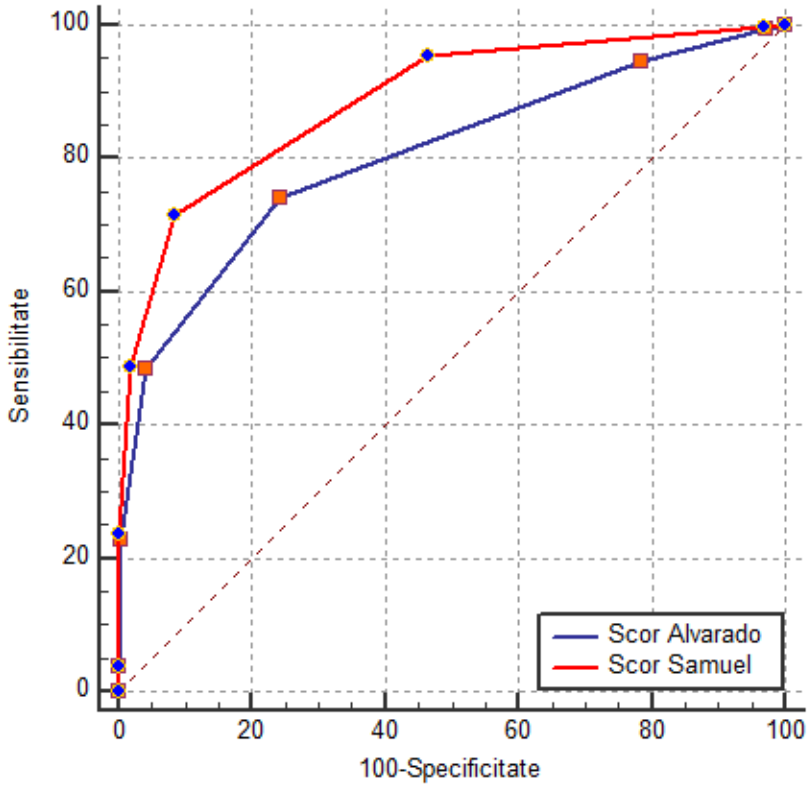


Figura 39 ROC curves for Alvarado and Samuel score – comparative

The difference between the two surfaces under the ROC curve is 0.0747 (confidence interval 95% 0.0511 - 0.0982), this being statistically significant (p <0.0001). Thus, the area under the ROC curve for the Samuel score is statistically significantly higher compared to the area under the ROC curve for the Alvarado score.

By comparing the ROC curves for the two scores in children under 10 and in children over 10 years, the ROC curve of the Samuel score was significantly better for both groups.

Complications

In the case of the retrospective group, the percentage of cases of complicated acute appendicitis was 13.5%, while in the case of prospective analysis the percentage was 12.5%, so the application of the scores did not significantly change the evolution towards complications.

Negative appendectomy In the absence of diagnostic score scores, 16.3% of surgical interventions did not have the diagnosis of confirmed confirmed appendicitis, while in the study group in which diagnostic scores were used, the percentage of negative surgical interventions Was 9.6%.

Reducing negative appendectomy to almost half confirms the usefulness of using scores in the rapid diagnosis of acute childhood appendicitis

Chapter VII: DISCUSSIONS

In the Discussion chapter we compared the results obtained with the results of other similar studies.

For the studied series we noted the following:

For the Alvarado score:

The high incidence of acute appendicitis at Alvarado scores 5 and 6 induces the need for iadmission for clinical reassessment and possibly imaging exploration. These low score values may be due partly to the early presentation of patients, when the clinical picture has not yet fully outlined (in this paper we have only processed records from patient presentation) or because of the inability of the examining physician to reveal signs of peritoneal irritation, harder to be emphasized in non-cooperative children (this leads to the decrease of the actual score by 1-2 points)

Assuming that only surgery with Alvarado scores over 7, the number of negative appendectomy would drop to 9.8% for the retrospective series and 6.7% for the prospective series instead we would have a high proportion of missed- 21.2% on the retrospective group and 16.1% on the prospective lot.

At an Alvarado score of 8, the negative appendectomy score would be only 3.5% for the retrospective group and 3.3% for the prospective group. From here it can be concluded that these patients can be operated immediately without further investigation

Patient management based on the Alvarado score is as follows

-below 5-discharge

-5-6-7-admission for further re-evaluation and possibly imaging exploration

-8,9,10- Surgery

For the Samuel score

In our PAS study above 6 we achieved a sensitivity of 71.7 and a specificity of 91.4.

If all patients with a Samuel score greater than or equal to 6 were subjected to surgery, we would have had a 2.7% missed diagnosis and 18.6% retrospective retrospective appendectomy and 3.8% missed diagnoses and 17 , 4% negative prospective appendectomy on the prospective series. For the threshold value of 7, the proportion of negative appendectomy would drop to 4.02% for the retrospective group and 5.8% for the prospective group instead, the proportion of missed diagnoses would be very high - 24% for the

retrospective group and 14.3% for the prospective . Given the very low rate of negative appendectomy in patients with 7 and above scores, they can be operated immediately without further investigation.

Patient management according to the Samuel score

· Under 5-discharge

· 5,6-admissions for re-evaluation and additional investigations

· 7,8,9,10 - immediate surgery

Chapter VIII: CONCLUSIONS

· Alvarado and Samuel scores are useful in the early diagnosis of acute childhood appendicitis.

· Scores significantly reduce the need for imaging explorations, being useful tools in resource-poor and modest staff.

· Scores are useful in patient management indicating which patients should be discharged, who need to be admitted for further re-evaluation and / or additional investigations and to be operated urgently

· By lowering the rate of negative appendectomy due to the application of scores, unnecessary material consumption is avoided and patients are exposed to unnecessary anesthetic and surgical risks. Moreover, the rate of negative appendectomy is a quality indicator of the activity of a surgical section.

· The presence of a large number of clinical criteria in the calculation of the scores reveals that the diagnosis of acute appendicitis is also an eminently clinical diagnosis in the age of imaging investigations.

· Samuel score has superior performance over the Alvarado score when applied to a pediatric population.

