Cardiac ischaemia and rhythm disturbances during elective colonoscopy

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Background The number of colonoscopic procedures continues to rise rapidly. With widespread adoption of colonoscopy based bowel screening programmes, this rising trend is set to continue.

Aims This study aimed to identify whether elective colonoscopy could provoke cardiac rhythm disturbances and/or myocardial ischaemia, as evidenced by 12 lead Holter ECG recordings and troponin I (cTnI) changes.

Materials and methods Patients were stratified into three groups based on the presence of cardiac disease or cardiovascular risk factors. They underwent real time 12 lead Holter monitoring before, during and after colonoscopy. Bloods were taken for pre- and post-procedure cTnI estimation.

Results Holter ECG recordings of the three groups showed a high incidence of new but silent ischaemic and arrhythmic ECG changes during the colonoscopy in patients with documented but stable heart disease and to a lesser extent in those patients with one or more risk factors for heart disease. Three patients had high cTnI concentrations both before and after colonoscopy. Two patients with known heart disease died within 30 days of colonoscopy.

Conclusions This study demonstrates for the first time the occurrence of potentially clinically significant ST-T wave changes and rhythm disturbances during elective colonoscopy in patients with known heart disease and to a lesser extent in those patients with a known cardiovascular risk profile.

Background

Since its introduction in the 1970s, colonoscopy has become the mainstay in the diagnosis and minimally invasive therapy of colorectal disease. Today, colonoscopy is considered as the optimal procedure for examining the colon¹ with nearly 300 000 colonoscopies being undertaken in the UK in 2005.² With the introduction of bowel screening, the numbers of elective colonoscopic procedures will rise even further.

Colonoscopy is considered to be a safe^{3 4} procedure with a perforation rate of 1/1000 and serious complication rate of 7/1000 procedures.⁵ However, the cardiovascular effects of this procedure have not been examined in detail although two controlled studies reported hypotension, bradycardia and excess ventricular ectopics during colonoscopy.^{6 7}

Populations are ageing in most countries. The combination of increasing life expectancy and reduction in old age mortality points to a further rise in the proportions of the above 65 age group in most populations.⁸ By 2030, it is projected that there will be a doubling of people aged between 65 and 80 years.¹ Increasing age is the most powerful predictor for coronary disease in asymptomatic individuals and autopsy studies have shown a prevalence of obstructive coronary artery disease increasing from 10–20% in the fourth decade to 50–70% in the eighth decade of life.⁹

Colonoscopy has been proposed as the preferred method of screening for colorectal neoplasia.^{10 11} With the launch of bowel screening programmes specifically targeting those aged over 60 years, the number of patients with both documented and silent cardiac comorbidities that will be recommended to undergo screening colonoscopy will also rise.

The main objectives of this double blind, prospective, non-randomised study were to determine whether elective colonoscopy could provoke cardiac rhythm disturbances and/or ST-T wave changes on 12 lead Holter ECG monitoring and/or evidence of myocardial injury, as observed through serial measurements of troponin I (cTnI).

Patients and methods

All patients included in this study underwent elective colonoscopy at a single site between February and December 2008.

Indications included surveillance colonoscopy or the investigation of large bowel symptoms and/or anaemia. None of the patients included in this study underwent colonoscopy as a screening procedure following a positive faecal occult blood test. All colonoscopies done were using air insufflation as per the standard operating protocols of the hospital. All colonoscopies were performed by consultant gastroenterologists or gastrointestinal surgeons of at least 5 years standing or by one year 6 specialist registrar, under consultant supervision.

Patients who were recruited to this study were classed into three groups according to their cardiac status.

Group A included patients who had known but stable heart disease. This included patients with stable angina or a history of angina in the past, myocardial infarction in the past, past history of coronary artery bypass grafting, documented poor left ventricular function, known valvular heart disease, pacemaker in situ and/or a documented history of cardiomyopathy.

