



Management of Appendicitis in a District General Hospital: The Potential Role of the Alvarado Score in Use of Investigation – Ultrasound, CT or Laparoscopy

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Abstract

Background: Appendicitis is often the primary diagnosis considered when patients present with acute right iliac fossa pain. Our primary aim assessed the diagnostic accuracy of ultrasound for acute appendicitis, including determining the role of Alvarado scoring, C-Reactive Protein (CRP) and Leukocyte count in directing subsequent management.

Materials and Methods: A retrospective analysis of all patients undergoing an appendicectomy over a 12-month period was performed. Patients having a pre-operative ultrasound scan were divided into three categories: Normal, inconclusive, or Acute Appendicitis (AA) and compared to histological reports. Symptomatology and biomarkers were used to calculate the Alvarado scores. Statistical analysis for ultrasonography, CT and diagnostic laparoscopy were also calculated.

Results: 226 patients underwent a laparoscopic appendicectomy. 77 patients had a pre-operative ultrasound, with 29 reported as AA, 15 as inconclusive, and 33 as normal. Sensitivity, specificity, positive and negative predictive value of ultrasound was 63%, 73%, 79% and 59% respectively. Specifically for males it was 57%, 100%, 100% and 33%. For females it was 67%, 70%, 67% and 70%. CT had values of 100%, 50%, 90% and 100% and laparoscopy 100%, 23%, 86% and 100%.

Alvarado scores of ≥ 6 and ≥ 7 in males and females indicated surgical intervention. Scores ≤ 4 and ≤ 6 suggested pre-operative imaging. Biomarkers could not permit a similar stratification in relation gender ($P=0.07$).

Conclusion: Ultrasound aids in confirming appendicitis in males with strong clinical suspicion. With females it is equivocal in confirming or excluding appendicitis. Alvarado scoring may help direct best management, either through investigation or direct to surgery.

Keywords: Ultrasound; Acute appendicitis; Diagnostic laparoscopy; Appendicectomy; Alvarado score

Introduction

The incidence of Acute Appendicitis (AA) in Western Europe is around 15 per 10,000, with an overall lifetime risk of 8.6% (males) and 6.7% (females) [1]. In the United Kingdom this accounts for more than 40,000 hospital admissions [1]. Acute appendicitis is often the primary diagnosis to be considered when patients present as an emergency with acute onset Right Iliac Fossa (RIF) pain [2]. Other differential diagnoses such as acute diverticulitis, mesenteric adenitis, ruptured ovarian cyst/luteal cyst (Mittelschmerz pain) and pelvic inflammatory disease are very much based upon features that include age and gender, family history and usually confirmed with radiological studies.

An element of diagnostic uncertainty in these patients leads to a greater amount of time and resources spent to establish a diagnosis [3]. This may lead to an increase in the complications such as perforation, gangrene, or abscess formation, thus elevating the risk of morbidity and mortality [4,5]. In individuals under 40 years of age, an ultrasound scan of the abdomen and pelvis is usually requested due to ready availability. It is often done on the same or next day and does not expose patients to radiation.

In our unit ultrasonography is the primary investigation of choice for acute right iliac fossa pain. It is mainly requested by junior doctors in situations where the diagnosis may not be clear or to confirm the clinical suspicion of acute appendicitis. It is not clear whether this 'heavy reliance' on an ultrasound abdomen and pelvis provides the most effective use of resources given the limitations

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Received Date: 25 May 2022

Accepted Date: 28 Jun 2022

Published Date: 04 Jul 2022

Citation:

Hamer J, Swati B, Deepak Singh R. Management of Appendicitis in a District General Hospital: The Potential Role of the Alvarado Score in Use of Investigation – Ultrasound, CT or Laparoscopy. Clin Surg. 2022; 7: 3539.

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with ultrasonography that include obesity, user experience and reporting accuracy and anatomical physiological issues such as a gaseous gastrointestinal tract.

This study investigates the value of the ultrasound abdomen and pelvis in the diagnostic accuracy of acute appendicitis in females and males. We ask the question as to which gender is this investigation most useful and if an established simple scoring system such as the Alvarado Score, C-Reactive Protein (CRP) or Leukocyte Count could provide a guide as to which patients benefit from this investigation. It is hoped that this would reduce diagnostic delay and improve resource utilization and patient morbidity. As a secondary outcome measure the negative appendectomy rate was determined in the cohort as a whole and by gender in relation to the ultrasound reporting. Appendix histology was used as the gold-standard against which comparisons were made.