· Taking into account the current trend of non-operator treatment of acute appendicitis, scores can be a selection criterion for cases that are appropriate to it.

Bibliography

1 Adamidis, D., Roma-Giannikou, E., Karamolegou, K., Tselalidou, E. & Constantopoulos, A. (2000). Fiber intake and childhood appendicitis. *Int J Food Sci Nutr, 51*(3), 153-157.

2 Addiss, D.G., Shaffer, N., Fowler, B.S. & Tauxe, R.V. (1990). The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol, 132*(5), 910-925.
3 Alvarado, A. (1986). A practical score for the early diagnosis of acute appendicitis. *Ann Emerg Med, 15*(5), 557-564.
4 Alves, J.G., Figueiroa, J.N. & Barros, I. (2008). Does breast feeding provide protection against acute appendicitis? A case-control study. *Trop Doct, 38*(4), 235-236. doi: 10.1258/td.2008.070404
5 Andersen, B.R., Kallehave, F.L. & Andersen, H.K. (2005). Antibiotics versus placebo for prevention of postoperative infection after appendicectomy. *Cochrane Database Syst Rev*(3), Cd001439. doi: 10.1002/14651858.CD001439.pub2
6 Andersson, M. & Andersson, R.E. (2008). The appendicitis inflammatory response score: a tool for the diagnosis of acute appendicitis that outperforms the Alvarado score. *World J Surg, 32*(8), 1843-1849. doi: 10.1007/s00268-008-9649-y
7 Andersson, R.E. (2004). Meta-analysis of the clinical and laboratory diagnosis of appendicitis. *Br J Surg, 91*(1), 28-37. doi: 10.1002/bjs.4464
8 Bachur, R.G., Hennelly, K., Callahan, M.J., Chen, C. & Monuteaux, M.C. (2012). Diagnostic imaging and negative appendectomy rates in children: effects of age and gender. *Pediatrics, 129*(5), 877-884. doi: 10.1542/peds.2011-3375
9 Barber, M., McLaren, J. & Rainey, J. (1997). Recurrent appendicitis. *British journal of surgery, 84*(1), 110-112.
10 Barrett, M.L., Hines, A.L. & Andrews, R.M. (2013). Trends in rates of Perforated Appendix, 2001–2010.
11 Basta, M., Morton, N.E., Mulvihill, J.J., Radovanovic, Z., Radojicic, C. & Marinkovic, D. (1990). Inheritance of acute appendicitis: familial aggregation and evidence of polygenic transmission. *Am J Hum Genet, 46*(2), 377-382.
12 Bemelman, W.A., Hugenholtz, E., Heij, H.A., Wiersma, P.H. & Obertop, H. (1995). Meckel's diverticulum in Amsterdam: experience in 136 patients. *World J Surg, 19*(5), 734-736; discussion 737.
13 Benaim, J., Pulaski, M. & Coupey, S.M. (1998). Adolescent girls and pelvic inflammatory disease: experience and practices of emergency department pediatricians. *Archives of pediatrics & adolescent medicine, 152*(5), 449-454.
14 Bhatt, M., Joseph, L., Ducharme, F.M., Dougherty, G. & McGillivray, D. (2009). Prospective validation of the pediatric appendicitis score in a Canadian pediatric emergency department. *Acad Emerg Med, 16*(7), 591-596. doi: 10.1111/j.1553-2712.2009.00445.x
15 Birnbaum, B.A. & Wilson, S.R. (2000). Appendicitis at the millennium. *Radiology, 215*(2), 337-348. doi: 10.1148/radiology.215.2.r00ma24337
16 Boleslawski, E., Panis, Y., Benoist, S., Denet, C., Mariani, P. & Valleur, P. (1999). Plain abdominal radiography as a routine procedure for acute abdominal pain of the right lower quadrant: prospective evaluation. *World J Surg, 23*(3), 262-264.
17 Bollinger, R.R., Barbas, A.S., Bush, E.L., Lin, S.S. & Parker, W. (2007). Biofilms in the large bowel suggest an apparent function of the human vermiform appendix. *Journal of theoretical biology, 249*(4), 826-831.
18 Bond, G.R., Tully, S.B., Chan, L.S. & Bradley, R.L. (1990). Use of the MANTRELS score in childhood appendicitis: a prospective study of 187 children with abdominal pain. *Annals of Emergency Medicine, 19*(9), 1014-1018. doi: 10.1016/s0196-0644(05)82566-1
19 Brender, J.D., Marcuse, E.K., Weiss, N.S. & Koepsell, T.D. (1985). Is childhood appendicitis familial? *Am J Dis Child, 139*(4), 338-340.