Group B included patients with no documented heart disease but with one or more risk factors for heart disease, namely regular smoking within the preceding decade, diabetes mellitus, hypertension, documented use of a statin, history of heart disease among first degree relatives or a history of young heart attacks (<40 years old) among first degree relatives.

Group C included patients with no documented cardiac disease or known risk factors for heart disease. This included patients who had stopped smoking over 10 years previously.

Exclusion criteria

- (1) patients with a history of large bowel resection
- (2) patients with known large bowel cancer who were having the colonoscopy preoperatively to rule out synchronous malignant lesions (completion colonoscopy)
- (3) flexible sigmoidoscopy performed instead of a colonoscopy on the day of the procedure
- (4) age <30 years
- (5) unable or unwilling to consent to inclusion in the study
- (6) emergency colonoscopies.

Bowel preparation

All patients attending for colonoscopy had undergone routine orthograde bowel preparation with two sachets of sodium picosulphate/magnesium citrate (Picolax; Ferring Pharmaceuticals, Langley, UK), taken 24 and 18 h before the procedure.

Troponin I estimation

Patients who consented to this study had blood taken before the procedure post-bowel preparation, for cTnI, sodium, potassium, urea and creatinine estimations. All aspects of their comorbidities were recorded before the procedure. A cardiovascular history was taken, and all risk factors and regular medications were documented. All patients provided a second sample of

blood for cTnI and serum sodium, potassium, urea and creatinine estimation 20–28 h after completion of the colonoscopic procedure.

All blood samples were coded and analysed by staff who had no knowledge of the assigned patient groups. The normal upper limit of cTnI in our laboratory is 0.08 µg/l.

ECG monitoring

A 12 lead microchip Holter monitor (GE systems, Chalfont St Giles, UK), was used for recording the ECGs whereby the rhythms were recorded onto a microchip. The 12 lead rhythm strip recordings commenced 15 min before the procedure (baseline ECG). Monitoring continued during the entire colonoscopic procedure (procedure ECG) and for a further 15 min after the procedure while the patient was in recovery (post-procedure ECG). Other vital parameters including heart rate, blood pressure and oxygen saturations were also documented. Records were kept of sedation dosages and medications.

All ECGs were coded for blinding to subgroup identity and analysed independently by two cardiologists (each of >5 years' specialty experience). In case of disagreement in findings, the review of a third equally qualified cardiologist was sought and a consensus between two out of three cardiologists was deemed the final interpretation.

New ECG changes that occurred during the colonoscopic procedure were identified by assessing the procedure ECG and comparing with the baseline ECG. The persistence of any such ECG changes was assessed by analysing the post-procedure ECG.

ECG changes that occurred during the colonoscopic procedure were classified into:

- (A) changes compatible with ischaemia
- (B) arrhythmias.

ECG changes compatible with ischaemia included:

- (1) peri- or post-procedure ST segment elevation or depression (>1 mm elevation or depression compared with baseline in at least two contiguous leads)
- (2) normalisation of a pre-existing ST segment abnormality during the procedure
- (3) new T wave changes
- (4) new onset left bundle branch block.

ECG changes compatible with arrhythmias included:

- 1) peri- or post-procedure transient atrial fibrillation or supraventricular tachycardia
- 2) asystole >3 s
- 3) new and profound sinus bradycardia (<30 beats/min)
- 4) transient second or third degree heart block
- 5) new onset bigemini or trigemini.

Assessment of 30 day mortality

Mortality within 30 days of colonoscopy was interrogated using the available hospital patient administration system and by examination of case notes and death certificates.

Statistical analysis

As no previous data were available regarding the ECG changes during colonoscopy, the study was powered based on cTnI data alone. On this basis, a minimum of 40 patients in each group was required to achieve an 80% statistical significance for any cTnI differences between the groups.

Baseline differences in age and body mass index, procedure duration and use of hyoscine butyl-bromide between the three groups were compared using the one way parametric analysis of variance (ANOVA) test and the differences between groups were analysed using the Tukey honestly significant difference test. The incidence of cTnI elevations in each of the three groups was compared using Fisher's exact test. Where statistical significance was detected, logistic regression was used to adjust for the age differences between the groups. A *p* value <0.05 was considered statistically significant.

