DEPARTMENT OF GENERAL SURGERY

LITHUANIAN UNIVERSITY OF HEALTHCARE SCIENCES

Differential diagnosis of acute appendicitis in female patients: value of the diagnostic tests

MARIA PRADOS QUIRANTES

FACULTY OF MEDICINE

SUPERVISOR : Dr. LINAS URBANAVICIUS

16/11/2016

TABLE OF CONTENTS

I.SUMMARY……..3

II. CONFLICTS OF INTEREST……..5

III. CLEARANCE ISSUED BY THE ETHICS COMMITTEE……..6

IV. ABBREVIATIONS……..7

V. INTRODUCTION……8

VI. AIM AND OBJECTIVES……11

VII. LITERATURE REVIEW……11

VIII. RESEARCH METHODOLOGY AND METHODS……16

IX. RESULTS……18

X. DISCUSSION OF RESULTS……19

XI. CONCLUSIONS……22

XII. REFERENCES……23

I. SUMMARY

Aim

To review the diagnostic studies that can assist in establishing the diagnosis of acute appendicitis in fertile women.

Objectives

1. To analyze and assess diagnostic criteria based on the clinical signs as well as laboratory tests and instrumental investigations among women of reproductive age who were diagnosed with acute appendicitis in our ED, but during the corresponding surgery, gynecological pathology was diagnosed.
2. To gather and analyze the most updated literature review regarding the topic.
3. To compare results of the study to the data from the literature.

Methodology

A retrospective study of 21 female patients, between 18 and 55 years old with a false-positive diagnosis of acute appendicitis from 2013 to 2015 who underwent laparoscopy at the Department of General surgery during which a gynecological pathology was diagnosed as the real etiology of the acute abdominal pain. The following patient-related characteristics were analyzed: body temperature, WBC count and CRP level, presence of pain in the right fossa, presence of Kocher's and Blumberg's sign as well as anorexia, nausea and vomiting. Alvarado score was calculated and its diagnostic value was assessed. The value of radiologic investigations (abdominal as well as transvaginal ultrasound and abdominal-pelvic CT) was assessed. The obtained data were compared to the data in the literature.

Results

Fever over 38°C was observed in 10% of the patients. CRP was elevated (>10 mg/l) in 61%, leucocytosis (> 11x10*9/l) in 45% and an increased neutrophils count (>70%) in 66%. Localized right fossa pain was present in 55% of the patients. Kocher's sign, was positive in 14% of the cases, while Blumberg's sign was positive in 52.3% of the cases. Vomiting or nausea was present in 60% of the patients, while the anorexia prevalence was 65%. 56% obtained an Alvarado score =/> 5. 43% obtained a score <5. In 66% of the patients the pain lasted longer or equal to 24h, while in the rest 34% < 24h. US findings showed some abnormalities in 41% of patients. CT was not performed at all. TVU was not helpful.

Conclusions

1. Clinical signs and laboratory parameters indicating AA were weakly expressed, thus, they were not informative enough to rule out AA. However, elevated Ne, anorexia, afebrile condition and pain onset =/> 24h may suggest a gynecological pathology.

2. Alvarado score ≤5 is not suggestive for AA in fertile women and these patients have to be referred to the gynecologist.

3. To improve the diagnostics when clinical, laboratory tests and AUS do not support the diagnosis of AA, abdominal-pelvic CT has to be considered.

4. To improve the gynecologic diagnostics TUS should be more widely applied in combination with AUS.

5. A closer cooperation between surgeon and gynecologist is warranted to avoid diagnostic mistakes.

6. A more detailed anamnesis and further clinical examination is required.

7. The number of false-positive diagnosis of AA remains high over the last few years indicating the need for more accurate diagnostic approach.

II. CONFLICTS OF INTEREST

The author reports no conflicts of interest.

III. CLEARANCE ISSUED BY THE ETHICS COMMITTEE

Tittle: Differential diagnosis of acute appendicitis in female patients

Date of issue: 2017-03-02

Number: BEC-MF-330

IV. ABBREVIATIONS

AA Acute appendicitis
ED Emergency department
L Leukocytes
AS Alvarado score
US Ultrasound
AUS Abdominal ultrasound
TUS Transvaginal ultrasound
PP Prior pregnancies
GA Gynecological anamnesis
MCD Menstrual cycle day
LF Laparoscopy findings
Ne Neutrophils
A Anorexia
N/V Vomiting/nausea
PO Pain onset
RFP Right fossa pain
K Kocher's sign
B Blumberg's sign
N Normal value/findings
? Not available data
NP Not performed
NA Negative appendectomy

V. INTRODUCTION

Acute appendicitis is the most common abdominal emergency requiring emergency surgery. [1]
Evaluating acute lower quadrant abdominal pain in fertile female patients remains a clinical challenge.
The accuracy of the diagnosis is complicated, since depending on the hospital policy and recommendations in the literature, different protocols are established at each center, and diagnosis is made hypothetically and sometimes with not enough criteria.

