

## Evaluation of clinical diagnosis of children with acute appendicitis at Rapareen Teaching Hospital

Received: 26/1/2014

Accepted: 2/6/2014

Wesam Amjad Kaka \*

Dlair A. K. Chalabi \*

### Abstract

**Background and objective:** Appendicitis is the most common acute surgical emergency of childhood. Decision-making in patients with acute appendicitis poses a diagnostic challenge worldwide. Among the reported diagnostic criteria, modified Alvarado score system and ultrasound findings were used to support diagnosis and even exclude complicated cases. The aim of this study was to detect clinical and sonographic features that distinguish children visited the emergency department with acute simple appendicitis and identify factors related to complicated cases.

**Methods:** This cross-sectional study included 76 children with the provisional diagnosis of acute appendicitis according to clinical findings attending the Emergency Department at Rapareen Teaching Hospital in Erbil between January and December 2012.

**Results:** Of 76 patients included in this study, 75 patients (99.7%) had appendicitis whether inflamed (63 patients, 82.9%) or complicated (13 patients, 15.8%) and only one patient had normal operative (non-inflamed appendix) findings. Delay of admission, high temperature at time of presentation, localized tenderness and MASS of  $\geq 7$  increased the risk of complicated appendicitis as do leukocytosis and positive ultrasound findings.

**Conclusion:** The study shows that use of certain clinical data (like duration of manifestations) with the modified Alvarado score system supported by leukocytosis and positive ultrasound findings in children suspected to have acute appendicitis provides a high degree of diagnostic accuracy of complicated cases rather than simple acute appendicitis.

**Keywords:** Acute appendicitis; MASS; Children; Ultrasonography.

### Introduction

Acute appendicitis is one of the most common surgical emergencies in both developed and developing countries, with a prevalence of approximately 1 in 7 worldwide.<sup>1</sup> Its incidence is 1.5 – 1.9 \ 1000 in male and female population.<sup>2</sup> Patients with acute appendicitis may present with different symptoms and signs varying from non-specific vague abdominal pain to typical findings of right lower quadrant pain, tenderness and rebound tenderness.<sup>3</sup> This variability has been attributed to a series of possible causes, including patient's age, inflammation severity and perforation, or a combination of these factors.<sup>4</sup> The diagnosis of acute appendicitis is purely based on history, clinical examination and

some laboratory investigations. Imaging techniques have been shown to add very little.<sup>5</sup> Surgery for acute appendicitis is the most frequent operation performed (10%) of all emergency abdominal operations.<sup>6</sup> A negative appendectomy rate of 20-40% has been reported, and many surgeons advocate early surgical intervention for the treatment of acute appendicitis to avoid perforation.<sup>7</sup> Removing normal appendix is an economic burden on both, patients and health resources. Misdiagnosis and delay in surgery can lead to complications like perforation and finally peritonitis.<sup>8</sup> Severe periappendiceal inflammation, periappendiceal or abdominopelvic fluid and abscess were significantly associated with perforated appendicitis and with a significant

\* Department of surgery, college of medicine, Hawler medical university, Erbil, Iraq.

\*\* Department of pediatric, college of medicine, Hawler medical university, Erbil, Iraq.

longer hospital stay.<sup>9</sup> In order to reduce the negative appendectomy rate, various scoring systems have been developing to support the diagnosis of acute appendicitis. One of the scoring systems is the Alvarado Scoring system that purely based on history, clinical examination and few laboratory tests and is very easy to apply.<sup>10</sup> The Modified Alvarado Scoring System (MASS) has been reported to be a cheap and quick diagnostic tool in patients with acute appendicitis.<sup>11</sup> The original Alvarado score describes a possible total of 10 points, but those medical facilities that are unable to perform a differential white blood cell count, are using a Modified Alvarado Score with total score of 9 points, which could be not as accurate as the original score.<sup>12</sup> The aim of this study was to detect clinical and radiological features that distinguish children visited the emergency department with acute simple appendicitis and identify factors related to complicated cases.

