

Clinical judgment and harmonic ultrasonography in the diagnosis of acute appendicitis: Experience with a modified score-aided diagnosis.

Ossama M Zakaria,^a MD; Tamer A Sultan,^b MD

a) Division of Pediatric Surgery, Department of Surgery, Suez Canal University, Egypt.

b) Division of Pediatric Surgery, Department of Surgery, Menoufyia University, Egypt.

Co''espondence: e-mail: ossamaz2004@yahoo.com

Abstract

Background: Appendicitis is the most common surgical emergency in children, yet diagnosis of equivocal presentations continues to challenge clinicians.

Aim: The objective of this study was to investigate the hypothesis that the use of a modified clinical practice and harmonic ultrasonographic grading scores (MCPGS) may improve the accuracy in diagnosing acute appendicitis in the pediatric population.

Patients & methods: Main outcome measures: Sensitivity, specificity, and accuracy of the modified scoring system. Five hundred and thirty patients presented with suspected diagnosis of acute appendicitis during the period from December 2000 to December 2009 were enrolled in this study. They were classified into 2 equal groups.

Group I (n=265): Included children who presented with suspected diagnosis of acute appendicitis. To these children a special clinical practice guideline system (CPGS) incorporating clinical judgment and results of gray scale US was applied),²

Group II (n=265): Included a similar group of children with equivocal diagnosis of acute appendicitis (AA), to whom a modified clinical practice guideline system (MCPGS) was applied.

Statistical analyses were carried out using Z test for comparing 2 sample proportions and student's t-test to compare the two quantitative data in both groups. Sensitivity and specificity for the 2 scoring systems were calculated using Epi-Info software.

Results: The Number of appendectomies declined from 200 (75.5%) in group I to 187 (70.6%) in group II ($P > 0.05$).

Specificity was significantly higher when applying MCPGS (90.69%) in group II compared to 70.47% in group I when CPGS was applied ($P < 0.01$). Furthermore, the PPV was significantly higher in group II (95.72%) than in group I (82.88%) ($P < 0.01$).

Conclusions: MCPGS tends to reduce the numbers of avoidable and unnecessary appendectomies in suspected cases of pediatric acute appendicitis that may help in saving hospital resources.

Key words: Acute appendicitis, children, Harmonic ultrasound scan, CPGS, MCPGS.

Introduction:

Certainty of clinical diagnosis is the most challenging task in clinical practice. It is relatively straight forward to look up the treatment once a correct diagnosis has been made. A single perfect diagnostic test for acute appendicitis does not exist.^{1,3}

Despite the number of algorithms and diagnostic tests available, about 200/o of patients with appendicitis are misdiagnosed.³⁻⁹

Presence of normal appendix ranges from 5-25% out of suspected cases of acute appendicitis.^{5,10-13} Negative appendectomies were thought to be relatively harmless; nevertheless, they result in considerable unnecessary clinical and economic costs.^{t4} Even despite the uncertainty of diagnosis, appendicitis demands prompt treatment in order not to be neglected and misdiagnosed leading to progression of the disease with its associated morbidity and mortality that may include the risk of perforation which happens in approximately one third of the cases.^{5, 15,16}

In an attempt to improve diagnosis, attention has turned to radiological imaging. The use of ultrasound scan (US) has been advocated as the readily available simple and fast imaging modality particularly in thin patients and children. A normal appendix is not frequently observed using gray-scale US, ¹⁷⁻¹⁸ however, on the other hand, Harmonic imaging (HI) increases the contrast and spatial resolution resulting in artifact-free images, and has been shown to significantly improve abdominal ultrasonography. However, only a handful of reports exist regarding its application in pediatric patients. Most of them do not encompass its use in acute appendicitis.^{t9} This work aimed to investigate and assess the hypothesis that the use of a modified clinical practice, judgment and harmonic ultrasonography as a modified score-aided diagnosis; MCPGS may improve the accuracy in diagnosing acute appendicitis in children with equivocal pictures of acute appendicitis and to compare these results with those of previously published data of CPGS),²

Patients and methods:

The study was carried out during the period from December 2000 to December 2009. Cases

of suspected pediatric acute appendicitis were included in the study. The first 265 cases were referred to as **Group I** to whom the clinical judgment and ultrasonography score aided CGPS was applied.¹ This was a modification of previously published scoring methods^{2,3} including certain subjective clinical parameters measured as 1 point such as fever of 38, anorexia and vomiting, tachycardia of more than 120 beats/minute. Abdominal pain parameters were also measured with special emphasis on guarding or rigidity, positive per-rectal examinations, however, a positive rebound tenderness was given 3 points in this score method as well as other clinical, laboratory and harmonic US measurements **Table(I)**; Results for this group are already published. ■ The next 265 cases were referred to as **Group II** to whom the proposed usage of harmonic ultrasonography clinical judgment and practice as a modified score aided system MCPGS was applied.