Diagnostic workup in this patient group is more difficult than in male patients, due to the local anatomical differences with numerous gynecological pathologies mimicking AA. A false positive diagnosis may lead to both unnecessary and negative appendectomy whereas a false negative diagnosis of acute appendicitis leads to serious complications such as appendicular perforation.

Therefore, it is of significant importance to determine the most accurate diagnostic methods in order to optimize the use of resources, diagnostic tools, as well as invasive procedures which can even compromise patient`s health and life.
Nowadays, despite numerous studies, the accuracy, specificity, sensitivity and likelihood ratio of updated diagnostic methods are still not efficient and effective enough.

Then, which systematic approach should be followed by emergency department physicians when facing acute abdominal pain in fertile women?

<u>Appendicitis</u>
Appendicitis is defined as an inflammation of the inner lining of the vermiform appendix that spreads to its other parts.
The appendix is a wormlike extension of the cecum.
Appendicitis is caused by obstruction of the appendiceal lumen from a variety of causes. Independent of the etiology, obstruction is believed to cause an increase in pressure within the lumen. Such an increase is related to continuous secretion of fluids and mucus from the mucosa and the stagnation of this material. At the same time, intestinal bacteria within the appendix multiply, leading to the recruitment of white blood cells and the formation of pus and subsequent higher intraluminal pressure.
If appendiceal obstruction persists, intraluminal pressure rises ultimately above that of the appendiceal veins, leading to venous outflow obstruction. As a consequence, appendiceal wall ischemia begins, resulting in a loss of epithelial integrity and allowing bacterial invasion of the appendiceal wall.Within a few hours, this localized condition may worsen because of thrombosis of the appendicular artery and veins, leading to perforation and gangrene of the appendix. As this process continues, a periappendicular abscess or peritonitis may occur.

<u>Appendectomy</u>
The median age at appendectomy is 22 years.
Appendectomy carries a complication rate of 4-15%, as well as associated costs and the discomfort of hospitalization and surgery.
Infertility in women of reproductive age after appendectomy procedure, is one of the main concerns nowadays.[2]

How does the scaring after either ruptured or non-ruptured appendectomy influence female infertility (infertility and ectopic pregnancy)?

This subject was studied by Tarig Elraiyah et al.,[3] in 2014, who found that appendicitis (whether complicated or not) does not lead to increased future infertility in women. However, the risk of ectopic pregnancy may be higher after appendectomy is performed.

Diagnosis

The most common symptom of acute appendicitis is abdominal pain. A history of mid-epigastric pain migrating to the right lower quadrant (Kocher's sign) is classic, and has a positive predictive value of 90% in adults with acute appendicitis. Nausea, vomiting, diarrhea, and anorexia are also common. Fever and leukocytosis may be present, and have been reported in approximately one-third of adults with acute appendicitis. However, many of these signs and symptoms may not be helpful in distinguishing acute appendicitis from urgent gynecological conditions.

The uterus, cervix, and adnexa share the same visceral innervation as the lower ileum, sigmoid colon, and rectum. Signals travel via the sympathetic nerves to spinal cord segments T10 through L1. Because of this shared pathway, distinguishing between pain of gynecologic and gastrointestinal origin is often difficult.

I period (pain onset up to 8-12h): obstruction of lumen, epigastric pain, anorexia signs, subfebrile fever (37-38ºC).

II period (12-24h): localized right fossa pain

III period (>24h): perforation

Appendicitis is misdiagnosed in 33% of nonpregnant women of childbearing age. [4]

Negative appendectomy

The overall accuracy for diagnosing acute appendicitis is approximately 80%, which corresponds to a mean negative appendectomy (NA) rate of 20%. Diagnostic accuracy varies by sex, with a range of 78-92% in male patients and 58-85% in female patients. [4]

Engin O. et al.,[5] through their study in 2010 of the different NA rates in males and females, found out that the leading cause of acute abdomen in women who underwent appendectomy had gynecological source, being ruptured right ovarian cyst the most common primary cause, followed by ruptured left ovarian cyst, tubo-ovarian abscess, ectopic pregnancy, salphingo-oophoritis, right ovarian torsion and finally, pelvic inflammatory disease.

According to Seetahal S.A. et al.,[6] the NA incidence decreased with years, being 14.7% and 8.47% during 1998 and 2007 respectively, where women comprised 71.3% of all NA. However, this decline cannot be attributed to the increased use of imaging modalities because the study did not have adequate data for that.

Women accounted for 71.3% of all NA studied. Mean age overall was 42 years. 76.2% were white ethnicity. Diagnosis for women aged from 18 to 44 years old, was predominantly benign diseases, whereas for women aged more than 44, main diagnosis switched to malignant diseases, where malignant ovarian disease counted 16.5%.

The most common urgent gynecological pathologies causing acute abdominal pain:

- **Pelvic inflammatory disease (PID)**
- **Endometriosis**
- **Ovarian torsion**
- **Ruptured ovarian cyst**
- **Ectopic pregnancy**

Early diagnosis of pelvic pain is important to prevent sequelae of delayed diagnosis, such as appendiceal perforation, infertility from PID and ovarian torsion, or hemoperitoneum from an ectopic pregnancy. Right-sided pelvic pain is especially challenging and can be confusing because of the close proximity of the appendix, uterus, right fallopian tube, and right ovary.

