Gas insufflation of minimal preparation CT of the colon reduces false-positives

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Objectives: Minimal preparation CT of the colon (MPCT colon) is used for investigation of suspected colorectal cancer in frail and/or elderly patients who would be expected to tolerate laxative bowel preparation poorly. Although it has good sensitivity for colorectal cancer it has a poor specificity. We wished to investigate whether distension of the colon with carbon dioxide alone would reduce the number of false-positives, but without making the test arduous or excessively uncomfortable.

Methods: 134 patients were recruited and underwent MPCT colon with gas insufflation and antispasmodics. Results were compared with a cohort of 134 patients undergoing standard protocol MPCT colon. The numbers of false-positives were compared, as was reader confidence. All trial patients were given a questionnaire documenting their experience.

Results: The number of false-positives was 15% in the control group and 5% in the trial group; this difference was statistically significant, ($p=0.01$). Reader confidence was increased in the trial group. Patient tolerance was good, with 95% saying they would have the test again.

Conclusion: Use of gas insufflation and antispasmodics reduces the false-positives from 15% to 5% without adversely affecting patient tolerance.

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Minimal preparation CT of the colon (MPCT) is an examination used for investigation of suspected colorectal cancer in frail or elderly people. It does not require starvation, high-dose laxatives, colonic gas insufflation or even intravenous contrast as do other methods of investigating the colon, and relies upon faecal tagging using oral diatrizoate meglumine [Gastrografin; Merck (previously Schering), Feltham, UK]. Although not as accurate as standard CT colonography, it is very well tolerated and has a good sensitivity for colorectal cancer. However, false-positives are quite common with this technique (up to 50% in some reports [1] with a pooled specificity of 90% [2]), thus further investigations are required. We wished to investigate whether distension of the colon with carbon dioxide and antispasmodics would reduce the number of false-positives, but without making the test arduous or excessively uncomfortable.

Methods and materials

Patient selection

Ethical approval was obtained from a local research ethics committee. Prior to study initiation, a power calculation was performed assuming that standard MPCT colon had a specificity of 90% and that gas insufflation would increase this to the rate seen for CT colonography, 98%. Using a χ^2 test for the difference of

proportions at 5% significance level, 80% power would require 134 patients per group.

134 patients were recruited from patients referred for MPCT colon. Referral criteria for this investigation in our institution are patients suspected of having colorectal cancer aged 75 years or over, or younger patients who are thought unfit for laxative bowel preparation. Patients younger than 75 or elderly patients who are exceptionally fit undergo standard CT colonography with full laxative bowel preparation where detection of polyps is more relevant. 134 control patients were identified from a consecutive series of historical patients before the start of this trial.

Patient preparation and imaging parameters

The faecal tagging regimen was as follows: 5 ml of diatrizoate meglumine (Gastrografin) diluted with 300 ml of water in the evening 3 days prior to the study, morning and evening doses 2 days before, morning and evening doses 1 day before, a morning dose on the day of the study. On arrival in the radiology department patients were given 5 ml of Urografin 150 in 750 ml of water, to be drunk over 45 min. Diet was not modified in any way and intravenous contrast was not used. No gas insufflation was used for control patients. For trial patients 20 mg of (hyoscine butylbromide Buscopan; Boehringer Ingelheim Ltd, Bracknell, UK) was administered intravenously unless there was a contraindication, and a thin rectal catheter was introduced into the low rectum. Carbon dioxide was introduced using a mechanical insufflator (Protocol; EZEM Ltd, Bicester, UK). Gas insufflation was performed until the patient experienced

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mild discomfort or colonic pressure reached 25 mmHg as recorded by the mechanical insufflator. The scout image of the CT was examined for colonic distension and more gas was introduced if desired. The volume of carbon dioxide introduced was recorded.

All control examinations and the first 50 trial patients were performed using a GE Lightspeed CT scanner (GE Healthcare, Little Chalfont, UK), 120 kV, 300 mA, with spiral acquisition. The last 84 trial patients were examined using a GE Lightspeed VCT scanner at 120 kV, variable milliamperes. All control patients and the first 50 trial patients were reconstructed to 5 mm slice thickness of a single supine series. The last 84 patients were reconstructed to 2.5 mm slice thickness axial and coronal series, but were reported on a workstation at 5 mm slice thickness in the axial plane only.