The normality of the data was tested using the χ^2 test against the normal distribution and no significant difference was obtained ($\chi^2=10.07$; *p*=0.26).

Results

On an intention to treat basis, 199 patients were recruited for the study. Two patients had a flexible sigmoidoscopy performed on the day of the procedure instead of a full colonoscopy and their results were excluded from the analysis.

Of the 197 patients studied, the caecum was reached in 190 patients (caecal intubation rate of 96%). The colonoscope could not be passed fully into the ascending colon of seven patients. Assessment of caecal intubation was based on two out of three observations: the tri-radiate fold, the appendicular orifice and/or visualisation of the ileocaecal valve.

Completeness of data in group A

Forty-four patients were recruited into group A. Four of these did not provide a second sample of blood for cTnI analysis. The ECGs of one patient were marred by artefact, rendering them uninterpretable.

Completeness of data in group B

One hundred and 12 patients were recruited to group B. One did not provide a second sample of blood for cTnI analysis. The ECGs of two patients were marred by artefact, rendering them uninterpretable.

Completeness of data in group C

Forty-one patients were recruited to group C. All had adequate quality ECGs and provided paired samples for cTnI estimation.

Baseline demographics and procedure characteristics

The mean age of patients in group A was higher than the ages of groups B and C. However, there were no differences between the groups regarding body mass index or duration of the colonoscopic procedure (calculated in minutes from time from anal intubation to time of extubation) (table 1).

All patients were given oxygen supplementation during the colonoscopic procedure as per the hospital protocol.

Although oxygen saturations were monitored throughout each colonoscopic procedure, they were not systematically documented for the purposes of this study. Based on the available data of oxygen saturations recorded during the procedure, there were no demonstrable differences between the three groups and no patient required a reversal agent.

All three groups had patients with coexisting but stable chronic obstructive pulmonary disease (four in group A, three in group B and three in group C) and analysis of the oxygen saturation recording data for this subgroup did not show any demonstrable difference in comparison with those without respiratory disease.

The most commonly used sedatives during colonoscopy were pethidine and midazolam, with no differences between the three groups in types of drugs or dosages used. Hyoscine butyl-bromide was used more commonly in group B but this difference did not reach statistical significance (*p*=0.43) (table 2). Hyoscine butyl-bromide, when it was used, was given at the same time as sedation and no correlation between the timing of hyoscine butyl-bromide injection and the development of ischaemic ECG changes was observed.

30 day mortality data

There were two deaths within 30 days of colonoscopy, with both patients being in group A (4.6%) (table 3).

Troponin I changes

Three patients had elevated cTnI concentrations on the pre-procedure blood estimation with a small but non-significant rise following the procedure (normal troponin concentrations for our laboratory <0.08 µg/l).

Table 1 Comparison of baseline demographics and procedure durations

Variable	Group A	Group B	Group C	<i>p</i> Value (ANOVA test)
Age (years)	69 (9)	60 (12)	53 (13)	<0.001
BMI (kg/m ²)	21 (5.8)	27 (5.1)	27 (3.7)	0.12
Duration of procedure (min)	34 (14.9)	32 (14.6)	31 (17)	0.65

Values are mean (SD).

ANOVA, analysis of variance; BMI, body mass index.

All three patients had documented normal cTnI concentrations within the past 2 years (table 4).

All three patients were asymptomatic during the colonoscopy and none displayed hypoxia or hypotension. Furthermore, neither their baseline ECGs nor those during the colonoscopy showed any evidence of cardiac ischaemia or arrhythmia.

The pre and post-procedure urea, creatinine, sodium and potassium levels were normal in all three patients. None of these three patients had any underlying renal dysfunction or any identifiable pre-existing pathology which may have caused the elevation in cTnI levels. The probability of patients in group A having an elevated cTnI was 7.5 times greater than the other two groups combined (ANOVA; $p=0.04$).