VI. AIM AND OBJECTIVES

Aim

To review the diagnostic studies that can assist in establishing the diagnosis of acute appendicitis in fertile women.

Objectives

1. To analyze and assess diagnostic criteria based on the clinical signs as well as laboratory tests and instrumental investigations among women of reproductive age who were diagnosed with acute appendicitis in our ED, but during the corresponding surgery, gynecological pathology was diagnosed.
2. To gather and analyze the most updated literature review regarding the topic.
3. To compare results of the study to the data from the literature.

VII. LITERATURE REVIEW

To most effectively explore this issue surrounding the differential diagnosis of AA in female patients and its value of the diagnostic tests, a subset of literature has been selected.

Until recently, many researchers have shown interest in the field of the differential diagnosis when a women of reproductive age presents in ED with acute abdominal pain, in the accuracy of the diagnostic tests and the side effects when a pathology is misdiagnosed. Their findings and suggestions are reviewed here.

1. Abdominal-pelvic CT

Shogilev et al.[1] (2014), evaluated the specificity and sensitivity of the different diagnostic methods of AA, to have an updated diagnostic approach to suspected appendicitis.

According to these authors, although CT proves its high specificity and sensitivity as well as its efficacy, incidence of appendiceal perforation, the most significant complication of appendicitis, was reported as unchanged by the use of CT.

On the other hand, concerns over increased exposure to radiation and long-term cancer risks seem to largely decrease its benefits.

Efforts have been made to limit CT's high radiation levels with low-dose CT imaging, but studies demonstrate that both, standard CT and low-dose CT, had similar negative appendectomy rates and no major differences in perforation rates. [7]

In 2014, Thomas Schok [8] published an article in which the benefits of the "Appendicitis Guideline" introduced by the Dutch Association for Surgery, where image screening (abdominal US and abdominal MRI for pregnant women, and abdominal CT and abdominal US for adults with suspicious appendicitis) was added for every clinical practice, were observed.

The author concluded that percentage of negative appendectomies, following image screening, remains close to the percentage declared as unacceptable by the publishers of the guideline.

S.A. Seetahal et al.,[6] through their study, aim to compare the appendectomy rates, with the incorporation of increased imaging technology (CT and US mainly), during past decade. The significant burden of negative appendectomy was also studied.

On the other hand, according to a study published in the June edition of Radiology, the number of appendectomies and the negative appendectomy rate in patients who presented to the emergency department saw significant reductions during an 18-year period, which is associated with increased use of preoperative abdominal CT.

Greenville Hospital System, University Medical Center, Greenville, South Carolina, USA (2007), examined CT effectiveness in making the diagnosis of AA in reproductive-age women with right lower quadrant abdominal pain and to determine if its use is cost-effective. Results showed a positive result of the diagnostic tool, being reliable, useful, and cost-effective.

As well as some other studies suggest that nontherapeutic appendectomy rate increases in adult women when preoperative diagnostic CT scan is not performed. [12]

2. **Abdominal US**

When talking about abdominal US, its limited sensitivity shows less efficacy than CT due to its considerable heterogeneity, however, neither radiation nor cancer risks are attributed to this radiological imaging. [4]

Moreover, the spatial resolution of a high-frequency US image is higher than that of a CT image. But this is only true if the target organ can be approached closely, which requires either a thin patient or the use of graded compression.[18]

Department of Surgery, Myongji Hospital, Kwandong University, Goyang, Korea (2013) concluded that ultrasonography/computed tomography should be performed routinely for diagnosis of AA. However, in view of its advantages, ultrasonography should be performed first. Also, if the result of a physical examination is negative, imaging studies after physical examination can be unnecessary.

Diagnostic imaging should be performed and is most likely to alter treatment when the diagnosis of appendicitis is clinically suspected but unclear. It may be useful in women of childbearing age with an unclear presentation. [12]

Ultrasonography effectively evaluates emergent entities such as ovarian cysts and rupture, tubo-ovarian abscesses, uterine fibroids, ectopic pregnancy, uterine rupture, and even ovarian torsion.[16]

The decision to obtain US or CT scan studies depends on institutional preference and the available user expertise, although patient age, sex, and body habitus are important influencing factors. US and CT scanning have similar diagnostic value for detecting an alternative diagnosis in a patient in whom acute appendicitis is suspected. Graded-compression US of the right

lower quadrant (RLQ) has been shown to be a useful examination because of this technique's safety and high accuracy (approximately 90%) in the diagnosis of acute appendicitis. Advantages of US include lack of radiation exposure, noninvasiveness, short acquisition time, and the potential for diagnosis of other causes of abdominal pain, particularly in the subset of patients who are women of childbearing age. Several authors suggest that US should be the first imaging method used in pregnant women and pediatric patients because x-ray exposure is especially undesirable in these groups. [19]

3. Transvaginal US

The results obtained in the department of Obstetrics and Gynecology, Kaplan Medical Center, Rehovot, Israel (2012) indicate that combined ultrasound (abdominal and transvaginal) has a high predictive value for the diagnosis of appendicitis and may assist in reduction of the use of CT scanning for diagnosis and in the negative appendectomy rate.(no reference)

Omer Engin et al.,[5] suggested in 2010 that the lack of urgent gynecologic US, CT and diagnostic laparoscopy when female presents with acute abdominal pain may lead to wrong diagnosis. General surgeons interpreted acute appendicitis through only physical examination, direct abdominal ultrasound and blood test, therefore, leading to negative appendectomies when the real cause was gynecological.