20 Buntain, W.L., Krempe, R.E. & Kraft, J.W. (1984). Neonatal appendicitis. *Ala J Med Sci, 21*(3), 295-299.
21 Buschard, K. & Kjaeldgaard, A. (1973). Investigation and analysis of the position, fixation, length and embryology of the vermiform appendix. *Acta Chir Scand, 139*(3), 293-298.
22 Buyukbese Sarsu, S. & Sarac, F. (2016). Diagnostic Value of White Blood Cell and C-Reactive Protein in Pediatric Appendicitis. *BioMed Research International, 2016*, 6. doi: 10.1155/2016/6508619
23 Cardall, T., Glasser, J. & Guss, D.A. (2004). Clinical value of the total white blood cell count and temperature in the evaluation of patients with suspected appendicitis. *Acad Emerg Med, 11*(10), 1021-1027. doi: 10.1197/j.aem.2004.04.011
24 Cariati, A., Brignole, E., Tonelli, E., Filippi, M., Guasone, F., De Negri, A., Novello, L., Risso, C., Noceti, A. & Giberto, M. (2001). [Laparoscopic or open appendectomy. Critical review of the literature and personal experience]. *Il Giornale di chirurgia, 22*(10), 353-357.
25 Carrol, E., Thomson, A. & Hart, C. (2002). Procalcitonin as a marker of sepsis. *International journal of antimicrobial agents, 20*(1), 1-9.
26 Chandel, V., Batt, S.H., Bhat, M.Y., Kawoosa, N.U., Yousuf, A. & Zargar, B.R. (2011). Procalcitonin as the Biomarker of Inflammation in Diagnosis of Appendicitis in Pediatric Patients and Prevention of Unnecessary Appendectomies. *Indian Journal of Surgery, 73*(2), 136-141. doi: 10.1007/s12262-010-0214-1
27 Chong, C.F., Adi, M.I., Thien, A., Suyoi, A., Mackie, A.J., Tin, A.S., Tripathi, S., Jaman, N.H., Tan, K.K., Kok, K.Y., Mathew, V.V., Paw, O., Chua, H.B. & Yapp, S.K. (2010). Development of the RIPASA score: a new appendicitis scoring system for the diagnosis of acute appendicitis. *Singapore Med J, 51*(3), 220-225.
28 Christian, F. & Christian, G.P. (1992). A simple scoring system to reduce the negative appendicectomy rate. *Ann R Coll Surg Engl, 74*(4), 281-285.
29 Claeys, R., Vinken, S., Spapen, H., ver Elst, K., Decochez, K., Huyghens, L. & Gorus, F.K. (2002). Plasma procalcitonin and C-reactive protein in acute septic shock: clinical and biological correlates. *Critical care medicine, 30*(4), 757-762.
30 Cloud, D.T. (1993). Appendicitis. In K. W. Ashcraft & T. M. Holder (Eds.), *Pediatric Surgery* (pp. 470-477): WB Saunders Company.
31 Cobben, L., Groot, I., Kingma, L., Coerkamp, E., Puylaert, J. & Blickman, J. (2009). A simple MRI protocol in patients with clinically suspected appendicitis: results in 138 patients and effect on outcome of appendectomy. *Eur Radiol, 19*(5), 1175-1183. doi: 10.1007/s00330-008-1270-9
32 Cobben, L.P., de van Otterloo, A.M. & Puylaert, J.B. (2000). Spontaneously Resolving Appendicitis: Frequency and Natural History in 60 Patients 1. *Radiology, 215*(2), 349-352.
33 Cochrane, J.M. & Phil, D. (2006). Imaging for diagnosis of appendicitis. *Radiology Rounds - A newsletter for referring physicians, Massachusetts General Hospital, Department of Radiology, 4*(1).
34 Crochot, W. (2006). Diagram of the stomach, colon and rectum.
35 Dado, G., Anania, G., Baccarani, U., Marcotti, E., Donini, A., Risaliti, A., Pasqualucci, A. & Bresadola, F. (2000). Application of a clinical score for the diagnosis of acute appendicitis in childhood: a retrospective analysis of 197 patients. *J Pediatr Surg, 35*(9), 1320-1322. doi: 10.1053/jpsu.2000.9316
36 Delevaux, I., Andre, M., Colombier, M., Albuisson, E., Meylheuc, F., Bègue, R., Piette, J. & Aumaître, O. (2003). Can procalcitonin measurement help in

differentiating between bacterial infection and other kinds of inflammatory processes? *Annals of the rheumatic diseases, 62*(4), 337-340.

37 Dickson, A.P. & MacKinlay, G.A. (1985). Rectal examination and acute appendicitis. *Arch Dis Child, 60*(7), 666-667.

38 Douglas, C.D., Macpherson, N.E., Davidson, P.M. & Gani, J.S. (2000). Randomised controlled trial of ultrasonography in diagnosis of acute appendicitis, incorporating the Alvarado score. *BMJ, 321*(7266), 919-922.

39 Dunn, J.C.Y. (2006). Chapter 98 - Appendicitis A2 - Grosfeld, Jay L. In J. A. O'Neill, A. G. Coran, E. W. Fonkalsrud & A. A. Caldamone (Eds.), *Pediatric Surgery (Sixth Edition)* (pp. 1501-1513). Philadelphia: Mosby.

40 Ein, S.H., Langer, J.C. & Daneman, A. (2005). Nonoperative management of pediatric ruptured appendix with inflammatory mass or abscess: presence of an appendicolith predicts recurrent appendicitis. *J Pediatr Surg, 40*(10), 1612-1615.

41 Ein, S.H. & Sandler, A. (2006). Wound infection prophylaxis in pediatric acute appendicitis: a 26-year prospective study. *J Pediatr Surg, 41*(3), 538-541. doi: 10.1016/j.jpedsurg.2005.11.052

42 Ein, S.H. & Ein, A. (2013). Open appendectomy for pediatric ruptured appendicitis: a historical clinical review of the prophylaxis of wound infection and postoperative intra-abdominal abscess. *Canadian Journal of Surgery, 56*(3), E7.

43 Emil, S., Mikhail, P., Laberge, J.M., Flageole, H., Nguyen, L.T., Shaw, K.S., Baican, L. & Oudjhane, K. (2001). Clinical versus sonographic evaluation of acute appendicitis in children: a comparison of patient characteristics and outcomes. *J Pediatr Surg, 36*(5), 780-783. doi: 10.1053/jpsu.2001.22960

44 Erkasap, S., Ates, E., Ustuner, Z., Sahin, A., Yilmaz, S., Yasar, B. & Kiper, H. (2000). Diagnostic value of interleukin-6 and C-reactive protein in acute appendicitis. *Swiss Surg, 6*(4), 169-172.

45 Escriba, A., Gamell, A.M., Fernandez, Y., Quintilla, J.M. & Cubells, C.L. (2011). Prospective validation of two systems of classification for the diagnosis of acute appendicitis. *Pediatr Emerg Care, 27*(3), 165-169. doi: 10.1097/PEC.0b013e31820d6460

46 Fa, E.M. & Cronan, J.J. (1989). Compression ultrasonography as an aid in the differential diagnosis of appendicitis. *Surg Gynecol Obstet, 169*(4), 290-298.

47 Fenyo, G., Lindberg, G., Blind, P., Enochsson, L. & Oberg, A. (1997). Diagnostic decision support in suspected acute appendicitis: validation of a simplified scoring system. *Eur J Surg, 163*(11), 831-838.

