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EVALUATION OF THE RECENT UPDATES REGARDING APPENDICITIS DIAGNOSIS AND MANAGEMENT

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Abstract

Background: *Acute appendicitis is one of the commonest acute medical condition that present to the emergency department and appendectomy is considered as one of the commonest surgical procedure worldwide. Diagnosis of appendicitis has remained a challenge for clinicians and negative appendectomy percentage is still considerably high despite the recent advancement of medicine. Appendicitis management has a lot of controversies that need to be tackled and discussed.*

Objective: *A lot of literatures have been done in order to provide patients with appendicitis a better outcomes, in our review we will evaluate the recent publications regarding diagnosis and management of appendicitis and its complications.*

Method: *PubMed database were used for articles selection. All relevant articles related to our review were chosen to cover the following topics: Appendicitis, Daignosis of Appendicitis, and Management. We excluded other articles, which are not related to our objectives. The data have been extracted according to specific form to be reviewed by the authors*

Conclusion: *Each and every clinical sign and symptom for appendicitis alone has a poor predictive value but their predictive ability becomes much stronger if they were combined. So, using a scoring system like Alvarado score has shown to be a useful diagnostic tool because it combines signs, symptoms and laboratory testing together. Anyhow, clinical examination cannot definitively confirm the diagnosis especially in children. Therefore, clinicians will continue to rely on radiological studies to evaluate potential appendicitis. CT has improved the diagnostic accuracy of appendicitis. high-quality Ultrasound is a safe alternative in order to avoid radiation hazard especially in children and pregnants. Appendectomy has been the standard practice for uncomplicated appendicitis across the world. The use of the laparoscopic approach became more preferable than the open procedure because it was associated with lower complications rate. For perforated appendicitis, nonsurgical treatment with antibiotics and abscess percutaneous drainage has shown to be successful and safe modality of treatment.*

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INTRODUCTION:

Conditions that can be treated by surgery pose a considerable health burden (1). Acute appendicitis is one of the commonest acute medical condition that present to the emergency department (2). Accordingly, appendectomy is considered as one of the common surgical procedure worldwide. In developed countries, appendicitis rate accounts for 100/100,000 per year, and it mostly affect people in the second and third decade of life with male predominance (3). It was the 11th cause of death among conditions requiring emergency surgery presented in the Global Burden of Disease Study 2010 (1).

In the recent years a lot of literatures have been done to evaluate the best diagnostic and management approaches in order to provide a better outcomes for the patients. In this paper, we aim to review the controversies related to the management and diagnostic approaches and provide a comprehensive yet a simplified a summary.

METHODOLOGY:

Sample

We performed comprehensive search using biomedical databases; Medline, and Pubmed, for studies concerned with assessment of stress ulcer prophylaxis published in English language between 2013 and 2018. Keywords used in our search through the databases were as {Appendecitis, Management, Diagnosis, Evaluation, Pathophysiology} More relevant articles were recruited from references lists scanning of each included study.

Analysis

No software was used, the data were extracted based on specific form that contain (Title of the study, name of the author, Objective, Summary, Results, and Outcomes). Double revision of each member's outcomes was applied to ensure the validity and minimize the errors.

DISCUSSION:

Appendicitis is inflammation of the vermiform appendix. Appendix is a hollow organ located at the tip of the cecum. It is usually in the right lower quadrant of the abdomen, near the ileocecal valve where the taenia coli converge. The term vermiform is Latin for worm-like and it belongs to its long, tubular architecture. The size of the appendix varies but averages 10 cm in length. In contrast to an acquired diverticulum, appendix is a true diverticulum of the colon and contains all of the colonic layers: mucosa, submucosa, longitudinal and circular muscularis, and serosa. The presence of B and T lymphoid cells in the appendicular mucosa and submucosa is what makes the appendix histologically different from the colon. This gut-associated lymphoid tissue in the lamina propria has led to the belief that appendix serves a function in immunity. However, there is no clear evidence to its function in humans. The vascular supply is from the appendicular artery, a branch of the ileocolic artery arising from the distal superior mesenteric artery. Venous and lymphatic drainage follow that of the arterial supply. The vessels, lymphatics, and nerves enter the appendix through its mesentery or mesoappendix to which it is adherent to the mesentery of the adjacent ileum (4). Appendix can be in a variety of positions like retrocecal, subcecal, pre-ileal and post-ileal, and pelvic. Moreover, posture, respiration, and distention of adjacent bowels are factors that can affect the position of the appendix. These variations in position can produce different symptoms which can cause clinical confusion in diagnosing appendicitis (5,6).