Intra-procedure ECG changes

ECG interpretation showed a high incidence of potentially significant ECG changes in group A (table 5) in

comparison with group B and group C (Fisher's exact test; $p\leq 0.001$). The results indicated a significant overall difference in ECG changes between the three groups, with the highest occurrence in group A and the lowest in group C. Comparing specific groups, there was a significant difference between group A and group B ($p=0.006$) and also between group A and group C ($p=0.003$). There was no difference between group B and group C ($p=1.00$).

After adjusting for age, a comparison between the three groups showed that the highly significant overall differences between the three groups were maintained. After adjusting for age, the odds of ECG changes were eight times greater in group A than in group C (table 6) (logistic regression test; $p=0.008$). Comparing specific groups, there was again a significant difference between group A and group B ($p=0.02$) and group C ($p=0.03$). There was no difference between group B and group C ($p=0.80$).

Table 2 Intravenous medications used during the colonoscopic procedure

Group	Pethidine	Midazolam	Fentanyl (%)	Hyoscine butyl-bromide (%)
Group A (n=44)	77% 50 mg (25–50)	93% 3 mg (1–5)	14	7
Group B (n=112)	72% 50 mg (25–50)	93% 3 mg (1–10)	14	20
Group C (n=41)	73% 50 mg (25–50)	95% 3 mg (1–7)	22	10

Values are median (range) or %.

Table 3 30 day mortality data

Patient data	Comorbidities	Indications for procedure	ECG changes during procedure	Colonoscopy findings	Date of death/cause of death
74 year/male	Diabetes/stable angina (last episode >10 years ago)	Lower GI bleed	Broad complex rhythm/ increasing ectopics	Angiodysplasia/<1 cm adenoma	Day 10 lower GI bleed myocardial infarction
64 year/male	Hypertension, MI 52 weeks, angina 56 weeks	Anaemia/bleeding P/R	New onset left bundle branch block	Normal	Day 22 myocardial infarction

GI, gastrointestinal; MI, myocardial infarction; P/R, bleeding per rectum.

Table 4 Pre- and post-procedure troponin I concentrations in three patients

	Group	Procedure ECG	Pre-procedure troponin I (µg/l)	Post-procedure troponin I (µg/l)	Electrolyte and urea estimation
Patient 1	Group A	Normal	0.21	0.23	Normal
Patient 2	Group A	Normal	0.15	0.16	Normal
Patient 3	Group B	Normal	0.12	0.13	Normal

Table 5 Summary of intra-procedure ECG changes in each group

		ECG changes during the procedure		
	No ECG changes	Present	Arrhythmic	Ischaemic
Group A (n=43)	28 (65%)	15 (35%)	6 (14%)	13 (31%)
Group B (n=110)	97 (88%)	13 (12%)	6 (5%)	10 (9%)
Group C (n=41)	39 (95%)	2 (5%)	1 (2%)	1 (2%)

Table 6 Ischaemic and arrhythmic changes during the colonoscopic procedure

	Group A (n=43)	Group B (n=110)	Group C (n=41)
Changes compatible with ischaemia			
ST segment elevation or depression >1 mm	6	6	1
Transient normalisation ST segment changes	2	1	0
New T wave changes	3	3	0
Transient left bundle branch block	2	0	0
Changes compatible with arrhythmias			
Asystole >3 s	1	1	0
Bradycardia <30 beats/min	4	2	0
New peri- or post-procedure atrial fibrillation	1	1	1
Supraventricular tachycardia	0	1	0
Transient bigemini	0	1	0

Ischaemic changes

Ischaemic ECG changes during the colonoscopic procedure were more common in group A (30%) compared with group B (9%) or groups B and C (7%) (table 6). Patients in group A had a 3.6-fold increased incidence of changes consistent with cardiac ischaemia compared with patients in groups B and C (ANOVA; $p=0.004$) or a threefold increased risk compared with group B alone (ANOVA; $p=0.016$).

These ischaemic changes persisted into the post-procedure phase ECG in 11 patients (46%).