**Methods**

A cross-sectional study was performed for all children with the diagnosis of appendicitis proven by operative findings at Rapareen Teaching Hospital in Erbil. Seventy-six children less than 18 years old between January and December 2012 with a provisional diagnosis of acute appendicitis admitted to the emergency department were included in this study. Exclusion criteria included chronic underlying illness and known case of gastrointestinal problem like inflammatory bowel disease. For the purpose of this study, a written official permission has been obtained from Research Ethics Committee of the College of Medicine/Hawler Medical University. Patients with proven appendicitis were divided according to operative findings into two groups: acute simple appendicitis and complicated appendicitis (perforated, gangrenous and with abscess formation). Age, gender, signs and symptoms (pain analysis, tenderness, temperature and associated symptoms), radiologic studies

(ultrasound), time of presentation to the emergency department, and operative findings were tabulated and analyzed. Modified Alvarado Scoring System was used (Table 1).<sup>13</sup> Sonographic findings were classified as:

- a. Appendix diameter ≥6
- b. Peri-appendicular fat tissue inflammation
- c. Peri-cecal fluid or abscess formation
- d. Both a. and c.
- e. Others (Blind-ended tubular structure , Non compressible , Appendicolith ,.....)<sup>14</sup>

Statistical package for the social sciences (version 21.0) was used for analysis with t-test to compare means and chi-squared test for categorical variables to check the relationship between clinical features, radiological findings and operative findings. A P value of ≤ 0.05 was considered statistically significant. OR (odds ratio) with CI (confidence intervals) were computed for a 2x2 table to estimate risk. Medcalc Version 12.7.7 software for windows used for claculating sensitivity and specificity.

**Table 1:** the Alvarado and Modified Alvarado Score

		Alvarado	Modified Alvarado
Symptoms	Migratory RIF pain	1	1
	Anorexia	1	1
	Nausea / vomiting	1	1
Signs	Tender RIF	2	2
	Rebound tenderness RIF	1	1
	Elevated temperature > 37.5	1	1
Laboratory investigations	Leucocytosis	2	2
	Shift to left neutrofiles	1	-
Total score		10	9

**Results**

Among 76 patients included in this study, 75 patients (98.7%) had appendicitis whether inflamed (63 patients, 82.9%) or

complicated (12 patients, 15.8%) and only one patient had normal operative (non-inflamed appendix) as shown in Table 2.

**Table 2:** Clinical manifestations and laboratory findings of suspected patients.

	No.	%
Chief complain :		
abdominal pain	70	92.1
Vomiting	5	6.6
Abdominal mass	1	1.3
Character of pain:		
dullache non specific	33	43.4
Migratory	26	34.2
localized	15	19.7
dullache and migratory	2	2.6
Site of pain :		
RTLQ (right lower quadrant)	42	55.3
RTUQ(right upper quadrant)	3	3.9
LTLQ(left lower quadrant)	3	3.9
Central	28	36.8
Rebound tenderness		
+ve	58	76.3
-ve	18	23.7
Tenderness		
+ve localised	37	48.7
+ve generalised	3	3.9
-ve	36	47.4
Modified Alvarado scoring system (MASS)		
< 7	49	64.5
≥ 7	27	35.5
WBC count		
≤10000	15	19.7
11000 - 15000	27	35.5
16000 - 20000	27	35.5
> 20000	7	9.2
Ultrasound		
no findings present	40	52.6
2. findings present :	36	47.4
a. appendix diameter ≥6	11	30.1*
b. peri-appendicular fat tissue inflammation	10	27.7*
c. peri-cecal fluid or abscess formation	9	25*
d. both a. and c.	3	8.3*
e. others	3	8.3*
Operative findings and diagnosis		
a.Normal appendix	1	1.3
b.Inflamed	63	82.9
C.Perforated	7	9.2
d.Gangrenous	3	3.9
e.Appendicular abscess	2	2.6

\* Percentage among positive ultrasound findings

This only patient was a male 11 years old complaining of localized right quadrant pain of 3 days duration with localized tenderness but no rebound tenderness with temperature of 36.6 C°, alvarado score of 3 and no leukocytosis or sonographic findings of appendicitis. Fifty seven out of 76 suspected appendicitis (75%) were of age group (5-10 years) while only 7 were below 5 year of age (9.2%). Most of patients had abdominal pain (92.1%) as chief complain which was mainly dull ache non specific (43.4 %), at lower right quadrant of abdomen (55.3%) with positive rebound tenderness (76.3 %) and MASS of < 7 in 64.5%, while 36

(47.4%) patients had ultrasound findings supportive of appendicitis diagnosis and 19.7 % had low white blood cells count of less than or equal to 10 000 (Table 2). In Table 3 and 4, after excluding the only patient with normal operative finding; cases of inflamed versus complicated appendicitis were compared by certain variables. Larger duration before time of admission, high temperature at time of admission, localized tenderness and MASS  $\geq 7$  (OR 14.68, CI: 2.91-74.27) increased the risk of complicated appendicitis as do leukocytosis (OR and CI not applicable) and positive ultrasound findings (OR 16.7, CI: 2.03-137.7).

