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Normal versus Pathological Appendix in Clinically Suspected Acute Appendicitis "Randomized Controlled Trials"

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Abstract

The therapy of acute appendicitis is aimed to early diagnosis and prompts operative intervention. However, this aim is not always easily accomplished since many patients do not seek medical attention in a timely manner and the diagnosis of appendicitis can be difficult due to negative laparotomy rate about 25% is common in many reports.

Aim: of this study is to correlate clinical diagnoses of acute appendicitis with results of pathology of appendix if it's normal or has under typing pathology.

Patient & Method: This is a prospective case study research, performed on 88 patients who underwent appendectomy for initial diagnosis of acute appendicitis between September 2014 and December 2014in Assiut University hospital Department of Surgery.

Results: Most of normal appendix patients were females (40%) but most of inflamed appendix patients were males (60%) and gangrenous appendicitis mostly found in female (75% of gangrenous appendicitis), tumor found in two patients one was female and male. Acutely inflamed appendix was (67.9%) of patients with leukocytosis (>11000 mm^3). The most clinic-pathological features found in 48% of patient.

Conclusion: The high result of negative appendectomy rate is higher than accepted standard in our study. Preoperative ultrasonography is essential for reduction of negative appendectomy rate especially.

Recommendations: To decrease high negative appendectomy rate, we should depend on experienced surgeons & radiologists. Laparoscopic diagnosis is useful in doubtful cases of acute abdomen. Routine histopathological examination of appendix is very important to exclude malignancy. Finally using of high resolution ultrasound scan and CT could improve the diagnostic yield of acute appendicitis.

Keywords: Negative; Positive appendectomy

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Introduction

Appendicitis is one of the most common causes of the acute abdomen in the Western world and is one of the most frequent indications for abdominal surgery. It occurs in 7% to 12% of the general population, and although it may occur at any age, it is most common in the 10 to 19 year-old age appendectomies are performed in the United States to avoid the potential complications of perforated appendicitis [1]. Perforation rates are correlated with delayed diagnosis and age. In the past two decades, the negative appendectomy rate has been relatively constant with slight decline after 2000, but the rates for perforated appendicitis seem to be increasing [2].

Acute appendicitis is the most common cause of an acute abdomen [3] .The life-time risk of appendectomy is 12.0% for men and 23.1% for women [4]. Although clinical symptoms are often characteristic, a high rate of misdiagnosis, often referred to as negative appendectomy, suggests otherwise. Several studies have shown that over 15% of appendectomies performed revealed no pathological evidence of appendicitis [5]. Despite the introduction of modern diagnostic imaging, such as CT, ultrasonography, population-based rates of negative appendectomy remain unchanged

over time [6]. Furthermore, a significant clinical and financial cost incurred by patients undergoing negative appendectomy exists throughout their presumed course of appendicitis [7].

The clinical diagnosis may be difficult to make without a classic presentation of periumbilical pain migrating to the right lower quadrant or in particular patient populations such as women of child bearing age whose gynecologic pathologies may present similarly. Owing to its increased morbidity, there is an ongoing need for early and accurate diagnosis of appendicitis before the onset of perforation. Depending on the pathologic stage of appendicitis, there are a variety of surgical and nonsurgical treatment options including laparoscopic or open appendectomy, primary antibiotic therapy, or percutaneous drainage of periappendiceal abscesses [8].

Females have a consistently higher reported incidence of negative appendectomies [1-3]. The main reason for this is thought to be due to the high incidence of gynecologic disorders in females, especially in the second and third decades of life. Such disorders include pelvic infections, ruptured ovarian cysts, and ectopic pregnancies. The range of ages of females with a negative appendectomy was 15 to 27 years [9].

Appropriate patient management is based of distinguishing complicated (gangrenous or perforated appendicitis) from uncomplicated appendicitis. In addition in patients with perforated appendicitis differentiate liquefied abscesses from indurated soft tissue, it is important to masses (phlegmonous inflammation) [10]. Obstruction of the lumen is the dominant factor for acute appendicitis and fecoliths are the usual cause of obstruction. Other causes of obstruction could be lymphoid hyperplasia, intestinal worms, tumors, or other conditions [11]. There are criteria for diagnosis are similar to those of other diseases of the gastrointestinal tract, and include granulomatous inflammation, transmural lymphoid aggregates, and fissuring-type ulcers [12]. However, the use of high resolution ultrasound scan and CT scan has improved the diagnostic yield of acute appendicitis in some studies [13]. The use of leukocyte count and determination of the neutrophil fraction has been suggested as a means to aid diagnostic accuracy [14].