Arrhythmic changes

Indirect evidence of cardiac disturbance during the procedure was inferred from the presence of arrhythmias (table 6). The patient in group A who developed the asystolic pause >3 s had multiple episodes as well as evidence of a sinus arrest and ventricular escape rhythm during the colonoscopic procedure. This abnormality resolved during the post-procedure phase. None of the patients exhibited persistence of the observed arrhythmic changes into the post-procedure phase.

Troponin I and ECG changes

There was no demonstrable correlation between the cTnI elevation and the occurrence of ECG changes (Fisher's exact test; $p=1.00$).

Discussion

Colonoscopy remains the gold standard for investigating the large bowel. The increasing reliance on colonoscopy has stimulated interest in the risk of the procedure relative to its benefit. Although other studies have reported on adverse events related to colonoscopy,^{5 12–20} to our knowledge our study is the first to investigate any real time intra-procedure ECG changes using a 12 lead ECG Holter monitoring system on a cohort of patients with pre-existing heart disease.

While flexible sigmoidoscopy is believed to be relatively safe in patients with a previous history of myocardial infarction,²¹ colonoscopy needs to be considered separately. This is because patients receive orthograde

bowel preparation before the procedure and the physiological stress before and during colonoscopy is significantly greater.²²

Thirty-day mortality rates following colonoscopy are difficult to establish because direct evidence of a relation between colonoscopy and mortality may be lacking. Studies report 30 day mortality rates to be in the range of 0.09%²³ to 0.007%.¹² Mortality in our study is higher (1.01%). Although both deaths in the present study occurred within 30 days of the procedure, direct evidence implicating the colonoscopy could be demonstrated only in the patient whose post-procedure bleed may have been a trigger for subsequent myocardial infarction. The link to colonoscopy in the other patient who died within 30 days was based on the development of new onset left bundle branch block during colonoscopy which persisted into the post-procedure ECG recording. This patient did not have any specific factor to precipitate the subsequent fatal myocardial infarction other than the presence of pre-existing heart disease and the colonoscopy.

The potential cardiac risks of colonoscopy have been considered in other studies^{12 24} where standard three lead Holter monitoring was used. The 12 lead continuous Holter monitoring that we used to record cardiac rhythms could provide a better demonstration of potentially significant ECG changes. No patient in our study—even those with ischaemic ECG changes or with sinus arrest and ventricular escape—developed any clinical features of cardiac failure during the procedure or recovery phase. This suggests that the proportion of patients who develop any clinically evident cardiac effects associated with colonoscopy underestimates potentially significant cardiac stress or strain associated with the procedure.

A potential contributing factor towards the cardiac phenomena we observed during colonoscopy could be patient discomfort. At the time of the study comfort scores were not being systematically recorded for every patient. Since 2008 the same endoscopists are being regularly monitored for their comfort scores,

which are zero, minimal or mild in >95% of cases. While we cannot rule out the possibility that patient discomfort could contribute to some of the findings, it is noteworthy that pathological ECG changes occurred in only two patients with no cardiovascular risk factors.

Although the clinical relevance of these pathological intra-procedure ECG changes is unclear, the efficacy and safety of colonoscopy need to be examined carefully before being recommended as a universal primary screening modality, especially in older age brackets. Cardiac pre-assessment before colonoscopy is not routinely done. A full evaluation and careful case selection before colonoscopy, along with active cardiac monitoring of the patient during the colonoscopic procedure, could reduce the risk of cardiovascular sequelae among patients with known heart disease who require lower gastrointestinal evaluation.

Adverse effects of bowel preparations have been reported previously²⁵ especially in older people and cardiovascularly compromised patients. The potential risks of bowel preparation have been highlighted recently by the national patient safety agency in the UK.²⁶ The observed elevation in cTnI concentrations might be accounted for by dehydration and electrolyte imbalances induced by bowel preparation prior to colonoscopy. The absence of clinical symptoms and the rarity of pre-procedure pathological ECG changes would be consistent with the hypothesis that an irritable myocardium could release troponin in response to bowel preparation induced dehydration and electrolyte imbalances.