Materials and Methods

A retrospective data collection was performed over a 12-month period (2017-18) for all patients undergoing laparoscopic appendectomy. Patients were divided into two subgroups: Preoperative ultrasound (Group A) and no pre-operative imaging (Group B). Group B patients were excluded from subsequent analyses as the basis for our investigation was to assess potential improvement in management in patients who had undergone preoperative ultrasound scans. Patients in Group A were then subdivided into 3 categories based on their Ultrasound Scan (USS) results: Acute Appendicitis (AA), inconclusive and normal (NAD). The accuracy of ultrasonography was ascertained by comparing the result against the gold-standard.

Data taken from patient records included symptom profile, CRP, leukocyte count and neutrophil count shift. The history, clinical findings and appropriate hematological results were used to calculate the Alvarado score (Table 1). Sensitivity, specificity, positive predictive and negative predictive values for ultrasound was calculated for the whole cohort and then with reference to gender. For all ultrasound groups Alvarado scores, CRP, leukocyte count and 'Positive' or 'Normal' histology were compared. Individuals under 17 years of age were excluded. All ultrasound scans were performed by experienced sonographers.

Results were expressed as Median (interquartile range) and where necessary non-parametric tests were employed with statistical significance set at a P value of ≤ 0.05 . Statistical analysis was conducted with IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, N.Y., USA) IRB approval and written consent was not required for this study. The focus of the study was on quality improvement of our existing management of acute appendicitis; however no active interventions such as implementation/omittance of new treatments, patient interviews or questionnaires were undertaken.

Results

226 patients underwent a laparoscopic appendectomy, of which 77 (34%) had a preoperative ultrasound (Figure 1). 57 were women and 20 men. 15 of 77 (19.5%) patients had an inconclusive report and were excluded in the sensitivity and specificity analyses.

Acute appendicitis was reported in 29 patients; median age 36.5 (18-63) years, male to female ratio 1:2.6 and 76% had histological evidence of appendicitis. A normal scan was reported

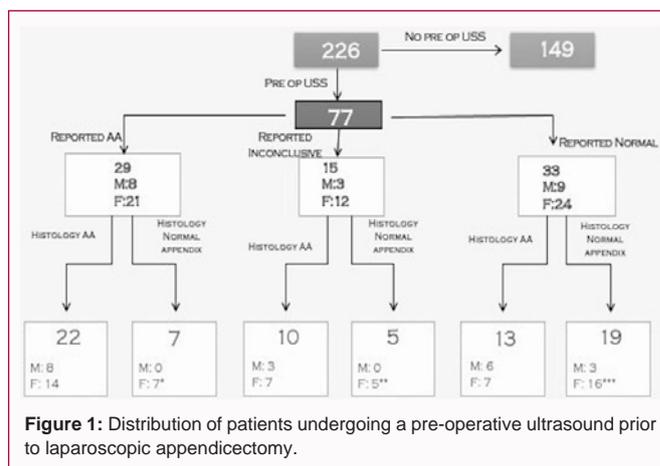


Figure 1: Distribution of patients undergoing a pre-operative ultrasound prior to laparoscopic appendectomy.

Table 1: Alvarado score denominations. A score of 5 or more implies appendicitis [6].

Parameter	Score
Migratory abdominal pain to RIF	1
Anorexia	1
Nausea	1
RIF tenderness	2
Rebound tenderness	1
Pyrexia	1
Leucocytosis	2
Left shift of Neutrophils	1
Total	10

Table 2: Value of ultrasonography as a diagnostic tool in patients with suspected acute appendicitis at a district general hospital.

Ultrasound Diagnostic Accuracy	(%)
Sensitivity	63
Specificity	73
Positive predictive value	79
Negative predictive value	59

in 33 patients with median age 31.9 (17-82) years, male to female ratio 1:2.7 and in 39% histology revealed appendicitis. The negative appendectomy rate for each category of ultrasound was acute appendicitis: 24%, inconclusive: 42%, normal: 61%.

When stratified by gender 17 out of 20 (85%) men had appendicitis on histology with a negative appendectomy rate of 15%. In females 28 out of 56 (50%) had a histological diagnosis of acute appendicitis and the negative appendectomy rate was 50%.

The sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) for acute appendicitis was 63%, 73%, 79% and 59% (Table 2).

Specifically for males these values were sensitivity 57%, specificity 100%, PPV and NPV 100% and 33%. Additional comparisons were made for males undergoing a pre-operative CT scan and patients proceeding to laparoscopy (Table 3).

With females the sensitivity, specificity, PPV and NPV were 67%, 70%, 67% and 70% respectively. Additional comparisons were made for females undergoing a pre-operative CT scan and additionally patients proceeding to laparoscopy (Table 4).