48 Field, A. (2007). *Discovering Statistics Using SPSS*: SAGE Publications.

49 Fitz, R.H. (1886). *Perforating inflammation of the vermiform appendix, with special reference to its early diagnosis and treatment*. Philadelphia: Dornan.

50 Funaki, B., Grosskreutz, S.R. & Funaki, C.N. (1998). Using unenhanced helical CT with enteric contrast material for suspected appendicitis in patients treated at a community hospital. *AJR Am J Roentgenol, 171*(4), 997-1001. doi: 10.2214/ajr.171.4.9762983

51 Gaensler, E.H., Jeffrey, R.B., Jr., Laing, F.C. & Townsend, R.R. (1989). Sonography in patients with suspected acute appendicitis: value in establishing alternative diagnoses. *AJR Am J Roentgenol, 152*(1), 49-51. doi: 10.2214/ajr.152.1.49

52 Gan, Q.F. (2014). Histology of gastrointestinal tract. from https://www.slideshare.net/QuanFuGan/histology-of-gastrointestinal-tract

53 Garcia, E.A. & Wiebe, R.A. (2000). Intussusception in childhood. *Pediatr Emerg Med Rep, 5*, 93-100.

54 Garnache, F., Simon, M. & Goffinet, P. (1997). Péritonites primitives à Streptococcus pneumoniae. *Journal de gynécologie obstétrique et biologie de la reproduction, 26*(6), 617-622.
55 Gillick, J., Velayudham, M. & Puri, P. (2001). Conservative management of appendix mass in children. *British journal of surgery, 88*(11), 1539-1542. doi: 10.1046/j.0007-1323.2001.01912.x
56 Goldman, R.D., Carter, S., Stephens, D., Antoon, R., Mounstephen, W. & Langer, J.C. (2008). Prospective validation of the pediatric appendicitis score. *J Pediatr, 153*(2), 278-282. doi: 10.1016/j.jpeds.2008.01.033
57 Golub, R., Siddiqui, F. & Pohl, D. (1998). Laparoscopic versus open appendectomy: a metaanalysis. *Journal of the American College of Surgeons, 186*(5), 545-553.
58 Goodman, D.A., Goodman, C.B. & Monk, J.S. (1995). Use of the neutrophil:lymphocyte ratio in the diagnosis of appendicitis. *Am Surg, 61*(3), 257-259.
59 Goulder, F. & Simpson, T. (2008). Pediatric appendicitis score: A retrospective analysis. *Journal of Indian Association of Pediatric Surgeons, 13*(4), 125-127.
60 Graif, M. & Itzchak, Y. (1988). Sonographic evaluation of ovarian torsion in childhood and adolescence. *American Journal of Roentgenology, 150*(3), 647-649.
61 Gronroos, J.M. (2001). Do normal leucocyte count and C-reactive protein value exclude acute appendicitis in children? *Acta Paediatr, 90*(6), 649-651.
62 Guida, E., Pederiva, F., Di Grazia, M., Codrich, D., Lembo, M.A., Scarpa, M.G. & Rigamonti, W. (2015). Perforated appendix with abscess: Immediate or interval appendectomy? Some examples to explain our choice. *International journal of surgery case reports, 12*, 15-18.
63 Hellberg, A., Rudberg, C., Kullman, E., Enochsson, L., Fenyö, G., Graffner, H., Hallerbäck, B., Johansson, B., Anderberg, B. & Wenner, J. (1999). Prospective randomized multicentre study of laparoscopic versus open appendicectomy. *British journal of surgery, 86*(1), 48-53.
64 Houry, D. & Abbott, J.T. (2001). Ovarian torsion: a fifteen-year review. *Annals of Emergency Medicine, 38*(2), 156-159.
65 Hsiao, K.H., Lin, L.H. & Chen, D.F. (2005). Application of the MANTRELS scoring system in the diagnosis of acute appendicitis in children. *Acta Paediatr Taiwan, 46*(3), 128-131.
66 Inci, E., Hocaoglu, E., Aydin, S., Palabiyik, F., Cimilli, T., Turhan, A.N. & Aygun, E. (2011). Efficiency of unenhanced MRI in the diagnosis of acute appendicitis: comparison with Alvarado scoring system and histopathological results. *Eur J Radiol, 80*(2), 253-258. doi: 10.1016/j.ejrad.2010.06.037
67 Jangjoo, A., Varasteh, A.R., Bahar, M.M., Meibodi, N.T., Aliakbarian, M., Hoseininejad, M., Esmaili, H. & Amouzeshi, A. (2011). Is C-reactive protein helpful for early diagnosis of acute appendicitis? *Acta Chir Belg, 111*(4), 219-222.
68 Jasonni, V. (2005). Appendectomy. In P. Puri & M. E. Höllwarth (Eds.), *Pediatric Surgery* (pp. 321-326): Springer.
69 Jecu, A. (2003). Patologia chirurgicală a apendicelui. In N. Angelescu (Ed.), *Tratat de patologie chirurgicală* (Vol. 2, pp. 1595-1610). București: Editura Medicală.
70 John, J., Hanini, S. & Popoiu, C.M. (2009). Acute apendicitis in ingants and toddlers: rare but challenging. *Jurnalul Pediatrului, 12*(45-46), 36-39.
71 Kharbanda, A.B., Taylor, G.A., Fishman, S.J. & Bachur, R.G. (2005). A clinical decision rule to identify children at low risk for appendicitis. *Pediatrics, 116*(3), 709-716. doi: 10.1542/peds.2005-0094

72 Kizilcan, F., Tanyel, F.C., Buyukpamukcu, N. & Hicsonmez, A. (1992). The necessity of prophylactic antibiotics in uncomplicated appendicitis during childhood. *J Pediatr Surg, 27*(5), 586-588.

73 Kokoska, E.R., Silen, M.L., Tracy, T.F., Jr., Dillon, P.A., Kennedy, D.J., Cradock, T.V. & Weber, T.R. (1999). The impact of intraoperative culture on treatment and outcome in children with perforated appendicitis. *J Pediatr Surg, 34*(5), 749-753.

74 Kokoska, E.R., Keller, M.S. & Weber, T.R. (2000). Acute ovarian torsion in children. *The American journal of surgery, 180*(6), 462-465.