All surgeons faced the prospect of normal looking appendix following appendectomy and the dilemma of removing such a normal looking appendix was in favor of removing it [15]. Now in the era of diagnostic laparoscopy to evaluate right iliac fossa pain especially in female patients. This dilemma is becoming even more important than ever before especially when no other pathology is found to explain patient symptoms. Some studies were in favor of removing the appendix while other studies favor a more conservative approach [16].

Significance of the Study

Early diagnosis and prompts operative intervention is a very important goal of acute appendicitis therapy. However, this goal is not always easily accomplished since many patients do not seek medical attention in a timely manner and the diagnosis of appendicitis can be difficult [17]. Many surgeons use an aggressive approach, accepting a certain number of negative appendectomies, traditionally 15 percent, although the use of imaging studies appears to have reduced the negative appendectomy rate to less than 10 percent [18].

In addition to the diagnosis of acute appendicitis in many patients can be difficult to establish a negative laparotomy rate about 25% is common in many report [19].

Aim of the Study

The aim of our study is to correlate clinical diagnoses of acute appendicitis with results of pathology of appendix if it's normal or has under typing pathology.

Patient and Method

Study design is a prospective case study; it performed in Assiut University hospital at department of surgery. We performed this study on 88 patients for suspected acute appendicitis and searched to identify all patients who underwent appendectomy to treat an initial diagnosis of acute appendicitis between September 2014 and December 2014. The demographic and histopathological data collected for each patient included age, sex, appendectomy surgery date, and macroscopic and microscopic properties of appendix. Patients who had received the appendectomy incidental to other surgeries, such as colorectal or gynecological cancer surgery or trauma surgery were excluded from study also Incidental appendectomy and appendicular inflammatory masses that resolved on conservative management were excluded from this study. In addition, pediatric patients younger than 16 years old were also excluded from study. Information entered included patient demographics, clinical symptoms and signs, duration of symptoms, white cell count, operative findings and histological findings. Appendectomy was indicated when there was a high suspicion of acute appendicitis, based on symptoms and signs. WCBs were used as a complementary finding and ultrasound scan was performed only when the clinical findings were equivocal. All specimens were routinely examined morphologically, and the final diagnosis was based on histology using the microscopic findings of each patient's appendectomy specimen that were recorded in the pathology report, the patients were classified into (1) inflamed appendix (2) Normal appendix (3) unusual histopathology findings.

Methods

Clinical data divided into the following

Patient history taken by resident and personal history including menstrual history in female patient; name, age, sex, Occupation and marital status also are reported. History of patient complaint with onset, course, duration, and gastrointestinal symptoms as fever, anorexia, vomiting, nausea and abdominal pain. In addition to associated symptoms as dysuria, hematuria are taken and past history of the same condition, surgical history and chronic disease. Examination of patient abdomen inspection, palpation (Abdominal examination (organomegal & McBurney tenderness, rebound tenderness, reverse tenderness, reverse rebound tenderness), percussion and auscultation and laboratory data especially white blood cells count.

Operative data

Presence of signs of inflammation hyperemia, pyogenic membrane, presence of pus or fecaliths. All patients incised by McBurney incision with muscle splitting the appendix took for histopathological examination.

Pathological data

All appendixes examined by 3 sections, firstly cut section from base of appendix then longitudinal section from the middle part of appendix and shelf section from tip of appendix.

Criteria of inflamed appendix: Presence of acute inflammatory

Table 1: Demographic data of the patients.

Demographics **1-Age**	Normal	Pathological	Total
<20 years old	4	6	10
20~30 years old	17	24	41
31~40years old	9	21	30
41~50 years old	1	4	5
>50 years old	0	2	2
2-Gender			
Male	16	30	46
Female	17	25	42
3-Marital status			
Male			46
Married	9	15	24
Not married	7	15	22
Female			42
Married	8	14	22
Not married	9	11	20

cells, presence engorged blood vessels and edema and presence of lymphocytes may be found in normal appendix.