PATHOPHYSIOLOGY AND ETIOLOGY:

Appendicitis mainly arises because of an obstruction of the appendicular lumen by an appendicolith which is stone of the appendix or due to fecalith. Carcinoid tumors, intestinal parasites, and hypertrophied lymphatic tissue can also cause an appendicular obstruction and thus appendicitis (7,8). When the appendicular lumen gets obstructed, bacteria will build up in the appendix. This will cause an acute inflammation with abscess formation (6). The mucosal and secretory function of the inflamed appendix continues. Due to the absence of a patent lumen, increased secretions will cause increased intraluminal pressure which will lead to bowel wall distention. This distention will manifest as visceral pain which is the earliest symptom. It will be poorly localized mid-abdominal pain for the reason that it is transmitted via afferent sympathetic autonomic nerve fibers of the splanchnic origin to the dorsal root ganglion of the thoracic spinal cord segments. These segments are shared with the other abdominal organs of midgut embryologic origin (4).

The exact etiology of acute appendicitis is unknown. Nobody could reach to the precise etiology of acute appendicitis. However, many believe that the etiology of acute appendicitis is multifactorial. In several studies, appendicitis had a peak incidence in the summer months with a winter nadir. (Sanda et al.) conducted a local study in northern Saudi Arabia on the seasonal variation of appendicitis. They found a high number of appendectomies in the spring months of March to May and a low in the winter months of December to February. Sandstorms are common

during spring season in this region and characterized by a strong winds blowing across the desert bringing dust that hangs in the air. It was suggested that they can be a source of allergens, pollens, and bacteria challenging the mucosa-associated lymphoid tissue (9).

The risk of appendicitis is roughly three-times higher in members of families with a positive history for appendicitis than in those with no family history, despite there is no defined gene has been identified (10).

CLINICAL FEATURES:

Appendicitis usually starts with periumbilical or epigastric pain which is resulted by hyperperistalsis of the appendix to overcome luminal obstruction and because the appendix is visceral in origin as mentioned earlier. Nausea and anorexia (with or without vomiting) are the following symptoms along with a consequence of bowel wall distention. Also, one of the most consistent symptom is anorexia. 24 hours after the onset of symptoms, the pain often shifts and becomes localized to the right lower quadrant with tenderness when the area gets palpated. As explained earlier, the localization and character of pain also varies because the anatomic position of the appendix varies. Fever follows as the infection progresses from a localized to a systemic inflammatory process. The condition may progress to perforation and peritonitis within 2 to 3 days of symptoms onset (11).

If perforation occurred, it will be enclosed by the patient's own defense mechanisms, by the formation of an inflammatory phlegmon or a circumscribed abscess. It is mostly called a palpable appendicular mass. It is an inflammatory tumor consisting of the inflamed appendix, its adjacent viscera and the greater omentum, whereas an abscess is a pus-containing appendicular mass. This enclosure will keep the infection localized to the right lower quadrant, causing continued right lower quadrant pain without signs and symptoms of peritonitis, and occasionally a mass is palpated (11).

Upon abdominal examination, the physician will find right iliac fossa tenderness, mostly associated with rebound tenderness (Blumberg's sign) which is explained by irritation of the parietal peritoneum as a result of the inflamed appendix. Other signs are Rovsing's sign, Dunphy's sign, Psoas sign, and Obturator sign. Rovsing's sign becomes positive when palpation of the left lower quadrant of the patient's abdomen increases the pain felt in the right lower quadrant. If abdominal pain increased with coughing, Dunphy's sign becomes positive. Psoas muscle is a retroperitoneal and it can be affected mostly in cases of retrocecal inflamed appendix. It is a hip flexor muscle in the abdomen and that is why the patient may feel pain when the doctor holds the patient's right thigh and passively extends the hip while the patient is lying on the left side. In this case, Psoas muscle becomes positive. The obturator test is done by flexing at ninety degrees and then internally rotating the hip. If the patient felt pain, obturator sign is positive (11, 12).