Focusing on TUS advantages and disadvantages when exploring non-pregnant female patients with RLQ pain, Tabbara et al., [9] concluded that its use resulted in 100% specificity and 80% sensitivity to provide a correct diagnosis, and that the incidence of true gynecological emergencies requiring urgent surgical intervention was very low.

Nevertheless, other authors, such as Bondi M. et al., [10] support the use of combined TUS and AUS, whose studies reflected a high predictive value for the diagnosis of appendicitis and may assist in reduction of the use of CT scanning for diagnosis and in the negative appendectomy rate.

Compared with endovaginal ultrasonography, transabdominal ultrasonography uses a lower frequency and can penetrate further, with a large field of view. Thus, fibroids, ovaries, or cysts located high in the pelvis may be out of the focal range of an endovaginal probe. Also a normal fallopian tube may not be visualized with endovaginal ultrasonography; however, a fluid- or pus-filled tube can be identified.[16]

The endovaginal transducer is preferred for obese patients because it has the ability to visualize pelvic organs far better than any other modality.[16]

4. Laboratory tests

Laboratory markers (WBC, CRP, granulocyte count) calculated alone, always contribute to appendicitis presentation, but they do not really help in differential diagnosis. However, when used in combination, they show better response.[1]

Novel markers (IL-6, SAA, leukocyte gene expression, cytokine profiles, G-CSF, LRG, Calprotectin) show a good early predictor for appendicitis diagnosis. However, they are not yet applied in clinical practice and further exploration of some of these markers is warranted. [1]

5. Alvarado score

The Alvarado score was developed to assist in diagnosing appendicitis.

A score is assigned by the following variables leading to a maximum of 10-points [17]:

+2 points - Right lower quadrant tenderness
+1 point - Elevated temperature (>37.3°C or 99.1°F)
+1 point - Rebound tenderness (Blumberg's sign)
+1 point - Migration of pain to the right lower quadrant (Kocher's sign)
+1 point - Anorexia
+1 point – Nausea/vomiting
+2 point - Leukocytosis > 10,000
+1 point - Leukocyte left shift (neutrophils >70%)

A score of 5 or 6 is "compatible" with the diagnosis of acute appendicitis. A score of 7 or 8 indicates a "probable" appendicitis, and a score of 9 or 10 indicates a "very probable" acute appendicitis.[17]

According to Ronald F Martin [12], a female patient who is not pregnant with a score of 7 to 9 would undergo diagnostic laparoscopy, then appendectomy if indicated by the intraoperative findings.

Notwithstanding, Robert Ohle et al., confirmed that patients with Alvarado score >5 have a sensitivity for appendicitis of 99%, then patients <5 are considered clinically at low risk for appendicitis, who should avoid ED CT and only proceed with future clinical examinations.[11]

In contrast, McKay et al., [13] recommend a CT scan for a score of 4-6 and surgical consultation for a score ≥ 7. For a score of ≤ 3, the authors suggest that a CT scan is unnecessary for diagnosing appendicitis given the low likelihood of appendicitis.

6. Other diagnostic scores

Following Kijja Jearwattanakanok et al., [14] article about their retrospective data analysis (2013), the present clinical scoring system may help to differentiate between females of reproductive age (15-50 years old) with appendicitis, common obstetrics and gynecological conditions (ectopic pregnancy, pelvic inflammatory disease, complicated ovarian cyst…) or nonspecific abdominal pain.

Significant differences are seen among the different diagnostic groups, such as shifting of pain, anorexia, nausea and vomiting or guarding/rebound tenderness, which are highly specific for appendicitis, or left lower quadrant tender and pregnancy, which are specific for common obstetrics and gynecological conditions.

Kijja Jearwattanakanok et al., [15] (2014) also studied medical records of reproductive aged women who were admitted for acute lower abdominal pain. The recently diagnostic score developed for acute lower abdominal pain in reproductive age female can guide ED physicians for proper management when appendicitis, obstetrics-gynecological conditions or nonspecific abdominal pain are suggested.

7. Conclusions

A low radiation dose preoperative CT, which is as useful as high radiation dose CT, may improve the diagnosis of AA, however some studies show its limited value.

Abdominal US may replace CT avoiding unnecessary radiation.

Gynecologic US may assist the abdominal US in diagnosing gynecologic pathology, especially in obese patients.

Laboratory tests (WBC, Ne, CRP) may be helpful if used in combination, however they lack specificity.