Table 3: Sensitivity, specificity, positive predictive value and negative predictive values in males undergoing a preoperative ultrasound, preoperative CT scan and laparoscopy.

Males	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Ultrasound	57	100	100	33
CT	100	50	90	100
Laparoscopy	100	23	86	100

Table 4: Sensitivity, specificity, positive predictive value and negative predictive values in females undergoing a preoperative ultrasound, preoperative CT scan and laparoscopy.

Females	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Ultrasound	67	70	67	70
CT	100	75	81	100
Laparoscopy	100	40	77	100

Table 5: BMI of males and females undergoing ultrasound scan categorized in relation to the report and histology findings. P=0.543 (Kruskal-Wallis test).

Ultrasound Report Category	Acute Appendicitis		Inconclusive		Normal	
	Acute Appendicitis	Normal	Acute Appendicitis	Normal	Acute Appendicitis	Normal
BMI Male	25 (21–28)		24 (22–25)		27 (22–30)	26 (22–34)
BMI Female	25 (23–28)	30 (21–35)	26 (20–32)	24 (24 -28)	27 (24–32)	30 (25–33)

Table 6: Median Alvarado scores in relation to histological diagnosis and investigative modality ultrasound, CT scan and diagnostic laparoscopy.

	Appendicitis		Normal Appendix	
	Male	Female	Male	Female
Ultrasound	6 (5–7)	7 (5–8)	4 (4–8)	5 (4–6)
CT Scan	6 (4–6)	6 (5–7)	4 (2–6)	4 (2–6)
Laparoscopy	6 (5–7)	6 (5–7)	5 (3–6)	4 (3–5)

Body habitus, as measured by BMI, did not influence the ultrasound report (P=0.54) (Table 5). A significant difference was not demonstrated in Alvarado scores between gender and ultrasound diagnosis of acute appendicitis (P=0.08). Additional comparison was made for patients undergoing a preoperative CT scan and laparoscopy and significance was not seen between gender and the investigation (Table 6).

CRP and Leukocyte counts for each of these groups were not significantly different between gender and ultrasound diagnosis (P=0.07) (Table 7).

In those patients with an inconclusive report 12 were females, whereby 7 had appendicitis confirmed upon histology. All the men (n=3) had appendicitis on histology.

147 patients did not have a preoperative ultrasound and 108 (72

males) underwent a diagnostic laparoscopy with appendectomy. 79 (59 males) of the 108 patients had appendicitis on diagnostic laparoscopy confirmed by histology. The remaining 29 patients (13 males) did not have appendicitis on histology.

Laparoscopic findings that resulted in the appendix being removed in these 13 male patients demonstrated that 7 males were to have an inflamed appendix. The remaining 6 males demonstrated that 1 had appendix serositis (appendix looked inflamed), 1 appendix faecolith (appendix looked injected), 1 to have pinworm (tip of appendix looked congested so removed) and the remaining 3 an inflammatory mass adherent to the anterior abdominal wall.

Out of the 16 females that did not have appendicitis upon histology the diagnostic laparoscopy suggested 6 to have an inflamed looking appendix, 3 to have appendix faecoliths, 1 to have appendix serositis, 1 to have mucosa swelling and another a firm feeling appendix. These were excluded from sensitivity and specificity analysis as they all exhibited histological pathology and not a true normal histology. The appendix although looking normal was removed in the presence of other pathology including multiple adhesions, free pelvic fluid with multiple ovarian cysts and blood in pouch of Douglas (n=2). Laparoscopy had a sensitivity and specificity, PPV and NPV of 100%, 23%, 86% and 100% for males and 100%, 40%, 77% and 100% for females (Table 3, 4).

Table 7: Median CRP and leucocyte values between males and females in relation to ultrasound and histology reports (P=0.071 and 0.74 respectively using the Kruskal-Wallis and Dunn's post hoc test).

Gender	Positive US and Appendix Histology		Normal US and Appendix Histology	
	Male	Female	Male	Female
CRP	83 (22.75 – 180)	35 (5.75 – 201.3)	4 (1 – 58)	9 (1 – 66)
Leucocyte Count	12.65 (9.68 – 13.8)	10.9 (7.23 – 14.35)	10.60 (7.4 – 10.8)	10.05 (6.9 – 13.35)

Table 8: Median age (interquartile range) in years with relation to histological diagnosis and investigative modality ultrasound, CT scan and diagnostic laparoscopy.