75 Kouame, D., Garrigue, M., Lardy, H., Machet, M., Giraudeau, B. & Robert, M. (2005). *Is procalcitonin able to help in pediatric appendicitis diagnosis?* Paper presented at the Annales de chirurgie.

76 Kumar, N.S., Balamuragan, R. & Zakkaria, M. (2016). FACTORS AFFECTING CONVERSION OF LAPAROSCOPIC CHOLECYSTECTOMY TO OPEN SURGERY IN A TERTIARY HOSPITAL IN SOUTH INDIA. *JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS, 5*(4), 256-261.

77 Lane, M.J., Katz, D.S., Ross, B.A., Clautice-Engle, T.L., Mindelzun, R.E. & Jeffrey, R.B., Jr. (1997). Unenhanced helical CT for suspected acute appendicitis. *AJR Am J Roentgenol, 168*(2), 405-409. doi: 10.2214/ajr.168.2.9016216

78 Lane, M.J., Liu, D.M., Huynh, M.D., Jeffrey, R.B., Jr., Mindelzun, R.E. & Katz, D.S. (1999). Suspected acute appendicitis: nonenhanced helical CT in 300 consecutive patients. *Radiology, 213*(2), 341-346. doi: 10.1148/radiology.213.2.r99nv44341

79 Lee, S.L., Walsh, A.J. & Ho, H.S. (2001). Computed tomography and ultrasonography do not improve and may delay the diagnosis and treatment of acute appendicitis. *Arch Surg, 136*(5), 556-562.

80 Li, X., Zhang, J., Sang, L., Zhang, W., Chu, Z., Li, X. & Liu, Y. (2010). Laparoscopic versus conventional appendectomy-a meta-analysis of randomized controlled trials. *BMC gastroenterology, 10*(1), 129.

81 Liang, M.K., Andersson, R.E., Jaffe, B.M. & Berger, D.H. (2014). Chapter 30 - The Appendix. In F. Brunicardi, D. Andersen, T. Billiar, D. Dunn, J. G. Hunter, J. Matthews & R. E. Pollock (Eds.), *Schwartz's Principles of Surgery, 10th edition*: McGraw-Hill Education.

82 Lintula, H., Pesonen, E., Kokki, H., Vanamo, K. & Eskelinen, M. (2005). A diagnostic score for children with suspected appendicitis. *Langenbecks Arch Surg, 390*(2), 164-170. doi: 10.1007/s00423-005-0545-8

83 Lintula, H., Kokki, H., Kettunen, R. & Eskelinen, M. (2009). Appendicitis score for children with suspected appendicitis. A randomized clinical trial. *Langenbecks Arch Surg, 394*(6), 999-1004. doi: 10.1007/s00423-008-0425-0

84 Liu, K. & Fogg, L. (2011). Use of antibiotics alone for treatment of uncomplicated acute appendicitis: a systematic review and meta-analysis. *Surgery, 150*(4), 673-683.

85 Livingston, E.H., Woodward, W.A., Sarosi, G.A. & Haley, R.W. (2007). Disconnect between incidence of nonperforated and perforated appendicitis: implications for pathophysiology and management. *Annals of Surgery, 245*(6), 886-892.

86 Lopez, A.F., Cubells, C.L., García, J.G. & Pou, J.F. (2003). Procalcitonin in pediatric emergency departments for the early diagnosis of invasive bacterial infections in febrile infants: results of a multicenter study and utility of a rapid qualitative test for this marker. *Pediatr Infect Dis J, 22*(10), 895-904.

87 Macari, M., Hines, J., Balthazar, E. & Megibow, A. (2002). Mesenteric adenitis: CT diagnosis of primary versus secondary causes, incidence, and clinical significance in pediatric and adult patients. *AJR Am J Roentgenol, 178*(4), 853-858. doi: 10.2214/ajr.178.4.1780853

88 Macklin, C.P., Radcliffe, G.S., Merei, J.M. & Stringer, M.D. (1997). A prospective evaluation of the modified Alvarado score for acute appendicitis in children. *Ann R Coll Surg Engl, 79*(3), 203-205.
89 Mandeville, K., Pottker, T., Bulloch, B. & Liu, J. (2011). Using appendicitis scores in the pediatric ED. *Am J Emerg Med, 29*(9), 972-977. doi: 10.1016/j.ajem.2010.04.018
90 Markar, S.R., Karthikesalingam, A., Falzon, A. & Kan, Y. (2010). The diagnostic value of neutrophil: lymphocyte ratio in adults with suspected acute appendicitis. *Acta Chir Belg, 110*(5), 543-547.
91 Marudanayagam, R., Williams, G.T. & Rees, B.I. (2006). Review of the pathological results of 2660 appendicectomy specimens. *J Gastroenterol, 41*(8), 745-749. doi: 10.1007/s00535-006-1855-5
92 Mason, R.J. (2008). Surgery for appendicitis: is it necessary? *Surg Infect (Larchmt), 9*(4), 481-488. doi: 10.1089/sur.2007.079
93 Mason, R.J., Moazzez, A., Sohn, H. & Katkhouda, N. (2012). Meta-analysis of randomized trials comparing antibiotic therapy with appendectomy for acute uncomplicated (no abscess or phlegmon) appendicitis. *Surg Infect (Larchmt), 13*(2), 74-84.
94 Mazuski, J.E., Sawyer, R.G., Nathens, A.B., DiPiro, J.T., Schein, M., Kudsk, K.A. & Yowler, C. (2002). The Surgical Infection Society guidelines on antimicrobial therapy for intra-abdominal infections: an executive summary. *Surg Infect (Larchmt), 3*(3), 161-173. doi: 10.1089/109629602761624171
95 McBurney, C. (1894). IV. The Incision Made in the Abdominal Wall in Cases of Appendicitis, with a Description of a New Method of Operating. *Annals of Surgery, 20*(1), 38-43.
96 McBurney, C.H. (1889). Experience with early operative interference în cases of disease of the vermiform appendix. *New York Medical Journal*(50), 676-684.
97 McKay, R. & Shepherd, J. (2007). The use of the clinical scoring system by Alvarado in the decision to perform computed tomography for acute appendicitis in the ED. *Am J Emerg Med, 25*(5), 489-493. doi: 10.1016/j.ajem.2006.08.020
98 Medcalc Software. (2017). ROC curve analysis. *Medcalc easy-to-use statistical software*. 2017, from https://www.medcalc.org/manual/roc-curves.php
99 Meyer, J.S., Harmon, C.M., Harty, M.P., Markowitz, R.I., Hubbard, A.M. & Bellah, R.D. (1995). Ovarian torsion: clinical and imaging presentation in children. *J Pediatr Surg, 30*(10), 1433-1436.
100 Migraine, S., Atri, M., Bret, P.M., Lough, J.O. & Hinchey, J.E. (1997). Spontaneously resolving acute appendicitis: clinical and sonographic documentation. *Radiology, 205*(1), 55-58.
101 Morris, K.T., Kavanagh, M., Hansen, P., Whiteford, M.H., Deveney, K. & Standage, B. (2002). The rational use of computed tomography scans in the diagnosis of appendicitis. *Am J Surg, 183*(5), 547-550.
102 Murao, Y., Ueda, S. & Miyamoto, S. (1996). Preoperative administration of antibiotics in patients with suspected acute appendicitis. *Surg Today, 26*(5), 314-322.
103 Nadler, E.P. & Gaines, B.A. (2008). The Surgical Infection Society guidelines on antimicrobial therapy for children with appendicitis. *Surg Infect (Larchmt), 9*(1), 75-83.
104 Narsule, C.K., Kahle, E.J., Kim, D.S., Anderson, A.C. & Luks, F.I. (2011). Effect of delay in presentation on rate of perforation in children with appendicitis. *Am J Emerg Med, 29*(8), 890-893. doi: http://dx.doi.org/10.1016/j.ajem.2010.04.005
105 Nemeth, L., Reen, D.J., O'Briain, D.S., McDermott, M. & Puri, P. (2001). Evidence of an inflammatory pathologic condition in "normal" appendices following