Alvarado score of <5 might help to exclude the diagnosis of AA.

VIII. RESEARCH METHODOLOGY AND METHODS

Retrospective study of 21 female patients with diagnosed appendicitis and who were admitted to the Department of General Surgery of LUHS, over the last three years (2013-2015). The data were obtained from Kaunas clinical hospital. The data analyses included clinical, laboratory and instrumental data that had confirmed the diagnosis of acute appendicitis.

Inclusion criteria were fertile women patients whose preliminary diagnosis was AA, based on clinical signs, symptoms, laboratory tests and imaging, in some cases, however, clinical diagnosis was confirmed as a gynecological pathology when laparoscopy was performed. Clinical, laboratory, instrumental data, gynecological anamnesis, and age was selected from the patient's case histories.

Exclusion criteria were non fertile aged women, any women patient who presented to emergency department with acute abdomen pain but no suspicion of appendicitis was present and those whose preliminary diagnosis was appendicitis indeed, but no gynecological etiology was found during surgery.

Age, Alvarado score, leucocytes and neutrophils counts, CRP, body temperature, onset of pain (in hours) and prior pregnancies median values were calculated as a whole group.

Signs and symptoms, such as pain onset and localization, vomiting/nausea, anorexia, Kocher and Blumberg's sign menstrual cycle day and relevant gynecological anamnesis were also obtained when available. Findings of abdominal and transvaginal ultrasound, CT and laparoscopy were assessed.

Laparoscopic appendectomies in female patients in 2013-2015:

Year	Number of diagnosed AA cases	Number of laparoscopic appendectomies	Number of gynecologic diagnosis	Percentage of false-positive AA diagnosis
2013	86	83	3	3,4%
2014	85	74	11	12,9%
2015	63	56	7	11,1%

	Age	CRP	ºC	L	Ne	A	N/V	RFP	K	B	AS	PO (h)	AUS	TUS	CT	GA	PP	MCD	LF
1. V.R. 13	40	37.4	39	12.5	42	+	-	-	-	+	5	24	N	NP	NP	Cervix surgery + pelvialgia	2	10	Morbus pelvis inflam.
2. L.R. 13	39	2	N	14.5	42	-	-	+	-	-	4	48	Free fluid	NP	NP	Foreign body in uterus + cervix surgery	0	?	?
3. R.J. 13	31	80.5	N	11.4	72.3	-	-	-	-	+	4	24	N	NP	NP	C.S., Adhesions	0	?	Pus + adnexa inflam.
4. L.K. 14	26	162	37.3	8	74	?	?	?	-	+	2	72	N	NP	NP	-	?	?	Pus + right adnexa inflam.
5. I.K. 14	29	178	N	13	78.2	+	+	+	-	-	7	36	Free fluid + tumor in right iliac adnexa	NP	NP	PID	?	?	Free fluid + adnexa and uterus inflam.
6. H.R. 14	36	31.8	37.3	13.7	78.4	-	-	-	-	-	3	20	N	NP	NP	Breast cancer + chemotherapy	?	1	15ml hemorrhagic fluid
7. N.J. 14	21	?	N	6.7	66.5	+	+	+	+	+	6	10	RF free fluid + appendix 7.7cm	NP	NP	-	?	?	Ruptured right ovarium, apoplexy
8. J.M. 14	35	?	N	?	?	+	+	+	-	-	4	36	NP	NP	NP	Cervix cancer+ radiation	?	?	Right area blood accumulation + right torsion ovarium + necrosis
9. M.J. 14	27	0.1	N	5.5	58.7	-	-	+	-	+	3	20	Free fluid	NP	NP	-	1	?	20ml blood Douglas pouch + uterus and adnexa inflam.
10. A.L. 14	48	47	N	9.9	76.6	-	-	-	-	-	1	12	NP	NP	NP	-	?	?	Right ovarium and uterus inflam.
11. A.S. 15	32	15.7	N	15.9	?	+	+	+	-	-	6	24	NP	NP	NP	-	1	?	Ruptured cyst + blood right ovarium
12. S.J. 15	47	9.5	?	10.8	?	+	+	+	-	-	6	24	N	NP	NP	RA	?	?	Hemorrhagic fluid next to uterus
13. M.R15	22	32	N	10.4	?	-	-	+	-	-	4	96	NP	NP	NP	-	0	?	Turbid fluid in douglas pouch
14. D.C. 15	31	1.2	N	10.8	82.8	+	+	-	-	-	5	?	N	NP	NP	-	?	?	Hemorrhagic fluid LRQ + uterus and adnexa inflam
15. G.D15	27	8.8	37.5	8.4	85.9	+	+	+	+	-	6	24	Free fluid next to uterus	NP	NP	-	?	?	Hemorrhagic fluid next to uterus + uterus and adnexa inflam.
16. J.V. 16	53	21.4	38.2	17.2	87.9	+	+	-	-	+	6	20	N	NP	NP	-	?	?	Pus left fallopian tube
17. V.C. 16	27	?	N	8.5	?	-	-	+	+	+	4	36	Fetus	NP	NP	-	19 wog	?	Yellow fluid 15 ml lower abdomen + cyst right ovari + endometriosis
18. B.K. 16	53	51.5	N	18.3	77.4	+	+	-	-	+	6	24	N	NP	NP	-	?	?	Inflam uterus and adnexa inflam.
19. V.D.16	21	6.8	N	11.8	?	+	+	-	-	+	5	72	Free fluid in lower abdomen	Free fluid	NP	-	?	22	400 ml hemorrhagic fluid in abdominal cavity + right ovari ruptured cyst
20. D.G16	19	0.1	N	10.3	55.1	+	+	+	-	+	7	12	N	N	NP	-	0	12	Uterus and adnexa inflam. + 50ml hemorrhagic fluid
21. G.S.16	25	48.4	N	10.1	77.9	+	+	-	-	+	6	29	Right ovarium cyst	NP	NP	-	?	?	Right ovari inflam. + free fluid next to uterus