0.001	Appendicitis		Normal Appendix	
	Male	Female	Male	Female
Ultrasound	34 (20–48)	37 (25–46)	29 (28–31)	27 (21–45)
CT Scan	54 (38–66)	61 (53–70)	50 (31–70)	50 (31–70)
Laparoscopy	29 (23–39)	35 (23–30)	32 (24–50)	33 (26– 44)

39 patients (22 males) underwent a preoperative CT scan. The average age was older than for ultrasound (Table 8). 20 out of 22 males had a CT diagnosis of appendicitis and 18 confirmed by histology. The other 2 males exhibited other pathology requiring ileocolic resection/right hemicolectomy (cecal volvulus and obstructing tumour). 17 women underwent a CT scan prior to surgery of which 13 had appendicitis. The other 4 females were reported to have appendix mottling, adhesions between cecum and appendix, appendiceal mass and slightly hyperemic appendix. In both sexes median Alvarado scores were similar to those seen for ultrasound (Table 6). Those with appendicitis on CT and histology had an Alvarado score of 6 and with a normal appendix less than 6. CT had a sensitivity of 100% and positive predictive value of 90% in males and 100% and 76% for females respectively.

Discussion

As a diagnostic tool, ultrasonography was introduced in the 1980's. Its use as being a quick, radiation free and speedier alternative to computed tomography gained momentum over the decade and was a topic of discussion for multiple studies. In our experience the overall sensitivity and specificity of ultrasound in the diagnosis of acute appendicitis is 63% and 73% with a positive and negative predictive value of 79% and 59%. This would imply that in our cohort ultrasound abdomen and pelvis would miss appendicitis in about 30% of patients and provide an incorrect diagnosis in about 40% of cases. For males, ultrasound abdomen pelvis had a positive predictive value and negative predictive value of 100% and 33%. This implies that it is excellent for confirming the diagnosis, however not as adequate for excluding it, thus leading to the clinicians to ultimately rely on clinical utility more often, or perhaps further scans that may involve the use of radiation. This leads to additional time lost until surgery and increased risk of complications. In females the findings were not as stark with a positive predictive value and negative predictive value of 67% and 70%. This consequently implies that ultrasound is better for excluding appendicitis but only in 70% of cases, however comparatively worse in confirming appendicitis when reflected against males.

Pinto et al. conducted a literature review in 2013 highlighting a sensitivity range from 44% to 100% and specificity range from 47% to 99% throughout 14 associated studies for ultrasound [7]. A more recent meta-analysis including 2,841 participants demonstrated a sensitivity and specificity of ultrasonography for diagnosis of acute appendicitis to be 69% (95% CI 59% to 78%) and 81% (95% CI 73% to 88%) respectively [8]. An analysis of the dataset published by Kaminski of 326 patients undergoing appendectomy revealed ultrasound to have a positive predictive value and negative predictive value in females of 82% to 89% and 22% to 25% and in males 92% to 94% and 19% to 20% [9]. The literature displays a wide variance in the performance of ultrasound; however results demonstrate similar issues to our unit, particularly in excluding appendicitis in males. Ultrasonography is an operator-dependent technique, and our findings can vary depending on who is performing the scan, patients body habitus, anatomical location of the appendix (retrocaecal or subhepatic plane) [10]. Such reasons can lead to the contribution of false negative; however do reflect the true process of a busy district general hospital. This would suggest that in certain patient groups other diagnostic modalities could be useful in diagnosis of acute appendicitis. We however did not see a significant difference in ultrasound and histology diagnosis between gender and BMI.

Di Saverio et al. displayed the overall sensitivity and specificity of Alvarado scores within 5960 patients in excluding appendicitis at 99% (95% CI 97% to 99%) and 43% (95% CI 36% to 51%) when scores were <5 and at 82% (95% CI 76% to 86%) and 81% (95% CI 76% to 85%) when <7 [11]. Group's data thus demonstrates a clinical cut off score of less than 5 can warrant the ability to rule out the clinical suspicion of acute appendicitis; however a score of less than 7 has not been substantiated significantly to either rule in or out the need for surgery [11].

The POSAW investigation also indicates that imaging with ultrasound was conducted in about 43% of patients and 29% underwent appropriate surgery following an accurate clinical examination and relevant blood results.

An Alvarado score of ≥ 5 confirmed appendicitis (using histology) in 89.8% of patients [12].