Increasing age is the most powerful predictor for coronary disease⁹ and the prevalence of detected and undetected cardiac disease (and the presence of a cardiovascular risk profile) will be greater among the >60 year age group compared with a younger age group. The mean ages of patients exceeded 60 years in both group A and group B. This may be clinically relevant, especially as colonoscopy based bowel screening programmes are aimed specifically at this age group. These patients could have an increased chance of developing potentially significant ECG changes during the colonoscopy. Conversely, our study shows a low risk for cardiovascular changes during colonoscopy in the healthy patient group.

The potential role of non-invasive tests such as CT colonography for investigating the colon in such high and medium cardiac risk patients is supported by our findings, but this requires further investigation. CT colonography, although known to have less morbidity,⁷ normally requires bowel preparation and in some clinical scenarios is not as cost effective as colonoscopy because it does not offer the ability to perform biopsy or polypectomy. Newer techniques of virtual colonoscopy²⁷ which obviate the need for full bowel preparation may further reinforce the role of CT colonography in older patients and those with cardiac disease.

Our demonstration of potentially significant cardiac rhythm disturbances during routine elective colonoscopy opens up new issues in the consent of patients for this procedure. For those with a history of heart disease, the risk of cardiac rhythm disturbances and ischaemia may need to be discussed with the patient in addition to addressing the recognised complications of pain, bleeding and bowel perforation.

Our study has several strengths. The three cohorts that we studied were matched in all respects (except for age). The use of 12 lead ECG Holter monitors and the recording of baseline ECGs immediately before the colonoscopy allowed accurate identification of the intra-procedure ECG changes during the colonoscopy.

Our analysis also has limitations. Our 30 day mortality data were based on significant although indirect evidence that may overestimate the true mortality associated with colonoscopy. Patients with a permanent pacemaker in situ in whom conventional ECG changes of ischaemia may not be inferred from standard monitoring were included in group A. This may have diluted the actual findings in this group. The study could have been strengthened by recording the 12 lead Holter ECGs of all patients for a 24 h period before and after the colonoscopy to help in identifying whether any ischaemic changes occurred during normal day to day activities of the high risk patients. Although this study included sufficient numbers to make the results robust, a larger study with higher patient numbers and longer periods of ECG Holter recordings will be useful in order to confirm and enlarge on the findings of our study.

While no clinical sequelae were evident during or immediately after these procedures, there may be a role for cardiac monitoring during the procedure in patients with known cardiac comorbidities. Advising clinicians to curtail the procedure on the basis of transient ECG changes may be premature. Moreover, it would be impractical to undertake 12 lead ECG monitoring while observing for ST-T wave changes during the procedure but, by the same token, standard three lead monitoring is probably underused.

In conclusion, our study demonstrates the increased occurrence of silent but potentially significant ECG changes among patients with established heart disease and those with a cardiovascular risk profile, undergoing colonoscopy. The risk of developing ischaemic or arrhythmic ECG changes during outpatient colonoscopy is strongly related to the presence of underlying cardiac comorbidities and to a lesser extent the presence of one or more risk factors for heart disease.

Our findings contribute to the ongoing clinical debate on the wider use of colonoscopy. Clinicians may need to address the issues of cardiovascular risks during pre-procedure discussions with patients before informed consent is taken. Finally, our findings may assist policy making for colorectal cancer screening of

patients with underlying cardiac comorbidity or risk factors for heart disease.

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Competing interests None.

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Contributors ATG, chief investigator, carried out the study and drafted the manuscript; AR carried out the study; CD carried out the study; CE provided statistical assistance; PGC, first cardiologist, provided cardiology support for reading the ECGs; HK, second cardiologist, provided cardiology support for reading the ECGs; MJ, third cardiologist, provided cardiology support for reading the ECGs; MCA, supervisor, co-wrote the manuscript; VLC, supervisor; KJS, supervisor/principal investigator.

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