IX. RESULTS

We calculated mean age, variance and standard deviation, obtaining as results 32.8, 102.90 and 10.14 respectively.

The mean body temperature 36.9ºC. Fever over 38°C was observed in 10% of the patients.

Looking at laboratory tests, mean value of CRP, leucocytes and neutrophils count were 40.8, 11.38 and 70.38 respectively, indicating, CRP was elevated (>10 mg/l) in 61%, leucocytosis (> 11x10*9/l) in 45% and an increased neutrophils count (>70%) in 66%.

However, CRP values which were registered, did not exceed 178.7 mg/L, and minimum value was 0.1 mg/L. CRP median was 21.4 mg/L.

Localized right fossa pain was present in 55% of the patients. For the rest of the cases, abdominal pain was diffused and not localized in the right lower quadrant.

Kocher's sign, was positive in 14% of the cases, while Blumberg's sign was positive in 52.3% of the cases.

Localized right fossa pain, Kocher's sign and Blumberg's sign, all together, were present in 9.5%.

Accompanying symptoms were also studied, being vomiting/nausea and anorexia the most prevalent. Vomiting or nausea was present in 60% of the patients, while the anorexia prevalence was 65%.

Based on above mentioned signs and laboratory tests, the Alvarado score was calculated for every patient.
The median Alvarado score was 5.
56% obtained a score =/> 5 (47% 5-6, 9% 7-8, 0% 9-10).
43% obtained a score <5.

The median duration from the onset of pain was 24h. In 66% of the patients the pain lasted longer or equal to 24h, while in the rest 34% < 24h.

US findings showed some abnormalities in 41% of patients who has it done; 23% with free fluid alone, one case with ovarian cyst and free fluid, one case with tumor and free fluid, and one case with free fluid and a thickened appendix, which was not found later during laparoscopy. However, 19% of patients did not have it done, while the remaining 81% had. Fetus was found in one case.

TVU was exclusively performed on one patient, however it was not able to exclude the diagnosis of AA.

Notwithstanding, CT was not performed at all.

All patients preoperatively were examined by gynecologist.

Only in 38% of them, a previous gynecological pathology was present, and not a specific one. Instead, the 62% of remaining patients presented with no relevant gynecological anamnesis (-).

During laparoscopy, following gynecological pathologies were found:

In 47% of cases, there was hemorrhagic fluid. Pus accumulation was found in 14%, and an inflammation (uterus, ovary, adnexa or pelvis) in 52% of patients.

Cysts were only found in three patients, being two of them already ruptured.

Ovarian torsion only in one patient.

X. DISCUSSION OF RESULTS

The purpose of this retrospective analysis and literature review, was to present the reader with an update on the diagnostic approach to rule out AA in fertile women by providing an evidence-based review of radiological imaging, clinical scoring system, laboratory testing, age, pain onset and gynecological anamnesis.

The whole sample was analyzed searching for the most predominant symptoms that where present, which had lead to a false-positive diagnosis of AA. From the whole sample, the next symptoms were selected, according to diagnostic criteria:

-Elevated CRP readings (61%)

-Fever over 38ºC (10%)

-Elevated white blood cells (45%)

-Elevated neutrophils (66%)

-Anorexia(65%)

-Nausea/vomiting (60%)