Data analysis

The patients were divided into four groups based on sex and age, women, men, girls, and boys. The negative appendectomy rate (NAR) and positive appendectomy (PR) was calculated for each group, in accordance with their preoperative evaluation. The NAR was defined as the proportion of patients who underwent removal of a normal appendix. PR was defined as the proportion of patients who had a pathological appendix, noted either at surgery or at pathologic examination, from all patients who had appendicitis proved at histologic examination. The sensitivity and positive predictive value (PPV) of clinically diagnosing acute appendicitis were also calculated. Statistical analysis was performed.

Results

The Table 1 showed that 10patients were blow 20 years old, four of them had normal appendix and six had pathological appendix (heavy acute inflammation reaching serosa). Forty-one patients aged between 20 to 30 years old, 17 of them had normal appendix versus twenty-four had pathological appendix. Third category of patients aged between 31 to 40 years old, 9 patients of them had normal appendix versus twenty-one had pathological appendix (two of patients had gangrenous appendicitis and one patient had carcinoid tumor). Fourth categories of patients were aged between 41 to 50 years old, one of them had normal appendix and four had pathological appendix (heavy acute inflammation reaching serosa except one patient cystic mucinous tumor with no invasion). Last category of patients was two and aged more than 50 years old and they had pathological appendix (heavy acute inflammation reaching serosa).

According to gender, there were 46 male and 42 female patients. 40% of female patients had inflamed appendix while 60% were males. The gangrenous appendicitis was appeared 3 patients mostly of them were females (75%) but tumor found in two patient one was female and other was male.

The Table 2 illustrated the clinical data of patients. Regarding

Table 2: Clinical data of the patients.

Clinical data	Normal	Pathological	Total
Symptoms			
1-Vomiting	8	30	38
2-Fever	6	23	29
Signs			
Rebound Tenderness	9	49	58
Vital signs			
Pulse			
Normal pulse	11	10	21
Tachycardia	20	47	67
Temperature			
Normal	27	32	59
Elevated	6	23	29
Investigations			
W.B.Cs			
Normal	30	10	40
leukocytosis	3	43	46
leucopenia	0	2	2

Table 3: Patient laboratory investigations.

W.B.Cs	Male	Female	Total
Normal	22	27	49
Elevated	9	28	37
Low	0	2	2

Table 4: Operative impression of patients.

Operative impression	Normal	Pathological	Total
Normal	25	1	26
Inflamed	8	54	62

to abdominal pain, all patients presented by abdominal pain mainly periumbilical fist then referred to right iliac fossa. Thirty-eight patients presented with vomiting and fifty patients had no vomiting when presented. Fever presented only in 29 patients, 19 of them had acute inflammation reaching to serosa and 4 patients had gangrenous appendicitis but 6 patients of them had normal appendix. There is no urinary and gynecological manifestations were reported. Regarding to vital signs pulse range from 80 b/m to 110 b/m, temperature from 37 to 38.5^{0}C.-Tachycardia >90 b/m were presented in 67 patients, 22 had normal appendix and 44 patients had acutely inflamed appendicitis, one patients with cystic mucinous tumors had tachycardia while all gangrenous appendix were had tachycardia. However patients with tumors were hadn't fever. Regarding signs, all patients included in this study had right iliac fossa tenderness. But rebound tenderness presented in 58 patients (65.9%). Thirty patients hadn't rebound tenderness.

The Table 3 showed that all patients in this study had abdominal ultrasound describe presence of acute inflamed appendicitis. Regarding laboratory, all patients investigated for WBCs counts, 49 patients had normal WBCs counts<11,000 mm^3, 37 patients had elevated WBCs count, and 2 patients had low WBCs count.

The Table 4 showed that 26 appendix had gross impression of being normal appendicitis. So that 7 appendix which grossly being acute inflamed appendicitis were pathologically had normal appendix.

Table 5: Pathological findings of participated patients.

Pathology	Total number	%
Heavy acute inflammation	53	60.3
Normal	33	37.5
Carcinoid tumor	1	1.1
Cystic mucinous tumor	1	1.1

Table 6: Clinico-pathological features patients with normal appendix.