**Table 3:** Association of certain demographic, clinical and laboratory variables with underlying operative findings.

Variables		Inflamed	Complicated	P
Gender	Male	39 (79.6 %)	10 (20.4%)	0.15
	Female	24 (92.3%)	2 (7.7%)	
Age in years	$\leq 10$ years	54 (84.4%)	10 (15.6%)	0.83
	> 10 years	9 (81.8%)	2 (18.2%)	
Tenderness	localised	28 (77.8%)	8 (22.2%)	0.008
	generalised	1 (33.3%)	2 (66.7%)	
	Absent	34 (94.4%)	2 (5.6%)	
MASS	< 7	47 (95.9%)	2 (4.1%)	<0.001
	$\geq 7$	16 (61.5%)	10 (38.5%)	
WBC	$\leq 10000$	14 (93.3%)	1 (6.7%)	0.016
	11000-15000	22 (84.6%)	4 (15.4%)	
	16000-20000	24 (88.9%)	3 (11.1%)	
	>20000	3 (42.9%)	4 (57.1%)	
Ultrasound findings	-ve	38 (97.4%)	1 (2.6%)	0.001
	+ve	25 (69.4%)	11 (30.6%)	

**Table 4:** T Test for comparing between means of inflamed compared to complicated cases

	Inflamed	Complicated	p
Duration before admission in hours (mean $\pm$ SD)	24.20 ( $\pm 15.74$ )	53.66 ( $\pm 28.19$ )	<0.001
Temperature at time of admission in Celsius (mean $\pm$ SD)	37.95 ( $\pm 0.68$ )	38.46 ( $\pm 0.74$ )	0.02

Both sensitivity and specificity of MASS and ultrasound were (83.3%, 74.6%) and (91.67 %, 60.32%) respectively. Agreement was 76% for MASS and 65% for ultrasound (Tables 5 and 6).

**Table 5:** MASS versus operative findings.

MASS	Complicated appendicitis	Inflamed appendix	Total
≥7	10	16	26
<7	2	47	49
Total	12	63	75

**Sensitivity:** 83.33 % (95% CI: 51.58 % to 97.42 %)

**Specificity:** 74.60 % (95% CI: 62.06 % to 84.73 %)

**Positive predictive value:** 38.46 % (95% CI: 20.25 % to 59.42 %)

**Negative predictive value:** 95.92 % (95% CI: 85.99 % to 99.38 %)

**Table 6:** Ultrasound findings versus operative findings.

U/S	Complicated appendicitis	Inflamed appendix	Total
+ve findings	11	25	36
-ve findings	1	38	39
Total	12	63	75

**Sensitivity:** 91.67 % (95% CI: 61.46 % to 98.61 %)

**Specificity:** 60.32 % (95% CI: 47.20 % to 72.43 %)

**Positive predictive value:** 30.56 % (95% CI: 16.37 % to 48.11 %)

**Negative predictive value:** 97.44 % (95% CI: 86.47 % to 99.57 %)

## Discussion

This study was conducted to evaluate the diagnostic value of MASS and other laboratory findings in patients with acute simple and complicated appendicitis. The goal of the clinical decision process in patients with acute abdominal pain is to make a correct diagnosis in the fastest and cheapest way.<sup>15</sup> The male predominance in this study is in agreement with the finding of other studies conducted previously.<sup>8,16,17</sup> This may be attributed to the fact that female patients with right iliac fossa pain