Group II (n=265): consisted of a similar group of children in whom our modified score aided system MCPGS with twenty five variables including harmonic ultrasound (US) examination and a marker of inflammatory response was assessed in multivariate analysis using the finding of AA at operation as the end point were enrolled in this study **Table(2)**. Exclusion criteria included those who were proved to have other causes of acute abdominal pain rather than acute appendicitis. Children were equally distributed regarding sex and age into 2 equal groups.

Ultrasonography was performed using linear and curved transducers with ultrasound frequencies ranging between 2.5 and 7.5 MHz, commercially available US systems (Sonoace XP8; Medison, Korea). The examination was performed with both conventional and harmonic imaging US. Scanning parameters were optimized for each method, and all images were obtained with the use of the same focal zone. An external video with cine playback mode was used to obtain identical images in two standard planes, longitudinal and transverse scans. Images were obtained with the two methods in random sequence to facilitate their masking for the observers. Harmonic images were acquired at a transmitting frequency of

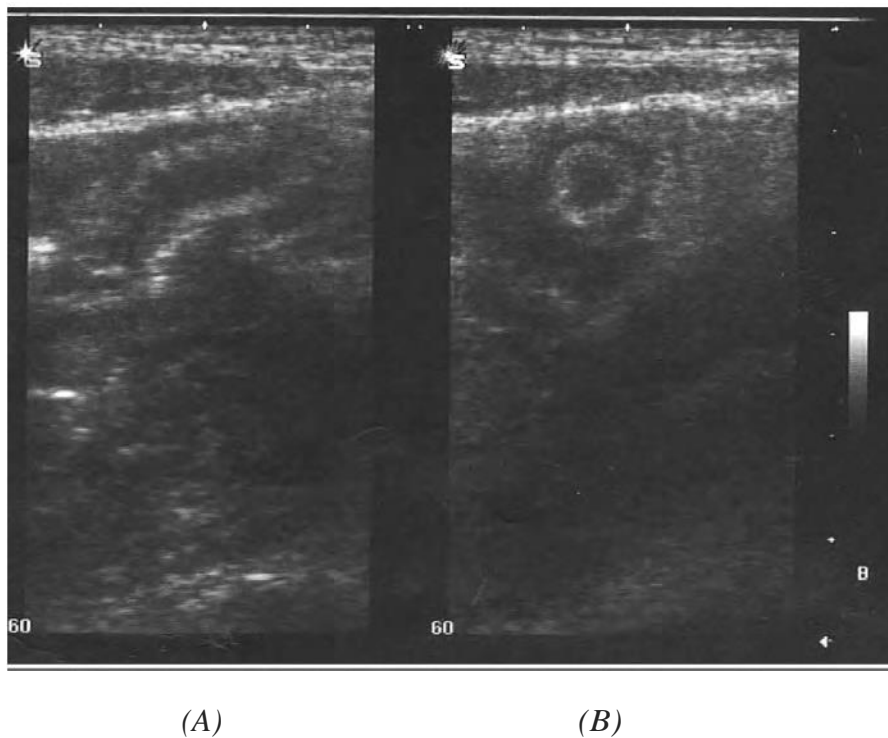
2.0 MHz and a receiving hannonic bandwidth of 4.0 MHz. Conventional US images were obtained at a frequency of 3.5 MHz, which is a frequency used commonly at abdominal imaging in adults. The harmonic and conventional US modes were switched by means of a toggle switch on the scanner control panel **Figure(1)**. In both groups the rationale of active watchful waiting in suspected appendicitis was a prudent and safe strategy with the use of at least one time repetition of conventional US or Harmonic US in groups I

and \mathcal{N} , respectively with no increase in the risk of perforation.