emergency appendectomy. *Arch Pathol Lab Med, 125*(6), 759-764. doi: 10.1043/0003-9985(2001)125<0759:EOAIPC>2.0.CO;2

106 Ohmann, C., Yang, Q. & Franke, C. (1995). Diagnostic scores for acute appendicitis. Abdominal Pain Study Group. *Eur J Surg, 161*(4), 273-281.

107 Pansky, B. (1982). *Review of Medical Embryology*: McGraw-Hill.

108 Paradise, J., Fleischer, G. & Ludwig, S. (2002). Pediatric and adolescent gynecology. *Fleisher GR, Ludwig S. Textbook of pediatric emergency medicine Philadelphia: Lippincott, Williams and Wilkins, 1053*.

109 Park, N.H., Oh, H.E., Park, H.J. & Park, J.Y. (2011). Ultrasonography of normal and abnormal appendix in children. *World J Radiol, 3*(4), 85-91. doi: 10.4329/wjr.v3.i4.85

110 Paulson, E.K., Kalady, M.F. & Pappas, T.N. (2003). Clinical practice. Suspected appendicitis. *N Engl J Med, 348*(3), 236-242. doi: 10.1056/NEJMcp013351

111 Pearl, R.H., Hale, D.A., Molloy, M., Schutt, D.C. & Jaques, D.P. (1995). Pediatric appendectomy. *J Pediatr Surg, 30*(2), 173-181.

112 Pena, B.M., Taylor, G.A., Fishman, S.J. & Mandl, K.D. (2002). Effect of an imaging protocol on clinical outcomes among pediatric patients with appendicitis. *Pediatrics, 110*(6), 1088-1093.

113 Pickuth, D., Heywang-Kobrunner, S.H. & Spielmann, R.P. (2000). Suspected acute appendicitis: is ultrasonography or computed tomography the preferred imaging technique? *Eur J Surg, 166*(4), 315-319. doi: 10.1080/110241500750009177

114 Pisacane, A., de Luca, U., Impagliazzo, N., Russo, M., De Caprio, C. & Caracciolo, G. (1995). Breast feeding and acute appendicitis. *BMJ, 310*(6983), 836-837.

115 Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. (2012). *Anesthesiology, 116*(2), 248-273. doi: 10.1097/ALN.0b013e31823c1030

116 Prișcu, A. (1994). *Chirurgie* (Vol. 2). București: Editura Didactică și Pedagogică.

117 Puapong, D., Lee, S.L., Haigh, P.I., Kaminski, A., Liu, I.-L.A. & Applebaum, H. (2007). Routine interval appendectomy in children is not indicated. *J Pediatr Surg, 42*(9), 1500-1503.

118 Puri, P. & Mortell, A. (2006). Appendicitis. In M. D. Stringer, K. T. Oldham & P. D. E. Mouriquand (Eds.), *Pediatric Surgery and Urology: Long-Term Outcomes* (pp. 374-382): Cambridge University Press.

119 Puylaert, J.B. (1986). Acute appendicitis: US evaluation using graded compression. *Radiology, 158*(2), 355-360. doi: 10.1148/radiology.158.2.2934762

120 Quarrie, R., Lindsey, D. & Bahner, P.D. (2014). Review of the incidence and management of Meckel's diverticulum. *Austin Journal of Surgery, 1*(3), 1-3.

121 Rao, P.M., Rhea, J.T., Novelline, R.A., McCabe, C.J., Lawrason, J.N., Berger, D.L. & Sacknoff, R. (1997). Helical CT technique for the diagnosis of appendicitis: prospective evaluation of a focused appendix CT examination. *Radiology, 202*(1), 139-144. doi: 10.1148/radiology.202.1.8988203

122 Rao, P.M., Rhea, J.T., Novelline, R.A., Mostafavi, A.A. & McCabe, C.J. (1998). Effect of computed tomography of the appendix on treatment of patients and use of hospital resources. *N Engl J Med, 338*(3), 141-146. doi: 10.1056/nejm199801153380301

123 Rautio, M., Saxen, H., Siitonen, A., Nikku, R. & Jousimies-Somer, H. (2000). Bacteriology of histopathologically defined appendicitis in children. *Pediatr Infect Dis J, 19*(11), 1078-1083.