have a wide range of differential diagnosis as a result acute appendicitis may be over-diagnosed. The results of Khawaja et al,<sup>18</sup> who conducted a study at Muhammed Medical College in Pakistan, and found that out of 100 patients, 62 patients (62%) had a MASS score of >7, among them 15 patients (24%) were females and 47 patients (76%) were males. Kanumaba et al<sup>19</sup> conducted a study including adults and children and found that simple appendicitis was equally in all age groups, whereas children aged 0-15 years had significant higher perforation rate compared to other age groups whereas our study showed no significant relation with equal incidence of complicated and simple appendicitis at different age groups. This may be attributed to having our study being restricted to children only, while another study of 204 children<sup>20</sup> support our findings. The commonest symptom was abdominal pain (92.1%) followed by vomiting. This is comparable with other studies in which children presented with abdominal pain (89–100%), fever (80–87%) and vomiting (66–100%), though our results showed that localized abdominal pain was less common compared to migratory pain.<sup>21</sup> This may be explained by difficulty in description of pain by younger children like those below 5 years of age who were included in our study. Again migratory abdominal pain mainly in right lower quadrant or tenderness was the commonest presentation in other studies<sup>22</sup> as expected. Several authors stress that the presence of right lower quadrant tenderness is probably the most sensitive physical finding in early appendicitis.<sup>23</sup> Localized tenderness (48.7%) with rebound tenderness (76.3%) showed in this study is nearly equal to findings of a study in which 43% of patients had lower quadrant localized tenderness, with rebound tenderness in 75%.<sup>24</sup> Our operative findings were nearly similar to a study by Hameed and Merdan<sup>25</sup> as inflamed appendix and complicated were 79 % and 27.3% respectively while normal

appendix was 2.4%. Inflamed appendix was the most common operative findings (62.9%, 51.2%)<sup>19,23</sup> followed by perforated appendices, gangrenous appendices and lastly abscess as shown in previous studies,<sup>19,23</sup> which supports our operative findings. The diagnostic accuracy for pediatric appendicitis was high (up to 80%) with mean WBC count was  $> 14.8 \times 10^4/L$ .<sup>16</sup> Physicians should not discount appendicitis in children with vomiting and laboratory evidence of leucocytosis, especially in those over five years of age. In our study WBC count (80.2%) were above 10000/L which nearly equal to findings of study of Sadidique et al where Leukocytes count was  $\geq 10 \times 10^9/L$  in 75.43% of cases and even higher WBC may be helpful in predicting complicated cases (mean of 13800 versus 15000/L) comparing acute simple appendicitis and perforated appendix respectively.<sup>20</sup> Perforation correlates strongly with delayed diagnosis.<sup>26</sup> The risk of perforation is highest in the first four years of life and has been reported in more than 70 percent of children in this age group<sup>27</sup> while most of patients in this study were below 10 years with perforated appendix constitute 2 among 7 patients below 5 years of age; this finding was consistent with many studies e.g. Chung et al<sup>28</sup> and Bickell et al<sup>29</sup> that had reported perforation rate were more in children  $\leq 4$  years. Longer duration of manifestations is associated with increased risk of complications, especially rate of appendiceal perforation in the misdiagnosed cases in this study, a similar findings were seen by Chung et al<sup>28</sup> and Bickell et al.<sup>29</sup> In latter study, the duration of illness in majority of patients was four days and seen by the admitting doctor in more than 24 hours after the onset of illness. This observation concurs with other reports.<sup>8,12</sup> The reasons for delay in seeking medical consultation in this study may be attributed to delay in referral from primary or secondary health centres, misdiagnosis or fear of surgery as a result they are treated conservatively with analgesics and

antibiotics to mask the symptoms. Delayed presentation is associated with increased morbidity and mortality due to appendiceal perforations and peritonitis. A high temperature ( $\geq 38^\circ C$ ) and a long duration of symptoms were associated with complicated appendicitis like perforation, which is compatible with our study.<sup>20,21</sup> The rate of perforation in our study was 7.9%, which is comparable to other reported rates 9.4%.<sup>26,27</sup> However, much higher perforation rates have been reported from other centres in Nigeria.<sup>16</sup> Several studies validated the Modified Alvarado Score System using different cut-off points as by Bukhari and Rana<sup>30</sup> where the cut-off points was 7 and (83%) of the patients had MASS of  $\geq 7$ ; in this study, 35.5% had MASS of  $\geq 7$  and this may be explained that most of patients were treated initially with symptomatic treatment and even with antibiotics as they were considered as URTI. Around 80% of perforation of appendices occurred mostly in patients with MASS  $\geq 7$  and this may determine role of MASS in early detection of perforated or complicated appendicitis. Despite limited studies support this findings as most articles focus on role of MASS in differentiating normal from inflamed appendix regardless if complicated or not, but Dey et al found That there were 6 patients with gangrenous appendicitis, 4 had perforated appendicitis in a retrospective study conducted in the Department of Surgery of a Medical College Hospital in Gangtokand and they all were within the score range (MASS) of  $\geq 7$ .<sup>31</sup> Ultrasound features of appendicitis were positive in 39.7 % of cases and negative in 60.3%, while in another study<sup>32</sup> it was positive in 54.2% and negative in 45.8%, such difference may be related to variation in sample size, age groups and time of doing ultrasound after had clinical features as we lack emergency ultrasound in most of night shift. Of the 55 patients with visualized appendix in the group with a final diagnosis of appendicitis,<sup>33</sup> most patients had an appendiceal diameter