All trial patients were given a questionnaire (Table 3) to take away and complete at home which recorded the patient experiences.

Image analysis

All CT data sets were examined by a consultant radiologist and a radiology trainee, the former with 8 years' experience of colonic CT. Data sets were classified according to the presence of colonic abnormalities requiring endoscopic investigation. If none was recorded, confidence was classified as "definitely normal", "probably normal" or "not confident, but does not warrant endoscopy". Where colonic abnormalities were recorded these were classified according to the confidence of the reporting radiologist that they represented malignancy, "unlikely", "might be", "not sure", "probable" or "definite", and which colonic segment they were in. In patients in whom a colonic abnormality was recorded, patient records were examined for subsequent investigations to determine if these abnormalities represented true pathology and its nature. Comparison of the true- and false-positive rates between the trial and control group was made. Bowel wall thickening associated with sigmoid diverticular disease is common in the elderly populations and the presence of diverticular disease or diverticulitis at endoscopy was not considered to be an abnormality.

Colonic distension was recorded in trial patients by one observer. Distension for each of the six colonic segments was graded on a scale from 0 to 3 using a system adapted from that of Taylor et al [3] and in which a grade of 0 indicated complete collapse; a grade of 1, partial collapse; a grade of 2, reasonable but suboptimal distension; and a grade of 3, optimal distension. Partial collapse (Grade 1) was defined as a situation where the thickest portion of the haustral folds measured, on average, >4 mm (on abdominal windows) in width and met within the lumen, thereby obliterating a clear central navigation pathway through the segment. Reasonable but suboptimal distension (Grade 2) was defined as a situation where there was an easily visible colonic wall with slightly thickened haustral folds that measured, on average, >2 mm in their widest portion but did not meet within the colonic lumen and therefore allowed a clear central navigation pathway. Optimal distension (Grade 3) was defined as a situation where the colonic wall was "pencil-thin" throughout the segment, with thin haustral folds that were <2 mm thick

throughout their length. The least-distended section of any individual segment was used to assign the overall distension score for that segment.

Statistical methods

The outcome measure was whether there was a false-positive or not, considered to be a binary outcome. Owing to the nature of this outcome, Fisher's exact test was used to compare between scan methods. This method was preferred to the χ^2 test because of the relatively small number of false-positive results.

Results

For the trial patients, the mean age was 80.0 years (range 55–96 years), with 86 (63%) being male. For the control group the mean age was 80.3 years (range 34–97 years), with 59 (44%) being male. The volume of carbon dioxide was recorded in 115 patients. The mean volume was 3.47 l, range 0.7–12 l. In seven patients the volume was not recorded, and in eight patients manual insufflation with room air was used because the mechanical insufflator was not available. Buscopan was not given in 18 (13%) patients owing to contraindications.

There was disagreement between the 2 readers in the presence of colonic abnormalities in 36 patients (13%), and a final result was reached by consensus review of the images. Among the trial group, 114 of 134 patients were reported as normal, 9 were true-positives (8 tumours, 1 benign polyp), 7 false-positives and in 4 patients there was inadequate information for follow up. In the control group, 101 of 134 patients were reported as normal, 7 were true-positives (6 tumours, 1 benign polyp), 19 were false-positives and 7 had inadequate follow-up information. These results are shown in Table 1.

Two sets of analyses were performed. For the first set all subjects who had a result other than false-positive were combined together into the "not false-positive group". However, it could be argued that the true-positives could not have a false-positive result, so a second analysis was repeated omitting the true-positives. For the purposes of both analyses, all subjects with an inadequate follow up were omitted from the analysis.

Fisher's exact test was used to compare the occurrence of false-positives between methods; a summary of the results is given Table 2. The figures reported are the number and percentage of patients with and without a false-positive for each of the two methods, and the *p*-values indicating the significance of the differences between the two groups.