All appendices were routinely sent for histopathological examination.

Collected data were statistically analyzed using X2 test. Continuous variables were analyzed using Z test and student's t-test.

.05 were considered statistically significant. Sensitivity and specificity were calculated for the CPGS. Kappa test was used to verify the specificity. All calculations were performed using SAS version 8.2.



*Figure (1): Acute appendicitis by conventional US
(A) Longitudinal scan showing a peristaltic non compressible blind ended tubular structure with distinct thickened wall/ayers and diameter > 6mm
(B) Transverse scan showing target sign appearance.*

Table (1): Clinical Practice Guideline Scoring System (CPGS) 1.

			1	0	Score	
Clinical data	General	-Fever	Yes	No		
		-HR	> 120/min.	<120/min.		
		-Vomiting	Yes	No		
		- Dehydration	Yes	No		
	Abdominal	Abd.pain				
		-Localized	Yes	No		
		-History of similar - attacks	No	Yes		
		-Character	Constant	Intermittent		
		-Severity	Intolerable	Tolerable		
		-Course	Progressive	Regressive		
		- Reliefby antispasmodic	No	Yes		
		- Bowel Habit alteration	Yes	No		
		-Rebound tenderness	Yes (3)	No		
		- Guarding or rigidity	Yes	No		
		- +veP.R. examination	Yes	No		
		Investigations Laboratory	-WBCs leukocytosis	Yes	No	
			- Urine analysis (Findings ofUTI)	Yes	No	
		Focused abdominal	- Appendicitis or mass	Yes	No	
			U.S.	- +ve fmdings in female Adnxae	No	Yes
		- +ve fmdings in liver, Gall bladder, billiary passages		No	Yes	
- +ve fmdings kidneys	No	Yes				
-Free fluid	Yes	No				
Total score						

Interpretation of results:

21- 15 =Highly suggestive of appendicitis.

14- 8 = Patient needs repeated evaluation for conclusive result.

7- 0 =The diagnosis of acute appendicitis is not likely.

Table (2): Modified clinical practice and harmonic ultrasonographic grading score (MCPGS).

			1	0	Score
Clinical data	General	-Fever	Yes	No	
		Abdominal			
		-HR.	>120/min.<120/min		
		-Vomiting	Yes	No	
		Abd.pain			
		-Localized	Yes	No	
		-History of similar - attacks	No	Yes	
		-Character	Constant	Intermittent	
		-Severity	Intolerable	Tolerable	
		-Course	Progressive	Regressive	
		-Relief by antispasmodic	No	Yes	
		-Bowel Habit alteration	Yes	No	
Laboratory		-tenderness	Yes	No	
		-Guarding or rigidity	Yes	No	
Investigations	Focused abdominal U.S.	--ve P.R.	Yes	No	
		Associated intra- abdomin., Disease	No	Yes	
		-High WBCs	Yes	No	
		-Elevated CRP	Yes	No	
		-Urine analysis (Findings ofUTI)	No	Yes	
		-Aperistaltic non- Compressible blind ended tubular structure	Yes	No	
		-Distinct thickened appendicial wall layers	Yes	No	
		-Outer diameter> 6mm			
		-Target sign appearance			
Total score		-Appendicolith(s)	Yes	No	
		-Periappendiceal fluid collection	Yes	No	
		-Echogenic Prominent pericecal fat	Yes	No	
		- +ve fmdings in female Adnexae	No	Yes	

Interpretation of results:

15- 25 =Highly suggestive of appendicitis.

8 - 14 =Patient needs repeated evaluation for conclusive result.

0 - 7 =The diagnosis of acute appendicitis in not likely.

Table (3): Sensitivity, specificity, PPV and NPV for Group II

MCPGS	Histopathology		Total
	+ve	-ve	
+ve	179	8	187
-ve	0	78	78
Total	179	86	265

Sensitivity= 100%

Specificity= 90.69%

PPV = 95.72%

NPV = 100%

The Number of appendectomies declined from 200 (75.5%) in group I to 187 (70.6%) in group II (P>0.05).

Results:

Our study included 530 children of whom 280 were males and 250 were females, with a male to female ratio of 1.12:1. Our patients aged between one year and 17 with a mean age of 12.6 ± 1.4 (mean \pm S.D.). No significant differences were observed between the two groups as regard age and sex distribution.

