

## Randomised controlled trial of ultrasonography in diagnosis of acute appendicitis, incorporating the Alvarado score

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### Abstract

**Objectives** To determine whether diagnosis by graded compression ultrasonography improves clinical outcomes for patients with suspected appendicitis.

**Design** A randomised controlled trial comparing clinical diagnosis (control) with a diagnostic protocol incorporating ultrasonography and the Alvarado score (intervention group).

**Setting** Single tertiary referral centre.

**Participants** 302 patients (age 5-82 years) referred to the surgical service with suspected appendicitis. 160 patients were randomised to the intervention group, of whom 129 underwent ultrasonography. Ultrasonography was omitted for patients with extreme Alvarado scores (1-3, 9, or 10) unless requested by the admitting surgical team.

**Main outcome measures** Time to operation, duration of hospital stay, and adverse outcomes, including non-therapeutic operations and delayed treatment in association with perforation.

**Results** Sensitivity and specificity of ultrasonography were measured at 95% and 89%, respectively. Patients in the intervention group who underwent therapeutic operation had a significantly shorter mean time to operation than patients in the control group (7 v 10 hours,  $P=0.02$ ). There were no differences between groups in mean duration of hospital stay (53 v 55 hours,  $P=0.84$ ), proportion of patients undergoing a non-therapeutic operation (9% v 11%,  $P=0.59$ ) or delayed treatment in association with perforation (3% v 1%,  $P=0.45$ ).

**Conclusion** Graded compression ultrasonography is an accurate procedure that leads to the prompt diagnosis and early treatment of many cases of appendicitis, although it does not prevent adverse outcomes or reduce length of hospital stay.

### Introduction

Acute appendicitis is one of the commonest surgical emergencies. Simple appendicitis can progress to perforation, which is associated with a much higher morbidity and mortality, and surgeons have therefore been inclined to operate when the diagnosis is probable rather than wait until it is certain.<sup>1</sup> A clinical decision to operate

leads to the removal of a normal appendix in 15% to 30% of cases.<sup>1</sup> This proportion may be reduced by observing equivocal cases for a period of time.<sup>2</sup> Reductions in the number of "unnecessary" or non-therapeutic operations, however, should not be achieved at the expense of an increase in number of perforations.<sup>3</sup>

It has been claimed that diagnostic aids can dramatically reduce the number of appendicectomies in patients without appendicitis, the number of perforations, and the time spent in hospital.<sup>1</sup> Methods advocated to assist in the diagnosis of appendicitis include laparoscopy,<sup>4,5</sup> scoring systems,<sup>6,7</sup> computer programs,<sup>8</sup> ultrasonography,<sup>9</sup> computed tomography,<sup>10</sup> and magnetic resonance imaging.<sup>11</sup> Imaging techniques have been shown to be particularly accurate.<sup>12</sup> Graded compression ultrasonography is the least expensive and least invasive of these and has been reported to have an accuracy of 71% to 95%,<sup>12</sup> but doubts have been raised about the influence of ultrasonography on patient outcomes.<sup>13</sup> Furthermore, it has been argued that findings at sonography should not supercede clinical judgment in patients with a high probability of appendicitis.<sup>14</sup> This raises questions about whether sonography should be performed at all in patients at high risk and whether there is some reliable means of selecting those who can benefit from imaging.

The Alvarado score is a 10 point scoring system for the diagnosis of appendicitis, based on clinical signs and symptoms and a differential leucocyte count. In his original paper Alvarado recommended an operation for all patients with a score of 7 or more and observation for patients with scores of 5 or 6.<sup>6</sup> Subsequent prospective studies have suggested that the Alvarado score alone is inadequate as a diagnostic test,<sup>15,16</sup> but it has been advocated as a means of selecting patients who should undergo imaging.<sup>17</sup>

We designed a diagnostic protocol incorporating graded compression ultrasonography and the Alvarado score. We then undertook a randomised controlled trial to assess whether the information provided by this protocol improved clinical outcomes.