124 Rice, H.E., Arbesman, M., Martin, D.J., Brown, R.L., Gollin, G., Gilbert, J.C., Caty, M.G., Glick, P.L. & Azizkhan, R.G. (1999). Does early ultrasonography affect

management of pediatric appendicitis? A prospective analysis. *J Pediatr Surg, 34*(5), 754-758; discussion 758-759.

125 Roosevelt, G.E. & Reynolds, S.L. (1998). Does the use of ultrasonography improve the outcome of children with appendicitis? *Acad Emerg Med, 5*(11), 1071-1075.

126 Rothrock, S.G. & Pagane, J. Acute appendicitis in children: Emergency department diagnosis and management. *Annals of Emergency Medicine, 36*(1), 39-51. doi: 10.1067/mem.2000.105658

127 Sack, U., Biereder, B., Elouahidi, T., Bauer, K., Keller, T. & Trobs, R.B. (2006). Diagnostic value of blood inflammatory markers for detection of acute appendicitis in children. *BMC Surg, 6*, 15. doi: 10.1186/1471-2482-6-15

128 Sakpal, S.V., Bindra, S.S. & Chamberlain, R.S. (2012). Laparoscopic appendectomy conversion rates two decades later: an analysis of surgeon and patient-specific factors resulting in open conversion. *Journal of Surgical Research, 176*(1), 42-49.

129 Saliu Oguntola, A., Layiwola Adeoti, M., Olayide Agodirin, S., Adeniyi Oremakinde, A. & K, O.O. (2014). Further exploration during open appendicectomy; assessment of some common intraoperative findings. *Pak J Med Sci, 30*(2), 316-321.

130 Samuel, M. (2002). Pediatric appendicitis score. *J Pediatr Surg, 37*(6), 877-881.

131 Sanford, A.P. (2010). Open Appendectomy. In C. M. Townsend & B. M. Evers (Eds.), *Atlas of General Surgical Techniques*: Elsevier Health Sciences.

132 Schneider, C., Kharbanda, A. & Bachur, R. (2007). Evaluating appendicitis scoring systems using a prospective pediatric cohort. *Ann Emerg Med, 49*(6), 778-784, 784.e771. doi: 10.1016/j.annemergmed.2006.12.016

133 Schuler, J.G., Shortsleeve, M.J., Goldenson, R.S., Perez-Rossello, J.M., Perlmutter, R.A. & Thorsen, A. (1998). Is there a role for abdominal computed tomographic scans in appendicitis? *Arch Surg, 133*(4), 373-376; discussion 377.

134 Schulte, B., Beyer, D., Kaiser, C., Horsch, S. & Wiater, A. (1998). Ultrasonography in suspected acute appendicitis in childhood-report of 1285 cases. *Eur J Ultrasound, 8*(3), 177-182.

135 Semm, K. (1983). Endoscopic appendectomy. *Endoscopy, 15*(02), 59-64.

136 Sengupta, A., Bax, G. & Paterson-Brown, S. (2009). White cell count and C-reactive protein measurement in patients with possible appendicitis. *Ann R Coll Surg Engl, 91*(2), 113-115. doi: 10.1308/003588409X359330

137 Sharma, R.K. & Jain, V.K. (2008). Emergency surgery for Meckel's diverticulum. *World Journal of Emergency Surgery : WJES, 3*, 27-27. doi: 10.1186/1749-7922-3-27

138 Shera, A.H., Nizami, F.A., Malik, A.A., Naikoo, Z.A. & Wani, M.A. (2011). Clinical scoring system for diagnosis of acute appendicitis in children. *Indian J Pediatr, 78*(3), 287-290. doi: 10.1007/s12098-010-0285-9

139 Shestobuz, S.V., Bodnar, B.M., Brozhyk, V.L. & Kukharchuk, O.L. (2000). [Differences in differential diagnosis between acute mesenterial lymphadenitis and appendicitis in children]. *Klin Khir*(7), 39-40.

140 Silen, W., Cope, Z. & Cope, Z. (1991). *Cope's early diagnosis of the acute abdomen*: Oxford University Press.

141 Simillis, C., Symeonides, P., Shorthouse, A.J. & Tekkis, P.P. (2010). A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis (abscess or phlegmon). *Surgery, 147*(6), 818-829.

142 Sivit, C.J., Newman, K.D., Boenning, D.A., Nussbaum-Blask, A.R., Bulas, D.I., Bond, S.J., Attorri, R., Rebolo, L.C., Brown-Jones, C. & Garin, D.B. (1992). Appendicitis: usefulness of US in diagnosis in a pediatric population. *Radiology, 185*(2), 549-552. doi: 10.1148/radiology.185.2.1410371