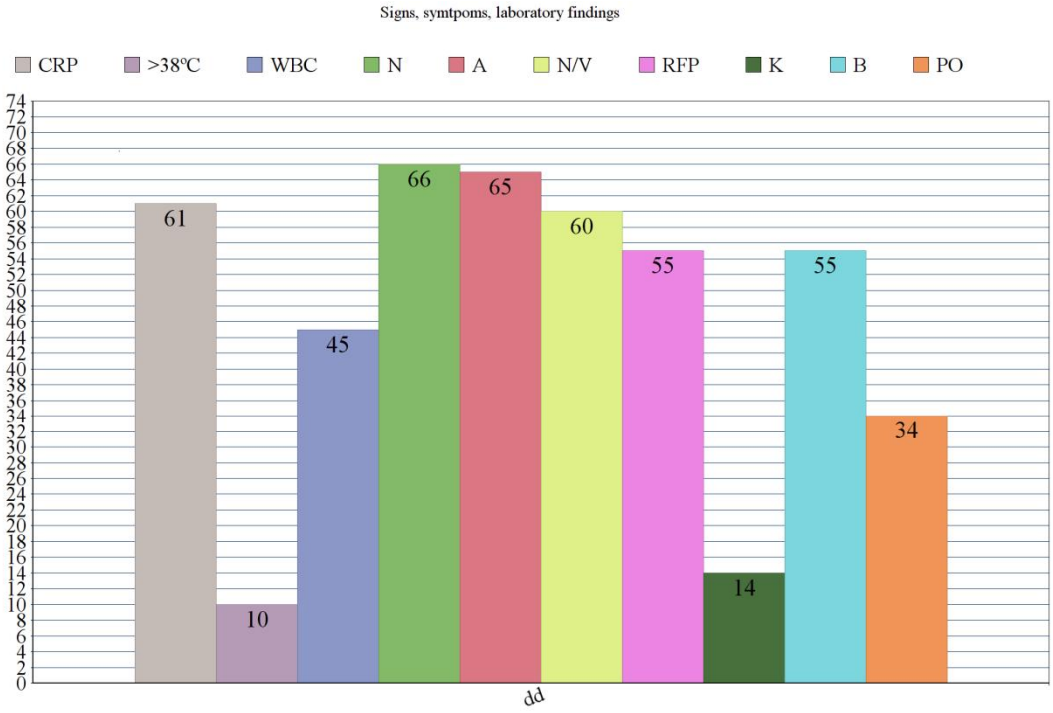
-Localized right fossa pain (55%)

-Positive Kocher's sign (14%)

-Positive Blumberg's sign (55%)

-Pain onset < 24h (34%)

-Alvarado score =/ >7 (9,5%)



We can observe a general distribution of all the symptoms that were previously mentioned depending on their prevalence between the 21 cases that were used for the study. Elevated neutrophils and anorexia was the most present in between the clinical data.

Nevertheless, afebrile condition (<38ºC) was present in 90% of the cases and pain onset = or > 24h in 66% of patients, in which acute appendicitis is already barely an option, and appendix perforation should happen, leading to a positive Blumberg's sign, which does not correspond to our results.

Regarding Alvarado score, 90.5% of patients presented with score <7.

Also, imaging tools were used (% of patients):

-AUS (81%)

-TUS (4%)

-CT (0%)

Imaging methods were not of great importance, due to the high percentage of patients lacking them and their poor specificity when performed. AUS was the most used screening method in our study, however, its findings, although not specific for AA, did not exclude it.

TVU was considerably missing. Only in one case it was performed, which may indicate that our gynecologists do not consider this a necessary diagnostic tool. According to Tabbara et al., it is a helpful tool if performed by a physician who is well trained in order to rule out a

gynecological pathology. Despite the fact that in this case TVU did not help to avoid a mistake, the wider use of it could possibly have improved the diagnostics.

Gynecological aspects such as prior diseases or pregnancies, as well as menstrual cycle day, did not help to rule out AA.

Based on our literature review and results of the study, we can assume that a different protocol, to diagnose AA, should be followed by physicians when a fertile patient presents with acute abdominal pain, in order to misdiagnose it and avoid possible future complications as those found either with a delayed diagnosis, or with negative appendectomies.

AUS should be always done. It is available fast enough, non invasive test with high predictive value for the diagnosis of AA. Ionizing radiation is avoided and does not violate women privacy. Furthermore, uses a lower frequency than TUS and can penetrate farther. Thicker appendix wall can be easily seen, as well as recognize adnexal cysts and hemoperitoneum.

TUS would be very useful, however its lack in most of EDs around the world and its required well trained specialist for its use, make it an unused tool. But its benefits should be enough reason to increase its use.
An enlarged ovary is the first sign of torsion, while the identification of a complex ovarian mass greater than 5 cm increases the probability of torsion.
Endovaginal scanning is the only modality to assess degree of color flow to and from the ovary and help in the diagnosis of ovarian torsion.
It is sensitive enough to differentiate between pregnancy, hemorrhagic ovarian cysts, endometriosis, ovarian torsion, and tubo-ovarian abscess.
Then, it should be included in all diagnostic protocols for reproductive women with RFP in order to rule out a gynecological source such as ovarian torsion, intrauterine pregnancy

CT should be used only when AUS are very unclear, to avoid women to expose to unnecessary radiation and consequent increased risk for cancer, especially, lung, colon and leukemia.

Nonetheless, clinical signs and symptoms as well as a deep clinical history is fundamental for any acute abdominal pain diagnosis among women. Consequently it can require some time from doctor, which might be compromised in ED.

Regarding signs and symptoms, many aspects should be considered in order to rule out or support some gynecological pathologies such as cervical motion tenderness or vaginal discharge (leucorrhea) characteristic for PID.