DIAGNOSIS:

Each and every clinical sign for appendicitis alone has a poor predictive value. However, their predictive ability becomes much stronger if they were combined, although not perfectly accurate. The use of Alvarado scoring system, which includes clinical examination findings and laboratory values combination, is helpful in ruling out appendicitis (table 1). Scores range from 1 to 10, with higher scores indicating a greater risk of appendicitis. The purpose of Alvarado scoring system is to identify low, intermediate, and high-risk patients for appendicitis (99% sensitivity and 81% specificity). When the score is low, appendicitis is uncommon, and imaging and other interventions can be avoided. (Ohle et al.) conducted a systematic review on 42 studies assessing diagnostic accuracy and calibration performance of the Alvarado score. They concluded that The Alvarado score is a useful diagnostic 'rule out' score at a cut point of 5 for all patient groups. The score is well calibrated in men, inconsistent in children and over-predicts the probability of appendicitis in women across all strata of risk. In terms of diagnostic accuracy at the cut-point of 7, which was recommended for 'ruling in' appendicitis and progression to surgery, the score performed poorly in each subgroup (12).

Table 1: Alvarado scoring system.

Scoring components		**Points**
Symptoms	Migratory right iliac fossa pain	1
	Anorexia	1
	Nausea or vomiting	1
Signs	Right iliac fossa tenderness	2
	Rebound tenderness	1
	Fever	1
Laboratory findings	Leukocytosis	2
	Neutrophilia (Left shift)	1
Total points		10

A compatible clinical history and physical examination remain the cornerstone of diagnosis. Other diagnostic tools such as inflammatory markers, imaging studies significantly help in the diagnostic process. They increase both efficiency and accuracy. However, initial evaluation misdiagnosis rates in children can reach up to 30%, despite all these diagnostic advances. This is mainly due to the variable and non-specific presentation of the disease and the wide differential diagnosis of abdominal pain in children. Misdiagnosis is associated with high rates of perforation (12-38%) leading to significant morbidity and negative appendectomy (2-30%). Discriminating appendicitis via inflammatory markers because their diagnostic accuracy is limited. For the reason that they are increased in many abdominal pain disorders. White blood cell count (WBC), absolute neutrophil count (ANC) and C-reactive protein (CRP) are the most studied and used in clinical practice (13, 14).

WBC is very commonly elevated in patients with acute appendicitis. However, it is not a specific marker and is commonly elevated in patients with other inflammatory conditions included in the differential diagnosis. A WBC cut-off of greater than 10,000-12,000 cell/mm3 yielded a range of sensitivity between 65-85% and specificity between 32-82%. CRP is an acute phase reactant. Its diagnostic significance is largely based on both its kinetic properties and its utility as a marker for complicated/advanced appendicitis. CRP levels show an increase between 8-12 hours after the onset of inflammatory processes with a peak between 24 and 48 hours, which is later than that of WBC. CRP serves as a strong predictor for appendicular perforation but is quite limited for appendicitis in general. A CRP cut-off of >10 mg/L yielded a range of sensitivity between 65-85% and a specificity between 59-73% (15). In response to the difficulty of making the accurate diagnosis of appendicitis and to decrease CT utilization and negative appendectomy rates, there has been much effort to search for novel markers. Therefore, (Prada-Arias et al.) assessed the diagnostic accuracy of the biomarker fibrinogen, along with the more traditional inflammatory markers WBC, ANC and CRP, to differentiate appendicitis from non-specific abdominal pain in children. They found that WBC and ANC are useful inflammatory markers to discriminate appendicitis from non-