143 Skandalakis, J.E. & Colborn, G.L. (2004). *Skandalakis' Surgical Anatomy: The Embryologic and Anatomic Basis of Modern Surgery*: PMP.
144 Soda, K., Nemoto, K., Yoshizawa, S., Hibiki, T., Shizuya, K. & Konishi, F. (2001). Detection of pinpoint tenderness on the appendix under ultrasonography is useful to confirm acute appendicitis. *Arch Surg, 136*(10), 1136-1140.
145 Soffer, D., Zait, S., Klausner, J. & Kluger, Y. (2001). Peritoneal cultures and antibiotic treatment in patients with perforated appendicitis. *Eur J Surg, 167*(3), 214-216. doi: 10.1080/110241501750099456
146 St-Vil, D., Brandt, M.L., Panic, S., Bensoussan, A.L. & Blanchard, H. (1991). Meckel's diverticulum in children: a 20-year review. *J Pediatr Surg, 26*(11), 1289-1292.
147 St. Peter, S.D. (2010). chapter 43 - APPENDICITIS A2 - Holcomb, George Whitfield. In J. P. Murphy, A. Editor & D. J. Ostlie (Eds.), *Ashcraft's Pediatric Surgery (Fifth edition)* (pp. 549-556). Philadelphia: W.B. Saunders.
148 Standring, S. (2008). *Gray's Anatomy: The Anatomical Basis of Clinical Practice*: Elsevier Health Sciences UK.
149 Stengel, A. (1908). Appendicitis. In W. Osler & T. McCrae (Eds.), *Modern Medicine* (Vol. V - Diseases of the Alimentary Tract). Philadelphia: Lea & Febiger.
150 Talukder, D.B. & Siddiq, A.K.M.Z. (2009). Modified Alvarado Scoring System in the Diagnosis of Acute Appendicitis. *Journal of Armed Forces Medical College, Bangladesh; Vol 5, No 1 (2009)*.
151 Tekin, A., Kurtoğlu, H., Can, I. & Öztan, S. (2008). Routine interval appendectomy is unnecessary after conservative treatment of appendiceal mass. *Colorectal Disease, 10*(5), 465-468.
152 Thompson, G. (2012). Clinical Scoring Systems in the Management of Suspected Appendicitis in Children. In A. Lander (Ed.), *Appendicitis - A Collection of Essays from Around the World*: InTech.
153 Toorenvliet, B., Vellekoop, A., Bakker, R., Wiersma, F., Mertens, B., Merkus, J., Breslau, P. & Hamming, J. (2011). Clinical differentiation between acute appendicitis and acute mesenteric lymphadenitis in children. *Eur J Pediatr Surg, 21*(2), 120-123. doi: 10.1055/s-0030-1267979
154 Tsuji, M., Puri, P. & Reen, D.J. (1993). Characterisation of the local inflammatory response in appendicitis. *J Pediatr Gastroenterol Nutr, 16*(1), 43-48.
155 Tugnoli, G., Giorgini, E., Biscardi, A., Villani, S., Clemente, N., Senatore, G., Filicori, F., Antonacci, N., Baldoni, F., De Werra, C. & Di Saverio, S. (2011). The NOTA study: non-operative treatment for acute appendicitis: prospective study on the efficacy and safety of antibiotic treatment (amoxicillin and clavulanic acid) in patients with right sided lower abdominal pain. *BMJ Open, 1*(1).
156 Tzanakis, N.E., Efstathiou, S.P., Danulidis, K., Rallis, G.E., Tsioulos, D.I., Chatzivasiliou, A., Peros, G. & Nikiteas, N.I. (2005). A new approach to accurate diagnosis of acute appendicitis. *World J Surg, 29*(9), 1151-1156, discussion 1157. doi: 10.1007/s00268-005-7853-6
157 Varadhan, K.K., Humes, D.J., Neal, K.R. & Lobo, D.N. (2010). Antibiotic therapy versus appendectomy for acute appendicitis: a meta-analysis. *World J Surg, 34*(2), 199-209.
158 Varadhan, K.K., Neal, K.R. & Lobo, D.N. (2012). Safety and efficacy of antibiotics compared with appendicectomy for treatment of uncomplicated acute appendicitis: meta-analysis of randomised controlled trials.
159 Vons, C., Barry, C., Maitre, S., Pautrat, K., Leconte, M., Costaglioli, B., Karoui, M., Alves, A., Dousset, B. & Valleur, P. (2011). Amoxicillin plus clavulanic acid versus

appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. *The Lancet, 377*(9777), 1573-1579.

160 Waisman, Y. (1997). Gastrointestinal Disorders. In R. M. Barkin (Ed.), *Pediatric Emergency Medicine Concepts and Clinical Practice* (pp. 852-854). St. Louis: Mosby.

161 Wang, L.T., Prentiss, K.A., Simon, J.Z., Doody, D.P. & Ryan, D.P. (2007). The use of white blood cell count and left shift in the diagnosis of appendicitis in children. *Pediatr Emerg Care, 23*(2), 69-76. doi: 10.1097/PEC.0b013e31802d1716

162 Wang, Y., Reen, D.J. & Puri, P. Is a histologically normal appendix following emergency appendicectomy always normal? *The Lancet, 347*(9008), 1076-1079. doi: 10.5555/uri:pii:S0140673696902792

163 Weyant, M.J., Eachempati, S.R., Maluccio, M.A., Rivadeneira, D.E., Grobmyer, S.R., Hydo, L.J. & Barie, P.S. (2000). Interpretation of computed tomography does not correlate with laboratory or pathologic findings in surgically confirmed acute appendicitis. *Surgery, 128*(2), 145-152. doi: 10.1067/msy.2000.107422

164 Williams, G.R. (1983). Presidential Address: a history of appendicitis. With anecdotes illustrating its importance. *Annals of Surgery, 197*(5), 495-506.

165 Williams, N. & Kapila, L. (1994). Acute appendicitis in the under-5 year old. *J R Coll Surg Edinb, 39*(3), 168-170.

166 Wilson, E.B., Cole, J.C., Nipper, M.L., Cooney, D.R. & Smith, R.W. (2001). Computed tomography and ultrasonography in the diagnosis of appendicitis: when are they indicated? *Arch Surg, 136*(6), 670-675.

167 Wise, S.W., Labuski, M.R., Kasales, C.J., Blebea, J.S., Meilstrup, J.W., Holley, G.P., LaRusso, S.A., Holliman, J., Ruggiero, F.M. & Mauger, D. (2001). Comparative assessment of CT and sonographic techniques for appendiceal imaging. *AJR Am J Roentgenol, 176*(4), 933-941. doi: 10.2214/ajr.176.4.1760933

168 Yazici, M., Ozkisacik, S., Oztan, M.O. & Gursoy, H. (2010). Neutrophil/lymphocyte ratio in the diagnosis of childhood appendicitis. *Turk J Pediatr, 52*(4), 400-403.

169 Young, P. (2014). La apendicitis y su historia. *Revista médica de Chile, 142*, 667-672.

170 Zuniga, R.V., Arribas, J.L., Montes, S.P., Fernandez, M.N., Abad, C.G., Martin, L.G. & Gonzalez-Sagrado, M. (2012). Application of Pediatric Appendicitis Score on the emergency department of a secondary level hospital. *Pediatr Emerg Care, 28*(6), 489-492. doi: 10.1097/PEC.0b013e3182586d34