The results indicated a significant difference in the occurrence of false-positives between the two CT

Table 1. Consensus results for presence of colonic neoplasia

Result	Control	Trial
Normal (n)	101	114
True-positive (n)	7	9
False-positive (n)	19	7
Inadequate-follow-up (n)	7	4
Total (n)	134	134

Table 2. Statistical analysis

Analysis	Result	Standard CT number (%)	Modified CT number (%)	p-value
All subjects	Not false-positive	108 (85)	123 (95)	0.01
	False-positive	19 (15)	7 (5)	
Omitting true-positives	Not false-positive	101 (84)	114 (94)	0.01
	False-positive	19 (16)	7 (6)	

methods for both sets of analyses. In both cases, there was a significantly reduced occurrence of false-positives using the modified CT method. When all subjects were considered, the false-positive occurrence was 15% using the standard method, and 5% for the modified method. The equivalent figures were 16% and 6% when the true-positives were omitted from the analysis. The positive predictive value for the trial group was 0.56 compared with 0.27 for the control group. Examples of true and false-positives are shown in Figures 1 and 2.

There were 122 questionnaires returned out of 134 (91%) trial group patients. The results are shown in Table 3.

The results of colonic distension are shown in Table 4. Included for comparison are equivalent results from Table 4 of Taylor et al [3].

The confidence with which an examination was reported as normal is shown in Table 5. The majority of the trial patients who were reported as normal were reported as "definitely normal", compared with less than a third for the control group.

Discussion

Colorectal cancer is a disease of elderly people [4], but the most popular tests for investigating colon cancer, CT colonography and colonoscopy, use high-dose laxatives. Full laxative bowel preparation is arduous for any individual [5], but it has risks for elderly people or those with comorbidity [6, 7], with adverse effects including bowel perforation [8]. MPCT colon is promoted by its advocates as a safe and well-tolerated test for colon cancer, although its sensitivity is less than other modalities. The

Figure 1. Axial CT image with gas insufflation shows an area of wall thickening (arrow) associated with diverticular disease that was incorrectly reported as a possible tumour. Subsequent flexible sigmoidoscopy was normal.

Figure 2. Axial CT image with gas insufflation shows an ulcerated soft tissue mass (arrow) in the sigmoid colon. Endoscopy confirmed this to be an adenocarcinoma.

most vociferous criticism is aimed at the low specificity, 50% in one study [1]. A meta-analysis showed a pooled specificity of 90% [2]. Clearly, MPCT colon is one end of a spectrum of the multitudinous published descriptions of

Table 3. Questionnaire results

Question	Number	Percentage
Overall I found the test		
Fine	75	61%
Not too bad	41	34%
Uncomfortable	5	4%
Unpleasant	1	1%
Taking the liquid (Gastrografin) with meals before the test		
Fine	67	55%
Not too bad	49	41%
Uncomfortable	4	3%
Unpleasant	2	2%
Having a tube placed in my back passage		
Fine	57	47%
Not too bad	53	43%
Uncomfortable	9	7%
Unpleasant	3	2%
Having gas blown into my bowel		
Fine	49	40%
Not too bad	52	43%
Uncomfortable	18	15%
Unpleasant	3	2%
During the test I experienced pain		
Not at all	69	57%
A little	48	39%
Quite a bit	5	4%
A lot	0	0%
Would you have the test again?		
Yes	116	95%
No	6	5%

Table 4. Results of colonic distension assessment. Absolute numbers (percentages)

Grade	Rectum (%)	Sigmoid (%)	Descending (%)	Transverse (%)	Ascending (%)	Caecum (%)	Overall (%)
0 or 1	26 (19)	71 (53)	26 (19)	12 (9)	17 (13)	11 (8)	163 (20)
2 or 3	108 (81)	63 (47)	108 (81)	122 (91)	117 (87)	123 (92)	641 (80)

Equivalent results extracted from Taylor et al [3] for 20 mg of hyoscine butylbromide