Patients' characteristics	***Result***
Patients (n)	33
age[mean 6 SD (range)], y	
Sex [n (%)]	
Male	16
Female	17
Histopathologic findings [n (%)]	
Fibrous obliteration	0
Carcinoid tumor	1
Evermicularis	0
Granulomatous inflammation	48
Endometriosis	0
Mucocele	0
Eosinophilic infiltration	5
T saginata	0
Appendicular diverticulitis	0
Surgical approach (n)Appendectomy	88

The Table 5 showed that 37.5 of cases had normal appendix, and 60% of cases had inflammed appendix. However, two cases have carcinoid reaching peritoneal fat, and another has Low grade cystic mucinous tumor with no invasion present 2.3% of all patients.

The Table 6 showed that the most histopathological findings were present in 48 of patients had granulomatous inflammation.

Discussion

Although it is more than 100 years since McBurney described his experience with early operative interference in cases acute appendicitis, it is perhaps surprising that only recently has attention been focused on the patient who not having inflamed appendix is nevertheless subjected to surgery and unnecessary appendectomy. Surgeons have believed it safer to remove a normal appendix than risk perforation if the organ is in fact inflamed. But this view has been challenged by studies which showed that it is possible to reduce the negative appendectomy rate significantly by intensive in hospital observation without at the same time increasing the perforation rate.

As Appendectomy is the most common operation performed in emergency services. Because of common occurrence of symptoms mimicking acute appendicitis, the diagnosis of acute appendicitis is a dilemma for surgeons. Between 15% and 30% of all these patients who are suspected of having acute appendicitis undergo surgery that demonstrates neither appendicitis nor any other surgically correctable disease [20]. But in this study 37.5% of patients suspected acute appendicitis had normal appendix.55.7% of patients had heavy acute appendicitis, 2.2% of patients had appendicular tumor and 4.5% of patients had gangrenous appendicitis. Periumbilical abdominal pain eventually localizing to right iliac fossa (RIF) with peritoneal signs, low grade fever, anorexia and elevated white blood count is the typical textbook presentation of a patient with acute appendicitis However not every patient has a typical clinical presentation has acute appendicitis.

The incidence of negative appendectomy in this study was 37.5% with representation of both males and females. Okobia et al. [21] in Benin City Nigeria reported an incidence of 32.2% with representation of both males and females. Similarly, Ogbonna et al. [22] reported a negative appendectomy rate of 29.7% in males and 47% in females over five year period in Jos, Nigeria. Kakande et al. [23] in Uganda reported a negative appendectomy rate of 29.5% over a five year period. Chang et al. [24] reviewed 184 cases of acute appendicitis in Taiwan and found a 79% diagnostic accuracy rate in men as opposed to 54% in women. In this series, there was an overall misdiagnosis rate of 33%. Gilmore in England reported a negative appendectomy rate of 22% [25].

The incidence of both genders is almost equal in this study. But female and male patients had also normal appendix equally (17 patients female & 16 patients males), so genders especially females must be evaluated well before they had been operated and also searching for other causes of right iliac fossa pain I.e. Ovarian cyst. But in other studies Females have a consistently higher reported incidence of negative appendectomies. The main reason for this is thought to be due to the high incidence of gynecologic disorders in females, especially in the second and third decades of life. Such disorders include pelvic infections, ruptured ovarian cysts, and ectopic pregnancies. In the present study, the range of ages of females with a negative appendectomy was 15 to 27 years. This finding is in keeping with other studies on negative appendectomy in females [26]. In some cases of negative appendectomy, the exact pathological diagnosis may not even be made intra operatively; in these cases the histology report determines the diagnosis of negative appendectomy. What may appear as an inflamed appendix to the surgeon may truly show no inflammation on histological review.

Right iliac fossa tenderness may cause by other differential diagnosis of acute appendicitis as it presented in patients had normal appendix, but rebound tenderness had significant p-value of presence of acute appendicitis (0.000) so rebound tenderness suggests acute appendicitis on other hand the p-value of absence of rebound tenderness in normal appendix is also significant so absence of rebound tenderness suggests other cause of right iliac fossa pain and normal appendix.