A good anamnesis (family diseases, social, sexual, obstetric/gynecological history) is of great importance due to the fact that many pathologies might be clearly differentiated upon the menstrual periods and cycles characteristics, prior pregnancies or abortions, diseases, scars, sexual activities, marital status and heredity.

For instance, regarding endometriosis, some signs and symptoms such as dysmenorrea, dyspareunia or alteration of menses can be a significant indication of the pathology.

Day of menstrual cycle should be added in all fertile women anamnesis because of the fact that increased levels of progesterone (during luteal phase) may have an important impact on body's temperature, increasing it. Therefore, body temperature might be altered giving false positive subfebrile/febrile status that may make us think about an infection.

Also ovulation should be considered, which its symptoms in some patients may mimic appendicitis.

If the patient's anamnesis is performed adequately it may provide multiple information and aids in establishment of the correct diagnosis.

In conclusion, the system developed nowadays in most of ED's, help to distinguish appendicitis and common obstetrics and gynecological conditions from nonspecific abdominal pain in pregnant age women with acute lower abdominal pain. However, the system is not accurate enough to be used in routine clinical practice.

XI. CONCLUSIONS

1. Clinical signs and laboratory parameters indicating AA were weakly expressed, thus, they were not informative enough to rule out AA. However, elevated Ne, anorexia, afebrile condition and pain onset =/> 24h may suggest a gynecological pathology.

2. Alvarado score ≤5 is not suggestive for AA in fertile women and these patients have to be referred to the gynecologist.

3. To improve the diagnostics when clinical, laboratory tests and AUS do not support the diagnosis of AA, abdominal-pelvic CT has to be considered.

4. To improve the gynecologic diagnostics TUS should be more widely applied in combination with AUS.

5. A closer cooperation between surgeon and gynecologist is warranted to avoid diagnostic mistakes.

6. A more detailed anamnesis and further clinical examination is required.

7. The number of false-positive diagnosis of AA remains high over the last few years indicating the need for more accurate diagnostic approach.

XII. REFERENCES

[1]Daniel J. Shogilev et al., “Diagnosing Appendicitis: Evidence-Based Review of the Diagnostic Approach in 2014” Review article. Western Journal of Emergency Medicine 2014.

[2] Articlesng “Female infertility effects in women child bearing age” 2013 http://articlesng.com/female-infertility-effects-women-child-bearing-age/

[3] Tarig Elraiyah et al., “The effect of appendectomy in future tubal infertility and ectopic pregnancy: a systematic review and meta-analysis” Journal of Surgical Research 2014

[4] Sandy Craig, MD Residency Program Director, Carolinas Medical Center; Associate Professor, Department of Emergency Medicine, University of North Carolina at Chapel Hill School of Medicine “Appendicitis differential diagnoses” 2017

http://emedicine.medscape.com/article/773895-differential

[5] Omer Engin et al., “Gynecologic pathologies in our appendectomy series and literature review” Journal of the Korean Surgical Society 2010.

[6] S.A. Seetahal et al., ”Negative appendectomy: 10-year review of a nationally representative sample” The American Journal of Surgery 2011

[8] Thomas Schok “Prospective Evaluation of the Added Value of Imaging within the Dutch National Diagnostic Appendicitis Guideline – Do we Forget our Clinical Eye?” 2015 S. Karger AG, Basel.

[9] Tabbara et al.,”Transvaginal ultrasound in fertile patients with suspected appendicitis: an experience report of current practice” Research article. Emergency medicine international 2012.

[10] Bondi M. et al., “Improving the diagnostic accuracy of ultrasonography in suspected appendicitis by the combined transabdominal and transvaginal approach” PubMed 2012.

[11] Robert Ohle et al., “The Alvarado score for predicting acute appendicitis: A systematic review” BMC Medicine 2011.

[12] Ronald F Martin “Acute appendicitis in adults: diagnostic evaluation” UpToDate 2014

[13] Mc Kay et al., “The use of the clinical scoring system by Alvarado in the decision to perform computed tomography for acute appendicitis in the ED” PubMed 2007.

[14] KijjaJearwattanakanok et al., Research Article “Clinical Scoring for Diagnosis of Acute Lower Abdominal Pain in Female of Reproductive Age” Emergency Medicine International 2013.

[15] KijjaJearwattanakanok et al., Research Article “Validation of the Diagnostic Score for Acute Lower Abdominal Pain in Women of Reproductive Age” Emergency Medicine International 2014.

[16]Shoreh Kooshesh, MD Resident Physician, Division of Emergency Medicine, Stanford University School of Medicine “Pelvic Ultrasonography Clinical Presentation” Medscape 2016 http://emedicine.medscape.com/article/797240-clinical.

[17] Clinical emergency radiology textbook from Cambridge Univeristy Press. J. Christian Fox.

[18] Julien Puylaert “Acute abdomen – Role of ultrasound” Department of radiology, MCH Westeinde Hospital, The Hague, The Netherlands.

[19] Lutfi Incesu, “Appendicitis imaging**”** Department of Radiology, Ondokuz Mayis University School of Medicine 2016.

[20] http://www.sciencedirect.com/science/article/pii/S0002961097001839