### Methods

Ethics committee approval was obtained for this trial. Patients were considered for inclusion in the study if they were referred to the surgical service at John

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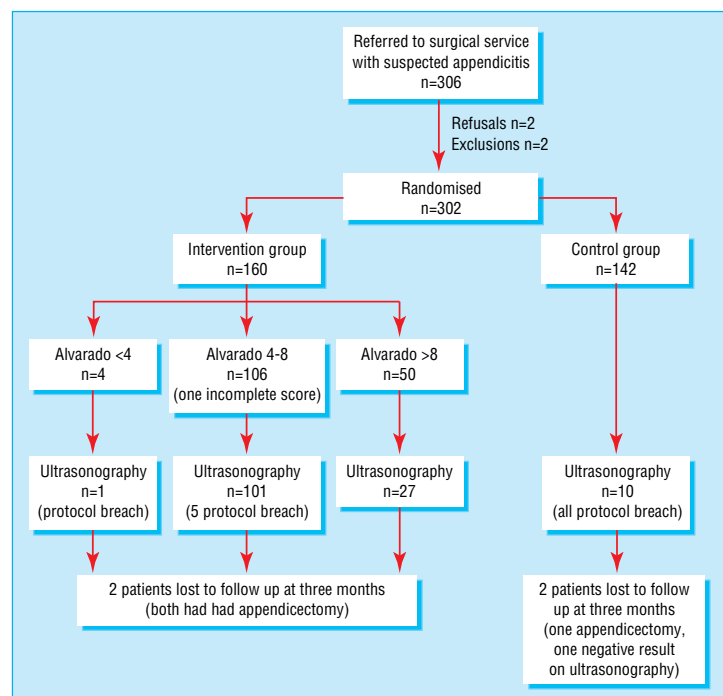
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Profile of trial of graded compression ultrasonography and Alvarado score compared with clinical methods in diagnosis of appendicitis

Hunter Hospital and John Hunter Children's Hospital with a provisional diagnosis of acute appendicitis between October 1997 and October 1998.

Patients were excluded from randomisation if they fulfilled any of the following criteria: age less than 5 years; evidence of generalised peritonitis; palpable mass in the right iliac fossa; evidence of acute confusional state or dementia; graded compression ultrasonography already performed. A project officer randomly allocated patients by coin toss to control (standard treatment) or diagnostic protocol (intervention) groups. He performed a clinical assessment from which he calculated the Alvarado score.

For patients in the control group, members of the admitting surgical team were not informed of the Alvarado score. They proceeded with appropriate clinical assessment and management. They were requested not to organise graded compression ultrasonography for 36 hours.

For patients in the intervention group, the admitting team was advised of the Alvarado score. Ultrasonography was then organised if the Alvarado score was between 4 and 8, inclusive. An Alvarado score of 9 or 10 was taken to be a relative indication for surgery, but the admitting team was given the option of organising graded compression ultrasonography; patients with an Alvarado of 3 or less were not eligible for ultrasonography. The admitting team was advised of the result of ultrasonography when this was done.

### Ultrasonography

Graded compression ultrasonography results were designated positive, negative, or equivocal by the attending sonographer by using the following criteria: positive—appendix identified, tender and non-compressible or appendiceal phlegmon or abscess seen; negative—appendix not identified, no other relevant abnormality seen; equivocal—appendix not

identified but abnormal amount of free fluid seen with thickened, dilated, or non-peristaltic bowel in the region of the caecum.

Ultrasonography was unavailable at this institution between 10 pm and 8 am, and patients entered in the study between these times had their examination at 8 am, unless the admitting surgical team deemed an immediate operation to be necessary.

### Surgery

All patients who underwent laparotomy or laparoscopy for suspected appendicitis had an appendicectomy. The diagnosis of appendicitis was made on histological grounds. Operations were considered to be therapeutic if disease was found, when the disease seemed to be the cause for the patient's pain, and when surgery was the appropriate treatment for that disease. All other operations were classed as non-therapeutic operations.

### Perforations

A designation of perforation of the appendix or bowel was based on an unequivocal finding or on objective microbiological or histopathological criteria.

### Delayed treatment in association with perforation

For patients with perforation, treatment was considered to be delayed if surgery had not started within 10 hours of randomisation.

### Follow up

Patients were reviewed at one week and three months.

### Outcomes

*Time to operation for therapeutic operations* was defined as the time in hours from randomisation to skin preparation.

*Duration of stay* was defined as the time in hours from randomisation to discharge from hospital.

*Rate of non-therapeutic operations* was the number of non-therapeutic operations (see above) as a proportion of the total number in each group.