Within our data, males with an Alvarado score of 6 or more (a strong clinical impression of appendicitis) are likely to have appendicitis and therefore would be recommended to undergo surgery, thus negating the need for preoperative diagnostic imaging. Where the condition is suspected but the Alvarado score is 4 or less, diagnostic modalities other than ultrasound may help to decide surgical intervention. In females with an Alvarado score of 7 or more, appendectomy is likely to be most appropriate management step. A score of 6 or less would indicate diagnostic imaging may be needed, with the modality tailored to gender, BMI and age. Whilst the Alvarado score may be useful in guiding management in certain patients, statistical significance was not achieved within our data, thus the need for further data collection and additional collaboration may be needed to confine more robust results to support the utilization of the Alvarado score.

CT for diagnosing appendicitis in equivocal scores of 4 to 6 in one study revealed a sensitivity and specificity of 90.4 and 95% respectively [13]. Adopting this policy may help reduce the burden on ultrasound, whilst also streamlining patients to the best diagnostic modality for management. Exposure to ionizing radiation with CT is of concern especially in the young and females. Focal CT using low dose radiation (one quarter of the standard dose) has provided similar results to standard CT regimens [14-16].

The negative appendectomy rate in males was 15% and in females 50%, however no judgments about this can be made until it is a larger sample size is studied. In female's ultrasound exhibited a positive predictive value mildly higher than the negative predictive value. In our case series a better method than ultrasound is needed to improve the negative appendectomy rate. Sonographer variation, body habitus are some factors that could have affected the diagnostic capability of ultrasound. Our findings seem to be different to those reported by others who record a much better diagnostic yield with ultrasound. Al-Ajerami noted a NPV in males of 100% and the same for PPV in females [17]. Benedetto recorded a sensitivity and specificity of ultrasound of 90.78 and 100% in 139 patients, with a negative appendectomy rate was 0% [18]. In our series 12 females out of 77 patients (undergoing ultrasound) had an inconclusive ultrasound report. Pelin suggested potential reasons to be age older than 31.1 ± 14 years, a BMI of 26.7 ± 4.3 , atypical appendix location and complicated appendicitis [19]. In individuals with high BMI, age over 31 years and suspicion of complicated appendicitis it may be worth considering an alternative diagnostic modality such as CT or

MRI or diagnostic laparoscopy.

A significant difference in symptom profile, hematological and biochemical parameters was not observed between the 3 ultrasound report categories and appendix histology. This would imply that in isolation reliance on CRP and leukocyte values may not be useful in deciding which patients may benefit from ultrasound imaging. Nasiri et al. noted that the diagnostic utility of WCC alone displayed a 44% positive predictive value, whereas CRP was 34% alone, however in conjunction, the positive predictive value improved to 56% [10].

Secondly, Tucker et al. displayed sensitivity of CRP it was 59% [20].

An alternative study revealed elderly patients exhibit higher CRP values in comparison to younger patients, whilst displaying a higher Leukocyte Particle Count (LPC) [11]. Overall, biochemical markers used in isolation to determine a clinical diagnosis of acute appendicitis are uncertain. Clinical chemistry needs to be partnered with diagnostic symptomatology and clinical assessment to form an accurate diagnosis prior to the use of ambulatory use of ultrasonography. If biochemical markers are used judiciously and within the parameters of the Alvarado scoring system, perhaps the rate of negative laparoscopy may lower, and mitigation of ultrasonography could be employed in certain circumstances.

Several measures were taken within this study design to ensure the efficacy of the study remained true, however certain limitations of the study must be considered. Firstly, data was collected retrospectively. Retrospective data analysis hinders outcome and exposure controls; however, selection bias is minimal within this study as all adult patients undergoing appendectomy were identified and analyzed. Involvement of children undergoing appendectomy may have provided key insight into the age effectiveness of ultrasonography; however, children were excluded from this study. Additionally, a relatively small sample size was used, and data was collected over 1 year within a single district hospital. Collections of data from alternative trusts, combined with a longer retrospective analysis may provide increase power and validity within the analysis of the data.

Conclusion

Imaging may be necessary for patients presenting with clinically indicated acute appendicitis, however our retrospective study displays ultrasonography as a poor modality for females for diagnosing appendicitis and poor for excluding appendicitis within males. The incorporation of scoring systems such as the Alvarado score alongside biochemical markers may aid in achieving a low negative appendectomy rate, however little statistical significance was seen between all ultrasound groups. In certain cases, the need for scans using radiation may be needed such as CT scan, which displayed good sensitivity. Overall, the use of laparoscopy needs to be balanced with the rates of negative laparoscopy. Additionally, data with larger patient sizes may need to be employed to seek greater clarification in the diagnostic utility of ultrasonography. The Alvarado score may help streamline patients for investigation or straight to surgery and possibly have a positive impact on length of stay and resource utilization.

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