specific abdominal pain. Fibrinogen and CRP are not very useful to discriminate appendicitis from non-specific abdominal pain, but they discriminate properly complicated from uncomplicated appendicitis and non-specific abdominal pain, with a similar diagnostic accuracy. In a child with suspected appendicitis, a plasma fibrinogen level (prothrombin time derived method) >520 mg/dl is associated to an increased likelihood of complicated appendicitis (13). Nevertheless, CT remains the best radiological modality for diagnosing appendicitis but radiation exposure and long term cancer risks are a major concern. If imaging is used, high-quality ultrasonography should be considered a first approach, but only in practice settings where its accuracy is sufficiently high. If high quality ultrasonography is not available or if ultrasonography fails to visualize the appendix, CT with lower-dose radiation protocols is often used (16).

In children, even more considerable variability exists in the diagnostic approach to acute appendicitis affecting both quality and costs of care. The diagnosis of appendicitis is more difficult to make in children. Clinical examination still plays a key part in determining whether the child with abdominal pain should undergo immediate surgical consultation for potential appendectomy or should undergo further diagnostic evaluation (17). Clinicians will continue to rely on radiological studies to evaluate potential appendicitis since the clinical examination in children cannot definitively confirm this diagnosis. The range of diagnoses that can mimic appendicitis is wide and includes right ureteric calculus, epiploic appendagitis, torsion of Meckel's diverticulum, mesenteric adenitis, inflammatory bowel disease, colitis, gynecological disorders, and right-sided diverticulitis. CT is useful in differentiating between these disorders (18). As mentioned earlier, CT has improved the diagnostic accuracy of appendicitis. (Balthazar et al.) reported a sensitivity of 96% and a specificity of 89% regarding CT use. Unfortunately, CT exposes the child to radiation. So, Ultrasound is a safe alternative with a sensitivity of 74% and specificity of 94% (19).

MRI may also be used to image the abdomen with similar results compared to CT but the advantage that favor MRI is it does not entail the radiation exposure. Therefore, in centers that provide 24-h MRI coverage, MRI can be standardized to be a modality of diagnosis because of its efficacy and its advantage over ultrasound regarding performance and over CT regarding radiation hazard especially in children and pregnants. In some studies, MRI has been used in combination with ultrasonography for the diagnosis of appendicitis in adults, maintaining a high sensitivity and specificity without effect on negative appendectomy or perforation rate (20).

MANAGEMENT:

Appendectomy has been the standard practice for uncomplicated appendicitis across the world. According to the American College of Surgeons, the Society for Surgery of the Alimentary Tract, and the World Society of Emergency Surgery, appendectomy, either laparoscopic or open, is the treatment of choice for appendicitis. Yet, it has a recognized risk of complications although it is considered routine and safe. Examples of the complications are postoperative abdominal wall infections, intraperitoneal infections, and bowel obstruction secondary to adhesions. Recently, for uncomplicated appendicitis, antibiotics have been proposed as a single treatment. However, it was associated with 25-35% failure rate at 1 year according to (Varadhan et al.) meta-analysis (21). Moreover, (Svensson et al.) in their RCT found that 38% of the included children needed subsequent appendectomy during their 1-year follow-up (22). (Bachur et al.) also found that patients who got treated with non-operative management had more subsequent Emergency Department visits and hospitalizations compared with those managed operatively at the index visit. In addition, a substantial proportion of patients who initially managed non-operatively eventually had an appendectomy (23). The benefits for the patients on antibiotic treatment are avoidance of surgery and thereby a decreased risk of complications that may sometimes be severe and life-long persistent (24). Therefore, all patients should receive adequate information about different treatment alternatives according to present evidence, which includes offered antibiotic treatment if they are willing to accept a risk of initial antibiotic failure or later on recurrence (24). The ordinary bowel bacteria are aerobic and anaerobic. So, they all should be covered by the prescribed antibiotics. The antibiotics should be given intravenously for 3 days and then should be continued orally for at least 1 week after.