*Rate of delayed treatment in association with perforation* was the number of cases of delayed treatment in association with perforation (as defined above) divided by the total number in each group.

### Power

This sample had a power of 80% to detect a difference between groups of 3.3 hours for mean time to theatre, 15.2 hours for mean duration of stay, and a reduction in the non-therapeutic operation rate from 11% to 2%.

### Data analysis

Data were analysed on an intention to treat basis. For calculation of sensitivity and specificity of graded compression ultrasonography we included cases only if a histological diagnosis was available. Diagnoses other than appendicitis were ignored. Equivocal ultrasonography reports were counted as positive.

### Results

In total 306 patients were referred and 302 patients were enrolled in the study (figure). The mean age was slightly lower in the intervention group (20 v 24 years,  $P=0.04$ ) but otherwise groups were comparable (table).

Sixteen patients were in breach of the trial protocol because the admitting surgeon in each case thought

that this was in the patient's interests. All were included in the reported analysis on an intention to treat basis.

### Ultrasonography

Graded compression ultrasonography was performed in 139 patients (see table 3 in the longer version of this paper on the *BMJ* website). The sensitivity and specificity of ultrasonography for diagnosing appendicitis was 95% (95% confidence interval 86% to 98%) and 89% (67% to 97%), respectively.

### Surgery

There were 170 operations performed: 95 of the 160 patients in the intervention group underwent surgery compared with 75 of the 142 patients in the control group (59% *v* 53%,  $P=0.25$ ). Appendicitis was confirmed histologically in 128 patients: 73 (46%) in the intervention group and 55 (39%) in the control group ( $P=0.23$ ). Twenty nine operations were non-therapeutic: 14 (9%) in the intervention group and 15 (11%) in the control group ( $P=0.59$ ).

### Perforations

Nineteen patients had a perforated appendicitis (15% of all cases of appendicitis), and five had other bowel perforations. Of all perforations, 14 were in the intervention group and 10 in the control group (perforations/number in group of 9% and 7%, respectively,  $P=0.58$ ).

### Delayed treatment in association with perforation

There were seven cases of delayed treatment in association with perforation (six cases of appendicitis and one of perforation of a caecal carcinoma). Five of these were in the intervention group, and two were in the control group (3% *v* 1%,  $P=0.45$ , Fisher's exact test).

### Follow up

There were no readmissions for appendicitis during the follow up period. Two patients required readmission for complications: one in the intervention group for drainage of an abscess and one in the control group for an early small bowel obstruction.

### Discussion

All our patients who underwent surgery after a positive result on ultrasonography proved to have appendicitis. Patients with equivocal signs of appendicitis are usually admitted to hospital for a day or night of observation. If the result on graded compression ultrasonography is positive, however, the surgeon can operate immediately. In our study, this led to a significant reduction in mean time to therapeutic operation. The reduced time to operation in the intervention group did not, however, result in a reduced duration of hospital stay or a reduction in incidence of adverse outcomes.

### Adverse outcomes

There are two outcomes that surgeons seek to avoid in cases of suspected appendicitis. The first is a non-therapeutic operation. The second is delayed treatment in a patient who is subsequently found to have perforation. In our study in each group the proportion of patients who had an adverse outcome was similar. The occurrence of several cases of delayed treatment in association with perforation, despite a low rate of perforated appendicitis (15%), suggests that rate of delayed treatment in association with perforation is a more appropriate measure of the consequences of delayed diagnosis than overall perforation rate.

Demographics and results according to allocation to diagnosis with graded compression ultrasonography and Alvarado score or clinical diagnosis only. Results are given with 95% confidence intervals unless stated otherwise

	Intervention (n=160)	Control (n=142)
No male	87	69
Mean age (years)	20.2	23.5
<b>Alvarado score</b>		
Mean score	7.18	6.93
No (%) with score >6	99 (61.9)	86 (60.6)
<b>Hospital data</b>		
Total No (%) of operations	95 (59.4; 52 to 67)	75 (52.8; 45 to 61)
No (%) of therapeutic operations	81 (50.6; 43 to 58)	60 (42.3; 34 to 50)
Mean time to therapeutic operation (hours)	7.0 (5.9 to 8.1)	10.2 (7.9 to 13)
Mean duration of stay (hours)	53.4 (47 to 60)	54.5 (46 to 63)
No (%) of non-therapeutic operations	14 (8.8; 5.3 to 14)	15 (10.6; 6.5 to 17)
No (%) with delayed treatment in association with perforation	5 (3.1; 1.3 to 7.1)	2 (1.4; 0.4 to 5.0)
Total (%) adverse outcomes (delayed treatment in association with perforation and non-therapeutic operations)	19 (11.9; 7.7 to 18)	17 (12.0; 7.6 to 18)