of  $\geq 6$  mm and this support our finding of a diameter of  $\geq 6$  mm as the commonest sonographic finding (11 out of 36). To determine the effectiveness of ultrasound at differentiating perforated from nonperforated appendicitis in children, Levin and colleagues<sup>34</sup> conducted a retrospective study of 161 consecutively registered children (mean age of 11 years) who had acute appendicitis and had undergone ultrasound and appendectomy. An abscess on ultrasound was associated with perforation, featuring a sensitivity of 36.2 % and a specificity of 99 % and ultrasound considered effective for differentiation of perforated from nonperforated appendicitis in children as in our study. Limitations of this study must be considered. The study design was based on a cross sectional evaluation of several ultrasound and clinical criteria, but lack histopathological findings which recommended in future studies.

### Conclusion

This study shows certain clinical data like duration of manifestations with high MASS supported by leukocytosis and positive ultrasound findings in children suspected to have acute appendicitis can help to identify those with complicated appendicitis from simple inflamed appendix.

### Conflicts of interest

The authors report no conflicts of interest.

### References

- Mohammed AA, Daghan NA, Abouds M. The diagnosis value of C-reactive protein, white blood cell count and neutrophils percentage in childhood appendicitis. *Saudi Med J* 2004 ;25:1212-5.
- Cuschieri A. The small intestine and vermiform appendix. In: Giles GR, Mossa AR *Essential surgical practice* 3<sup>rd</sup> ed. London: Butter worth Heinemann; 1995:1325-8.
- Schwartz SI. Appendix. In: Schwartz SI, Shires GT, Spencer FC. *Principles of surgery*, 5<sup>th</sup> ed. New York: Mc Graw – Hill; 1989: P.1315 .
- Prukprasert P, Maipang T, Greater A , Apakupakul N, Ksantigi JP. Accuracy in diagnosis of appendicitis by Comparing C- reactive protein measurement, Alvarado score and clinical impression of surgeons. *J Med Assoc Thail* 2004 ;25:296 -303 .
- Dado G, Anania G, Baccarani U, Macrotti E, Donini A , Risaliti A. Application of a clinical score for the diagnosis of acute appendicitis in childhood. *J Pediatr Surg* 2000; 35:1320–2.
- Matthysens LE, Zioli M, Barrat C, Champault G. *Routine Surgical Pathology in General*. *Br J Surg* 2006 ; 93:362-8 .
- Kalan M, Talbot D, Cunliffe WJ, Rich AJ. Evaluation of the MASS in the diagnosis of acute appendicitis : a prospective study . *Ann R Coll Surg* 1994; 76: 418 –9 .
- Ohmann C, Yang Q, Franke C. Diagnostic scores for acute appendicitis. *Eur J Surg* 1995;161:273– 81 .
- Siddiqui AH, Afzal S .Perforated appendicitis: accuracy of ct diagnosis and correlation CT findings with the length of hospital stay. *J Coll Physicians Surg Pak*. 2007; 17(12):721-5.
- Alvarado A. A practical score for the early diagnosis of acute appendicitis. *Ann Emerg* 1986 ;15 : 557 – 65 .
- Fenyo G, Lindberg G, Blind P, Enochsson L, Oberg A: Diagnostic decision support in suspected acute appendicitis : Validation of a simplified scoring system . *Eur J Surg Med* 1997; 163:831 –8 .
- Khan I, Rehman A. Application of Alvarado scoring system in diagnosis of acute appendicitis. *J Ayub Med Coll Abbottabad* 2005;17: 41-4.
- Almujamaee B. the assesment of modified Alvarado Score in the diagnosis of acute appendicitis. *Diyala J Med* 2011; 1(1): 1-5.
- Hassan M, Tawfiq S, Brayyich A, Aljabbar L. The sensitivity and specificity of ultrasound in diagnosis of acute appendicitis. *Tikrit Med J* 2009; 15(2):132-40
- Hoffmann J, Rasmussen OO. Aids in the diagnosis of acute appendicitis. *Br J Surg* 1989; 76: 774-9.
- Edino ST, Mohammed AZ, Ochicha O, Anumah M. Appendicitis in Kano, Nigeria: A 5 yr. review of pattern, morbidity and mortality. *Ann Afr Med* 2004, 3:38-41.
- Beltra'n MA, Almonacid J, Vicencio A, Gutie´rrez J, Cruces KS, Cumsille MA. Predictive value of white blood cellcount and C-reactive protein in children with appendicitis. *J Paediatr Surg* 2007; 42:1208–14.
- Khawaja AM, Khoohoro Y, Majeed N. The Alvarado Score for the diagnosis of acute appendicitis at Muhammed Medical College Hospital Mirpurkhas. Evaluation of validity of Alvarado Scoring System for diagnosis of acute appendicitis. *Pak J Med Sci* 2009;25.
- Kanumba E, Mabula1J, Rambau P, Chalya P. Modified Alvarado Scoring System as a diagnostic tool for Acute Appendicitis at Bugando Medical Centre, Mwanza, Tanzania. *BMC Surgery* 2011, 11(4):1-5.
- Siddique K, Baruah P, Bhandari S, Mirza S, Harinath G. Diagnostic accuracy of white cell