Most patients with acute appendicitis will present with complaints of right lower abdominal pain, nausea, vomiting and anorexia. Tenderness is often elicited over the right iliac fossa. However, some other abdominal conditions may also present with these features. On the other hand, some patients with acute appendicitis may not present with nausea, vomiting and anorexia. Okobia et al. [21] reported vomiting and anorexia in only, 41% and 24.4% of cases respectively. In our study, the incidences of vomiting and anorexia were 34.1% in those patients with histologically confirmed appendicitis. These features clearly cannot be entirely relied upon in making a diagnosis of acute appendicitis. In other studies the incidence of nausea, vomiting and anorexia was found to be higher and more reliable in patients who had histologically confirmed appendicitis.

The use of various diagnostic tools has also been suggested as a means of reducing the rate of negative appendectomy. The use of leukocyte count has been suggested as a means to aid diagnostic

accuracy. Kpolugbo et al. [14] in Benin City reported a reasonable correlation between neutrophilia and acute appendicitis [7,17]. However, in the present study, use of leukocytosois and neutrophilia in making a diagnosis of acute appendicitis was particularly helpful. Out of the 53 cases of histologically confirmed appendicitis, only 40 cases had a leukocytosois and 33 cases had normal appendix, 30 cases had normal leukocytic counts.

The use of high resolution ultrasound scan and CT scan has improved the diagnostic yield of acute appendicitis in some studies. In the present study, use of ultrasound scan was not particularly helpful. Accuracy of ultrasound diagnosis in appendicitis is likely to be very operator dependent; in this center and other centers in developing countries, the use of ultrasound scan may not be diagnostically helpful in making a diagnosis of appendicitis. CT scan is readily available in most developed countries. Consequently our diagnosis of appendicitis rested mainly on clinical assessment.

Gross impression of appendix by surgeon intra operatively is important as if this inflamed appendix is the cause of right iliac fossa pain, and unless it is inflamed appendix surgeon will explore to find the cause of pain i.e. ovarian cysts or inflammatory bowel disease Crohn's disease. The p-value of inflamed and normal appendix is significant (0.000). But surgeon impression of malignancy not significant.

Gangrenous appendicitis in this study affected female patients' more than male patients this may be due to defect in evaluation of patients by junior surgeons which lead to delays of operations. All patients in this study were complaining of acute abdominal pain migrating to right iliac fossa with Mc-Burney's tenderness and abdominal ultrasound suggested presence of acute appendicitis. This had an important cause of our high result of normal appendix 37.5% due to junior resident who done abdominal ultrasound .We recommends senior to do abdominal ultrasound.

Conclusion

The high result of negative appendectomy rate (normal appendix) is higher than accepted standard in our study (37.5%) and is more in female patients due to several factors that lead to diagnosis of acute appendicitis. Also the high result of appendicular malignancy (2.2%) is histologically surprise so we recommend routine histological examination of appendix after appendectomy. It is clear that even when the macroscopic appearance of a respected appendix is normal, histopathological assessment of specimens will allow early diagnosis of malignant and infectious appendicular diseases. The proper history taking and clinical examination by an experienced surgeon supported by ultrasonography is the best way to establish the diagnosis of acute appendicitis. Despite the improvements in various imaging modalities, still a negative appendectomy rate of 15% to 20% has been considered an acceptable standard to minimize the risks of diagnostic delay and perforation. Preoperative ultrasonography in especial circumstances is essential for reduction of negative appendectomy rate especially when performed by highly trained and experienced radiologist with close rapport between surgeons and radiologist.

Recommendations

Due to high rate of negative appendectomy in this study, the study recommendations focused on decrease the high negative appendectomy rate through the following.

- Experienced surgeons could achieve a lower negative appendectomy rate than can their more junior colleagues.
- Experienced radiologist could do abdominal ultrasound to achieve lower negative appendectomy rate than their more junior colleagues.
- Laparoscopic diagnosis of suspected patients is useful in doubtful cases of acute abdomen.
- Routine histopathological examination of appendix also very important due to high malignancy rate in this study.
- The use of high resolution ultrasound scan and CT scan could improve the 7+.

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