In the intervention group, many adverse outcomes were associated with a clinical management decision that was at odds with a correct diagnosis under the intervention protocol. Of particular note is the fact that 11 patients had a non-therapeutic operation after a negative result on graded compression ultrasonography. If surgeons had relied on the results of the protocol these unnecessary operations would have been avoided. But what would have happened to other patients in the study?

The protocol, if allowed to override clinical judgment, would have led to operations in at least six patients who recovered without surgery and in two patients who did in fact undergo non-therapeutic operations (one with an Alvarado score of 10 and one with an incorrect sonographic diagnosis of ovarian cyst). More importantly, rigid adherence to the management indicated by the protocol would have required that no patient with a negative result could have an operation. There were three patients with appendicitis who had a negative result on ultrasonography, and in each case the appendix was gangrenous or perforated. Had graded compression ultrasonography been relied on, these patients would have had an indefinite delay in treatment.

### Availability of ultrasonography

Seventy patients were enrolled in the study between 10 pm and 8 am and could not undergo ultrasonography immediately. A secondary analysis was performed with these patients excluded, but there was still no significant difference between groups with respect to duration of stay or adverse outcomes.

### Selection of patients for imaging

We used the Alvarado score as an objective means of stratifying patients according to risk so that those with a high or low probability of appendicitis need not have unnecessary imaging. Whether the Alvarado score or some other form of risk stratification is used, selection of patients for imaging is an issue that cannot be ignored. Had we performed graded compression ultrasonography on all patients in the intervention group the results would probably have been worse (see the longer version of this paper on the *BMJ* website for further details). Our diagnostic protocol incorporating

### What is already known on this topic

Ultrasonography is an accurate test for the diagnosis of acute appendicitis

Few studies have examined the effect of diagnostic ultrasonography on clinical outcomes, and there have been no randomised controlled trials

### What this study adds

This study confirmed the accuracy of ultrasonography and found a reduction in mean time to operation for patients undergoing therapeutic operation

There was no benefit of ultrasonography in terms of length of hospital stay, rate of non-therapeutic operations, or rate of delayed treatment in association with perforation

False negative tests occurred in patients with gangrenous and perforated appendixes

Ultrasonography remains a test of unproved benefit and should not be used by those who are inexperienced in the clinical diagnosis of appendicitis

the Alvarado score was, if anything, safer, faster, and more accurate than graded compression ultrasonography alone, but it still failed to produce better outcomes than unaided clinical diagnosis.

#### General comments

When performed by experienced sonographers, graded compression ultrasonography is an accurate test. In this trial the accuracy was over 93%, equal to that of computed tomography without colonic contrast.<sup>12</sup> False negative reports, however, do occur: in our study 5% of negative results were incorrect. There is no certain way of determining which negative result is a false negative, and the consequences of not operating may be serious. Patients cannot be safely sent home after a negative result unless there are also clinical grounds for their discharge. It is therefore inappropriate for graded compression ultrasonography to be used by those who lack experience in the clinical diagnosis of appendicitis.

#### Conclusion

The diagnosis of acute appendicitis aided by graded compression ultrasonography has not been shown to produce better outcomes than clinical diagnosis alone. Further studies of graded compression ultrasonogra-

phy and other diagnostic methods in suspected appendicitis should be randomised trials.

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Contributors: CDD initiated the study, formulated the study hypotheses, proposed the study design, analysed the data, was the principal author of the paper, and is the guarantor. NEM managed the running of the trial, contributed to study design, collected the data, initiated and participated in data analysis, and helped to write the paper. PMD initiated the research in ultrasonography, supervised the running of the trial, facilitated and coordinated involvement of different departments, contributed to data interpretation, and helped to edit the paper. JSG contributed to study design, supervised the running of the trial, contributed to data interpretation and analysis, and helped to write and edit the paper.

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