- count and C-reactive protein for assessing the severity of paediatric appendicitis. *J R Soc Med Sh Rep* 2011; 2:59.
21. Rothrock SG, Pagane J. Acute appendicitis in children: emergency department diagnosis and management. *Ann Emerg Med* 2000; 36:39–51
  22. Williams N, Kapila L. Acute appendicitis in the preschool child. *BMJ* 1991;66:1270.
  23. Velanovich V, Savata R. Balancing the normal appendectomy rate with the perforated appendicitis rate: implications for quality assurance. *Am Surg* 1992; 58:264-9.
  24. Colvin JM, Bachur R, Kharbanda A. The presentation of appendicitis in preadolescent children. *Pediatr Emerg Care* 2007; 23:849-55.
  25. Hameed H & Merdan I. The effectiveness of ultrasound imaging in the diagnosis of acute appendicitis. *Bas J Surg.* 2012;18: 89-96.
  26. Blisard D: Institutioning a clinical guideline to decrease the rate of negative appendectomy. *American Surgeon* 2003, 69:796-8.
  27. Larsson PG, Tronstard SE: Laparoscopy reduces unnecessary appendectomy and improves diagnosis in fertile woman. A Randomized study. *Surgical endoscopy* 2001, 15:200-2.
  28. Chung CH, CP Ng, Lai K. Delay by patient, emergency physician, and surgeon in management of acute appendicitis. *HK MJ* September 2000 ;6 (3).
  29. Bickell NA et al. How time affects the risk of rupture in appendicitis. *J Am Coll Surg* 2006; 202 (3); 401-6.
  30. Bukhari SAH, Rana SH. Alvarado Score. A new approach to acute appendicitis. *Pak Armed Forces Med J* 2002 ; 52:47-50.
  31. Dey S, Mohanta P, Singh V. Alvarado Scoring in Acute Appendicitis: Clinicopathological Correlation. *Indian J Surg* 2010 August; 72(4): 290–3.
  32. Sivit C. Imaging children with acute right lower quadrant pain. *Pediatr Clin North Am* 1997; 44: 575-89.
  33. Ameen MK. Ultrasound Evaluation of Suspected Appendicitis. *J Fac Med Baghdad* 2007; 49(1): 95-100
  34. Blumfield E, Nayak G, Sirinivasan R, Muranaka MT, Blitman NM, Blumfield A et al. Ultrasound for differentiation between perforated and nonperforated appendicitis in pediatric patients. *AJR* 2013; 200(5):957-60.