In group I, traditional clinical judgment and grey scale US score aided CPGS were performed. 200 patients (75.5%) underwent appendectomy, of them 35 appendices (17.5%) were normal at histopathological evaluation. The remaining 65 patients (24.5%) were discharged from the Pediatric Surgical Facility as not having appendicitis. Yet, out of those 65, 3 children (4.6%), (2 males and 1 female) were re-admitted. Ultrasonography was repeated suggesting acute appendicitis. They underwent appendectomy with positive pathological results. A total of 203 appendectomies (76.6%) were performed in this group.

In group II, 187 patients (70.6%) have undergone appendectomy, of them 90 patients (48.1%) showed an MCPGS score between I5 and 22, those patients were kept with no oral feeding (NPO), intravenous fluid infusion (IV fluid) of appropriate type and amount according to patient's age before undergoing appendectomy.

Only 8 out of the total appendectomies (4.3%) were normal at histopathological evaluation.

The remaining 97 patients (36.6%) initially showed MCPGS of 8-I4. On repeated evaluation every 2 hours for a maximum of 6

times and repetition of harmonic US during the repeated evaluation for at least one time, their score progressed to 15 or more [61 patients (62.9%) with a MCPGS of I5-I7, II patients (II.3%) with MCPGS of 18, and 25 patients (25.8%) with MCPGS of I9]. During the observation period, these patients were kept with nothing to be taken orally (NPO), intravenous (IV) fluids were administered as appropriate. No antibiotics were given in order not to alter the clinical picture. However, antibiotics were started once the diagnosis was confirmed. No false negative cases were recorded when using MCPGS.

On the other hand, 78 children (29.4%) did not undergo appendectomy, 48 of them (61.5%) showed MCPGS of 8 or less at the initial examination. They were referred to the Pediatric Medical Care with no need for surgical interventions. Thirty patients (38.5%) showed MCPGS between 9 and 14 declining with repeated examinations until their score became definitely 8 or less, they were managed medically.

Specificity of MCPGS was higher than that of CPGS, this may be attributed to the use of harmonic US in this modified scoring system that seems to be significantly superior to the conventional grey scale US 90.69% in group I! Table(3) compared to a specificity of 70.47% in group II (Z=5.999, P<0.01). Also the Positive Predictive Value for group II (95.72%) was significantly higher than that of group I! (Z=4.727, P<0.01). Applying Kappa analysis on that data of Table(1) revealed the Kappa Measure for Agreement to be 0.929 (93%), Confidence intervals (88.1-97.7),

(MCPGS vs. Histopathology), Z Kappa=15.1, P value of 0.0001. These results show the high specificity of our finding in the MCPGS group.

Discussion:

Acute appendicitis traditionally has been a clinical diagnosis and remains so to this day. The diagnosis can be difficult to make in many children who may present with atypical symptoms or an equivocal physical examination.¹⁸

In our current study, the newly advocated score aided guideline system (MCPGS) based on clinical judgment, laboratory investigations for inflammatory response and harmonic US studies (Hn in association with the strategy of active watchful waiting performing repeated clinical examinations as well as at least one time repetition of Harmonic US before the decision-making process. It was highly accurate in the diagnosis of acute appendicitis in children. The specificity of the MCPGS was 90.69% compared to a specificity of 70.47% in the children to whom CPGS and active watchful waiting strategy was applied. In addition, we observed a statistically significant decrease in the negative appendectomy rate in group II compared with those in group I. The decrease in negative appendectomies occurred without a rise in the perforation rate. In fact, the perforation rate was lower under the MCPGS, although this change was not significant.

The inclusion and exclusion criteria of group formation in our study aimed at avoiding any selection bias as regards the patient's age and sex, attending hospital staff, investigatory facilities whether laboratory or radiological and the pediatric surgical team. Our study aimed at avoiding the selection bias mentioned before in similar scoring system.¹⁹ Screening ultrasound scanning for pediatric appendicitis has suboptimal accuracy, particularly in obese children with a low likelihood of appendicitis who should not routinely undergo ultrasound scanning. However, when followed by a second ultrasound scanning or a clinical reassessment, it offers high diagnostic accuracy in lean children.²⁰

Targeted abdominal examination as well as harmonic ultrasound scan HI constituted around

75% of our MCPGS scoring system with the aim of increasing its specificity without affecting the system sensitivity.