Nowadays, appendectomy is performed laparoscopically in 60 to 80% of cases in USA, with hospitalization lasting an average of 1 to 2 days and a rate of complications of 1 to 3%. The use of the laparoscopic approach became more preferable instead of open procedure. It depends on availability and expertise. The concept of low-cost laparoscopy, with the use of straightforward, inexpensive, reusable devices can lead to equivalent costs and outcomes, even in complex appendicitis. According to

(Jaschinski et al.), the comparison between laparoscopic approach and open approach has been intensively analyzed in over 70 RCTs and both approaches were found to be equally safe and effective procedure. Anyhow, pain scores and wound infections were lower and hospital length of stay and recovery period were shorter after laparoscopic surgeries. On the other hand, the risk of abdominal abscesses was higher for laparoscopic surgery and the duration of surgery was shorter using the open approach (25).

Postoperative wound Infection is not uncommon complication after non-perforated appendicitis with a reported rate of less than 10% while perforated appendicitis has an infection rate of 15–20%. Postoperative wound Infection can increase the morbidity and lead also to increased length of postoperative hospital stay, increase expense, higher rates of hospital readmission. Consequently, it can lead to increase in postoperative pain, sepsis and patient dissatisfaction (26). Appendectomy for non-perforated appendicitis is a clean contaminated surgery, and preoperative antibiotics has been shown by several studies to be a preventive method against postoperative infective complications by 50% (27). For all the patients undergoing appendectomy, single dose prophylactic antibiotics should be given half to one hour before surgery. However, continuing antibiotic prophylaxis in the postoperative period did not add an appreciable clinical benefit in these patients (28).

In case of the presence of a palpable mass, or if the patient had symptoms for more than 3 days, delay in presentation and elevated temperature (> 38.8 °C), the diagnosis of appendicular mass should be suspected. It is more common in extreme ages such as in children especially in those age less than 5 years and in elderly who age more than 55 years. Imaging with CT or even with US is more preferable for appendicular mass cases than clinical picture. Most of the time, the diagnosis is made by finding a palpable mass while examining the right lower quadrant after the induction of anesthesia before making the incision (11).

Appendicular masses which are perforated appendicitides should be treated conservatively (29). Conservative treatment has shown great improvement of the clinical symptoms and it has a success rate of 93%. Perforated appendicitis mostly causes generalized peritonitis and cannot be drained. Therefore, many may need percutaneous drainage of abscesses. Absence of generalized peritonitis and presence of percutaneously or surgically drainable abscess are considerable indications of drainage. Nonsurgical treatment is associated with lower morbidity, shorter hospital stay and fewer overall complications such as wound infection, abdominal/pelvic abscess, ileus/bowel obstruction, and reoperation compared with immediate appendectomy as found in (Simillis et al.) meta-analysis (30). However, these results were not similar to those in some other studies (31, 32). Anyhow, primary nonsurgical treatment also known as Ochsner-Sherren regimen should be provided to the patient initially (33). It consists of antibiotics and abscess drainage as needed. No later or interval appendectomy is indicated in some cases. Nevertheless, the patient should be informed and educated regarding the risk of recurrence especially in the presence of appendicolith. In patients above the age of 40 years, long-term follow-up with a colon examination and/or a CT scan or US is recommended because another underlying condition such as cancer or Crohn's Disease is suspected even if the risk of missing it is low (11, 26).

CONCLUSION:

Each and every clinical sign and symptom for appendicitis alone has a poor predictive value but their predictive ability becomes much stronger if they were combined. So, using a scoring system like Alvarado score has shown to be a useful diagnostic tool because it combines signs, symptoms and laboratory testing together. Anyhow, clinical examination cannot definitively confirm the diagnosis especially in children. Therefore, clinicians will continue to rely on radiological studies to evaluate potential appendicitis. CT has improved the diagnostic accuracy of appendicitis. High-quality Ultrasound is a safe alternative in order to avoid radiation hazard especially in children and pregnants. Appendectomy has been the standard practice for uncomplicated appendicitis across the world. The use of the laparoscopic approach became more preferable than the open procedure because it was associated with lower complications rate. For perforated appendicitis, nonsurgical treatment with antibiotics and abscess percutaneous drainage has shown to be successful and safe modality of treatment.

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