Grade	Rectum	Sigmoid	Descending	Transverse	Ascending	Caecum	Overall
0 or 1	39 (30)	82 (62)	33 (25)	44 (33)	2 (2)	5 (4)	205 (26)
2 or 3	93 (70)	50 (38)	99 (75)	88 (67)	130 (98)	127 (96)	587 (74)

how to perform a CT of the colon. In its original description [9], it uses a small dose of Gastrografin, no diet modification, no intravenous (iv) contrast or antispasmodic, no gas insufflation and a single supine series. CT colonography with high-dose laxatives, starvation, iv contrast, antispasmodic and prone and supine positioning is at the other end of this spectrum. We have investigated an intermediate form consisting of low-dose Gastrografin, iv antispasmodic, gas insufflation, no diet modification, no iv contrast and a single supine series. We have shown that use of gas insufflation with antispasmodic significantly reduces the incidence of false-positives from 15 to 5%. The confidence with which an examination was reported as normal was greatly increased (88% *vs* 30%). Although questionnaires were not given to the control group and so a direct comparison cannot be made, it is clear that this "hybrid" investigation was still well tolerated. No patients dropped out of the study. The vast majority reported each aspect of the examination "fine" or "not too bad", and 95% would have the test again if required.

Diet modification was not used in this study in common with other descriptions of MPCT colon. CT colonography always uses a modified diet, mainly falling into two camps of low-fibre diet or liquid diet only. The latter is the original CT colonography technique used with high-dose laxatives [10, 11], essentially transferred from barium enema bowel preparation. A low-fibre diet can be successfully used with faecal tagging [12–15]. If the diet is not modified, then whichever faecal tagging regimen is used would be expected to result in some untagged faecal material due to the presence of macroscopic fibrous plant residue. However, Johnson et al [16] report good results with no diet modification or laxative and barium faecal tagging, in particular a high specificity (100%) for large adenomas. This is surprising, and other studies using this technique have produced poor results [17]. Most practitioners using barium tagging would combine it with at least a reduced dose of laxatives [18, 19].

Table 5. Reader confidence for CT examinations reported as normal

Result	Trial (%)	Control (%)
Definitely normal	100 (88)	30 (30)
Probably normal	13 (10)	25 (25)
Not confident, but does not warrant endoscopy	2 (2)	46 (46)
Total	114	101

Although there is clear evidence that the use of supine and prone or lateral decubitus series produces better colonic distension and improves diagnostic accuracy [20, 21–23], the discomfort associated with a second scan has not been investigated. Anecdotally, frail and elderly patients find prone scanning difficult, and it is not clear if the advantages are worth the discomfort.

MPCT colon uses Gastrografin faecal tagging at a low dose of 10 ml per day. Higher doses of Gastrografin have been successfully used for CT colonography, both with and without laxatives [12], but it is clear that Gastrografin itself is a laxative and at higher doses produces diarrhoea and abdominal symptoms [14].

Grading of colonic gaseous distension was performed, and the results compared with those of a previously published trial (Table 4 [3]). Although direct comparison of these two sets of results is limited owing to different patient populations, trial design and readers, the results are suggestive that distension was similar between this trial and standard protocol CT colonography. Gas insufflation was performed until the patient experienced mild discomfort or colonic pressure reached 25 mmHg as recorded by the mechanical insufflator. An "aggressive" approach to colonic distension more typical of CT colonography (insufflating the colon until discomfort and/or until a well-distended scout view is seen) was deliberately not used. In our opinion, it seems less painful to distend the colon using the MPCT technique than CT colonography with Picolax, although this has not been quantified by this study. This may be due to the solid or semi-solid nature of the colonic contents in MPCT colon compared with the liquid residue produced by Picolax. The latter may produce an "air lock" within the colon, requiring higher pressures to overcome. No formal comparison was made as part of our study, but this would be an interesting area of future research.

Study limitations

This was a non-randomised study and so there may have been inherent differences between the two groups due to their different selection methods. The two groups were not well matched for sex; it seems that more men volunteered to take part in the trial arm. The nature of the intervention in the trial arm, gas insufflation, meant that the readers could not be blinded to which arm the patients were in.

A complete reference standard was not available for all patients. If a CT was reported as normal, no further investigations took place, so we do not know how many cancers were missed in the two groups. However, false

negatives are generally low for MPCT colon [24], and it would seem reasonable to assume that gas insufflation would increase sensitivity. It could be possible to re-analyse these two groups of patients after a 3 year follow-up as other authors have done [24], assuming that missed cancers would present and could be identified using the cancer registry, thus providing a more complete reference standard.

Other variables, such as use of a prone series and diet modification, could be investigated.

Conclusion

Modification of the standard MPCT colon technique with carbon dioxide insufflation and antispasmodic reduces the number of false-positives, but maintains good patient acceptability in a frail/elderly population.

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