Results showed the superiority of harmonic imaging over conventional US for lesion visibility, with harmonic imaging being preferred over conventional US for 65% of cases. The findings were clearer and better defined with harmonic imaging which thereby improved the detection of subtle lesions. Harmonic imaging theoretically improved signal-to-noise ratios by reducing noise from side lobe artifact in the near field and echo detection from multiple scattering events.

This reduced noise was most likely responsible for the superiority of harmonic imaging over conventional US in the visualization of the findings and improved the confidence of diagnosis for most cases. Harmonic imaging was superior to conventional US in the visualization of lesions containing highly reflective tissues such as fat, calcium and air. It is therefore recommended to be used in obese patients. Better definition of the posterior acoustic shadows in calcifications and appendicolith(s).²¹⁻²⁸

In our study the negative appendectomy rate in groups I and II was 17.5 and 4.3%, respectively. Contrary to our results of group I some did show a negative appendectomy rate of 5.5% by applying somewhat similar scoring system.¹⁹ The reason for such difference may be their use of CT scanning in their system. However, the difference in the negative appendectomy rate does not support the use of such an expensive sophisticated and hazardous radiological tool to children. CT scanning is not always available in all centers limiting its incorporation in clinical practice guideline scoring system. A recently published study of a practice guideline found that CT scan did not improve the accuracy of diagnosis in patients with suspected appendicitis.²⁹ Their guideline did not specifically address the appropriate use of CT scan. Our study results of MCPGS, however, did show a great decline in the rate of negative appendectomies. This goes with data of some authors who showed that an imaging protocol using US followed by CT in their patients with equivocal presentations improved the accuracy of

diagnosis of appendicitis.³⁰ We present our current results of MCPGS which evolved from this and other studies recommending ultrasound as the imaging modality of choice in most patients. In addition the recommendation of MCPGS was not limited to imaging alone. Most clinical practice guidelines encourage, but do not require complaints with recommendations)! Measuring complaints can be challenging because guidelines can include numerous recommendations and because patients do not, especially children do not always match preconceived scenarios.³² Although many barriers limit physician acceptance of guidelines, ³³the compliance with our MCPGS is consistent with other developed practice guidelines.^{2,3,6-9,34} A considerable portion of the improvement seen in our study could be because of the utilization and accuracy of suitable imaging. Practice guidelines and clinical pathways have been implemented for many conditions, ²⁶ including acute appendicitis)^{6,30,35} Analysis of such guidelines can focus on any combination of patient outcome, resource utilization or complaints with recommendation.^{16,34-36}

Although most appendicitis guideline and pathways focus on decreasing postoperative treatment cost, a few concentrate on diagnosis itself. One such pathway in a pediatric hospital achieved a significant reduction in the number of laboratory tests and X-rays without adversely affecting the incidence of negative appendectomies or perforation.³⁴ However, in our proposed MCPGS we included the minimum necessary laboratory investigations to measure the inflammatory response and time and effort saving harmonic abdominal ultrasound scan in order to decrease the probabilities of misdiagnosing acute abdominal pain due to other reasons as acute appendicitis.

In our current study both groups underwent the active watchful waiting strategy. This excludes that the decision-making process did result strictly from the MCPGS scale, and was not rather based on the repeated clinical reevaluation that was adopted also on PGCS. This exactly shows that our proposed score is superior to the real life common clinical practice.

It may be concluded that the use of a modified clinical and harmonic ultrasonographic grading score (MCPGS) with the rationale of active watchful waiting in suspected appendicitis with at least one time repetition of Harmonic US was a prudent and safe strategy. It may improve the accuracy of diagnosing acute appendicitis in the pediatric population as it is superior to the real life common clinical practice. It leads to fewer negative appendectomies compared with those children to whom it was not applied or other scoring systems were applied as the CPGS with the same strategy of active watchful waiting and repeated US, without a significant change in the perforation rate. Moreover, inpatient observation for serial examinations was reduced significantly. Guidelines such as this can have considerable impact on the diagnosis of acute appendicitis in children. A larger cohort is necessary to validate our findings.

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